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SOP 15B: RESEARCH REGULATED BY THE FOOD AND DRUG ADMINISTRATION (FDA): INFORMATION AND POLICIES FOR INVESTIGATIONAL DEVICE EXEMPTION (IDE) APPLICATIONS

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SOP 15B: RESEARCH REGULATED BY THE FOOD AND DRUG ADMINISTRATION (FDA): INFORMATION AND POLICIES FOR INVESTIGATIONAL DEVICE EXEMPTIONS (IDE) APPLICATIONS

15B.1 DEFINITIONS AND LINKS TO WEBSITES

Terms that first appear below in bold and with an asterisk are defined in Appendix A "Definitions". Links to websites are provided in Appendix B "Links to Websites".

15B.2 PURPOSE

This policy describes additional specific procedures to be followed by NIH **investigators***, NIH IRBs, NIH institutional officials and others as appropriate when FDA-regulated research involving medical devices (see Appendix B "Links to Websites") is conducted at the NIH. Where noted, this policy also describes some of the requirements under applicable laws and FDA regulations. For a more comprehensive listing of FDA's requirements for the conduct of human device studies, refer to 21 CFR parts 11, 50, 54, 56, and 812.

15B.3 POLICY

Investigations involving investigational devices must be conducted in accordance with applicable FDA regulations, including the investigational medical devices at 21 CFR Part 812 (see Appendix B- Links to Websites). Such investigations should also be conducted consistent with **Good Clinical Practice (GCP)*** (see Appendix B "Links to Websites") and with the policies contained in SOP 15 "Research Regulated by the Food and Drug Administration (FDA): General Procedures for IND and IDE Applications." Also see "Device Advice", in Appendix B "Links to Websites".

15B.4 REQUIREMENT TO SUBMIT AN IDE TO THE FDA

FDA regulations at 21 CFR 812.2 describe the types of clinical investigations for which an **IDE*** does **<u>not</u>** need to be submitted to the FDA. For all other clinical investigations of devices, an IDE must be submitted.

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15B.5 RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI)

The responsibilities listed here relate specifically to FDA-regulated device research conducted at NIH, and are in addition to those provided in SOP 19 “Investigator Responsibilities” and SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”.

A. Investigations involving non-significant risk devices (NSR)*. An investigation is considered to have an approved application for an IDE unless the FDA has notified the sponsor that approval of an IDE application is not required or the IRB makes a determination as described in Section 15B.6.2.B NSR device studies, if the device is not a banned device, generally do not require an IDE application approved by the FDA, if the sponsor, or NIH PI as applicable, does all of the following:

    1. Labels the device in accordance with 21 CFR 812.5.

    2. Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk (SR) device*, and maintains such approval.

    3. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by an IRB under 21 CFR 56.109(c).

    4. Complies with the requirements of 812.46 with respect to monitoring investigations.

    5. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10)

    6. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and

    7. Complies with the prohibitions in 812.7 against promotion and other practices.

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B. The following categories of device investigations are generally exempted from 21 Part 812 including the requirement to submit an IDE:

1. A device, other than a **transitional device*** in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time (812.2(c)(1));

2. A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence. (812.2(c)(2));

3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) (see Appendix B "Links to Websites", see 812.2(c)(3)) and if the testing:

    a. Is noninvasive.

    b. Does not require an invasive sampling procedure that presents significant risk.

    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.

4. The research involves a device 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 subjects at risk (812.2(c)(4));

5. The research involves a device intended solely for veterinary use (812.2(c)(5);

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6. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5 and 812.2(c)(6);

7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution (812.2(c)(7)).

15B.5.1 MAKING THE DETERMINATION OF THE NEED FOR AN APPLICATION FOR AN INVESTIGATIONAL DEVICE EXEMPTION (IDE)

Under FDA regulations at 21 CFR 812.20, **sponsors***, including **sponsor-investigators***, are required to submit to FDA an IDE if the sponsor intends to use a significant risk (SR) device in an investigation, intends to conduct an investigation that involves an exception from informed consent under 21 CFR 50.24, or if FDA notifies the sponsor that an application is required for an investigation. Consistent with this requirement, NIH sponsor-investigators will make a preliminary determination whether or not an IDE is needed. All NIH investigators, including investigators who are not sponsor-investigators, will do the following:

A. If the NIH investigator believes that an IDE is not required, the investigator will submit the protocol to the IRB with an explanation of criterion met for exemption from need for IDE requirement.

B. If a sponsor or the FDA has identified a device as a NSR device as used in the study, then the PI will provide written documentation of the determination to the IRB.

C. If an IDE is required from the FDA, the PI will provide the IRB with IDE documentation. Documentation of the IDE in the form of a dated written communication from the FDA issued at the time the IDE number is assigned should be submitted as an attachment to the initial protocol application.

15B.5.2 STORAGE AND USE OF DEVICES

Under FDA regulations, investigators are responsible for the control and disposition of medical devices under investigation (see 21 CFR 812.100 and 812.140(a)). Consistent with FDA requirements, it is NIH policy that:

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A. Investigational medical devices received for a study must be kept under the PI's control and stored in a locked environment under secure control with limited access. If a device is dispensed, the PI must keep a log regarding the receipt, use, and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

B. The protocol should specify plans for handling or disposition of investigational devices at termination of the study, including how handling or disposition will be documented.
C. If, after use, the PI keeps the devices, he/she must maintain a log regarding the receipt, use and/or re-dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

15B.5.3 ADDITIONAL INVESTIGATOR COMMUNICATIONS AND REPORTS WHEN CONDUCTING MEDICAL DEVICE STUDIES

A. Investigator communication with the IRB:

1. Reporting unanticipated problems, including adverse events and **unanticipated adverse device effects***. The PI will promptly report to the IRB any unanticipated problems involving risks to subjects and others and any unanticipated adverse device effects (see FDA regulations 21 CFR 812.150(a)(1)), according to the IRB-approved protocol and SOP 16 "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations".

2. Upon request by a reviewing IRB or the FDA, investigators must also provide information about any aspect of the investigation to the reviewing IRB or the FDA, respectively.

B. Investigator reporting to the sponsor: Under 21 CFR 812.150(a), investigators are required to submit to the sponsor the following reports: unanticipated adverse device effects, withdrawal of IRB approval, progress report, deviations from the investigational plan, when the investigator uses a device without obtaining informed consent, and a final report. 21 CFR 812.150(a) specifies time frames for these reports.

C. Sponsor reports: Under 21 CFR 812.150(b), sponsors, including NIH Sponsor-Investigators, are required to provide the following reports:

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Subject of report	Entities to receive the report
Unanticipated adverse device effects	FDA, reviewing IRBs and participating investigators
Withdrawal of IRB approval	Reviewing IRBs and participating investigators
Current investigator list	FDA
Progress reports	Reviewing IRBs and, if a significant risk device or treatment IDE, the FDA
Any request that any investigator return, repair, or otherwise dispose of any units of a device	FDA and reviewing IRBs
Final report	For all devices, to all reviewing IRBs, and for a significant risk device, also to all participating investigators and the FDA
A copy of the report provided by an investigator of the use of a device without obtaining informed consent	FDA
A copy of an IRB's determination that the device is a significant risk device	FDA

Table 1. FDA reporting requirements for Sponsors and Sponsor-Investigators

Upon request by a reviewing IRB or the FDA, sponsors must also provide information about any aspect of the investigation to the reviewing IRB or the FDA, respectively.

D. Supplemental applications submissions from sponsor to FDA: Under 21 CFR 812.35, sponsors must obtain IRB approval when appropriate and FDA approval of a supplemental application before implementing a change to an investigational plan or facility. Prior approval is not required when a device is used for **emergency use*** in certain circumstances (see 15.B.7.1), or with certain developmental changes in the device, or with some changes to the clinical protocol as defined in 21 CFR 812.35(a)(3). However, the FDA must be notified within five days of certain of these changes (See 21 CFR 812.35 (a)(3)).

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15B.6 RESPONSIBILITIES OF THE IRB WHEN REVIEWING RESEARCH INVOLVING IDES

15B.6.1 REVIEW OF PROPOSED IDE STATUS

The IRB administrative staff, in collaboration with the IRB Chair, will review the documents provided by the PI and confirm whether the research requires an IDE and that there is appropriate supporting documentation.

15B.6.2 IRB REVIEW OF RESEARCH INVOLVING INVESTIGATIONAL DEVICES

A. Significant Risk Devices
   1. Determination of Significant Risk (SR) devices by the FDA: If the FDA has made an SR determination for the study then the IRB does not make an independent risk determination. The PI will note the FDA's determination in the written protocol and will provide the IRB with the FDA's IDE approval letter.

   2. Determination of Significant Risk (SR) devices by the IRB: If the FDA has not made a risk determination for the study, the IRB should review the sponsor's proposed risk determination. If the IRB determines that the device used in the study is NSR, then submission of an IDE application to the FDA is not required. If the sponsor has determined that the device used in a study is NSR but the IRB disagrees and determines that the device is SR, the IRB must notify the investigator and, where appropriate, the sponsor (see 21 CFR 812.66, see Appendix B "Links to Websites"). In making this determination of significant risk, the IRB will take into account how the device is used in the study and apply FDA IDE guidelines. For more information about significant risk and non-significant risk medical device studies see Appendix B "Links to Websites".

      a. If the IRB believes the protocol is a significant risk device study, the IRB may approve the study but the study cannot begin until the FDA approves the IDE or the FDA determines that an IDE is not needed.

      b. The IRB will not review studies involving significant risk devices under expedited review procedures.

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B. Non-Signification Risk Devices

1. Determination of Non-Significant Risk Devices (NSR) by the FDA. If the FDA has already made an NSR determination, the IRB does not need to duplicate the effort by making an independent risk determination.

2. Determination of NSR by the IRB:

   a. If the FDA has not already made the NSR determination, the IRB should review the sponsor's proposed risk determination. If the IRB determines that the device used in the study is NSR, then submission of an IDE application to the FDA is not required. If the sponsor has determined that the device used in a study is NSR but the IRB disagrees and determines that the device is SR, the IRB must notify the investigator and, where appropriate, the sponsor (see 21 CFR 812.66, see Appendix B "Links to Websites").

   b. If the IRB makes a NSR determination, submission of an IDE application is not required but the study must be conducted in accordance with the abbreviated requirements of IDE regulations (see 21 CFR 812.2(b), see Appendix B "Links to Websites").

C. If a sponsor or the IRB needs help in making the SR/NSR determination, it may ask for written guidance from the FDA.

D. The IRB will document its determination regarding device risk in the minutes. The IRB will also notify the PI in writing of its determination and the rationale for the determination.

15B.7 EXPANDED ACCESS TO INVESTIGATIONAL DEVICES

15B.7.1 EMERGENCY USE

Emergency situations may arise in which there will be a need to use an investigational device in a manner inconsistent with the approved investigational

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plan or by a physician who is not part of the clinical study. Emergency use may be appropriate if the device is intended to treat or diagnose a serious disease or condition, there are no alternative treatments available to the patient, and there is no time to obtain FDA approval. Deviations from an approved IDE must be reported to FDA within 5-working days after the sponsor learns of it (see 812.35(a)(3) and 812.150(a)(4)). For more information refer to FDA regulations at 21 CFR 812.35.

15B.7.2 COMPASSIONATE USE (OR SINGLE PATIENT/SMALL GROUP ACCESS)

The FDA may allow compassionate use access to investigational devices for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. Compassionate use is typically approved for individual patients but may be approved to treat a small group. Compassionate use may be allowed if the device is intended to treat or diagnose a serious disease or condition, and there are no alternative treatments available to the patient. Prior FDA approval is needed before compassionate use occurs. In order to obtain FDA approval, sponsors, including sponsor-investigators, should submit an IDE supplement requesting approval for a protocol deviation under section 812.35(a) in order to treat the patient. For more information, refer to FDA regulations at 21 CFR 812.35.

15B.7.3 TREATMENT USE

FDA regulations at 21 CFR 812.36 describe the criteria, safeguards, application procedures, and reporting requirements applicable to treatment use of an investigational device. In general, a device that is not approved for marketing may be under clinical investigation for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available. During the course of a clinical trial or prior to a final action on a marketing application, it may be appropriate to use the device in the treatment of patients not in the trial under the provisions of a treatment IDE. Criteria that the FDA will consider for a treatment IDE include:

A. The device is intended to treat or diagnose an immediately life-threatening or serious disease or condition.

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B. There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition in the intended patient population

C. 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; and

D. The sponsor of the investigation is actively pursuing marketing approval/clearance of the investigational device with due diligence.

15B.7.4 CONTINUED ACCESS

The FDA may allow continued enrollment of subjects after the controlled clinical trial under an IDE has been completed in order to allow access to the investigational medical device while the marketing application is being prepared by the sponsor or reviewed by FDA. Continued access may be allowed if there is a public health need, or there is preliminary evidence that the device is likely to be effective and that no significant safety concerns have been identified for the proposed indication (see Appendix B “Links to Websites”).

15B.8 HUMANITARIAN USE DEVICES (HUD)*

15B.8.1 GENERAL CONSIDERATIONS

FDA regulations at 21 CFR 814.100-814.126 implement section 520(m) of the Federal Food, Drug, and Cosmetic Act (FDCA). The purpose of section 520(m) is, to the extent consistent with the protection of the public health and safety and with ethical standards, to encourage the discovery and use of devices intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year (21 CFR 814.100)**.**

15B.8.2 IRB REVIEW

In accordance with 21 CFR 814.124, the holder of a Humanitarian Device Exemption (HDE) is responsible for ensuring that an approved HUD is administered only in facilities that have an IRB in compliance with the requirements for in 21 CFR part 56. A HUD may be administered only if such use has been approved by the IRB located at the facility or by a similarly constituted IRB that has agreed to oversee such use

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and to which the local IRB has deferred in a letter to the HDE holder that is signed by the IRB chair or an authorized designee. Except in an emergency situation, a HUD may only be administered at NIH if such use has been approved by an NIH IRB.

15B.8.3 EMERGENCY SITUATIONS

If a physician in an emergency situation determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior IRB approval (see 21 CFR 814.124(a)). In such a situation, FDA regulations require that within 5 days of the use of the HUD, the physician must notify the IRB Chair in writing of the patient involved, the date on which the device was used, and the reason for the use (21 CFR 814.124(a)). It is NIH policy that the information regarding the patient involved should include specific information that is medically important and relevant to the IRB's retrospective review of the HUD use, but should not include information that identifies the patient.

15B.8.4 NOTIFICATION OF THE FDA

Under FDA regulations, HDE holders (including investigators who may hold HDEs) are required to notify the FDA of any IRB withdrawal of approval for use of the HUD, within 5 working days after being notified of the IRB's withdrawal of approval. NIH Investigators are reminded that an approved HDE provides marketing approval for a HUD, and is not equivalent to an IDE.

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LIST OF APPENDICES

Appendix A: Definitions

Appendix B: Links to Websites

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APPENDIX A: DEFINITIONS

Except where noted otherwise, the definitions listed below are for the purpose of this SOP and are not necessarily found in the Federal Food, Drug, and Cosmetic Act (FDCA), the Public Health Service Act, FDA regulations, or other applicable laws and regulations.

A. **Adverse event** means any untoward medical occurrence temporally associated with the use of a drug in humans, whether or not considered drug related.

B. **Biological products** - see definition for "test article".

C. **Case Report Form (CRF)** is a protocol-specific form designed by the Principal Investigator or sponsor to enable the sponsor to collect data from each participating site and on each patient participating in a clinical trial.

D. **Emergency use**: FDA regulations define emergency use as "the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval." 21 CFR 56.102(d).

E. **The Guideline for Good Clinical Practice (GCP)**: GCP is an international ethical and scientific standard developed by the International Conference on Harmonisation (ICH) for designing, conducting, recording and reporting trials involving the participation of human subjects consistent with the principles of the Declaration of Helsinki. FDA published this guidance in the Federal Register on May 9, 1997 (62 FR 25692). (See Appendix B "Links to Websites".)

F. **Human subject**: FDA regulations define a human subject as "an individual who is or becomes a participant in research, either as a recipient of the test article [see definition of "test article"] or as a control. A subject may be either a healthy human or a patient." 21 CFR 50.3(g); see also 21 CFR 56.102(e).

   1. For drugs, a subject "means a human who participates in an investigation, either as a recipient of the investigational new drug [see definition of "investigational drug"] or as a control. A subject may be a healthy human or a patient with a disease." 21 CFR 312.3(b).

   2. For medical devices, a subject "means a human who participates in an investigation, either as an individual on whom or on whose specimen an

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investigational device [see definition of "investigational device"] is used or as a control. A subject may be in normal health or may have a medical condition or disease." 21 CFR 812.3(p).

G. **Humanitarian Use Device (HUD)**: A medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. 21 CFR 814.3(n).

H. **Investigation**: a clinical investigation or research involving one or more subjects [see definition of "human subject"] to determine the safety or effectiveness of a device. 21 CFR 812.3 (h). The terms research, clinical research, clinical study, study and clinical investigation are synonymous for the purposes of this SOP.

I. **Investigational device**: "means a device, including a transitional device that is the object of an investigation." 21 CFR 812.3(g).

J. **Investigational drug**: "means a new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes" 21 CFR 312.3(b).

K. **IDE**: An IDE means an application for an Investigational Device Exemption in accordance with 21 CFR part 812.

L. **Investigator**: "[A]n individual who conducts a clinical investigation, i.e., under whose immediate direction the test article [see definition of "test article"] is administered or dispensed to, or used involving a subject, or, in the event of an investigation conducted by a team of individuals, is the **responsible leader of that team."** 21 CFR 50.3(d).

M. **Investigator's Brochure**. "A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) on human subjects."

N. **Non-Significant Risk (NSR) Device**: An investigational device that does not meet the definition of a significant risk device [see definition of "significant risk device"].

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O. Non-Therapeutic Trial: In the Guideline for Good Clinical Practice, the FDA describes this as a trial in which there is no anticipated direct clinical benefit to the subject. (see GCP at sections 4.8.13 and 4.8.14.)

P. Serious adverse event: An adverse event or suspected adverse reaction is considered "serious" if, in the view of the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization, or prolongation of existing hospitalization, a persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Q. Significant Risk (SR) Device is defined in FDA regulations as an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or

2. 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; or

3. 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

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

R. Sponsor: A person (or other entity) "who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article [see definition of "test article"] is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A[n] [entity] other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct a clinical investigation that it has initiated is considered to

be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators." 21 CFR 50.3(e); see also 21 CFR 56.102(j).

S. **Sponsor-investigator**: An "individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency" (see 21 CFR 312.3 and 21 CFR parts 50.3(f) and 56.102(k).)

T. **Test article**: "Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the [FDCA] or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n)." 21 CFR 50.3(j); see also 21 CFR 56.102(l). The definitions of the various examples of test articles are as follows:

1. Medical devices: A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory which is-- (1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, (2) 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 (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve 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 its primary intended purposes" Section 201(h) of the FDCA (see Appendix B "Link to websites".)

2. Biological products: Under the Public Health Service Act (42 USC 262(i)), the term "biological product" "means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings" (see Appendix B "Link to Websites".)

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U. **Transitional device** means a device subject to section 520(l) of the act; that is, a device that FDA considered to be a new drug or an antibiotic drug before May 28, 1976.

V. **Unanticipated Adverse Device Effect**: An unanticipated adverse device effect is any serious adverse effect on health or safety, 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 application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. See FDA regulations at 21 CFR 312.64(b) and 812.150(a)(1).

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APPENDIX B: LINKS TO WEBSITES

A. FDA Form 1572:
http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf

B. Medical devices: Is The Product A Medical Device?:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm

C. IDE Approval Process:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm

D. FDA IDE regulations (21 CFR part 812):
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=812

E. FDA IDE regulations, “Abbreviated Requirements” (21 CFR 812.2(b)):
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=812.2

F. IDE Early/Expanded Access (includes FDA emergency device use):
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#compassionateuse

G. FDA regulations 21 CFR 814, Premarket Approval of Medical Devices (Subpart H – Humanitarian Use Devices):
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=814&showFR=1&subpartNode=21:8.0.1.1.11.7

H. FDA Device Advice:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm

I. Guideline for Good Clinical Practice (GCP):
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

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