

Clinical Device Trials in Countries with No Regulatory Systems

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Components of Regulatory System

- Product Oversight (e.g., CDRH/FDA)
 - Premarket Approval; Postmarket Surveillance
- Human Subject Protection Oversight (HRPP)
 - Organization (i.e., study site)
 - Administrative oversight
 - Available resources
 - Research Ethics Committee (IRB)
 - Protocol Review and Approval
 - Informed Consent Documentation
 - Responsible and Competent Investigator (team)



Distinction: SR/NSR Device

■ Significant Risk (SR) Device

- intended as an implant, or
- for use in supporting or sustaining human life, or
- 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 potential for serious risk to a subject.

■ Non-Significant Risk Device

- does not meet the definition for an SR device.



Major Differences – SR vs. NSR Device Study

- Significant Risk (SR) Device Studies
 - All IDE regulations (21 CFR 812) must be followed.
 - IDE application must be approved by FDA before proceeding.
- Nonsignificant Risk (NSR) Device Studies
 - Must follow abbreviated requirements (21 CFR 812.2(b))
 - Labeling, IRB approval, informed consent, monitoring, records, reports, prohibition against promotion; no need for submitting progress reports or final reports to FDA
 - IDE application approved by FDA not required
 - No report of IRB approval of NSR device study to FDA
 - IRB may approve NSR device study and investigator may conduct study without FDA knowing about it
 - Thus, IRB serves as FDA's surrogate for review, approval, and continuing review of the NSR device studies



Responsibilities for Device Risk Determination

- Sponsor must make initial risk determination and present it to IRB
- IRB must review sponsor's risk determination for every investigational medical device study and modify the determination if IRB disagrees
- FDA final arbiter of device study as SR or NSR
 - FDA makes determination when IDE submitted or if asked by sponsor, PI, or IRB (21 CFR § 812.2(b)(1))
 - FDA available to help sponsor, investigator, and/or IRB in making risk determination.



Early Communication Meetings

- Pre-IDE meeting (informal)
 - Feedback non-binding on either party
- Pre-IDE Determination Meeting (formal)
 - Prior to Pre-market Approval (PMA) or Product Development Protocol (PDP)
 - Purpose: FDA determination of type of valid scientific evidence necessary to demonstrate that device is effective for intended use
 - Binding on FDA unless contrary to public health
- Pre-IDE Agreement Meeting (formal)
 - Available to anyone planning to investigate safety or effectiveness of class III product or any implant; also submitters of 510(k)s for eligible devices
 - Purpose: agreement on key parameters of investigational plan (see 21 CFR 812.25), including clinical protocol
 - Binding on FDA; changed with written agreement of applicant or for scientific issue essential to determining safety or effectiveness of device



FDA Jurisdiction over foreign sites

- FDA does not have prospective jurisdiction over clinical device studies conducted outside of the United States. We encourage sponsors conducting studies in the US and abroad to follow the same protocol, controls, etc. so that the data may be pooled. For studies that will be conducted solely outside the US, we also encourage the use of the pre-IDE process, so sponsors can obtain early feedback on their trial design.
- FDA may or may not accept data from a non-US clinical device study based on criteria found in 21 CFR 814.15.



Research conducted outside US - 21 CFR 814.15

- FDA will accept foreign clinical device study only if
 - Data are valid, and
 - Study conforms to ethical principles in 1983 Declaration of Helsinki or with laws and regulations of country where research conducted, whichever provides greater protection of human subjects
 - Note: 21 CFR 814.15 issued in 1986, when 1983 version of Declaration in effect.
- PMA based solely on foreign data may be approved if
 - Foreign data applicable to U.S. population and medical practice
 - Studies performed by competent investigators, and
 - Data considered valid (with/without on-site inspection)



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 - Responsible and Competent Investigator (team)
- International Ethical Standards
 - Declaration of Helsinki, 2004; WHO CIOMS Guidelines, 2002; ICH E-6 Good Clinical Practice Guidelines.

