Backgrounder on Medical Device Regulation

For general information on how to market a medical device please refer to the following FDA website: http://www.fda.gov/training/cdrhlearn/default.htm. This is a link to the CDRH web page for multimedia industry education that includes learning modules describing many aspects of medical device and radiation emitting product regulations, covering both premarket and postmarket topics.(Note: This material has been adapted from an FDA Public Workshop on Brain Computer Interfaces held on November 21, 2014. http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm410261.htm)

A. Medical Device Classification

There are three classes of devices: Class I (general controls), Class II (special controls), and Class III (premarket approval), with the level of regulatory control increasing from Class I to Class III based on the types of regulatory controls considered necessary to provide reasonable assurance of safety and effectiveness[4]. For more information on device classification please refer to the following FDA website: http://www.fda.gov/medicaldevices/deviceregulationandguidance/overview/classifyyourdevice/default.htm

B. Marketing Applications

Information on the various types of marketing applications can be found on the following FDA websites:

- Premarket Notification (510(k)): http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketnotification510k/default.htm

- Premarket Approval (PMA): http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketapprovalpma/default.htm

- Humanitarian Device Exemption (HDE): http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/HumanitarianDeviceExemption/default.htm

- Evaluation of Automatic Class III Designation (*De Novo* Classification Process): http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf

C. Investigational Device Exemptions (IDEs)

Section 520(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)[5] establishes a framework for FDA to study medical devices for investigational use. This provides an exemption from certain requirements so that experts qualified by scientific training and experience can investigate their devices' safety and effectiveness. This exemption is known

[4] 21 Code of Federal Regulations (CFR) 860.3(c)
[5] 21 U.S.C. § 360j(g)

as an Investigational Device Exemption (IDE). The FDA considers most implanted devices to be "significant risk devices" because they are "intended as an implant and present a potential for serious risk to the health, safety, or welfare of a subject."[6] In order to study a significant risk device in human subjects, a sponsor (defined here as the person responsible for initiating the investigation) must receive approval of an investigational device exemption (IDE) application prior to beginning the investigation.[7] Investigational neurological devices are generally evaluated by the Division of Neurological and Physical Medicine Devices, one of the divisions in CDRH's Office of Device Evaluation (ODE).

A number of pathways exist for investigational studies including:

- Early Feasibility Study (EFS): a limited clinical investigation of a device early in development, typically before the device design has been finalized, for a specific indication (e.g., innovative device for a new or established intended use, marketed device for a novel clinical application).[8]

- First in Human (FIH) Study: a type of study in which a device for a specific indication is evaluated for the first time in human subjects.

- Traditional Feasibility Study: a clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan an appropriate pivotal study.

- Pivotal Study: a clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It may or may not be preceded by an early and/or a traditional feasibility study.

D. Benefit-Risk Evaluation

In making decisions regarding premarket submissions, the FDA weighs benefits and risks. There are a multitude of factors to consider assessing benefits and risks and some of these are listed in Table 1 below.[9]

E. Medical Device Master Files (MAFs)

Often a sponsor submitting a premarket submission (i.e., an applicant) needs to use another party's product (e.g., ingredient, subassembly, or accessory) or facility in the manufacture of the device. In order that a sound scientific evaluation may be made of the premarket medical device submission, the review of data and other information related to the other party's product, facility, or manufacturing procedures is required. The other party, while willing to allow FDA's confidential review of this information, may not want the applicant to have direct access to the information. To help preserve the trade secrets of the ancillary medical device industry and at the same time facilitate the sound scientific evaluation of

[6] 21 CFR 812.3(m)
[7] 21 CFR 812.20
[8] http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103.pdf
[9] Please refer to the FDA guidance documents referenced at the end of this discussion paper for additional information regarding benefit-risk evaluations in premarket submissions.

medical devices, FDA established the device master file system. Please refer to the following FDA webpage for additional information on device master files: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/ucm142714.htm

Table 1 – Factors to Consider when Evaluating Benefits and Risks

Considerations for Assessing Benefits	**Considerations for Assessing Risks**
• Type • Magnitude • Probability of patient experiencing one or more benefit • Duration of effect(s)	• Severity, type, number and rates of harmful events associated with the device • Probability of harmful event • Duration of harmful event
Additional Benefit-Risk Considerations	
• Type of submission • Stage of Device Development • Uncertainty • Characterization of Disease • Patient tolerance for risk and perspective on benefit • Availability of alternative treatments • Risk Mitigation	

Selected FDA Guidance Documents

The following is a list of current FDA guidance documents that may of interest when developing premarket submissions:

Benefit-Risk

- "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/UCM296379.pdf

IDE

- "Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies" http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidance documents/ucm279103.pdf

- "Guidance for Sponsors, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff" http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidance documents/ucm279107.pdf

- "Design Considerations for Pivotal Clinical Investigations for Medical Devices" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/UCM373766.pdf

- "Significant Risk and Nonsignificant Risk Medical Device Studies" http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

- "Procedures for Handling Inquiries Regarding the Need for an Investigational Device Exemptions Application for Research Involving Medical Devices" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm126598.htm

510(k)

- "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/UCM284443.pdf

PreSubmission

- "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff"

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/UCM311176.pdf

Technical

- "Recognition and Use of Consensus Standards" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/ucm077295.pdf

- "Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocume nts/ucm107705.htm

- "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/ucm089593.pdf

- "Radio Frequency Wireless Technology in Medical Devices - Guidance for Industry and Food and Drug Administration Staff" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/ucm077272.pdf

- "Off-The-Shelf Software Use in Medical Devices" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidan ceDocuments/ucm073779.pdf

Developing Guidance Documents

- "Food and Drug Administration Report on Good Guidance Practices" http://www.fda.gov/downloads/AboutFDA/Transparency/TransparencyInitiative/UCM285124.pdf

Acronyms and Abbreviations

510(k): Premarket Notification

CDRH: Center for Devices and Radiological Health

EFS: Early Feasibility Study

FDA: U.S. Food and Drug Administration

FIH: First in Human

HDE: Humanitarian Device Exemption

HUD: Humanitarian Use Designation

IDE: Investigational Device Exemption

MAF: Master File

ODE: Office of Device Evaluation

PMA: Premarket Approval