Workshop Materials

Discussion Paper: "External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals"

Posted Date: November 13, 2015

Table of Contents

I. Introduction

The FDA is releasing this discussion paper in preparation for the public workshop "External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals", which will be at FDA's White Oak Campus in Silver Spring, Maryland on November 20, 2015.

It is important to the FDA to ensure that the regulatory landscape for medical devices is transparent to the public (e.g., manufacturers, health care professionals, patients, consumers, consumer advocates, academia, and other government agencies), and FDA's meetings enable stakeholders to understand applicable regulatory requirements which may afford an opportunity to clarify the methodologies and data needed to bring safe, effective, and innovative devices to market. The agency is holding this workshop to open discussion and obtain public feedback on scientific and clinical considerations associated with external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals.

The workshop is open to all stakeholders to promote awareness of an emerging product area and discuss considerations in the regulation of these devices. The FDA hopes that open discussion and dialogue will help successfully advance this product area. The information and feedback collected by FDA from the workshop will help further develop an appropriate risk-based regulatory framework for these devices that will promote advances in the technology while maintaining appropriate user protections. This framework will be supplemented by the future development of FDA guidance for this technology.

For the purposes of this workshop, the FDA defines these products as devices that apply external electromagnetic neurostimulation to the head, with the intent of improving, enhancing, or otherwise favorably altering normal cognitive function in healthy individuals. This is in contrast with traditional therapeutic neurostimulation devices that are intended to prevent or treat (either alone or as an adjunct) diagnosed medical conditions.

This discussion paper provides background information and questions for workshop attendees to consider in advance, and will help facilitate discussion. While the information and questions provided represent FDA's focus, we look forward to hearing other considerations and questions at the workshop.

The information and questions contained in this document are not binding and do not create new requirements or expectations for affected parties, nor is this document meant to convey FDA's recommended approaches or guidance. Rather the information contained in this document offers background and the basis for discussions at the Public Workshop.

II. Regulatory Considerations for External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals

The field of external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals is progressing rapidly from fundamental neuroscience discovery and proof-of-concept to real-world application. The FDA recognizes the value of supporting medical device innovation to address consumer needs in an area where alternative methodologies of improving normal cognitive function are unavailable, ineffective, or associated with substantial risks to user safety. As a starting point, the workshop will consider scientific and clinical issues associated with these devices in the following areas:

A. Perspectives on Regulatory Assessment of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals;

B. Current State of Science of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals;

C. Benefits and Risks of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals;

D. Clinical Trial Design Considerations of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals; and

E. Ethical Considerations of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals.

During the workshop, and through an open public docket (available to collect public comments starting August 14, 2015), the feedback we collect will inform our development of a regulatory framework for these devices. *As part of the workshop discussion paper, a brief overview of device regulation is also provided (Appendix A).*

A. Perspectives on Regulatory Assessment of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals

A common understanding between device developers, manufacturers, consumers, and regulators regarding the regulatory assessment of external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals is important to promote device innovation and availability for use by consumers.

Medical devices are defined in section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act, in part, as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is … intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease … or intended to affect the structure or any function of the body of man… " (See Appendix A).

Generally, a product meets the definition of a medical device if it is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which (1) is not dependent upon being metabolized for the achievement of any of its primary intended purposes and is 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 (2) is intended to affect the structure or any function of the body of man; this latter provision of the device definition, "intended to affect the structure or any function of the body" is a central discussion of this workshop. We believe it is important to highlight the distinction between medical devices intended for diagnostic, preventive, or therapeutic use vs. medical devices intended to affect the structure or any function of the human body.

Medical devices are also categorized as Class I, II or III according to the level of regulatory control that is needed to provide a reasonable assurance of safety and effectiveness. The class of a particular medical device determines, among other things, the type of premarketing submission/application required for FDA marketing authorization[1] (See Appendix A). Class I devices have the lowest level of regulatory oversight. Moderate risk devices are Class II devices and typically require the submission of a premarket notification (510(k)), while Class III devices are the highest risk and require a premarket approval application (PMA). External electromagnetic neurostimulation devices that are intended to treat patients with specific conditions or disorders are currently classified in either class II or class III, depending on their intended use. (See footnotes 3-6).

FDA's regulatory paradigm allows oversight tailored to the risks of the device. The Agency has identified certain factors as important in the regulatory assessment of external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals including but not limited to:

- Whether the use of the device presents "a potential unreasonable risk of illness or injury."

- The information provided in the labeling and/or promotional materials describing how the device may affect the structure (anatomy) or function (physiology) of the human body.

- How these devices relate to other medical devices that may also deliver energy externally to the head for therapeutic effect (even if the intended uses are different). Some examples of medical devices that may be similar to external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals are Transcranial Magnetic Stimulation (TMS)[2], Transcutaneous Electrical Nerve Stimulation (TENS)[3], Cranial Electrotherapy Stimulation (CES)[4], and Electroconvulsive Therapy (ECT)[5] devices.

[1] See Appendix A
[2] 21 Code of Federal Regulations (CFR) 882.5805 and 21 CFR 882.5808
[3] 21 CFR 882.5890 and 21 CFR 882.5891
[4] 21 CFR 882.5800
[5] 21 CFR 882.5940

Questions for Consideration
With regard to perspectives on the regulatory assessment of external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals, consider the following questions in preparation for the workshop:

1. What kind of labeling or promotional materials of a product which applies electromagnetic neurostimulation externally to the head would have implied claims that fit within the definition of a medical device?

B. Current State of Science of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals

In general, there are two approaches in the scientific literature that investigate these devices which include either (1) studying the change in the anatomy or underlying physiology from use of the device or (2) studying the change in cognitive function, with or without a change in anatomy/physiology. While FDA historically has not required conclusive evidence supporting a specific mechanism of action claim(s) deriving from studies of anatomy and/or physiology that do not investigate cognitive function, such devices may appear to describe what would otherwise be considered a mechanism of action. In the case of claims deriving from studies of cognitive function, it would likely not be necessary to provide evidence of a mechanism of action.

The scientific literature underlying external electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals is limited. This may be due to a number of factors; for example, claims that are strictly related to anatomy and physiology – while of interest from a research perspective – would not likely receive attention from patients and consumers if not correlated with a type of benefit or risk that is meaningful to a user (e.g., faster reaction time).

Reports of the physiological effects of these devices typically focus on the neuromodulatory effects that electromagnetic stimulation has on neural structures and networks in the brain. Such neuromodulatory effects include modulation of neuronal excitability, modulation of the connectivity across neural networks, increasing or decreasing activity in particular neuronal structures, entrainment of specific patterns of activity, and modulating brain activity in certain frequency bands. However, the underlying cellular/molecular changes induced by external electromagnetic neurostimulation are less well-known, and it is not clear exactly how various methods of external electromagnetic neurostimulation achieve their effect at the cellular level.

External electromagnetic neurostimulation devices are believed to expose the brain to an electromagnetic field that interacts with neuronal tissue differently depending upon orientation and positioning of the device, the method by which this electromagnetic field or current is generated, the specific device stimulation parameters used, as well as the duration and number of the stimulation sessions. These variables, combined with the numerous potential anatomical targets, the numerous cognitive domains, and the numerous methods of assessing each cognitive domain has contributed to debate in the scientific community regarding the effectiveness of these devices in improving normal cognitive function in healthy individuals. However, there does not appear to be strong evidence in support of meaningful effects on specific cognitive faculties (e.g., working memory). Additionally, it is not clear whether improvement in one cognitive domain may occur at the expense of

cognitive function in another domain. Cognitive function is typically assessed across a number of different domains, such as attention and concentration, verbal and non-verbal memory, speech and language function, executive function, and visuospatial function. An individual's performance in each of these cognitive domains is affected by complex processes across a number of neuronal structures, and while a large amount of neuroimaging research in the past decade has contributed to our understanding of these processes, there still lacks a complete understanding of the physiological mechanisms by which each of these processes occur.

Questions for Consideration
With regard to the current state of scientific evidence, consider the following questions in preparation for the workshop:

1. How can the current gaps in scientific and clinical understanding be addressed to help us better understand different external electromagnetic neurostimulation device technologies? For example, are there physiological studies that can be performed to provide a better understanding of the potential stimulation targets and thereby potentially improve device effectiveness?

2. Are there areas of non-clinical testing, research, and medical device comparisons that need to be addressed for these external electromagnetic neurostimulation devices? For example, can modeling the currents induced in the brain tissue help us better understand how these devices work or help predict device effectiveness?

C. The Benefits and Risks Associated with External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals

As part of the decision-making process for device applications, FDA carefully considers the probable benefits to health as well as the probable risks from the use of the device. Along with descriptions of these and other factors that contribute to this analysis, this process is outlined in a 2012 guidance document, "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and De Novo Classifications."

Potential Benefits Associated with External Electromagnetic Neurostimulation Devices
External electromagnetic neurostimulation devices may be designed to benefit healthy individuals by improving their cognitive function. As discussed in Section II.B., depending upon the stimulation parameters and targeted anatomical location, a particular external electromagnetic neurostimulation device may modulate cortical structures to influence one or more cognitive domains. However, at this time, there does not appear to be substantial evidence to characterize the benefits these devices may confer. On the other hand, the magnitude of benefit for devices that solely target the anatomy or physiology of the human brain, in the absence of cognitive improvement, may also be hard to quantify.

Potential Risks Associated with External Electromagnetic Neurostimulation Devices
During the course of a medical device review, FDA evaluates and leverages evidence between technologically similar devices that are intended to diagnose, prevent, or treat a condition or disease, such as during the premarket notification process (510(k)); in some

cases, there is a large body of evidence for one, or in some cases, both devices characterizing the benefits and risks. The extent to which comparisons are appropriate depend on the devices similarity and use conditions, which may vary significantly. However, the available evidence generally focuses on short-term effects. What is unclear is what effects long-term use of these external electromagnetic neurostimulation may have. Long-term psychological or behavioral effects of external electromagnetic neurostimulation have not been evaluated and carry potential risk of unintended behavioral modifications. The degree of risk could vary between potential user populations (e.g., children versus adults), and could therefore impact the benefit-risk analysis.

Questions for Consideration
With regard to the benefits and risks, consider the following questions in preparation for the workshop:

1. What does a claim of "improvement in cognitive function" mean? Is it too vague to be meaningful to users; what specific types of benefits might users consider meaningful? What potential benefits related to cognitive function, if any, can be derived from data collected only on anatomy or physiology? And how can either benefits or risks be quantified?

2. A factor in FDA's assessment of a device's potential benefit and risk is an individual's tolerance for risk. Since these devices are intended to be used by healthy individuals, how should an individual's tolerance for risk be considered in the absence of a clinical or medical condition?

3. The levels of cognitive function in healthy individuals are not well-defined. What types of variation across healthy individuals should be considered when assessing either the potential benefits or risks associated with these devices?

D. Clinical Trial Design Considerations for Evaluating External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals

Whether or not a sponsor would need to collect data from human studies for their device will depend on a number of factors. For example, there may be cases where non-clinical testing would be sufficient and others where some degree of clinical data would be needed.. In other cases where clinical data may be needed, the development of adequate clinical study designs for evaluating use of these devices by healthy individuals is essential to furthering our understanding of these devices and to promoting their safe and effective use. The following are considerations that FDA believes would be useful important in designing trials, whether for research purposes or for marketing applications.

Intended Use Populations
Selection of an appropriate study population representative of the intended use population of external electromagnetic neurostimulation devices is critical to proper evaluation of their safety and effectiveness. It is important to understand what factors may influence safe and effective use of the device and the amount of variation that may be present within the healthy population. While these devices may broadly be intended for use by healthy individuals, there is likely variation in their effectiveness within different populations based upon a variety of individual traits or other characteristics. For example, there may be

biological reasons for variations in effectiveness of such a device based upon age of the individual users. There may also be individual-specific traits that influence whether a particular device effectively improves their level of cognitive function.

Similarly, the motivation for an individual to seek improvement in their normal cognitive function may vary and therefore affect the amount of risk they are willing to tolerate, as well as the amount of benefit that they would describe as meaningful. For example, an individual who is trying to learn how to better remember names of new acquaintances may have a different approach to the use of an external electromagnetic neurostimulation device from that of a student who is trying to improve performance on tested materials.

It is also important to understand the differences between use of external electromagnetic neurostimulation devices under the supervision of healthcare professionals in a medical setting and use of these devices by the lay user in their homes. Studies that take home-use environments into account may more adequately reflect how an individual will actually use the device.

Clinical Metrics

Clinical metrics or endpoints are important for defining the potential benefits and risks of medical devices. Metrics should be clinically meaningful, measure how an individual functions or feels or both, and ideally should be validated for the indicated use population. While there are a number of outcome measures that assess cognitive function, some may be less useful depending on the intended use of the device.

The following are important factors to consider when developing or selecting metrics for evaluating study success for external electromagnetic neurostimulation device clinical studies:

- The intended use population for which the device can be used and the type and level of benefit achieved through use of the device. For example, an individual seeking to improve their proficiency at studying materials may primarily benefit from improved memory function, while an individual seeking to improve their focus during their job or important daily activities may primarily benefit from improved attention.

- The level of potential benefit needed to outweigh the potential risks associated with a device may depend on the risk tolerance of the intended use population.

- Both the benefits and the risks associated with a device may change significantly depending upon the frequency of use of the duration of use.

Questions for Consideration

With regard to clinical trial design considerations, consider the following questions in preparation for the workshop:

1. What factors will be important in identifying a population of normal cognitive healthy users?

2. What outcome measures may be most relevant to assessing the safety and effectiveness of a device?

3. How should studies be conducted? What approaches may be used for blinding? Sham treatment arms?

4. How long should follow-up continue to evaluate potential long-term benefits? Risks?

E. Ethical Considerations of External Electromagnetic Neurostimulation Devices Intended to Improve Normal Cognitive Function in Healthy Individuals

The difference between a device intended to prevent or treat a disease or condition and one that is intended to improve or enhance an otherwise healthy individual is important. For example, powered muscle stimulators intended for muscle conditioning (mentioned earlier) can be considered a form of exercise equipment, and there are few, if any, that assert this type of device presents ethical concerns. External electromagnetic neurostimulation devices intended to improve normal cognitive function in healthy individuals could also be considered to be "exercising," but for the brain versus the body. While some might assert that there is little difference between the two, changes in cognitive function may impact an individual on a more profound level than changes in the structure and function of skeletal muscle.

Discussions about the ethical implications of using devices or drugs to improve normal cognitive function are not new. In the context of this workshop, medical devices under discussion are being designed specifically to improve or enhance an otherwise healthy individual and FDA believes this is an opportune time to address how ethics may be considered a part of these discussions.

Questions for Consideration
With regard to ethical considerations, consider the following questions in preparation for the workshop:

1. Under what circumstances would it be appropriate to make external electromagnetic neurostimulation device technologies available by prescription only? Over the Counter (OTC)?

2. To what extent would making these devices available only by prescription mitigate ethical concerns? Would it depend on the user population?

3. What types of claims may raise ethical concerns? Are there claims that would not raise ethical concerns?

III. Submitting Public Comments

Regardless of attendance at the public workshop, if you have information related to this workshop that you wish the FDA to consider, please post your material to Docket Number FDA-2015-N-2711 at http://www.regulations.gov. Instructions for posting material can be found at: http://www.fda.gov/RegulatoryInformation/Dockets/Comments/ucm089193.htm or in writing to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers

Lane, rm. 1061, Rockville, MD 20852 (Docket ID: FDA-2015-N-2711). Both individuals and groups may submit materials.

Please note that the docket will be public, and not appropriate for addressing individual confidential medical device concerns.

IV. Appendix A: A 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.

Additional resources are provided as follows:

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[6]. 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

- 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)[7] 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 as an Investigational Device Exemption (IDE). 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.[8]

A number of pathways exist to study medical devices including:

[6] 21 CFR 860.3(c)
[7] 21 U.S.C. § 360j(g)
[8] 21 CFR 812.20

- 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).[9]

- 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.[10]

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 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

[9] http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103.pdf
[10] 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.

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	

V. Appendix B: 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/GuidanceDocuments/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/guidancedocuments/ucm279103.pdf

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

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

510(k)

- "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/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/GuidanceDocuments/UCM311176.pdf

Technical

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

- "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"
  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/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/GuidanceDocuments/ucm077272.pdf

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

Developing Guidance Documents

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

VI. Appendix C: Glossary of Acronyms and Abbreviations

510(k): Premarket Notification

CDRH: Center for Devices and Radiological Health

CES: Cranial Electrical Stimulation

DBS: Deep Brain Stimulation

ECT: Electroconvulsive Therapy

EFS: Early Feasibility Study

FDA: U.S. Food and Drug Administration

FIH: First in Human

IDE: Investigational Device Exemption

MAF: Master File

ODE: Office of Device Evaluation

OTC: Over The Counter

PMA: Premarket Approval

PMS: Powered Muscle Stimulator

tDCS: transcranial Direct Current Stimulation

TENS: Transcutaneous Electrical Nerve Stimulation

TMS: Transcranial Magnetic Stimulation