BASIC FDA CDRH MEDICAL DEVICE RESOURCES

I. INTRODUCTION/PURPOSE

You have this innovative idea and want to bring it to market so patients and health care professionals can start using it and changing lives. But before it can even be marketed in the US, it's likely you'll need to get your invention cleared/approved/granted by the US Food and Drug Administration (FDA) to assure the invention is safe and effective for patients. Occasionally, even investors want to see FDA approval or clearance letter before they commit.

While this may seem like a bridge you'll cross when you're closer to finalizing and launching your invention, there are some regulatory requirements, such as clinical studies and Investigational Device Exemptions, which apply to medical devices before they are officially marketed. It can also be beneficial to start considering the regulatory implications for your invention in the early stages of development to be more prepared when it comes time to submit a marketing submission to the FDA. For example, FDA marketing submissions require and involve the FDA review of some level of design documentation (specifically for software) and performance/safety/effectiveness test data (whether bench, animal, and/or clinical), which are often completed months-years before you submit your marketing submissions. It can be a setback if you do an animal study in a model or for a duration that FDA doesn't agree with, leading to a request for new and additional testing. Having an idea of the type of data FDA requires can help you design and plan your testing approaches accordingly and in advance, potentially saving time, redesigns, repeat testing, and costs.

As you start to consider your regulatory strategies, review the **Med Device Regulation Questions** document in the JHTV Digital Library to get a general overview of some aspects of medical device regulation that can impact your invention's journey to market.

Next, you can refer to the sections in this guide to get:

- Acquainted with regulatory terms and learn some regulatory basics through useful FDA links
- A basic overview of the regulatory submission types and framework
- A focused overview on the 510(k) pathway and strategies for finding a predicate device
- A generalized table of some potential regulatory approaches for some regulatory scenarios

Lastly, if you are a faculty or staff project, reach out to FastForward and if you are a student venture, reach out to FastForward U for additional information and resources. Please note that FDA policy, information, and programs can adapt over time – while this serves as a basic overview of the major, and long-established principles and programs of FDA/CDRH regulatory processes, it is important to check current FDA sites and resources related to topics of interest to ensure you are informed of the most recent policies.

II. USEFUL LINKS FOR GETTING STARTED

- **FDA CDRH Learn**: Multimedia industry education site with recorded learning modules on basic regulatory topics. *Recommended to watch some modules prior to reading this guide to get acquainted with terminology*
- **FDA CDRH Device Advice**: Landing page for various FDA/CDRH medical device regulation resources)
- **Medical Device User Fees**: Cost for different FDA/CDRH Medical Device submissions
- **Device Advice – How to Study and Market Your Device**: Broad approach for getting a device on the market, broken down into 4 Main Steps. Last step includes guidance on administrative processes for submitting to FDA
- **How to Find and Effectively Use Predicate Devices**: Specific resource for the 510(k) Pathway
- **How to Prepare a Traditional 510(k)**: Broad approach, includes format and content of 510(k)
- **PMA Application Contents**
- **IDE Application**: Includes required, recommended content and formatting
- **Guidance for Industry and Food and Drug Administration Staff- Requests for Feedback and Meetings for Medical Device Submissions:** The Q-Submission Program: includes description of the Q-submission program and recommended content to include in pre-submissions
- **FDA Guidance Documents Search**: Website for searching for guidance documents that may be applicable to your medical devices
- **Medical Device Webinars and Stakeholder Calls**: Website for more specialized, current topics such as webinars on COVID-19 related medical device, recent guidance documents that have been finalized, introducing new regulatory programs intended to foster innovation

III. REGULATORY SUBMISSION TYPES AND FRAMEWORK

The 1976 amendment to the Federal Food, Drug, and Cosmetic Act of 1938 established the risk-based medical device classification system used by FDA. Generally, each medical device is assigned to one of three regulatory classes—Class I, Class II, or Class III—based on the level of risk and "control" necessary to provide reasonable assurance of the device's safety and effectiveness. "Controls" are understood to be provisions outlined by laws, requirements that can take various forms such as but not limited to guidelines/principles that must be upheld or avoided (e.g., misbranding), administrative steps (e.g., registering your device with FDA), labeling information that must be included with device packaging, and testing that should be completed in order for a device to marketed in the US.

When considering level of risk, FDA Center for Devices and Radiological Health (CDRH) evaluates a number of factors, both individually and in the aggregate. The factors include but are not limited to severity, types, numbers and rates of harmful events associated with the use of the device, probability of a harmful event, duration of harmful events, and risk from false-positive or false-negative results for diagnostics. Controls are requirements listed in Title 21 of the Code of Federal Regulations (CFR) that must be met in order to sell a medical device in the United States.

In most cases, Class I devices are considered low risk, Class II are moderate risk, and Class III devices are high risk. Classification includes factors related to both the technology and the device

intended use (i.e., the general purpose of the device or its function) and the device indications for use (i.e., the disease or condition the device will diagnose, treat, prevent, cure or mitigate including a description of the patient population for which the device is intended).

In addition to the three risk-based classes of medical devices, the following types of medical devices exist:

- Pre-amendment devices: a device that was on the market prior to the enactment of the Medical Device Amendments to the FD&C Act on May 28, 1976.
- Unclassified medical devices: pre-amendments device that have not been assigned a regulation number. Unclassified devices require submission of a 510(k) premarket notification to CDRH.
- "Not-classified device": a post-amendments device for which the Agency has not yet reviewed a marketing application or for which the Agency has not made a final decision on such a marketing application.

FDA/CDRH uses device-specific regulation numbers posted in the 21 Code of Federal Regulations (e.g., 21CFR XXX.XXXX) as general identifiers for the medical devices it regulates. The Code of Federal Regulations (CFR) is a codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the Federal Government. Title 21 of the CFR is reserved for rules of the Food and Drug Administration.

FDA/CDRH also further subdivides device-specific regulations into three-letter classification product codes. Classification product codes help to delineate technology and indication subgroups within a device-specific regulation. They can also serve to categorize unclassified or Class III (PMA) devices.

Clinical specialties identified as "review panels" (e.g., Neurology, Cardiovascular, General Surgery) are also used to further organize device-specific regulation numbers and classifications.

The type of submission that should be submitted for a device depends on the risk level of the medical device. There are three main pre-market submissions companies can submit to FDA in order to market a medical device in the United States (US) and are listed below. Please note this is not an exhaustive list of all pre-market submission types. Additional details on the main pre-market submissions are summarized in the Table 1:

- **510(k) Notification:** Submission to demonstrate that the device to be marketed is as safe and effective, or "substantially equivalent", to a legally marketed device referred to as a **predicate device**. The medically devices eligible for 510(k) are typically Class I and Class II devices (low-to-moderate risk).
- **De Novo Classification Process**: Submission to classify novel medical devices that provide reasonable assurance of safety and effectiveness for the intended use, but for which there is no legally marketed **predicate device**. De Novo classification is a risk-based classification process, typically classifying medical devices as Class I and II (low-to-moderate risk).
- **Pre-Market Application (PMA)**: Submission for scientific and regulatory review to evaluate the safety and effectiveness of Class III (high risk) medical devices. Class III devices support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.

Table 1: Basic Summary of Three Main FDA Pre-market Submissions

Pre-market Submission Type	Level of Risk	Classification	Regulatory Controls	Review Timeline	Cost**	Additional Details/Regulatory Outcomes
Pre-market Notification "510(k)"	Low-to-Moderate	Class I, II, Unclassified	**General Controls** (e.g., registration and listing, abstaining from misbranding), and sometimes **Special Controls** (depending on device regulation, e.g., special labeling requirements, conformance with **performance standards**)	~ 90* (for Traditional 510(k) submissions)	Standard: $12,745 Small Business: $3,186	Device is "cleared" for marketing if the submission demonstrates that the device is "substantially equivalent" to a predicate (i.e., previously cleared/marketed) device. If the device is not "cleared" then it is found "not substantially equivalent" (NSE), and cannot be marketed.
De Novo Classification Process "De Novo"	Low-to-Moderate	Class I, II	General Controls and Special Controls	~120*	Standard: $112,457 Small Business: $28,114	The device has no predicate device. Device is "granted" de novo designation and can be marketed and a new device classification is created. May be used as a predicate for future 510(k) notifications. If not "granted" designation, then the submission is "denied" and device cannot be marketed. Evidence must demonstrate that general and special controls provide reasonable assurance of safety and effectiveness.
Pre-Market Application "PMA"	High	Class III	General Controls	~180*	Standard: $374,858 Small Business: $93,714	The submission is "approved" if it demonstrates reasonable assurance of safety and effectiveness. If not approved, the device is "disapproved" and the device may not be marketed.

*The review timelines reflect the number of **calendar days** during which the FDA will actively review and engage in "interactive review" with companies for the submission. "Interactive review" is when the FDA will ask clarifying questions, request additional information and data from company via email or teleconference when the review is active. When information is requested during "interactive review," the review timeline or "review clock" continues and is limited by the number of days in the table above. FDA will identify via email or phone request the information requested and the number of days (e.g., 2-15 days) and/or a date by which a company should provide the information via email reply. Additionally, the number of days noted in the table above is not considered the "total review time", which includes hold times during which the FDA will place a submission "on hold" and temporarily stop the review timeline to request more in-depth information from companies in the format of a "hold letter. "When a submission is "on hold," companies usually have a maximum of 180 days to provide a reply and provide the requested information. The response provided to address a "hold letter" is required to be sent to FDA via mail as both a paper and electronic copy, like the original submission.
Medical Device Use Fee Amendments (essentially the cost of each submission type) is subject to change each government fiscal year. Click here for the most current cost for FDA CDRH Submissions.**

In addition to the three main marketing submissions described above, there are other submissions that can be submitted to FDA and are described below:

- **Investigational Device Exemptions (IDE):** Submission for obtaining FDA/CDRH approval to initiate a clinical study to evaluate the safety and effectiveness of a medical device. IDE studies often collect data that can be submitted to support a pre-market submission.
- **Humanitarian Device Exemption (HDE)**: Submission for devices intended for diseases or conditions that affect small (rare) populations (i.e., no more than 8000 individuals in the US per year).
- **513(g) Request for Information:** Submission for obtaining FDA/CDRH feedback on the classification/regulation number, product code, and regulatory requirements (i.e., type of pre-market submission) that may be applicable to your device.
- **Q-submissions:** *Free* submissions to obtain FDA feedback on specific questions related to future clinical studies and marketing submissions for medical devices.

IV. 510(K) PATHWAY- FINDING A PREDICATE DEVICE

510(k) submissions are the most common pre-market submission type and are intended to be a more streamline process for getting medical devices on the US market. For this reason, this guide has included this section for the 510(k) pathway and approaches for identifying a predicate device. For information on the other submission types, please refer to Section I and II above.

It's recommended that you watch the **Webinar from CDRH Learn on "The 510(k) Program"** for an overview of the 510(k) regulatory pathway.

A. GENERAL DEFINITIONS

- **Guidance documents:** As **defined by the FDA here**, documents prepared by FDA for FDA staff, regulated industry, and the public that describe the agency's interpretation of or policy on a regulatory issue. Guidance documents include, but are not limited to, documents that relate to:
  - the design, production, labeling, promotion, manufacturing, and testing of regulated products
  - the processing, content, and evaluation or approval of submissions
  - inspection and enforcement policies
  - Guidance documents do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statue, regulations, or both.
- **Product code:** as defined in FDA's Guidance for Industry and Food and Drug Administration Staff, "Medical Device Classification Product Codes", a three letter code created to assist in accurate identification and tracking of medical devices and easy reference to predicate device types.
- **Sponsor**: term FDA uses to refer to company/organization submitting a pre-marketing submission (can be a company, consulting group, academic institution, contract research organization)

B. 510(K) PATHWAY DEFINITIONS

- **Clearance**: terminology used to note a low-moderate risk-level device can be marked in US, was reviewed under the 510(k) regulatory pathway, and found to be substantially equivalent to another device that is currently on the market
- **Pre-amendment device**: Legally marketed in the U.S. by a firm before May 28, 1976 (date of Medical Device Amendments to the Federal Food, Drug and Cosmetic Act) which have not been significantly changed or modified since then and for which FDA has not issued a PMA regulation.
- **Predicate device**: a legally marketed device to which a device is compared/contrasted to in the 510(k) pathway in order to determine substantial equivalence
- **Primary predicate device**: when multiple predicate devices are identified in a 510(k) submission, a primary predicate is the one with indications for use and technological characteristics most similar to the new device under review
- **Reference device**: devices that may be identified in a 510(k0 to support scientific methodology or standard reference values applicable to the new device under review
- **Substantial equivalence**: a new low-moderate risk device is as safe and effective as a legally marketed device (i.e., predicate device)
- **Intended use**: as defined in FDA Guidance for Industry and Food and Drug Administration Staff "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]" the general purpose of the device or its function and encompasses the indications for use
- **Indications for use**: as defined in 21 CFR 814.20(b)(3)(i), describes the disease or condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended.

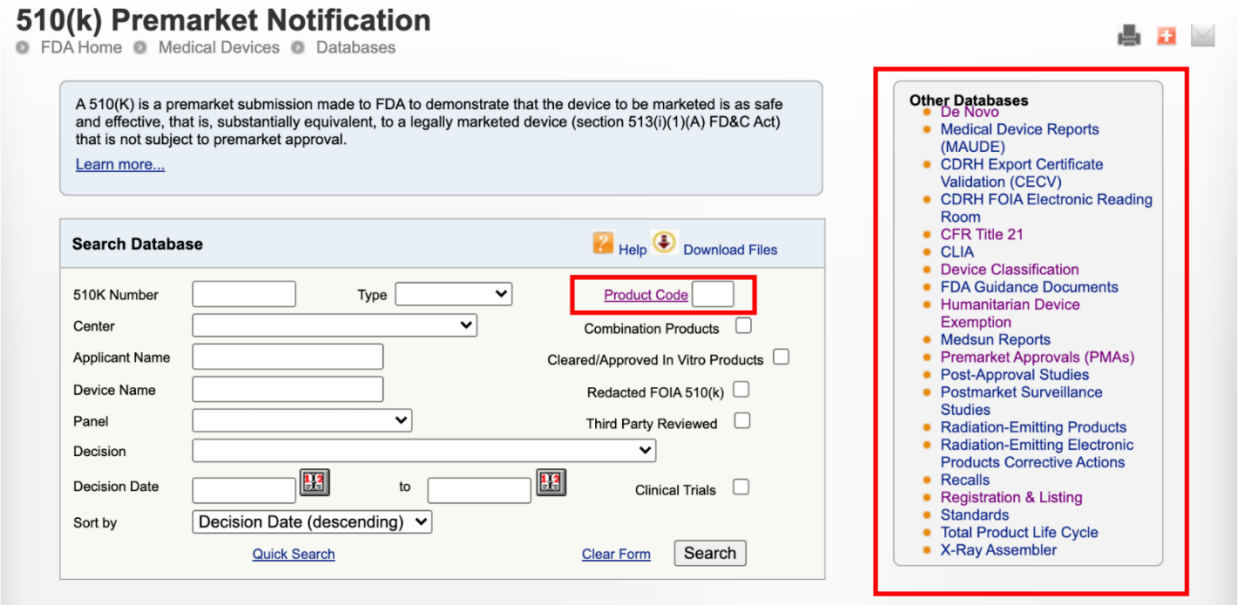
- **Unclassified device**: as defined in FDA's Guidance for Industry and Food and Drug Administration Staff, "Medical Device Classification Product Codes" a pre-amendments device for which a classification regulation has not been promulgated. Unclassified devices require submission of a 510(k) premarket notification to FDA.

C. APPROACHES TO CONSIDER

*Examples noted in screenshots below were randomly selected and do not represent good or bad examples of medical devices, marketing submissions, or regulatory experiences.

If you have no idea where to start:

- Identify generic terms related to your device, related to the indications for use/clinical application, mechanism of action, and technological characteristics. Google the term with "FDA"+ "CDRH" to help identify potential examples of similar devices that have obtained FDA clearance/approval. Look for web addresses that include **accessdata.fda.gov** or **fda.gov**. All devices that have obtained marketing clearance/approval/grant[ing] are posted on FDA's websites/databases (see following bullet point below). Each device has a page includes key information that can be helpful in your search for a predicate.
- The **510(k) database** is a public FDA website where you can search for medical devices cleared under the 510(k) process. More importantly to note, is the right-hand panel of "Other databases" with links to other databases such as "De novo," "Device Classification," "CFR Title 21," "Humanitarian Device," "Premarket Approvals (PMAs)." This site and panel of links are a great landing page to all the useful databases you may want to use in a regulatory search. When searching on these databases:
  - It is usually best to complete **only one** box in the online search form per search. The search engine searches for an exact match of text. Therefore, **one** descriptive word in the "device name" box is recommended.
  - Searching for predicate devices by product code (and only the product code, no other search term or search field) is a good place to start.
  - Please note – some devices have *multiple product codes*.

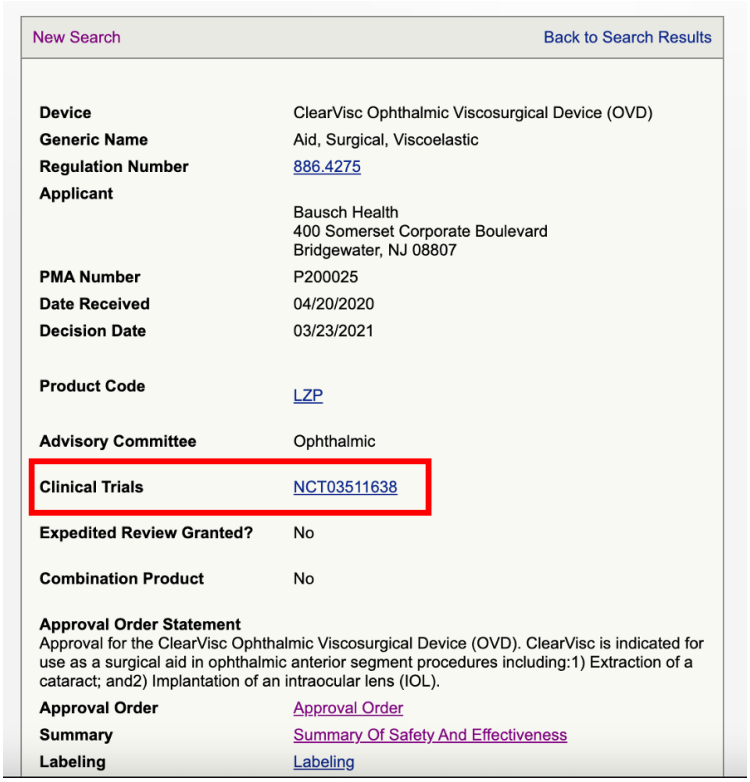


- When you find a device/devices that appears to be similar to yours and its corresponding FDA website, take note of the product code, classification name, regulation number, specific 510(k) number, manufacturer, review panel, CDRH Office. These details are important and can serve as search terms when using the FDA databases to look for more information.
  - Each FDA website for an approved/cleared/granted summary document that can be useful for understanding the regulatory experience and data required for the clearance/approval, which may be potentially applicable to your device and can be helpful resources in finding the type of clinical trials and other performance testing that was conducted to support the device clearance/approval. The name of each summary document is different depending on the marketing submission"
    - 510k → **"510(k) summary" example**
    - PMA → **"Summary of Safety and Effectiveness" example**
    - HDE → **"Summary of Safety and Probable Benefit" example**
    - De Novo → **"Decision Summary" example**

      The link to the summary document is on the on the accessdata.fda.gov FDA websites for approved/cleared/granted devices through the databases (example):

Device Classification Name	Stimulator, Neuromuscular, External Functional
510(K) Number	K200262
Device Name	L100 Go System
Applicant	Bioness Inc. 25103 Rye Canyon Loop Valencia, CA 91355
Applicant Contact	Mercedes Bayani
Correspondent	Bioness Inc. 25103 Rye Canyon Loop Valencia, CA 91355
Correspondent Contact	Shanna Hu
Regulation Number	882.5810
Classification Product Code	GZI
Subsequent Product Code	IPF
Date Received	02/03/2020
Decision Date	03/04/2020
Decision	Substantially Equivalent (SESE)
Regulation Medical Specialty	Neurology
510k Review Panel	Neurology
Summary	Summary
Type	Special
Reviewed By Third Party	No
Combination Product	No

- Unfortunately, **no** public summary document or FDA database exists for finding *approved clinical studies* through the IDE process. However, **clinicaltrials.gov** may be a useful resource to search for clinical studies on similar devices. The link to the associated clinical trial on **clinicaltrials.gov** is sometimes included on the **accessdata.fda.gov** FDA websites for approved PMAs and HDEs found through the databases: **EXAMPLE**



New Search | Back to Search Results

Device	ClearVisc Ophthalmic Viscosurgical Device (OVD)
Generic Name	Aid, Surgical, Viscoelastic
Regulation Number	886.4275
Applicant	Bausch Health 400 Somerset Corporate Boulevard Bridgewater, NJ 08807
PMA Number	P200025
Date Received	04/20/2020
Decision Date	03/23/2021
Product Code	LZP
Advisory Committee	Ophthalmic
Clinical Trials	NCT03511638
Expedited Review Granted?	No
Combination Product	No

Approval Order Statement
Approval for the ClearVisc Ophthalmic Viscosurgical Device (OVD). ClearVisc is indicated for use as a surgical aid in ophthalmic anterior segment procedures including:1) Extraction of a cataract; and2) Implantation of an intraocular lens (IOL).

Approval Order	Approval Order
Summary	Summary Of Safety And Effectiveness
Labeling	Labeling

- It's helpful to review the summaries of *multiple devices* that are similar to yours that are within the same product code and compare/contrast how their technological characteristics, indications for use statements, and level of testing completed may vary. The more devices you review and compare/contrast, the better understanding you'll have of the type of technology that exists, indications that have been cleared/approved/granted, and level of data needed that could be applicable to your device.
- If your device is used as a component or accessory to another device or used in a system, Google the device/system name with "FDA" to find whether the component/accessory/system has FDA approval/clearance. If you find any relevant FDA websites for the component/accessory/system on one of the FDA databases using the proprietary device name/trade name.
- Longer, less direct approach – Go to the **FDA Device Classification database**, pick a "Review Panel" relevant to your medical device (e.g., Neurology review panel for a neurosurgical device) and click "search" to get a full list of the product codes under the relevant review panel. Expand the results to the maximum number you can view on one page. Ctrl+F terms relevant to your medical product (e.g., "surger-", "pain, "elect-", "catheter"). Click and review information on product code that appear to be most relevant to your medical device, including device classification (i.e., Class I, II, III), submission type, premarket review office, recognized consensus standards.

V. BASIC REGULATORY SCENARIOS AND POTENTIAL APPLICABLE REGULATORY APPROACHES

Scenario	FDA/CDRH Submission that may be needed
You plan on conducting a clinical study to: - Evaluate a medical device and collect safety and effectiveness data - Collect preliminary performance data on an early-stage medical device	Investigational Device Exemption * There are some exemptions to IDE requirements. For example (but not only exemption), **non-significant risk studies** and some ***in vitro* diagnostics**. * **Institutional Review Board (IRB)** approval is pretty much always required for clinical studies of medical devices regardless of IDE exemption Q-submission (Q-sub) - Pre-submission to obtain feedback on clinical study design or non-clinical studies being conducted to support the clinical study - Risk-Determination Q-sub to obtain feedback on whether your study is significant risk/non-significant risk and applicable regulatory requirements (i.e., IDE or IDE exempt)
You have a device that is *identical or very similar* to another device on the market in how it is used, clinical condition, patient population, technical characteristics and presents low-moderate risk to the patient/user (e.g., not life sustaining or supporting, risks of minor-moderate injury when used as intended or in error)	510(k)
You have a device that is *similar* to another device on the market but has differences in - Indications for use (clinical condition - Technological characteristics - Ways it's used	510(k) DeNovo PMA **ANY* submission type is possible, but depends on factors such as, but not limited to the types of risks and benefits the difference between devices could pose, the intended patient population (e.g., pediatrics vs adults, pregnant women, older adults), use environment (e.g., home vs doctor's office vs hospital) 513(g) Request for information – obtain FDA's current thinking of the device classification and applicable regulatory requirements

Scenario	FDA/CDRH Submission that may be needed
You have a completely *new* device with an innovative approach to addressing a clinical condition that has never been done before	PMA- if life sustaining, supporting, of substantial importance, high risk, etc. De Novo- if low-moderate risk, not life-sustaining or supporting
You have a device intended for an "orphaned" patient population (<8000 cases per year in the US).	HDE
You have questions about: - Planned non-clinical and clinical testing on a medical device - Regulatory approaches/strategies for a pre-market submission - Early stage innovation intended to treat/diagnose a specific patient population and intent to market in the US	Q-submission - Pre-submission to request FDA feedback to specific questions
You have an idea of what device classification and pre-market submission you might need to submit (or are exempt from submitting) to be able to market your medical device in the US, but want some level of assurance	513(g) Request for information – obtain FDA's current thinking of the device classification and applicable regulatory requirements