

## A Primer on US Marketing Authorisations for Medical Devices - Part I: Premarket Notifications

*Diane Mandell and Karen Becker* look at the fundamentals of US regulatory requirements for medical devices.

This article is Part I of a two part series designed as a basic primer on the regulations and processes for obtaining marketing authorisation for medical devices in the United States. The text provides a summary of the applicable regulations, information on practical aspects of the manner in which these regulations are implemented, and reference to resources for more detailed information. The first part of this series describes the regulatory framework and procedures for marketing authorisation applicable to the vast majority of medical devices marketed in the United States, namely, those cleared through the Premarket Notification process, also known as a 510(k) submission. The second means of marketing authorisation, the Premarket Approval process, will be the subject of the second part of this series. Throughout the text, references to the Code of Federal Regulations are cited as [CFR] and these may be accessed via the Internet<sup>1</sup>.

In fiscal year 2000, the US FDA received approximately 4 200 original 510(k) submissions for review, compared to 43 original Premarket Approval Applications (PMAs)<sup>2</sup>. Thus, only a very small percentage of products are subject to the PMA process for marketing authorisation in the United States. The average elapsed time for review and approval of a PMA in fiscal year 2000 was 363 days, compared to the much more rapid 102 days for a 510(k) submission.

Generally, if intellectual property and/or confidentiality issues are not a factor, sponsors seek to obtain marketing authorisation via the 510(k) process because it is less burdensome in terms of data requirements, size of submission, and review time. The sponsor must comply with applicable regulations (as described *below*), but opportunities to pursue a 510(k) Premarket Notification route rather than a PMA route occasionally occur if it is appropriate to modify the intended use and/or performance characteristics of a product to adapt to that paradigm.

### Statutory definition of a medical device

Medical devices comprise a very large number of products (tens of thousands), with a wide range of performance characteristics and intended uses. Tongue depressors, bed pans, hospital beds, wound dressings, sutures, dental equipment, implantable pacemakers, orthopaedic implants, catheters, infusion pumps, *in vitro* diagnostics and so on, are all examples of medical devices. The total number of products regulated as devices by the FDA numbers in the tens of thousands. Medical devices are regulated by the FDA through the Center for Devices and Radiological Health (CDRH).

The definition of a medical device from Section 201 of the Federal Food, Drug and Cosmetic Act [FDCA]<sup>3</sup> is as follows:

*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) recognised 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 metabolised for the achievement of its primary intended purposes.*

*Majority of devices in the US are cleared via the 510(k) process*

*Why choose the PMN vs PMA route?*

*Definition of 'medical device' is in FDCA Section 201*

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*Distinguishing devices from drugs relies on certain aspects of the definitions*

There are two critical aspects of this definition that are important to bear in mind when considering the statutory and regulatory framework for medical devices in the US. First, a medical device is a product that incorporates a 'structure/function' claim within its intended use; that is, the product is intended to impact on the condition of the body (diagnose, prevent, mitigate, treat or cure) and the principal mode of action of the product is via physical rather than chemical means. This latter requirement distinguishes medical devices from drugs. In some cases, a device will have an intended use that incorporates a 'structure/function' claim, but the product has more than one mode of action, thereby calling into question whether or not the product is to be regulated as a drug or a medical device. For example, an eye drop that provides lubrication via physical properties of the solution may also have antimicrobial action due to the addition of an active drug substance. Wound dressings are another common example of such 'combination products' in which the dressing accomplishes its intended use via physical means, but the effectiveness of the product may be augmented by the addition of a drug or growth factor to enhance the rate of healing or minimise the risk of infection.

*FDA has a system for handling disputes over classification of combination products*

Generally, the classification of a product as a device or a drug is based on the primary mode of action, and the FDA has established a basic framework for deciding on the definition and the appropriate centre to review products that may be considered combinations<sup>4-6</sup>. Combination products are increasingly the subject of discussion and debate regarding the most appropriate regulatory pathway, but the FDA has an effective management system in place to adjudicate such disputes and identify the appropriate venue as well as personnel to resolve these matters. In some circumstances, history and precedent are relied upon in settling the regulatory framework for a product, leading to some inherently contradictory or confusing determinations. Hyaluronic acid products (injectable products approved for the treatment of osteoarthritis of the knee), for example, are regulated as medical devices due to precedent, regardless of the fact that in some cases the primary mode of action may be unknown, or be due to chemical rather than physical means.

With certain exceptions noted below, Class I and Class II medical devices are marketed via the 510(k) notification process, through which the sponsor demonstrates that the intended use and performance characteristics of the product are 'substantially equivalent' to a 'pre-amendment device', that is, a device in commercial distribution prior to 28 May 1976, or a subsequently marketed device for which there has been a cleared 510(k) notification. These are termed 'predicate devices'. If a difference in the intended use or performance characteristics is sufficient to pose an impact on the safety and effectiveness of a product, or if the product is classified as a Class III (significant risk) device, as defined below, the device will be the subject of a PMA instead.

### **Classification of medical devices**

*Devices are designated as Class I, II or III...*

Following the Medical Device Amendments to the FDCA on 28 May 1976 when the FDA was provided the means to regulate medical devices to ensure their safety and effectiveness, the FDA classified more than 1 700 categories of medical devices 'by regulation into either Class I (general controls), Class II (special controls) or Class III (premarket approval), depending on the level of regulatory control required to provide reasonable assurance of the safety and effectiveness of the device' [21 CFR 860.84].

The designation of Class I, II, or III of these devices is recommended by individual classification panels that are assembled 'for the purposes of

- (A) determining which devices intended for human use should be subject to the requirements of general controls, performance standards, or premarket approval, and
- (B) providing notice to the manufacturers and importers of such devices to enable them to prepare for the application of such requirements to devices manufactured or imported by them' [FDCA §513(b)].

Classification panels are assembled according to medical speciality, e.g. Clinical Chemistry and Clinical Toxicology Devices Panel, Microbiology Devices Panel, and in making their determination, they take into account the evidence of the safety and effectiveness of the device and the definition of each class. The intent of this regulation was to make available to the public safe and effective medical devices, in a manner that protects the public health while at the same time avoiding the imposition of unnecessary or onerous burdens on the regulated industry.

The three classes of medical devices, each regulated in an increasingly rigorous manner, are as follows [FDCA §513(a) and 21 CFR 860.3]:

**Class I, General Controls**

*Class I means the class of devices that are subject to only the general controls authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration), 516 (banned devices), 518 (notification and other remedies), 519 (records and reports), and 520 (general provisions) of the act. A device is in class I if (i) general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, or (ii) there is insufficient information from which to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but the device is not life-supporting or life-sustaining or for a use which is of substantial importance in preventing impairment of human health, and which does not present a potential unreasonable risk of illness or injury.*

*...with Class indicating level of regulatory control needed to assure safety and effectiveness*

**Class II, Special Controls**

*Class II means the class of devices that is or eventually will be subject to special controls. A device is in class II if general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness and there is sufficient information to establish special controls, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidance documents (including guidance on the submission of clinical data in premarket notification submissions in accordance with section 510(k) of the act), recommendations, and other appropriate actions as the Commissioner deems necessary to provide such assurance.*

**Class III, Premarket Approval**

*Class III means the class of devices for which premarket approval is or will be required in accordance with section 515 of the act. A device is in class III if insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls described in paragraph (c)(2) of this section would provide such assurance and if, in addition, the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.*

**General description of Classes I, II, and III**

Class I devices are considered to pose the least possible risk to health and Class III devices are higher risk. In general, Class I devices require compliance with *General Controls* (described below) and submission and clearance of a 510(k) *Premarket Notification* (referred to as a '510(k)' or a 'PMN') application before the device can be marketed in the US, unless they are exempt from the 510(k) submission requirement (also described below). The 510(k) submission is so called because the law originates in Section 510(k) of the FDCA [FDCA §510(k)]. This section states that 'to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use shall, at least ninety days before making such introduction...report to the secretary.'

*Class I and II devices require clearance of 510(k) submission prior to US marketing...*

In the premarket notification submission, the manufacturer must demonstrate substantial equivalence of a new Class I or II device to a device already on the market. That is, if the new device is comparable in intended use and technological characteristics to the already-marketed device, then it (like the already-marketed device) can be considered safe and effective. 'For the purposes of determinations of substantial equivalence...*substantial equivalence* means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and has the same technological characteristics as the predicate device' [FDCA §513(i)]. In addition, devices that have been in commercial distribution before 1976 fall into the 510(k) category.

Class II devices must comply with General Controls, and may require compliance with additional specific controls (called *Special Controls*, which may include special labeling requirements, mandatory performance standards and postmarket surveillance) as part of the 510(k) submission requirement. The 510(k) documentation for cleared devices is generally publicly available.

*...and the submission documents become publicly available*

*Class III devices are cleared via the more lengthy PMA process...*

*...with only the Summary Basis of Approval being made publicly available*

As described above and in FDCA §513(a), if the device cannot be classified as a Class I device, and it cannot be classified as a Class II device, and it is purported for use in supporting or sustaining human life or preventing impairment of human health or presents unreasonable risk of illness or injury, it is considered a Class III device. Class III devices require submission and approval of a PMA application prior to marketing; 21 CFR 814.20 defines a PMA as a 'premarket approval application for a Class III medical device, including all information submitted with or incorporated by reference therein'. This involves a more lengthy testing and validation process, and is required to provide reasonable assurance of safety and effectiveness in a significant proportion of the population studied, with adequate directions for use and a benefit that outweighs possible risks. The PMA submission is confidential, with only the Summary Basis for Approval available to the public. In a PMA submission, the safety and effectiveness of the new device is demonstrated affirmatively in clinical trials with human subjects. It is the goal of the FDA to protect the public from potential risks that could occur with new and unproven devices. Certain Class III devices i.e. pre-amendment devices for which the FDA has yet to require the submission of PMAs and that have been in commercial distribution, may be modified and marketed via the 510(k) route [FDCA§513(f)].

### **Determining the class and exempt status of a new device**

To determine the Class for a new device, the appropriate *Device Classification Name* and *Regulation Number* should first be identified using one of two readily available resources. Classification Names and Regulation Numbers are listed in the Code of Federal Regulations beginning in 21 CFR 860, as well as in an Internet-based searchable database called the FDA Classification Database,<sup>7</sup> in which the device class and exemption status are listed. This listing provides the regulation number, device name, panel, classification (I, II, or III), exemption status, and whether there are Special Controls.

#### **Example**

If a manufacturer has a new oximeter to measure haemoglobin, a search of the Classification Database reveals that this product falls under the jurisdiction of the Hematology Panel, is a Class II device, and is not 510(k) exempt. The Code of Federal Regulations citation is also provided; in this case it is 21 CFR 864.7500. Exemption status can also be determined by consulting with Federal Register publications on the topic<sup>8</sup> or with Device Advice, a part of the CDRH website<sup>9</sup>.

*Device Class can be determined using tools on the Internet*

Using the Regulation Number for the new device, the manufacturer can determine the correct class (I, II, or III) and determine what level of control is required by the FDA. The appropriate regulatory submission must then be crafted to obtain approval for commercial distribution of the new device in the US.

## **General Controls and overview of requirements for Class I and Class II devices**

### **General Controls**

All device classes (I, II, and III) are subject to General Controls as provided by the 28 May 1976 Medical Device Amendments to the FDCA which include the following requirements:<sup>10</sup>

- *Establishment Registration* (Form 2891), in which the owner/operator registers the name and place of business [21 CFR 807.20];
- *Medical Device Listing* (Form 2892), which lists the devices in commercial distribution [21 CFR 807.20];
- devices must be manufactured according to Quality Systems Regulations (previously called Good Manufacturing Practices) [21 CFR 820];
- devices must be labeled according to regulations [21 CFR 801 for general devices, 21 CFR 809 for *in vitro* diagnostics]; and
- provisions must be made for adulteration; misbranding; banned devices; notification, including repair, replacement, or refund; records and reports; restricted devices [21 CFR 860.3(c)(1)].

**Class I requirements**

Regulatory requirements for Class I devices are presented in FDCA §513. Class I devices are subjected to the lowest level of regulatory control and include such examples as elastic bandages and manual stethoscopes. As mentioned above, Class I devices must comply with general controls even if they are considered exempt (most Class I devices are considered exempt). The exempt status for a device, which is established using the appropriate Classification Number, only relates to whether the sponsor is required to submit a 510(k) premarket notification application prior to commercial distribution. Approximately half of all medical devices fall in the Class I category<sup>11</sup> and most of these are exempt from the 510(k) premarket notification requirement.

*Exempt Class I devices must still comply with General Controls*

A 510(k) premarket notification must be submitted to the FDA at least 90 days in advance of the sponsor’s intent to market a new medical device or when there is a significant modification of an already-approved device. The goal of the notification is to allow the FDA to determine if the new device is substantially equivalent to the predicate device in order to support ‘reasonable assurance of safety and effectiveness’. The contents and sections of a 510(k) are described in detail in a number of resources which are searchable and available on the FDA website:

- regulations as outlined in FDCA §510(k) and in 21 CFR 807.87;
- CDRH guidance documents;
- policy and precedents as presented in CDRH Blue Book Memoranda; *and*
- devices previously cleared by the FDA using the 510(k) premarket approval process.

The most important part of the 510(k) application is the section on substantial equivalence. In this section the sponsor establishes that the intended use and performance characteristics are comparable to a predicate device and do not raise any new issues of safety and effectiveness. The choice of predicate(s) can be discussed with the FDA prior to submitting the 510(k) application. The FDA is technically allowed 90 days from the time of submission in which to clear a 510(k) application. In the year 2000, approximately 4 200 510(k) submissions were reviewed by the FDA, with an average FDA review time of 77 days, and an average of 102 days total elapsed time from sponsor submission until FDA decision<sup>2</sup>.

*Substantial equivalence is the key element of a 510(k) application*

The question of when to file a 510(k) is summarised by the FDA as follows: ‘medical device manufacturers are required to submit a premarket notification if they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. Such change or modification could relate to the design, material, chemical composition, energy source, manufacturing process, or intended use.’<sup>12</sup>

**Class II Requirements**

About 40% of all devices fall into the category of Class II with a minority exempt from 510(k) submission requirements. Class II devices require Special Controls in addition to the General Controls described above. Special Controls may include special labeling requirements, mandatory performance standards and postmarket surveillance. The required Special Controls are listed in the *Device Classification* and in the Regulation Number for that device.

*Special Controls include labelling, performance standards and postmarketing surveillance*

For some devices, a *Special Controls Guidance Document* details the requirements for that particular device.

**Example**

21 CFR 864.5220 describes the Automated Differential Cell Counter, which can be classified as a Class II device with Special Controls that required a 510(k) submission to the Hematology and Pathology Devices Panel. A corresponding document titled *Class II Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells; Final Guidance for Industry and FDA* is available on the FDA website, which provides all required performance standards and testing requirements for this device.



**Contents and submission of a 510(k) Premarket Notification**

The information required in a 510(k) is described in 21 CFR 807.87 and in a number of documents on the FDA website,<sup>13</sup> with further detail regarding format and delivery of the submission to the FDA provided in 21 CFR 807.90.

*There are eleven elements to a 510(k) submission...*

There are eleven required elements for a 510(k) submission:

1. Device name (proprietary name and trade name) and classification name;
2. Establishment registration number, if applicable;
3. Device Class, panel, or statement that no appropriate classification exists with an explanation as to the basis for that statement;
4. Action taken by the sponsor to comply with performance standards, if any;
5. Proposed labeling, including user manuals, package labeling, and advertisements. There are a number of Blue Book and FDA guidance documents on device labeling, which detail the requirements for this section. The appropriate labeling guidance should be consulted and followed;
6. Substantial equivalence statement and table, indicating how the new device is similar to or different from other products that are on the market [the predicate device(s)] and that were previously cleared by the FDA. This section should focus on a comparison between the new device and the predicate(s), in the areas of intended use and technology (including materials, design, energy used or delivered by the device, and principles of operation);
7. 510(k)s are submitted for a cleared device that will undergo modifications, or for a new intended use for a device. These applications must contain data that demonstrate the consequences of this change to safety and effectiveness of the device;
8. A 510(k) summary [21 CFR 807.92] or a 510(k) statement [21 CFR 807.93];
9. A financial disclosure statement and Form 3455 or Form 3454, which is signed by the clinical investigator participating in clinical studies that were submitted as part of the 510(k). There is a form for investigators with financial arrangements to disclose (3455) and a form if there is nothing to disclose (3454), intended to reveal to FDA the financial interests and arrangements of the clinical investigators;
10. Class III devices that are subject to 510(k) requirements (a minority of device submissions) require certain information described in 21 CFR 807.87(j); and
11. A truthful and accurate statement (stating that data and information in the 510(k) are truthful and accurate, and that no material fact has been omitted).

*...with substantial evidence being the most important*

Also any additional information required for a substantial equivalence determination. This could include (as needed or requested) a description of the medical device, testing data, clinical data, information on sterilisation, information on biocompatibility, information on computer software, and manufacturing information. The additional information that is required can be determined by reading the relevant guidance for the type of device in development, or by conversations with the FDA review team for the submission.

The above listing of necessary components for the 510(k) submission illustrates that several steps are necessary prior to submitting the 510(k) application:

**1. Identify a predicate device**

The sponsor should identify a predicate device, one that has been cleared by the 510(k) process (a PMA-cleared device cannot serve as a predicate device; all information in a PMA is proprietary) and one that has similar intended use and technological characteristics. The Classification Number, certain generic words in the device name, and the manufacturer are all terms that can be used for searching the FDA 510(k) database<sup>14</sup> to identify possible predicates.

## 2. Define specific submission requirements

It is important that, early in the process of product development, the appropriate guidance documents,<sup>15</sup> performance standards (if applicable) and other relevant information be obtained from the FDA website to define the specific requirements of the new medical device prior to development of the submission. For example, any medical device that is computer-controlled or is dependent on computer software has special requirements for software development and validation that are detailed in FDA guidance documents.

After the 510(k) is assembled and checked for completeness, it should be sent to the FDA with a return receipt requested. The FDA will use a checklist to determine that the application is complete. If the application has all of the necessary components, a letter from the FDA will be sent to the sponsor in two weeks with an assigned 510(k) number (beginning with the letter K; PMA numbers begin with the letter P). The FDA assigns a review team and distributes the 510(k) to appropriate individuals. The FDA can request additional information if it is necessary to perform an adequate review, and the sponsor must submit the required data within 30 days of the request being made in order for the application to remain active. The FDA will then complete their scientific review, and notify the sponsor of the outcome. If the FDA determines that the device is substantially equivalent, the device can then be marketed in the US.

*What happens after a 510(k) submission is lodged?*

## Special 510(k) and Abbreviated 510(k) submissions

Following is a brief overview of two other options for obtaining premarket clearance for certain devices, the Special 510(k) and Abbreviated 510(k). These options were developed by the FDA in an effort to streamline the 510(k) review process. The FDA has written a guidance document with explicit details of these two optional approaches.<sup>16</sup> The guidance document states that 'while the New Paradigm maintains the traditional method of demonstrating substantial equivalence under section 510(k) of the Act, it also presents the 'Special 510(k): Device Modification' option, which utilises certain aspects of the Quality System Regulation, and the 'Abbreviated 510(k)' option, which relies on the use of guidance documents, special controls, and recognised standards to facilitate 510(k) review'.

If a sponsor wishes to submit a modification of a cleared device, a Special 510(k) could be submitted 'if the modification does not affect the intended use of the device or alter the fundamental scientific technology of the device' [21 CFR 807.81(a)(3)]. The Special 510(k) consists of summary information which verifies and validates that appropriate design control processes are in place, and this summary information can serve as the basis for clearing the 510(k) application.

*The Special 510(k) option can be used for clearing product modifications*

The Abbreviated 510(k) may be submitted if the following conditions exist:

- a guidance documents exists;
- a Special Control has been established; *or*
- FDA has recognised a relevant consensus standard.

The Abbreviated 510(k) is a summary report that includes information regarding the sponsor's efforts to conform with the appropriate guidance document and/or special control(s) and should outline any deviations. Details of these alternative 510(k) premarket notification submissions should be obtained from FDA guidance documents.

*Abbreviated 510(k)s can be used where a relevant standard has been recognised by FDA*

## Glossary

See overleaf for glossary of key US regulatory terms for medical devices.

## Conclusion

This article was written as an introduction to the concepts and general procedures for submission of a 510(k) Premarket Notification to the FDA. Part II of this series will be on the Premarket Approval process, which is appropriate for the majority of Class III devices.

**Glossary of Key US Regulatory Terms for Medical Devices**

Reference: FDA website, including the pages of 'Device Advice'

**Center for Devices and Radiological Health (CDRH)**

Branch of the US Food and Drug Administration (FDA) responsible for ensuring safety and effectiveness of medical devices and eliminating unnecessary human exposure to man-made radiation from medical, occupational or consumer products. Within CDRH, the Office of Device Evaluation (ODE) advises the Center Director and other Agency officials on all premarket notification (510(k)) and premarket approval applications (PMA).

**Code of Federal Regulations (CFR)**

Codification of the general and permanent rules published by the Government Printing Office (GPO) in the Federal Register (FR) by the Executive departments and agencies of the Federal Government. The Code is divided into 50 titles, which represent broad areas subject to Federal regulation. Each title is divided into chapters, which usually bear the name of the issuing agency. Each chapter is further subdivided into parts covering specific regulatory areas; e.g. CFR parts 800-1299, Food and Drugs.

**Device Classification Name**

Terminology used by the FDA and its classification panels to describe a device or class of devices for purposes of classifying devices under section 513 of the act [21 CFR 807.3].

**Device Listing**

'An owner or operator of an establishment not exempt under section 510(g) of the Act or subpart D of this part, who is engaged in the manufacture, preparation, propagation, compounding, assembly or processing of a device intended for human use, is required to submit listing information of those devices in commercial distribution, except that listing information may be submitted by the parent, subsidiary or affiliate company for all the domestic or foreign establishments under the control of one of these organisations when operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments ... An owner or operator is required to list devices whether or not the output of the establishments or any particular device so listed enters interstate commerce.' [21 CFR 807.20] Device listing information should be submitted at the time of registration [21 CFR 807.21].

**Establishment Registration**

An owner or operator is required to register its name, places of business, and all establishments 'An owner or operator of an establishment not exempt under section 510(g) of the Act or subpart D of this part, who is engaged in the manufacture, preparation, propagation, compounding, assembly or processing of a device intended for human use is required to register.' [21 CFR 807.20].

**Exemption from Premarket Notification**

'A device is exempt from the premarket notification requirements of this subpart if the device intended for introduction into commercial distribution is not generally available in the finished form for purchase and is not offered through labeling or advertising by the manufacturer, importer or distributor thereof for commercial distribution ...' [21 CFR 807.85].

**Federal Food, Drug and Cosmetic Act (FDCA)**

The *Food Drug & Cosmetic Act*, sometimes referred to as 'the Law' or 'the Act', is included in the *Compilation of Laws Enforced by FDA and Related Statutes* accessible through the FDA website.

**Federal Register**

Official daily publication for Rules, Proposed Rules and Notices of Federal agencies and organisations, as well as Executive Orders and other Presidential Documents.

**General Controls**

FDCA §513 establishes:

'(A) CLASS I, GENERAL CONTROLS —

- (i) A device for which the controls authorised by or under section 501, 502, 510, 516, 518, 519, or 520 or any combination of such sections are sufficient to provide reasonable assurance of the safety and effectiveness of the device.
- (ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but because it -
  - (I) is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
  - (II) does not present a potential unreasonable risk of illness or injury, is to be regulated by the controls referred to in clause (i).'

**Indication for Use**

A subset of the 'intended use' for a device (*see below*), because it is a specialised indication that is added to the device labeling. Specific indications are clearly defined, such as appropriate clinical settings, defined target population or anatomical sites.

**Intended Use**

Refers to the objective intent of the persons legally responsible for the labeling of devices. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. The intended uses of an article may change after it has been introduced into interstate commerce by its manufacturer. If, for example, a packer, distributor, or seller intends an article for different uses than those intended by the person from whom he received the device, such packer, distributor, or seller is required to supply adequate labeling in accordance with the new intended uses. But if a manufacturer knows, or has knowledge of facts that would give him notice that a device introduced into interstate commerce by him is to be



used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a device which accords with such other uses to which the article is to be put [21 CFR 801.4]

**Panels**

There are 16 panels divided according to medical speciality and each panel reviews submissions in its own area of specialisation e.g. Ear, Nose, and Throat, or Cardiovascular.

**Performance Standards**

'The Food and Drug Administration may determine that a performance standard, as described under special controls for Class II devices in Sec. 860.7(b) of this chapter, is necessary to provide reasonable assurance of the safety and effectiveness of the device. *Performance standards* may be established for:

- (1) A Class II device;
- (2) A Class III device which, upon the effective date of the standard, is reclassified into Class II; *and*
- (3) A Class III device, as a condition to premarket approval under section 515 of the act, to reduce or eliminate a risk or risks associated with such device.' [21 CFR 861.1(b)]

**Postmarket Surveillance Study**

A study conducted after marketing of a product as it is intended to be used in the general population, with the primary objective being to study the performance of the device in the 'real world' environment. Postmarketing surveillance generally applies to higher risk devices, or as determined necessary by the FDA.

**Predicate Device**

A legally marketed device to which a submitter claims equivalence. 'A legally marketed device to which a new device may be compared for a determination regarding substantial equivalence is a device that was legally marketed prior to May 28, 1976, or a device which has been reclassified from Class III to Class II or I (the predicate), or a device which has been found to be substantially equivalent through the 510(k) premarket notification process.' [21 CFR 807.92].

**Substantial Equivalence**

An identification of the legally marketed device to which the submitter claims equivalence. 'A legally marketed device to which a new device may be compared for a determination regarding substantial equivalence is a device that was legally marketed prior to May 28, 1976, or a device which has been reclassified from Class III to Class II or I (the predicate), or a device which has been found to be substantially equivalent through the 510(k) premarket notification process.' (21 CFR 807.92). If a device is determined to be substantially equivalent to another already-marketed device, it usually has (a) similar intended use, and (b) similar technology. If either intended use or technology are different, the submitter must demonstrate that these differences do not impact on safety or effectiveness of the device. In some cases clinical research is necessary to demonstrate no impact on safety or effectiveness.

**References**

1. Code of Federal Regulations, <http://www.access.gpo.gov/nara/cfr/index.html>
2. Office of Device Evaluation Annual Report, Fiscal Year 2000, CDRH, FDA
3. FDCA, Federal Food, Drug, and Cosmetic Act, as amended by Congress through the first quarter of 2000 (21 CFR starting from Section 301)
4. 21 CFR 3.5, Procedures for identifying the designated agency component
5. Intercenter Agreement Between CBER and CDRH, <http://www.fda.gov/oc/ombudsman/bio-dev.htm>
6. Intercenter Agreement Between CDER and CDRH, <http://www.fda.gov/oc/ombudsman/drug-dev.htm>
7. FDA Classification Database, <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm>.
8. List of Class I exempt devices, *Federal Register*, February 2, 1998, 63(21)
9. Class I/II Exemptions, CDRH, [http://www.fda.gov/cdrh/devadvice/3133.html#exempt\\_devices](http://www.fda.gov/cdrh/devadvice/3133.html#exempt_devices)
10. General Controls for Medical Devices, CDRH, <http://www.fda.gov/cdrh/devadvice/363.html#introduction>
11. General Information on Medical Device Regulations – 510(k) and Premarket Approval (PMA), CDRH, <http://www.fda.gov/cdrh/consumer/geninfo.html>
12. 510(k) Overview, CDRH, <http://www.fda.gov/cdrh/510k.html> ;  
Deciding When to Submit a 510(k) for a Change to an Existing Device, 510(k) Memorandum #K97-1, CDRH, <http://www.fda.gov/cdrh/ode/510kmod.html>; *and*  
21 CFR 807.81, When a premarket notification submission is required.
13. Contents of a 510(k), CDRH, <http://www.fda.gov/cdrh/devadvice/314312.html#contents>
14. CDRH, Premarket Notification Searchable Database, <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>
15. Guidance Documents and Reports, CDRH, <http://www.fda.gov/cdrh/guidance.html>
16. The New 510(k) Paradigm Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications Final Guidance, CDRH, 20 March 1998, <http://www.fda.gov/cdrh/ode/parad510.pdf>