NOTE: On October 26, 2002, the President signed the Medical Device User Fee and Modernization Act (MDUFMA) of 2002. Under this new law, you must pay a fee before FDA will review your Premarket Notification 510(k). Please see "Premarket Notification 510(k) Review Fees." http://www.fda.gov/cdrh/devadvice/314a.htmlfor details on submitting user fees.

Please see http://www.fda.gov/cdrh/mdufma/ for further information on the Medical Device User Fee and Modernization Act.

PREMARKET NOTIFICATION 510(k): REGULATORY REQUIREMENTS FOR MEDICAL DEVICES

HHS Publication FDA 95-4158

PREMARKET NOTIFICATION 510(k):

REGULATORY REQUIREMENTS FOR MEDICAL DEVICES

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Division of Small Manufacturers Assistance

Office of Health and Industry Programs

CENTER FOR

DEVICES AND

RADIOLOGICAL HEALTH

CDRH

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service Food and Drug Administration Center for Devices and Radiological Health Rockville, Maryland 20850

FOREWORD

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA), develops and implements national programs to protect the public health in the fields of medical devices and radiological health. These programs are intended to assure the safety, effectiveness, and proper labeling of medical devices, to control unnecessary human exposure to potentially hazardous ionizing and non-ionizing radiation, and to assure the safe, efficacious use of such radiation.

The Center publishes the results of its work in scientific journals and in its own technical reports. These reports disseminate results of CDRH and contractor projects. They are sold by the Government Printing Office and/or the National Technical Information Service.

We welcome your comments and requests for further information.

D. Bruce Burlington, M.D.
Director
Center for Devices and
Radiological Health

PREFACE

The Medical Device Amendments of 1976 mandated the establishment of "an identifiable office to provide technical and other nonfinancial assistance to small manufacturers of medical devices to assist them in complying with the requirements of the Federal Food, Drug, and Cosmetic Act." The Division of Small Manufacturers Assistance (DSMA) in the Office of Health and Industry Programs (OHIP) was established to meet this requirement. DSMA develops educational materials and sponsors workshops and conferences to provide firms with firsthand working knowledge of medical device requirements and compliance policies.

This manual covers premarket notification [510(k)] submission requirements and addresses the basic regulatory requirements that all manufacturers and distributors must consider when they plan to market medical devices, including medical device kits, trays or packs, in the United States.

The DSMA staff and the Office of Device Evaluation (ODE), in the Center for Devices and Radiological Health (CDRH) provided valuable assistance in preparing this manual.

For further information, contact the appropriate office within CDRH or call DSMA at 800-638-2041, 301-443-6597 or FAX 301-443-

8818. Comments on this manual, related workshops, and other DSMA activities, are always welcome.

John Stigi
Director
Division of Small Manufacturers Assistance

ABSTRACT

L. Rice and A. Lowery, Project Officers. Division of Small Manufacturers Assistance, Office of Health and Industry Programs. Premarket Notification 510(k): Regulatory Requirements For Medical Devices. HHS Publication FDA 95-4158 (August 1995)(pp. 116).

This manual covers premarket notification [510(k)] requirements for medical devices. It contains guidance of significance to manufacturers and distributors of medical devices. This manual incorporates changes required by the Safe Medical Devices Act of 1990 and the Medical Device Amendments of 1992. This manual is an update of HHS publication FDA 92-4158, "Premarket Notification 510(k): Regulatory Requirements for Medical Devices".

This is a manual used in the Division of Small Manufacturers Assistance (DSMA) medical device workshops.

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1 OVERVIEW OF THE MEDICAL DEVICE REGULATIONS

INTRODUCTION

Products meeting the definition of a device under section 201(h) of the Federal Food, Drug and Cosmetic Act (FD&C Act or "the Act") are regulated by the Food and Drug Administration (FDA). Medical devices are subject to general controls and other controls in the FD&C Act. General controls of the FD&C Act are the baseline requirements that apply to all medical device manufacturers. Unless specifically exempted, medical devices must be properly labeled and packaged, be cleared for marketing by the FDA, meet their labeling claims, and be manufactured under Good Manufacturing Practices (GMP), which is a mandated quality assurance system.

FDA regulates devices to assure their safety and effectiveness. To fulfill provisions of the FD&C Act, FDA develops and promulgates rules to regulate devices intended for human use. These rules regulate various aspects of the design, clinical evaluation, manufacturing, packaging, labeling, commercial distribution, and postmarket surveillance of devices. These regulations are published in the *Federal Register*. Final regulations are codified annually in the Code of Federal Regulations (CFR). Most device regulations are in Title 21 CFR Parts 800 to 1299.

MEDICAL DEVICE DEFINITION

What is a Medical Device

The definition of a device appears in section 201(h) of the FD&C Act. A device is:

"...an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component, part, or accessory, which is:

recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

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

intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes..."

Accessories and Components

Certain components such as blood tubing sets, major diagnostic x-ray components, and stand-alone software are regulated by the FDA as finished devices because they are accessories to finished devices and meet the above definition of a device. Software that is to be marketed to enhance the performance of a device is regulated as an accessory to that device. Software that enhances the performance of a group of different devices is regulated as an accessory to the device that poses the greatest risk to the patient. The

manufacturer of accessories is subject to the medical device regulations when the accessory is labeled and marketed separately from the primary device for a health-related purpose to a hospital, physician, or other end user.

CLASSIFICATION

FDA has established classifications for approximately 1,700 different generic types of devices and grouped them into 16 medical specialties referred to as panels. Each of these generic types of devices is assigned to one of three regulatory classes based on the level of control necessary to assure the safety and effectiveness of the device. The three classes and the requirements which apply to them are:

CLASS	REGULATORY CONTROLS
Class I.....	General Controls
Class II.....	General Controls and Special Controls
Class III.....	General Controls and Premarket Approval

The class of most devices can be found in the classification regulations in Title 21 CFR Parts 862 to 892 as listed below:

DEVICE CLASSIFICATION PANEL OR SPECIALTY GROUP	21 CFR PART
Anesthesiology	868
Cardiovascular	870
Clinical Chemistry and Clinical Toxicology	862
Dental	872
Ear, Nose, and Throat	874
Hematology and Pathology	864
Immunology and Microbiology	866
Gastroenterology and Urology	876
General and Plastic Surgery	878
General Hospital and Personal Use	880
Neurology	882
Obstetrical and Gynecological	884
Ophthalmic	886
Orthopedic	888
Physical Medicine	890
Radiology	892

GENERAL CONTROLS

As noted above, general controls are the baseline requirements of the FD&C Act that apply to all medical devices, Class I, II, and III. These are:

prohibition of adulteration; section 501 of the Act;

prohibition of misbranding; section 502 of the Act;

banned devices; section 516 of the Act;

notification; and repair, replacement or refund; section 518 of the Act;

records and reports; section 519 of the Act; and

restricted devices; section 520 of the Act.

Unless specifically exempted by regulation, general controls contain **requirements** for device manufacturers or other designated persons to:

register their establishment with FDA on form FDA-2891;

list their devices with FDA on form FDA-2892;

comply with labeling regulation in 21 CFR Part 801, 809 or 812;

submit a premarket notification [510(k)] to FDA ; and

design and produce devices under good manufacturing practices (GMP).

The controls in the above list are briefly described in this chapter.

Registration and Listing

Section 510 of the FD&C Act requires that United States (U.S.) device manufacturers and distributors register their establishments with FDA on form FDA-2891. Foreign manufacturers marketing devices in the U.S. are not required to register, but FDA encourages them to do so. All manufacturers are required to list the generic type of devices they have in U.S. commerce with FDA on form FDA-2892. Establishment registration and medical device listing should be submitted prior to commercial distribution. Requirements for establishment registration and medical device listing can be found in 21 CFR Part 807.20.

PLEASE NOTE: The submission of an establishment registration, form FDA-2891, and medical device listing, form FDA-2892, does **not** constitute marketing clearance by FDA.

Labeling

All medical devices in U.S. commerce must be properly labeled. Device labeling requirements of the FD&C Act are found in the following parts of Title 21:

General Device Labeling.....21 CFR Part 801

In Vitro Diagnostic Products.....21 CFR Part 809

Investigational Device Exemptions.....21 CFR Part 812

Good Manufacturing Practices.....21 CFR Part 820

General Electronic Products.....21 CFR Part 1010

The FD&C Act, section 201 defines the terms "label" and "labeling" as they apply to medical devices as follows:

Section 201(k) defines **"label"** as a "display of written, printed, or graphic matter upon the immediate container of any article..." The term "immediate container" does not include package liners. Any word, statement, or other information appearing on the immediate container must also appear "on the outside container or wrapper, if any there be, of the retail package of such article, or is easily legible through the outside container or wrapper."

Section 201(m) defines **"labeling"** as: "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." The definitions of label and labeling apply to devices held for delivery for shipment or for sale after shipment in interstate commerce. The term "accompanying" is interpreted liberally to mean more than physical association with the product. It extends to posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, etc. "Accompanying" includes labeling that is brought together with the device held for delivery for shipment or after shipment in interstate commerce..

Labeling and advertising can be used for a similar purpose, i.e., to provide information about the device. Therefore, under certain circumstances, advertising may be considered by FDA to be labeling also.

Under no circumstances may the labeling of any medical device bear the firm's facility registration number, device listing number, 510(k) premarket notification clearance or premarket approval number. Any representation that creates an impression of official approval by FDA related to these numbers will misbrand the device. Any phrase, such as "FDA approved", which connotes FDA approval of the device, is also prohibited under section 301(l) of the FD&C Act.

Basic labeling requirements and recommended labeling for medical devices can be found in the Center for Devices and Radiological Health (CDRH) booklet, *Labeling; Regulatory Requirements for Medical Devices*, available from DSMA.

Premarket Notification

A premarket notification [510(k)] is a marketing application submitted to FDA to demonstrate that the medical device you wish to market is as safe and as effective or **substantially equivalent** to a legally marketed device that was or is currently on the U.S. market and that does not require premarket approval. The premarket notification requirements are found in 21 CFR Part 807, Subpart E.

Most devices are cleared for commercial distribution in the U.S. by the premarket notification [510(k)] process. Most class I devices are exempt from the 510(k) requirement by regulation. However, they are not exempt from other general controls, such as establishment registration and device listing. Before marketing a medical device which is not exempt from the marketing clearance process, the manufacturer must submit a premarket notification [510(k)] or a premarket approval (PMA) application to FDA. The manufacturer cannot market the device unless the firm receives a marketing clearance letter from FDA as stated in section 513(I)(1)(A) or section 515(d)(1)(A)(I) of the FD&C Act.

For more information on the premarket notification requirements, see chapters 2 and 3 of this manual.

Good Manufacturing Practices

As required by section 520(f) of the Act, the Good Manufacturing Practices (GMP) regulation covers the methods used in, and the facilities and controls used for the design, manufacture, packaging, storage, and installation of devices. The GMP regulation is codified in 21 CFR Part 820. Some Class I devices, such as an manual surgical instruments for general use, 21 CFR section 878.4800, are exempt by regulation from **most** of the GMP requirements.

The GMP regulation contains general quality assurance (QA) or quality system requirements in areas of concern to all manufacturers of finished devices. Among other requirements, it covers the following general areas:

organization and personnel;

design practices and procedures (proposed);

buildings and environmental control;

design of labeling and packaging;

controls for components, processes, packaging and labeling;

device holding, distribution and installation;

device evaluation;

device and manufacturing records;

complaint processing; and

QA system audits.

SPECIAL CONTROLS

In addition to general controls, Class II and III devices are subject to further requirements such as special controls and premarket

approval.

Class II devices are defined in section 513(a)(1)(B) of the FD&C Act to include any device for which reasonable assurance of safety and effectiveness can be obtained by applying "special controls". Only general controls will apply to Class II devices until special controls are established by regulation(s). Special controls may include special labeling requirements, mandatory performance standards, patient registries and postmarket surveillance.

PREMARKET APPROVAL

Premarket approval (PMA) is the process by FDA to evaluate the safety and effectiveness of Class III devices. Class III is the most stringent regulatory category for medical devices. Class III devices are usually those that 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. Due to the level of risk associated with Class III devices, FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of Class III devices. Therefore, these devices require a premarket approval (PMA) application under section 515 of the Act, in order to obtain marketing clearance.

The PMA requirements are found in 21 CFR Part 814. Not all Class III devices require an approved PMA to be marketed at this time. Class III devices that are substantially equivalent to devices legally marketed before May 28, 1976, **and** do not currently require premarket approval may be marketed through the premarket notification [510(k)] process until FDA publishes a regulation requiring the submission of a premarket approval (PMA) application for those Class III devices.

Detailed guidance on PMA requirements can be found in the *Premarket Approval Manual*, available from DSMA.

INVESTIGATIONAL DEVICE EXEMPTIONS

To allow manufacturers of devices intended solely for investigational use to ship devices for use on human subjects (clinical evaluation), the FD&C Act authorizes FDA to exempt these devices from certain requirements of the Act that would apply to devices in commercial distribution. Clinical evaluation of devices not cleared for marketing, unless exempt, requires an approved investigational device exemption (IDE) either by an institutional review board (IRB) or an IRB and FDA, informed consent for all patients, adequate monitoring and necessary records and reports. These requirements can be found in 21 CFR Parts 50, 56, and 812.

Detailed guidance on the IDE requirements can be found in the *Investigational Device Exemptions Manual*, available from DSMA.

RADIOLOGICAL DEVICES

Electronic medical devices, including devices which emit radiation, have additional requirements which may have to be met before and during marketing. These requirements may include:

Filing initial reports for electronic products (21 CFR section 1002.10)

Annual reports (section 1002.11)

Reports of model changes (section 1002.12)

Reports of accidental radiation occurrences (section 1002.20)

Reporting defects or non-compliance with required standards (sections 1003.10 and

Performance standards (Parts 1010, 1020, 1030, 1040, and 1050).

All manufacturers of radiation-emitting electronic products must file an initial report before introducing the device into commercial distribution.

CDRH TECHNICAL ASSISTANCE

The publications mentioned throughout this manual are available from the Division of Small Manufacturers Assistance (DSMA), CDRH, FDA. DSMA also offers technical assistance to the medical device industry by conducting seminars and answering inquiries. The address and phone numbers for DSMA are:

Division of Small Manufacturers Assistance (DSMA), HFZ-220
Food and Drug Administration
1350 Piccard Drive
Rockville, Maryland 20850 USA

Voice Phone: 800-638-2041; or 301-443-6597; Fax 301-443-8818;

CDRH Facts-on-Demand: 800-899-0381; or 301-827-0111 (you call this automated system from a telephone and it transmits your selections to your fax);

Facts-on-Demand

The CDRH Facts-on-Demand system requires having a touch tone phone and a receiving fax machine. As directed by the requester's phone input, FDA sends the requested documents to the requester's fax machine automatically. The system will accept international calls. Most device specific guidance documents are on this system. Request the index and then choose the documents wanted.

Additional Sources of Information

The following is a list of agencies and key standards organizations that provide useful documents and standards.

Division of Small Manufacturers Assistance (DSMA)	See above.
Federal Register	202-523-5240
Foods, Plastics and Color	202-254-9515
Government Printing Office (GPO)	202-512-1800 FAX 202-512-2250
International Trade Administration (ITA)	202-482-2867
National Technical Information Service (NTIS)	703-487-4650
National Institutes of Standards and Technology (NIST)	301-975-2027
Naval Publications and Forms Center	215-697-3321
U.S. Small Business Administration (SBA)	202-205-6720
American National Standards Institute (ANSI)	212-354-3300
American Society for Testing and Material (ASTM)	202-737-6815 PA 215-639-4025
Assoc. for Advancement of Medical Instrumentation (AAMI)	703-525-4890
Health Industries Manufacturers Association (HIMA)	202-452-8240
National Committee for Clinical Laboratory Standards (NCCLS)	215-525-2435
Parenteral Drug Association, Inc.(PDA)	215-564-6466
Underwriters Laboratories, Inc.(UL)	312-272-8800
U.S. Pharmacopoeia (USP)	301-881-0666

2 PREMARKET NOTIFICATION

WHO MUST SUBMIT A 510(k)
510(k) EXEMPTIONS

INTRODUCTION

In order to market a medical device in the United States (U.S.), manufacturers must go through one of two evaluation processes: premarket notification [510(k)], unless exempt, or premarket approval (PMA). Most medical devices are cleared for commercial distribution in the U.S. by the premarket notification [510(k)] process. In certain instances, devices legally on the market prior to May 28, 1976 may not require either a 510(k) or PMA submission.

WHAT IS A PREMARKET NOTIFICATION [510(k)]

A premarket notification [510(k)] is an application submitted to the FDA. The purpose of a 510(k) is to demonstrate that the medical device to be marketed is **substantially equivalent (SE)** to a legally marketed device that was or is currently on the U.S. market.

Predicate Device. A predicate device is a device that was legally marketed in the U.S. prior to May 28, 1976 (**preamendment**), **OR** a device which has been reclassified from Class III to Class II or I **OR** a device which has been found to be substantially equivalent through the premarket notification 510(k) process**.** The term predicate device only applies to devices undergoing 510(k) review and not devices requiring premarket approval (PMA) since the basis of the PMA is not a comparison of one device to another.

Substantial Equivalence. A device is substantially equivalent if, in comparison to a legally marketed device, it:

has the same intended use as a predicate; **and**

has the same technological characteristics as the predicate device;

or

has the same intended use as a predicate; **and**

has different technological characteristics, and the information submitted to FDA;
- does not raise new questions of safety and effectiveness, and
- demonstrates that the device is as safe and as effective as the legally marketed device.

Different technological characteristics include, but are not limited to, changes in materials, design, energy sources, and principles of operation.

A claim of substantial equivalence does not mean the devices must be identical. Substantial equivalence is established with respect to: intended use, design, energy used or delivered, materials, performance, safety, effectiveness, labeling, biocompatibility, standards, and other applicable characteristics.

Substantial equivalence is codified in section 513(I)(1)(A) of the FD&C Act. More detailed information on how FDA determines substantial equivalence can be found in the Office of Device Evaluation (ODE) Bluebook Memorandum K86-3 "Premarket Notification Review Program" dated June 30, 1986, included in the Appendixes to this manual.

If FDA finds the device to be substantially equivalent (SE), FDA will send the manufacturer a marketing clearance letter, referred to as an "SE letter", and the device may be marketed as described in the 510(k). If FDA finds the device not to be substantially equivalent (NSE), FDA will send a not-substantially equivalent letter. In the latter instance, the firm may chose to resubmit another 510(k) with new information, may petition FDA requesting the device be reclassified into Class I or II, as described in Section 513(f) of the Act, or may submit a PMA.

Manufacturers may not place their device into U.S. commerce until they receive a marketing clearance/SE letter from FDA.

Preamendment Device. For purposes of 510(k) decision-making, the term "preamendment device" refers to devices legally marketed in the U.S. by a firm before May 28, 1976 **and** which have not been:

significantly changed or modified since then; **and**

for which a regulation requiring a PMA application has not been published by FDA.

Devices meeting this description are referred to as "grandfathered" and do not require a 510(k). Submitters of 510(k)s should review the section on "Modifications" in this chapter to confirm preamendment status.

Documenting Preamendment Status. In order for a firm to claim that they have a preamendment device, they must be prepared to demonstrate that their device was labeled, promoted and distributed in interstate commerce for the declared intended use.

FDA may consider the following as demonstrating preamendment device status:

Proof that the device was placed into interstate commerce for other than research uses or as part of a plant-to-plant transfer and was actually labeled, and promoted for the intended use to which the submitter of the premarket notification is claiming substantial equivalence. This may be accomplished by providing copies of the firm's advertisements, catalog pages, or other promotional material **dated** prior to May 28, 1976 **and** shipping documents such as invoices, bills of lading, receipts, etc., showing the **interstate** transit of the device dated prior to May 28, 1976.

If copies of the above documentation are not available, an affidavit may be used. The affidavit must be obtained from a current or former employee of the firm that distributed the device prior to May 28, 1976, who is, or was, in a position to be aware of the labeling and promotional information used for the device prior to May 28, 1976 and that the device was, indeed, distributed prior to May 28, 1976. The affidavit should contain a statement explaining why any invoices or shipping records of pre-May 28, 1976 distribution are not available.

If it is not possible to obtain an affidavit from a current or former employee of the firm that distributed the device prior to May 28, 1976, the submitter should provide an affidavit documenting their efforts and explaining why it was not possible to locate a current or former employee of the firm. An affidavit as described below should also be submitted.

In further support of the above affidavit, an affidavit from a credible person who used the device prior to May 28, 1976 should be obtained. The affidavit must state:

- that the user has personal knowledge that the device was received after it traveled in interstate commerce prior to May 28, 1976;
- the name of the source and the state from which it was shipped;
- a statement that it was labeled, promoted and purchased prior to May 28, 1976 for the intended use in question; and
- that it was not received as part of a research study or for investigational use prior to May 28, 1976.

Any statements provided **should be notarized** and **should include a statement concerning the financial interest in the device or firm**, if any, of the person signing the affidavit. Affidavits from individuals residing in other countries may be taken into consideration when accompanied by affidavits signed by persons residing in the U.S.

WHEN TO SUBMIT A 510(k)

According to 21 CFR section 807.81 a premarket notification submission is required when:

a device that requires 510(k) clearance is marketed for the first time by a medical device firm who is required to register; **or**

an existing device with 510(k) clearance or a preamendment device is being marketed and is to be changed or modified in a way that could significantly affect its safety or effectiveness (e.g., significant change or modification in design, material, chemical composition, energy source or manufacturing process); or

a major change or modification in the intended use for a preamendment or 510(k) device is claimed.

The 510(k) is not required if:

the device has been exempted by the classification regulations in 21 CFR Parts 862-892 [most Class I devices are exempt subject to the limitation on exemptions (e.g., 21 CFR 878.9), see Appendixes.]; **or**

the device requires a Premarket Approval Application (PMA); **or**

the device was legally distributed by your firm in the U.S. prior to May 28, 1976; i.e., preamendment/grandfathered; **and** it has **not** been significantly changed since then; **or**

the rights to market a preamendment or 510(k) cleared device has been acquired from a firm **and** the device has **not** been significantly changed since then, **and** the new owner does not intend to make **any** changes to the device (see sections on

"Documenting Preamendment Status" and "Modifications" in this chapter); **or**

the device is being distributed under a "Private Label", i.e., a preamendment device or device with a valid 510(k) which is being placed into commercial distribution for the first time by a distributor under their own name or a repackager who places their own name on a device provided **no** changes are made to the device or its indications for use, and it is not further processed, e.g.. sterilized.

Modifications

As described in 21 CFR section 807.81(a)(3), a **new** complete 510(k) application is required for changes or modifications to an existing device, where the modifications could significantly affect the safety or effectiveness of the device, **or** the device is to be marketed for a new or different indication.

When a manufacturer decides to modify an existing device, they must decide whether the proposed device modification requires submission of a 510(k). It is not FDA's intent that a 510(k) must be submitted for every modification. However, all changes in indications for use require the submission of a 510(k). More information about submitting 510(k)s for modifications made to devices can be found in the August 1, 1995 document "Deciding When to Submit a 510(k) for a Change to an Existing Device," available from DSMA.

Examples of modifications that **may** require a 510(k) submission include, but are not limited to, the following:

Sterilization method

Structural material

Manufacturing method

Operating parameters or conditions for use

Patient or user safety features

Sterile barrier packaging material

Stability or expiration claims

Design

FDA believes that the manufacturer is best qualified to determine when modifications to their device could significantly affect safety or effectiveness. Therefore, every modification to the device should be reviewed by appropriate personnel to determine if it affects safety or efficacy. If it is determined that the modification **is not significant,** the basis for this decision should be documented with supporting data in the manufacturer's device master file. If it is determined that the modification is **significant**, then a complete 510 (k) must be submitted to FDA.

FDA has not established provisions for a 510(k) amendment, supplement or an abbreviated 510(k). Therefore, each 510(k), whether for an original device, or modifications thereto, must be complete and include all information required by 21 CFR Part 807, Subpart E.

Combination Products

Combination products may be composed of any combination of a device, drug or biological product. As per section 503(g) of the FD&C Act, FDA will determine the primary mode of action of a combination product, then designate a center within FDA to have primary jurisdiction over the premarket review. Usually, the primary FDA center jurisdiction is based on the intended use of the product. For example, a human growth factor-coated hip implant is intended to be used as a bone replacement and not as a drug or biologic. Therefore, this implant is regulated as a device. The regulation for combination products can be found in 21 CFR Part 3. More information about combination product review can be found in the Intercenter Agreements between CDRH and the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER), available from DSMA.

WHO MUST SUBMIT A 510(k)

The FD&C Act and regulations do not specify who must apply for a 510(k) -- anyone may do so. Instead, they specify which actions,

such as introducing a device to the U.S. market, require a 510(k) submission.

Based on the specified actions, the following parties must submit a 510(k) to the FDA :

domestic manufacturers introducing a device to the U.S. market;

specification developers introducing a device to the U.S. market;

foreign manufacturers/exporters or U.S. representatives of foreign manufacturers/exporters introducing a device to the U.S. market which can include distributors of imported medical devices;

repackers or relabelers who make labeling changes, other than in name, or whose operations significantly affect the device.

Only one premarket notification [510(k)] is needed for each specific device, whether domestic or foreign unless the device is exempt by regulation. The foreign manufacturer or one of the U.S. distributors may submit the 510(k) application to FDA. It is not necessary for **every** U.S. representative or importer of a foreign manufactured device to submit a 510(k) premarket notification for the same device. Once a device from a foreign manufacturer is cleared for commercial distribution, that device can be sold to any U.S. distributor, unless the device is significantly altered to accommodate a new U.S. distributor.

Only one firm can hold the rights to a 510(k) as the 510(k) applies to a specific device. Be careful to accurately state the **510(k) applicant** (the person doing the paperwork) versus the **510(k) submitter** [the person required to submit the 510(k); i.e, 510(k) holder] in the 510(k) cover letter.

510(k) EXEMPTIONS

As previously mentioned, some devices are exempt from the premarket notification 510(k) submission. Additionally, some are exempt from the GMP requirements with the exception of complaint files and general record keeping requirements. However, these devices are not exempt from other general controls. All medical devices must be manufactured under a quality assurance program, be suitable for the intended use, be adequately packaged and properly labeled, and have establishment registration and device listing forms on file with the FDA.

Devices exempted from 510(k) are:

preamendment devices not significantly changed or modified; **or**

Class I devices specifically exempted by regulation.

See appropriate sections in this chapter on when a 510(k) application is required, documenting preamendment status, and the list of exempted Class 1 devices in the Appendixes to confirm an exempt status.

3 510(k) CONTENT AND FORMAT

INTRODUCTION

Manufacturers are required to submit a premarket notification [510(k)] to the Center for Devices and Radiological Health (CDRH) and must receive clearance to market before introducing a device into interstate commerce or otherwise holding or offering the device for commercial distribution, unless the medical device is a Class I device specifically exempt by regulation, or a preamendment

device which has not been significantly altered. Each 510(k) must include all required information and data as described in this chapter. **FDA will NOT accept or review an administratively incomplete 510(k) application**. Before marketing a device, the manufacturer must receive an order, in the form of a letter, from FDA which finds the device to be substantially equivalent (SE) and states that the device can be marketed in the U.S. This order "clears" the device for commercial distribution.

GENERAL INFORMATION

The goal of the 510(k) submitter is to prepare and submit a complete application in order to obtain marketing clearance. To facilitate FDA review of the data, analysis, and conclusions in the application, the manufacturer should check for the:

logical presentation of the data;

scientific soundness of the test and data analysis;

relevance of the test program to the device and the intended use; and

completeness of the summary report of the tests or studies.

A description of the tests and the results obtained are essential. Reasonable and sufficient details of all test procedures and results should be submitted to FDA.

The following suggestions will help assure that your application is complete.

Obtain and use the right guidance. This manual provides basic guidance taken directly from 21 CFR Part 807 Subpart E and the CDRH Screening Checklist For all Premarket Notification 510(k) Submissions. Both can be found in the Appendixes. Use the Division of Small Manufacturers Assistance (DSMA) Facts on Demand and the CDRH Electronic Docket to search for and obtain FDA guidance documents including device specific guidance for the preparation of your marketing application.

Understand the FDA decision-making process by reviewing the Office of Device Evaluation (ODE) Bluebook Memorandum K86-3 "Premarket Notification Review Program" included in the Appendixes to this manual.

Use the Premarket Submission Cover Sheet and the **510(k) Elements List** to prepare your submission. The cover sheet is a "fill-in-the-blank" format which satisfies many of the 510(k) requirements. The elements list is a duplicate of the Screening Checklist For all Premarket Notification 510(k) Submissions. The cover sheet and elements list are included in the Appendixes. However, for some products for which device specific guidance exists, the guidance may also require the submission of a **cover letter**.

510(k) CONTENTS

A 510(k) consists of a cover letter and/or coversheet and supporting information. The submission should be bound into a volume or volumes if necessary and submitted on standard sized paper. Submit two copies of the original including two copies of the cover letter or coversheet. Include the following information so that FDA can contact you; and to assure that your 510(k) application is complete which will enable ODE to determine if your device is substantially equivalent to a legally marketed device:

Identification. The cover letter should be designated **"510(k) Notification"** which identifies your document as a **premarket notification [510(k)] submission**. The cover letter should include:

- date of the application.
- applicant's and/or manufacturer name and street address,*
- contact person (if different from applicant),*
- telephone and FAX numbers of applicant or contact,
- signature of the applicant; and
- address(es) of manufacturing and sterilizing site(s), as appropriate.

*If the applicant, contact person, or address changes during the review, you must notify FDA in writing, referencing the 510(k) document control number, since this person is the official FDA contact for the 510(k) submission, and cannot be changed by anyone other than the current applicant or contact person in FDA's records.

Table of Contents. The table of contents should list each required item with page numbers, including a list of attachments and appendices.

Truthful and Accurate Statement. All 510(k) submitters must include a statement certifying that all information submitted in the 510(k) is truthful and accurate and that no material fact has been omitted. The statement may be in the 510(k) cover letter or may be on a separate page identified in the table of contents. (A sample of the form below can be found in the Appendixes).

PREMARKET NOTIFICATION

TRUTHFUL AND ACCURATE STATEMENT

[As required by 21 CFR 807.87(k)]

I certify that, in my capacity as *(The Position Held in Company)* of *(Company Name)*, I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

_____
(Signature)

_____
(Typed Name)
_____
(Dated)

_____
*(Premarket Notification [510(k)] Number)

* For a new submission, leave the space for the 510(k) number blank. You will receive your 510(k) number in your 510(k) acknowledgment letter. Document control numbers begin with the letter **K** followed by **6 digits**.

The truthful and accurate statement **must** be signed by a responsible person of the firm required to submit the premarket notification -- **NOT** a consultant for the 510(k) submitter.

Device Name. The device name, including both the trade, common, or proprietary name and the classification name of the device [807.87(a)].

Registration Number. The establishment registration number, if applicable, of the owner or operator submitting the premarket notification [807.87(b)]. If you do not have a registration number, so state. Registration is **NOT required** in order to submit a 510(k), however registration is required within 30 days of marketing the device.

If applicable, include the registration number and address of each facility used to manufacture the finished devices including contract sterilizers. The manufacturing process at each facility must be essentially the same and produce the same device as described in your premarket notification submission or state the differences.

Classification. Include the **class**, such as Class I, II, III, or not classified, in which the device has been placed under section 513 of the Federal Food, Drug and Cosmetic (FD&C) Act. If your device is not classified, state how you reached the non-classified conclusion, e.g., you were unable to find your device listed in the classification regulations, 21 CFR Parts 862-892 [807.87(c)].

If known, include the appropriate **panel** such as anesthesiology, orthopedic, etc.

Provide the **product code**, if known. The product code is a 2-digit, 3-letter code that CDRH assigns to devices such as, 80FMF, Piston Syringe.

The classification information required in this section can be found in 21 CFR Parts 862-892, and the CDRH publication "Classification Names for Medical Devices and In Vitro Diagnostic Products" by accessing the CDRH electronic docket or contacting DSMA.

Accessories to classified devices take on the same classification as the "parent" device. An accessory such as software that accepts input from multiple devices usually takes on the classification of the "parent" device with the highest risk, i.e., class.

Performance Standards. If your device meets any mandatory or voluntary standards, identify the standard or requirement of each standard that your device meets [807.87(d)]. If you are claiming substantial equivalence to one or more devices that meet a given standard, then your device should meet the same standard.

Labeling. Include **proposed** labels, labeling, and advertisements, sufficient to describe the device and its intended use [807.87(e)]. This would include: package label, instructions for use, package inserts, prompts, directions, labeling in software, other labeling and advertisements or promotional materials. The directions for use should include a specific intended use statement and any warnings, contraindications, or limitations.

The 510(k) must include a **"statement of indications for use"** prepared by the applicant and listed in the table of contents, as a separate item.

Substantial Equivalence Comparison. You should include a comparison table **AND** discussion of the **similarities and differences** of your device compared to one or more predicate devices to which you are claiming equivalency. The comparison table should identify relevant similarities and differences in areas such as:

1.
· indications for use	· chemical safety	· thermal safety
· target population	· anatomical sites	· radiation safety
· design	· human factors	
· materials	· energy used and/or delivered	
· performance	· compatibility with environment and other devices	
· sterility	· where used: hospital, home, ambulance, etc.	
· biocompatibility	· standards met	
· mechanical safety	· electrical safety	

The discussion of the similarities and differences should elaborate on the similarities identified in the table of comparisons and justify the differences with supporting rationale and/or data.

It is advisable to submit labeling for the device to which you are claiming equivalency.

The equivalence information should be provided in a clear and comprehensible format. A chart, table or other side-by-side comparison is a systematic way to compare the two devices. Side-by-side comparisons, wherever possible, are desirable. For some devices a simple table of comparison which lists characteristics will be sufficient to establish equivalence. Often, information is necessary to resolve questions of safety or effectiveness, especially where differences in technology exists between the predicate and the new device. It must be shown that technological differences **do not** adversely affect safety and effectiveness. Supporting information can be obtained from bench testing, animal studies, or clinical studies (verification).

State whether the legally marketed device for comparison is a preamendment device, or a Class I, II, or III device which has been granted marketing clearance by FDA following the submission of a 510(k). Provide the 510(k) document control number (i.e., **K** followed by **6 digits**) for the device to which you are claiming equivalency, if known. [510(k) numbers for devices that have been granted marketing clearance after 1984 are available on the CDRH Electronic Docket. See CDRH Technical Assistance in chapter 1 on how to use this system.]

For more information on substantial equivalence which has been granted marketing clearance by FDA following the submission of a 510(k). Provide the 510(k) document control number (i.e., **K** followed by **6 digits**) for the device to which you are claiming equivalency, if known. [510(k) numbers for devices that have been granted marketing clearance after 1984 are available on the CDRH Electronic Docket. See CDRH Technical Assistance in chapter 1 on how to use this system.]

For more information on substantial equivalence see chapter 2 and review the ODE Bluebook memorandum K86-3 "Premarket Notification Review Program" included in the Appendixes.

510(k) Summary or Statement.

REQUIREMENTS FOR A 510(k) SUMMARY OR STATEMENT

Definitions

A 510(k) summary means a summary, submitted under section 513(I)(3)(A) of the Act, of the safety and effectiveness information contained in a premarket notification submission upon which a determination of substantial equivalence can be based. The 510(k) statement in the format presented in this section is the same as the **definition** of the 510(k) statement. The 510(k) summary and statement are defined in 21 CFR section 807.3.

A person submitting a premarket notification [510(k)] to FDA **must** include either:

a summary of the 510(k) safety and effectiveness information upon which the substantial equivalence determination is based; OR

a statement that the 510(k) safety and effectiveness information supporting the FDA finding of substantial equivalence will be made available by your firm to **ANY** person within 30 days of a written request.

If a 510(k) submitter chooses to provide a statement to satisfy the conditions in (2) above, written requests by any individual for a copy of the 510(k), excluding patient identifiers and trade secret and confidential commercial information, must be fulfilled by the statement certifier within 30 days of receipt of the request. FDA publishes the name of certifiers on the monthly list of 510(k) submissions for which substantial equivalence determinations have been made [807.93(b)]. 510(k) submitters may not charge requesters for compiling and disseminating this data.

Non compliance with the 510(k) statement will be deemed a prohibited act under section 301(p) of the FD&C Act and FDA may choose to use its enforcement powers to obtain compliance.

The choice between the 510(k) summary and 510(k) statement should be made before the 510(k) is submitted. However, a submitter may elect to change their choice between the summary or statement **before** the substantial equivalence determination is reached. **After this determination is made, a submitter cannot change their choice of a 510(k) summary or 510(k) statement.**

Premarket Notification [510(k)] Summary

If you choose to meet the conditions **for a 510(k) summary**, then a summary **must** be submitted with your 510(k) submission and clearly marked as such in order for FDA to **begin** its scientific review of the 510(k) submission. A complete and correct summary as described below must be submitted in order for FDA to **complete** its review of the 510(k) submission. As required by section 807.92 (a), FDA will accept summaries or amended summaries until FDA issues a determination regarding substantial equivalence.

Please make a copy of the following to use as a checklist and check off each item to **make sure** your summary is adequate and complete.

[ ]

The summary is a separate section of the submission, beginning on a new page and ending on a page not shared with any other part of the premarket notification submission, and is clearly identified as "510(k) Summary" as required by section 807.92(c).

[ ]

The summary contains on the first page, preferably on your letterhead paper, the submitter's name, address, phone and fax numbers, name of contact person, and date the summary was prepared [807.92(a)(1)].

[ ]

The summary includes the name of the device, including the trade or proprietary name if applicable, the common or usual name, and the classification name, if known [807.92(a)(2)].

Example:

Trade name - DRAG@N LATEX EXAMINATION GLOVES

Common name - exam gloves

Classification name - patient examination glove (per 21 CFR section 880.6250)

[ ]

The summary identifies the legally marketed device to which your firm is claiming equivalence [807.92(a)(3)].

[ ]

The summary includes a description of the device [807.92(a)(4)].

[ ]

The summary describes the intended use of the device [807.92(a)(5)].

[ ]

Per section 807.92(a)(6), the 510(k) summary contains a summary of the technological characteristics of your device compared to the predicate device. If your device has different technological characteristics from the predicate device, the 510(k) summary contains a summary of how the technological characteristics of your device compare to a legally marketed device to which you are claiming equivalence.

[ ]

If the determination of substantial equivalence is also based on an assessment of non-clinical performance data, the summary includes a brief discussion of the nonclinical tests and how their results support a determination of substantial equivalence [807.92(b)(1)].

[ ]

If the determination of substantial equivalence is also based on an assessment of clinical performance data, the summary includes a brief discussion of clinical tests and how their results support a determination of substantial equivalence [807.92(b)(2)].

Clinical data is not needed for most devices cleared by the 510(k) process.

[ ]

Per section 807.92(b)(3), the summary includes the conclusions drawn from the nonclinical and clinical tests in (b1) and (b2). (See steps 8 and 9 above.)

[ ]

Per section 807.92(d), the summary includes any other information reasonably deemed necessary by FDA. Such requests will be made directly to the applicant by FDA or the requirements will be published in guidance documents such as this document. Additional information requested by FDA during review of the 510(k) may include additional safety and effectiveness information which may necessitate an update of your summary **if requested by FDA**.

Please make sure you have included all of the information listed above and verify that the following criteria have been met.

The summary includes **only** information that is also covered in the body of the 510(k).

The summary does **not** contain any puffery or unsubstantiated labeling claims.

The summary does **not** contain any raw data, i.e., contains only summary data.

The summary does **not** contain any trade secret or confidential commercial information.

The summary does **not** contain any patient identification information.

Make a copy of your complete 510(k) including the summary for your records. Submit the complete original 510(k) including the summary **and** a complete copy of the 510(k) including the summary to FDA.

In instances where a 510(k) submitter provides a 510(k) summary of the safety and effectiveness information upon which the SE determination is based with the 510(k) submission to FDA, written requests by individuals for copies of the 510(k) summary will be furnished by FDA through the Freedom of Information (FOI) process within 30 days after determining that the device is substantially equivalent to another device.

Premarket Notification [510(k)] Statement

For persons who choose to submit a 510(k) statement with their 510(k), the specific statement shown below **must** be submitted with

the 510(k) in order for FDA to **begin** the review process. The statement should be clearly identified as "510(k) Statement," signed by the certifier -- NOT a consultant to the 510(k) submitter, and must include the specific language beginning with "I certify ...", shown in the following sample as required by 21 CFR section 807.93:

510(K) STATEMENT
(As required by 21 CFR 807.93)

I certify that, in my capacity as (*the position held in company by the person required to submit the premarket notification, preferably the official correspondent*), of (*company name*), I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secret and confidential commercial information, as defined in 21 CFR 20.61.

_____
(Signature of certifier)

_____
(Typed Name)

_____
(Dated)

_____
*(Premarket Notification [510(k)] Number)

* For a new submission, leave the space for the 510(k) number blank. You will receive your 510(k) number in your 510(k) acknowledgment letter. The 510(k) document control number begins with the letter **K** followed by **6 digits**.

Make a copy of your complete 510(k) including your signed statement for your records. Submit the complete original 510(k) including the statement **and** a complete copy of the 510(k) including the statement to FDA.

Class III Certification and Summary. A 510(k) submitted for a Class III device **must include** a Class III certification and summary. Class III summary means: a summary of the types of safety and effectiveness problems associated with the type of device being compared and a citation to the information upon which the summary is based. The summary must be comprehensive and describe the problems to which the type of device is susceptible and the causes of such problem. [807.3(q)]

The certification should be signed by the certifier -- NOT a consultant to the 510(k) submitter, clearly identified as "Class III Certification and Summary", and listed in the table of contents. Attach the summary of problem data, bibliography or other citations upon which the summary is based, to the certification statement. The language to be used in the certification statement is shown below. (A sample of the form below can be found in the Appendixes.)

CLASS III CERTIFICATION AND SUMMARY
[As required by 21 CFR 807.94]

I certify that, in my capacity as (*the position held in company*), of (*company name*), that I have conducted a reasonable search of all information known or otherwise available about the types and causes of safety or effectiveness problems that have been reported for the (*type of device*). I further certify that I am aware of the types of problems to which the (*type of device*) is susceptible and that, to the best of my knowledge, the following summary of the types and causes of safety or effectiveness problems about the (*type of device*) is complete and accurate.

_____
(Signature of certifier)

_____
(Typed Name)

_____
(Dated)

_____
*(Premarket Notification [510(k)] Number)

* For a new submission, leave the space for the 510(k) number blank. You will receive your 510(k) number in your 510(k) acknowledgment letter. The 510(k) document control number begins with the letter **K** followed by **6 digits**.

Description. Include narrative and physical descriptions of the device. The narrative description of the "new" device should include the indications for use, principles of operation, power source, composition and other information necessary to understand the device. If the 510(k) is for an accessory or component sold to an end-user, describe a typical device with which the accessory or component will be used. **List all variations of the "new" device which you intend to market.**

As applicable, the physical description of the "new" device may include labeled diagrams, **photographs or pictures, engineering drawings**, schematics, etc. These may include all internal and external, assembled and unassembled, interchangeable, etc., parts of the device and should address the name and function of all parts of the device. The description should include the length, width, height, diameter, weight, etc., of the device. Identify any parts which are intended for single use.

The device specifications are the basis for the comparison of features between the new and the legally marketed device to which compared.

Note: Device specific guidance documents usually provide extensive information on level of detail which needs to be included in the specifications list. Copies of these are available from DSMA. (See "CDRH Technical Assistance" section in Chapter 1 on obtaining documents.)

Performance. When applicable, performance data should be provided to help demonstrate safety and effectiveness of your device to one or more legally marketed devices. The data may include results from engineering, bench, design verification, human factors, animal, and clinical studies. Tests should be conducted on all sizes and models of the device in a manner as similar as possible to how the device will be used.

Biocompatibility. For devices in direct contact with the patient or user, an exact identification and composition of all materials that contact the patient should be provided and a statement regarding any material differences from the legally marketed device should be explicitly stated. If the materials are identical to the legally marketed device and are identically processed and sterilized, then this should be stated. If the materials, manufacturing processes, and intended use are not identical or this information is not available for the legally marketed device, biocompatibility testing must be performed.

Therefore, manufacturers will need to provide biocompatibility test data for any new materials when the new device is compared to a legally marketed device of different materials. The data should be in a separate, identified biocompatibility section, be organized, and be complete.

FDA is currently using the ISO-10993 Biological Testing of Medical and Dental Materials and Devices, in the evaluation of manufacturers' biomaterial testing program for medical devices. This guidance can be found in ODE Bluebook Memorandum G95-1, which may be obtained from DSMA.

14.1

Color Additives. For devices containing color additives which come in contact with the user or patient, either directly or indirectly; such as gloves, condoms, contact lens, etc., you should provide an exact identification of all colors in inks, dyes, markings, radiopaque materials, etc., used to make the device . Identify any colorant changes from the legally marketed device. If the colors are identical to those in the legally marketed device, then this should be explicitly stated. Include biocompatibility test data on any color additive changes in the new device; state how the colors or markings are processed such as etched, bands, in material, etc.; and state whether the color contacts skin, mucosa, etc.

Software. If the device is computer controlled, software and/or hardware, validation and verification information must be included in the 510(k). The test data must support all performance and safety claims.

The "*Reviewer's Guidance for Computer Controlled Medical Devices Undergoing 510(k) Review"* provides information on 510(k) requirements for these devices and is available from DSMA.

Software that is to be marketed to enhance the performance of a device is regulated as an accessory to that device. Software that enhances the performance of a group of different devices is regulated as an accessory to the device that poses the greatest risk to the patient. The 510(k) submission should include the data noted above including any information, prompts, and cautions displayed by the system. This is considered to be labeling and such displays must meet the labeling regulations as well.

Databases, software, and computers that only process manually input data and is not used in the diagnosis, treatment, etc. of the patient is usually exempt from 510(k) requirements. However, it is a medical device and should be properly labeled and meet its claims. Examples include; patient data management programs or record keeping programs.

Sterility. Information regarding devices that are **labeled** sterile **must** include the following:

- the sterilization method;
- the method used to validate the sterilization cycle, but not the validation data itself;
- the sterility assurance level (SAL) for the device that the manufacturer intends to meet;
- the packaging to maintain the device sterile (do not include packaging integrity test data in the 510(k) submission);
- the maximum levels of residues of ethylene oxide, ethylene chlorohydrin, and ethylene glycol on the device when ETO is used to sterilize (information on current residue limits may be obtained from DSMA);
- for devices that contact blood or cerebrospinal fluids, state whether the device is non-pyrogenic and describe the method used to make that determination; and
- the radiation dose, or dose methodology, if radiation sterilization will be used.

If the entire device is not labeled sterile or non-pyrogenic, the labeling must clearly identify which parts are sterile and non-pyrogenic. Guidance on sterility is in ODE Bluebook Memorandum K90-1 *"510(k) Sterility Review Guidance"* which may be obtained from DSMA.

16.1

Pyrogens. If the device will be labeled as non-pyrogenic, state what process controls will be used to control pyrogens; and, state what method, such as the Limulus Amebocyte Lysate (LAL) or USP Rabbit test, will be used to determine that each lot is non-pyrogenic. This information is required for devices that contact blood or cerebrospinal fluids.

16.2

Sterilization by User. The labeling for devices intended to be sterilized by the user must identify one validated method of sterilization. The instructions should be detailed and specific enough for the user to follow and obtain the required sterility assurance level. The instructions should also adequately describe any precautions to be followed such as:

- special cleaning methods required;
- any changes in the physical characteristics of the device that may result from reprocessingand re-sterilization, especially those which may affect the safety,effectiveness, or performance; and
- any limit on the numberof times re-sterilization and reuse can be done without adversely affecting the safety, effectiveness, or performance of the device.

Kits, Packs, or Trays. If this device is to be marketed as a kit, identify all devices and other products in the kit and provide the certification stated below acknowledging that each product falls under 1, 2, or 3:

Para.1. I certify that the following devices in my kit:

1. are either legally marketed preamendment devices; or
2. are exempt from premarket notification [consistent with the exemption criteria described in the classification regulation(s) and the limitations of exemptions from 21 CFR Parts 862-892; or
3. have been found to be substantially equivalent through the premarket notification process for the use(s) for which the kit is to be intended [i.e., I am not claiming or causing a new use for the included devices/components].

If you cannot make the above referenced certification statement (paragraph 1) for each component of your kit, you must itemize the devices/components without preamendment, exempt, or premarket notification status. In this case the 510(k) review of these devices/components will continue as it would for any new device.

Para.2. I further certify that these devices/components are not purchased in "bulk", but are purchased in finished form, i.e., they are packaged, labeled, etc., consistent with their preamendment, exempt, or premarket notification status.

If you cannot make the above referenced certification statement (paragraph 2) for each device/component of your kit, you must itemize these devices/components, state whether they are preamendment, exempt, or have been found substantially equivalent through the 510(k) process, and describe how you further process them such as sterilization, packaging and/or repackaging, labeling and/or relabeling, etc.

17.1

Gloves in Kits. If your sterile kit contains examination gloves that are purchased in bulk, your 510(k) application must contain both of the following:

- data demonstrating or certification that the **finished sterile** examination gloves in the kit meet the American Society for Testing and Materials (ASTM) standards for examination gloves, ASTM D 3578 - 91, ASTM D 5250 - 92, or equivalent; **and**
- data demonstrating or certification that the **finished sterile** examination gloves pass the FDA 1000 milliliter water leak test in accordance with the sample plan and test method published in the *Federal Register,* 55 FR 51254-51258. (On a design basis, the gloves must pass the leak test after undergoing the accelerated aging in ASTM D 3578, D 5250 or equivalent. Please check with your supplier.)

17.2

Sutures in Kits. If the kit contains sutures, provide evidence that the sterilant does not contact the sutures during sterilization of the kit. (Some kit assemblers package the sutures separately from the main tray. After processing and sterilizing the main tray, the package of sutures is piggybacked onto the main tray.) Based on the evidence submitted, FDA can conclude if the sutures are or are not further processed. However, including sutures as a component in your kit requires you to comply with the following conditions:

- The labeling, packaging, and method of sterilization of the sutures you have listed cannot be changed without prior notification, review, and clearance by FDA; and
- The supplier(s) of the sutures included in your kit cannot be changed without prior notification, review, and clearance by FDA.

17.3

Drugs in Kits. If the device kit contains components which are subject to regulation as drugs, a substantially equivalent determination of the included devices by CDRH **does not apply** to the drugs in the kit. For information on applicable FDA requirements for marketing the drugs in a kit, you should contact the Center for Drug Evaluation and Research (CDER) at the following address.

Center for Drug Evaluation and Research
Division of Drug Labeling Compliance (HFD-310)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857 USA
Phone 301-594-1065

HOW TO FORMAT A 510(k)

The format and information required in a premarket notification [510(k)] for medical devices is found in 21 CFR sections 807.87, 807.90, 807.92, 807.93 and 807.94.

Include name, telephone, facsimile number (if available), and address of submitting official. If at any time during the 510(k) review this information changes, you must notify the Document Mail Center in writing, at the address below.

Include a detailed Table of Contents.

Use 8.5" x 11" (21.5 cm x 27.8 cm) 3-hole punched, white paper **only;** do not use colored paper.

Leave a 1.5" (3.8cm) margin between the left edge of the paper and the left margin of the text. This leaves enough space for FDA to bind the 510(k) in the review jacket.

Place the 510(k) in an inexpensive jacket or non-permanent binding. All 510(k)s are removed from the shipping binder and placed in standard jackets. The shipping binder will be discarded.

Use numbered or lettered tabulation sheets to separate the sections in the 510(k). This will make it easy for the reviewer to refer or search back and forth during the review.

Number the pages correctly, double check the page numbering when finished, then have someone else check it as well. Make sure the page numbering or pagination corresponds to the page numbers or section numbers in the Table of Contents.

Numbering pages by section is acceptable as is done in this manual. For example: Section 1 pages could be numbered 1-1, 1-2, 1-3.

Section 2 pages will then be numbered 2-1, 2-2, 2-3, etc. Numbering by section is a little faster than sequential numbering, helps reduce errors, and is easier to correct if a page is added or removed.

If any diagrams, drawings, figures, illustrations, photos, charts, or tables are used, give them a title and number. Make sure citations in the text refer to them correctly.

When you receive a letter regarding substantial equivalence, attach a copy to your copy of the original 510(k) submission. Attach any additional information sent to FDA, in response to FDA's request for data, to your copy of the 510(k) and maintain for your files.

WHERE TO SEND THE 510(k)

Premarket notification [510(k)] submissions should be sent to the following address by a method such as registered mail that returns to you proof of delivery. Submit 2 complete copies to FDA, and keep a complete copy for your files.

Document Mail Center (HFZ401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850 USA

WHEN FDA REQUESTS ADDITIONAL INFORMATION

After you submit your premarket notification, if FDA requests additional information by telephone, FAX, or letter, you should:

either submit the information within 30 days or request an extension for submitting information and state the time needed to submit;

identify the additional information you submit with your company name and 510(k) number; and

state where the information should be included in your application such as by topic, section and/or page numbers. You may find it necessary to submit a revised table of contents.

Please Note: Any information submitted to FDA to be added to the 510(k) submission whether required by FDA or voluntarily submitted must include the 510(k) document control number. Information submitted without the 510(k) document control number may be misrouted or improperly logged into the 510(k) database.

POINTS TO CONSIDER

The following suggestions will assist you in presenting your 510(k) to FDA in a format which is manageable by the Document Mail Center, administrative and scientific reviewers, and your own regulatory affairs personnel.

Review the Screening Checklist For all Premarket Notification 510(k) Submissions as an outline for your submission. The checklist is included in the Appendixes to this manual.

Use the Premarket Submission Cover Sheet and the 510(k) Elements List to assure completeness of the 510(k). The coversheet with elements list is included in the Appendixes.

Make sure you have obtained and read all device specific guidances for your device.

Make sure you have followed instructions in "How to Format a 510(k)" above.

4 510(k) REVIEW PROCESS AND PROGRAMS

INTRODUCTION

This chapter is intended to familiarize you with the review process so that you may better understand the steps, time frames, and terminology referred to while a 510(k) submission is under review. This chapter also addresses the 510(k) programs instituted in June of 1993 to increase resource efficiency.

510(k) REVIEW PROCESS

Log-In Procedures

Upon receipt in the Document Mail Center (DMC), 510(k) submissions are date stamped and logged into the DMC computer where a unique control number is assigned to the document. This number is referred to as the "**document control number**", "**510(k) number**", or just "**K number**". The document control number begins with the letter "**K**" followed by **6 digits**. The first two digits designate the calendar year the application was received; the last four digits represent the submission number for the year.

The database program will assign the 510(k) a due date and sequential position in the queue based on the receipt stamp date. The database program will generate an "acknowledgment letter" with the assigned 510(k) number. The acknowledgment letter will be mailed to the submitter or applicant if different from the submitter. **The acknowledgment letter is not a marketing clearance letter.**

Division Acceptance

After the 510(k) is logged in by the DMC, it is sent to the reviewing division appropriate for the classification of the device within the Office of Device Evaluation (ODE). These divisions are as follows:

Division of General and Restorative Devices

Division of Clinical Laboratory Devices

Division of Cardiovascular, Respiratory, and Neurological Devices

Division of Ophthalmic Devices

Division of Reproductive, Abdominal, Ear, Nose, and Throat and Radiological Devices

Including accurate classification information on the cover sheet or cover letter, such as, panel, Code of Federal Regulations reference, and product code will facilitate delivery to the proper reviewing division.

A designated person within the division will review the submission against the "Refuse to Accept" checklist. A recommendation to accept the 510(k) or issue a "Refuse to Accept" letter will be forwarded to the division supervisor for concurrence. A copy of the Refuse to Accept policy and checklist is included in the Appendixes.

If the recommendation to accept has concurrence, the 510(k) will be assigned to a division reviewer. In this case, you will not receive an acceptance letter.

If the recommendation not to accept has concurrence, a Refuse to Accept letter, detailing the omissions and inadequacies, will be mailed to the submitter or applicant within approximately 30 days of receipt of the original application. The letter will specify what administrative data must be submitted if the manufacturer wishes to pursue clearance for marketing.

If you receive a Refuse to Accept letter, send FDA the required information **or** a letter requesting an extension of time to obtain the information requested to the DMC within 30 days. If neither is received within 30 days, the 510(k) may be deleted from the system.

Reviewer Assignment

If the 510(k) is complete, it is assigned to a division reviewer and checked against the division "Triage List" to determine the "tier category" to which the device type belongs; tier I, II or III [see the 510(k) Programs section in this chapter for information on tier categorization]. The tier designation will determine the extent or intensity of review which must be performed. The reviewer also checks to see if the device warrants "Expedited Review", based on the expedited review policy [see the 510(k) Programs section in this chapter for information on the expedited review policy].

Most reviewers are assigned 510(k)s, IDEs and PMAs for review at the same time. Some 510(k)s are awaiting review, some may be on hold waiting for additional information, and some are under active review. The 510(k)s are reviewed, in order, according to the original or additional information receipt date which is based upon the due date assigned by the Document Mail Center computer database.

Several things can affect how quickly 510(k)s are reviewed, such as:

IDEs and PMAs have statutory due dates and therefore take priority over 510(k)s;

510(k)s and PMAs granted expedited review are taken out of turn and reviewed first;

If additional data is requested from FDA by letter, the application is put on hold; and

Consulting review of 510(k) by another CDRH office or another FDA Center.

FDA Requests Additional Information

When the reviewer needs additional information to complete the review he or she will either telephone the applicant with a simple request or prepare a deficiency letter which will detail what additional information is needed. In the latter case, while the reviewer is waiting for the additional information, the application is placed on "hold" and thus is not considered to be under active review.

These written requests for additional information usually request a response within 30 days. If additional time is needed to gather the requested information, the 510(k) submitter may request an extension within the 30 days of FDA's request for information. Any information to be added to the 510(k) file must be submitted in writing to the DMC, clearly identified as additional information or a request for an extension of time, and must include the 510(k) document control number. The 510(k) number may be deleted from the DMC database if there is no response to the request for additional information within 30 days of FDA's request letter.

Please Note: Any information submitted to FDA to be added to the 510(k) submission whether required by FDA or voluntarily submitted must include the 510(k) document control number. Information submitted without the 510(k) document control number may be misrouted or improperly logged in.

Administrative Review

After the technical review is completed, the reviewer's recommendation is forwarded to the division director for concurrence. Not substantially equivalent (NSE) recommendations, concurred with by the division director, are forwarded to the ODE 510(k) staff for concurrence prior to signature.

Before an SE letter can be issued, ODE will contact the Office of Compliance (OC) to verify the current Good Manufacturing Practices (GMP) status of the 510(k) submitter. The purpose of this process is to prevent issuing marketing clearances to 510(k) submitters with significant GMP violations, reasonably related to the device, that could result in the production of unsafe and/or ineffective devices until such time as the device related violations are corrected .

510(k) submitters with such violations will be issued a letter from the Office of Device Evaluation indicating the processing of the 510(k) is being postponed until outstanding GMP problems, reasonably related to the device, are resolved. This letter will instruct the manufacturer to contact the FDA district office to determine what corrective actions are necessary to resolve the deficiencies. Once the deficiencies are resolved, the district office will notify CDRH and the SE letter will be issued.

If the 510(k) submitter does not have a record of GMP violations, reasonably related to the device, the SE letter may issue.

A similar program exists for Class III devices seeking 510(k) clearance which is referred to as the "Class III Pre-Clearance Program". When a 510(k) is received for a Class III device in the Document Control Center, the OC is notified. The 510(k) takes its normal route through the ODE while the OC contacts the 510(k) submitter and the FDA District Office to confirm the current GMP status of the manufacturer.

If the manufacturer has been inspected within the last two years and no GMP violations had been noted, this information is relayed to ODE and the 510(k) review is not impeded.

If there is no current inspectional information available for the manufacturer, the OC will issue an inspection of the firm. If the inspection reveals no GMP violations, the ODE is notified and the 510(k) review continues. If the previous or current inspection reveals a GMP problem, reasonably related to the device, a determination of SE cannot issue until such time that the device related violations are resolved with the district office and the Office of Compliance.

Decision Letter Issued

The Office of Device Evaluation will issue the decision letter to the submitter upon receipt of the completed 510(k) documentation from the reviewing division and clearance from the Office of Compliance. The DMC staff will enter the final decision into the database and prepare the complete 510(k) file for electronic imaging into the computer. After completion of electronic imaging, and back-up microfilming, the original 510(k) files are destroyed.

510(k) PROGRAMS

Refuse to Accept Policy

Approximately one-third of all 510(k) applications received by ODE are incomplete and lack essential information needed for FDA to perform a thorough review. The Refuse to Accept procedures were implemented to assure that 510(k) submissions meet a minimum threshold of acceptability. Otherwise, ODE will refuse to accept the submissions for review. As part of the Refuse to Accept policy, FDA has developed a checklist of required information that must be included in all 510(k) applications. The *Refuse to Accept* Blue Book Memorandum K94-1, describing this policy and the Screening Checklist For all Premarket Notification 510(k) Submissions are included in the Appendixes.

Tier Categorization/Triage Review

FDA has established a three-tier categorization system of review based on the risk, technology, and characteristics of the device. All five ODE review divisions categorized the devices they are responsible for into one of three tier categories. These tier categorization lists are available from DSMA.

Tier 1 devices are those with low risk with no significant differences in technology or characteristics. Tier 1 devices will receive a labeling review to assure the indications for use are consistent with other devices in the same classification.

Tier 2 devices are considered to be moderate risk devices with which FDA has experience with the safety and effectiveness concerns. Tier 2 devices will receive a routine scientific and labeling review.

Tier 3 devices are high risk devices with which FDA has little or no experience with the safety and effectiveness concerns. Tier 3 devices will receive an intense scientific and labeling review, using a team approach. Advisory panel input is highly recommended for this tier of devices. The *Triage Review Procedures* Blue Book Memo G94-1 is included in the Appendixes.

Expedited Review

The FDA believes it is in the interest of the public health to review PMAs and 510(k)s for certain devices in an expeditious manner. Granting expedited review status means that the selected marketing application will receive priority review before other pending PMA and 510(k) applications, i.e., the application will be placed at the beginning of the review queue. The decision to expedite a marketing application should be made by the reviewing division, within 30 days of receiving a 510(k), and within the 45-day filing review for PMAs. It is advisable for the 510(k) submitter to request expedited review in writing to the DMC, including a justification for the device meeting the expedited review criteria.

Expedited review will be considered for devices intended for or meeting one or more of the following criteria:

Life-threatening or irreversibly debilitating conditions with no alternative modality;

Life-threatening or irreversibly debilitating conditions with alternative devices, but where the new device provides significant improvement over the existing alternatives;

New (revolutionary) device with significant advantage over existing technology; or

Device with specific public health benefit.

These conditions usually pertain to Class III devices requiring Premarket Approval. The *PMA/510(k) Expedited Review* Blue Book Memorandum G94-2 is included in the Appendixes.

510(k) Status Request Program

Applicants may request information on their 510(k) review status 90 days after the initial log-in date of the 510(k). Thereafter, the applicant may request status reports every 30 days following the initial status request. To obtain a 510(k) status report, the applicant should complete the status request form included in the Appendixes, and fax or mail it to DSMA. Within 3 working days after a status request is received, DSMA will send the applicant a fax or letter that includes:

The branch to which the 510(k) is assigned;

The last action, and date of action, that ODE has taken regarding the 510(k);

The position of the 510(k) in the reviewer's queue; and

The average review time for the division or branch.

Appendixes