37

Medical Devices

Regulations & requirements in Europe, USA ,Jordan & Saudi Arabia

Prepared by: Muna Jardaneh
Najwan Al-Titi
Rania Shaqlous
Rula Kawar

10/24/2010

Medical Devices

Regulations & requirements in Europe, USA ,Jordan & Saudi Arabia

Prepared by: **Muna Jardaneh**
Najwan Al-Titi
Rania Shaqlous
Rula Kawar

10/24/2010

Table of contents:

4.4 How to use the rules
4.5 Practical example
4.6 Explanations of individual rules
4.7 Graphical summary – medical devices classification guidance chart for initial identification of probable device class
4.8 General explanation of rules / Practical issues / examples

- Rule 1 - Devices that either do not touch the patient or contact intact skin only
- Rule 2 - Channeling or storing for eventual administration
- Rule 3 – Non-invasive devices that modify biological or chemical composition of blood, body liquids or other liquids intended for infusion into the body.
- Rule 4 - Non-invasive devices which come into contact with injured skin
- Rule 5 - Devices invasive with respect to body orifices
- Rule 6 - Surgically invasive devices intended for transient use (< 60 minutes*)*
- Rule 7 - Surgically invasive devices intended for short-term use *(>60 minutes, <30 days)*
- Rule 8 - Implantable devices and long-term surgically invasive devices (> 30days)
- Rule 9 - Active therapeutic devices intended to administer or exchange energy.
- Rule 10 - Active devices for diagnosis
- Rule 11 - Active devices intended to administer and/or remove medicines, body liquids or other substances to or from the body
- Rule 12 - All other active devices
- Rule 13 - Devices incorporating, as an integral part, a medicinal product or a human blood derivative.
- Rule 14 - Devices used for contraception or prevention of sexually transmitted diseases
- Rule 15 - Specific disinfecting, cleaning and rinsing devices.
- Rule 16 - Devices to record X-ray diagnostic images
- Rule 17 - Devices utilising animal tissues or derivatives

5. Clinical Evaluation of Medical Devices

5.1 MEDDEV Guidance for clinical evaluation.
5.2 Clinical investigation of medical devices.
5.3 EN ISO 14155 Parts 1 and 2.

6. Medical Device Regulation in the United States:

6.1 Introduction & Definitions
6.2 US Classification.
6.3 Establishment registration and medical device listing.
6.4 Performance /effectiveness requirements.
a. Premarket notification - 510(k)
b. Premarket approval.
c. Product development protocol.
d. Clinical data (International and Domestic)
e. Pre-IDE process.
f. Pre-IDE meetings.
f. Good manufacturing practices.
g. Postmarket surveillance/tracking

h. Postmarket surveillance studies.
i. Device tracking.
j. Medical device reporting.
k .Medwatch
l. Performance standards.
m. Radiation standards.
n. Labelling.
o. Making-country of origin.
p. Procedures for the export of medical devices from the US

7. Medical Device Regulation in the Jordan

7.1 Medical device Regulations in Jordan by the JFDA
7.2 Medical Device Requirement for registration

8. Medical Device Regulation in Kingdom of Saudi Arabia

Introduction:

The term ***"medical devices"*** includes everything from highly sophisticated computerized medical equipment down to simple wooden tongue depressors. Like medicines and other health technologies, they are essential for patient care – at the bedside, at the rural health clinic or at the large, specialized hospital. Medical devices include a wide range of products varying in complexity and application. Examples include: tongue depressors, medical thermometers, blood sugar meters, total artificial hearts, fibrin scaffolds, stents and X-ray machines.
Specific regional definitions of medical device vary slightly as detailed below. The medical devices are included in the category: Medical technology.

Medical devices also cost governments a substantial amount of money. In 2000, the estimated one and a half million different medical devices available on the market represented over US$145 billion. With innovation and the rapid advancement of technologies, medical devices are currently one of the fastest growing industries. The global market of medical devices reached roughly 209 billion US Dollar in 2006 and is expected to grow with an average annual rate of
6 - 9% through 2010.

Yet many countries lack access to high-quality devices and equipment that are appropriate for their specific epidemiological needs. This is particularly true in developing countries, where health technology assessments are rare and where little regulatory controls exist to prevent the importation or use of substandard devices. With the vast majority of devices in developing countries being imported, this leaves them prey to unscrupulous market influences and puts patients' lives at risk.
Governments need to put in place policies that will address all elements related to medical devices, ranging from access to high quality, affordable products, through to their safe and appropriate use and disposal. The health technology life cycle diagram illustrates the policy process that needs to be in place. However, policies will be unsuccessful unless they are translated into national regulations that are enforced by legislation and correlating sanctions and that form an integral part of the overall national health system.

Surprisingly, regulatory controls for medical devices are scarce in the developing world, even though implementation of national medical device regulations will often address the very issues raised in countries as major concerns for patient safety. Examples of these issues include the illegal re-processing and re-packaging of used syringes for re-sale; the availability on the market of equipment that fails minimum quality and safety standards; or simply no trace of what devices are being sold in the country, nor by whom. Such a listing is essential to enable governments to issue alerts or recalls for unsafe or ineffective items.

This will allow countries with weak regulatory systems to place emphasis and initial resources on areas such as vendor and device registration, training, and surveillance and information exchange systems on the assessment of medical devices in use.
WHO is reinforcing its role in providing technical support to Member States who wish to implement improved medical device regulatory systems.
We hope to provide a useful framework about medical devices and address their needs to populations and their regulatory requirements.

1. Definition.

A country may develop its own guidance document for any detailed descriptions they may require

1.1 European Union Definition (EMA):

Directive 2007/47/EC defines a medical device as:
"any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings. Devices are to be used for the purpose of:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease.
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap.
- Investigation, replacement or modification of the anatomy or of a physiological process
- Control of conception

This includes devices that do not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means."
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:247:0021:0055:en:PDF.

1.2 Definition in USA by the Food and Drug Administration:

A medical device, according to the U.S. Food and Drug Administration (FDA):
"*A device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory,* which is:

- *recognized in the official National Formulary, or the United States Pharmacopoeia, 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 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 its primary intended purposes*".

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm127086.htm.

1.3 Definition in Saudi Arabia by SFDA.

Medical Device means: *"any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article:*
A) Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:
− Diagnosis, prevention, monitoring, treatment or alleviation of disease,
− Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
− Investigation, replacement, modification, or support of the anatomy or of a physiological process,
− Supporting or sustaining life,

− Control of conception,
− Disinfection of medical devices,
− Providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body;

B) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means."

In-vitro medical device: means a medical device, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. This includes reagents, calibrators, control materials, specimen receptacles, software and related instruments or apparatus or other articles.

http://www.sfda.gov.sa/NR/rdonlyres/7BF70791-912B-4DC0-AB7E-65CC929B002E/0/MedicalDevicesinterimregulation.pdf

1.4 Global Medical Device Nomenclature (GMDN)./ (WHO)

The Global Harmonization Task Force GHTF has proposed the following harmonized definition for medical devices.

Achieving consistency in nomenclature is fundamental to the overall goal of international harmonization, particularly for the identification of devices involved in adverse incident reports.
In 1993, the European Commission mandated the 'Comité Européen de Normalisation'(CEN) to produce a *standard* indicating the structure of a nomenclature system that could meet the needs of the global market. The International Standards Organization was invited to participate to ensure that international considerations were addressed. The resulting standard was adopted as 'EN/ISO 15225 Nomenclature – Specification for a nomenclature system for medical devices for the purposes of regulatory data exchange'.
Before the creation of the Global Medical Device Nomenclature (GMDN) in 1997, a multitude of nomenclatures were being used, including the Universal Medical Device Nomenclature System. With the introduction of the European Directives for medical device regulations, the need for a standardized international nomenclature became clear. WHO supports wide consultation to adopt a single, harmonized option.
The GMDN, endorsed by the GHTF as the global nomenclature to be used by regulators for the classification and registration of medical devices, is intended:

1) To give a common generic description for every general term that describes characteristics of a medical device. This is to be used for identifying similar devices to those involved in an adverse incident report;
2) To identify a device, using the generic term, for having been awarded a specific design or other certificate;
3) To serve as a basis for E-commerce – to provide a generic basis for purchasing individual types of manufactured devices, by establishing a heading for comparison of products from different manufacturers.

The harmonized definition: 'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or other similar or related article:

a) intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices,
- providing information for medical or diagnostic purposes by means of *in vitro* examination of specimens derived from the human body; and

b) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.

Note 1: The definition of a device for *in vitro* examination includes, for example, reagents, calibrators, sample collection and storage devices, control materials, and related instruments or apparatus. The information provided by such an *in vitro* diagnostic device may be for diagnostic, monitoring or compatibility purposes. In some jurisdictions, some *in vitro* diagnostic devices, including reagents and the like, may be covered by separate regulations.

Note 2: Products which may be considered to be medical devices in some jurisdictions but for which there is not yet a harmonized approach, are:

- aids for disabled/handicapped people,
- devices for the treatment/diagnosis of diseases and injuries in animals,
- accessories for medical devices (see Note 3),
- disinfection substances,
- devices incorporating animal and human tissues which may meet the requirements of the above definition but are subject to different controls.

Note 3: Accessories intended specifically by manufacturers to be used together with a 'parent' medical device to enable that medical device to achieve its intended purpose should be subject to the same GHTF procedures as apply to the medical device itself. For example, an accessory will be classified as though it is a medical device in its own right. This may result in the accessory having a different classification than the 'parent' device.

Note 4: Components to medical devices are generally controlled through the manufacturer's quality management system and the conformity assessment procedures for the device. In some jurisdictions, components are included in the definition of a 'medical device'.
(see GHTF document SG1/N029R11). Further information on the GMDN can be found at http://www.gmdn.info.

2. List of Medical Devices

2.1 High-risk devices

High-risk devices are life supports, critical monitoring, energy emitting and other devices whose failure or misuse is reasonably likely to seriously injure patient or staff. Examples include:

- Anesthesia units
- Anesthesia ventilators
- Apnea monitors
- Argon enhanced coagulation units
- Aspirators
- Auto transfusion units
- Cardiac defibrillator, external or internal
- Electrosurgical units
- External pacemaker
- Fetal monitors
- Heart-lung machine
- Incubators
- Infusion pump
- Invasive blood pressure units
- Pulse oximeters
- Radiation-therapy machines
- Ventilator
- Stent

2.2 Medium-risk devices

These are devices including many diagnostic instruments whose misuse, failure or absence (e.g. out of service) with no replacement available would have a significant impact on patient care, but would not be likely to cause direct serious injury. Examples include:

- ECG
- EEG
- Treadmills
- Ultrasound sensors
- Phototherapy units
- Endoscopes
- Human-implantable RFID chips
- Surgical drill and saws
- Laparoscopic insufflators
- Phonocardiographs
- radiant warmers (adult)
- Zoophagous agents (e.g., medicinal leeches; medicinal maggots)
- Lytic bacteriophages

2.3 Low-risk devices

Devices in this category are those whose failure or misuse is unlikely to result in serious consequences. Examples include:

- Electronic thermometer,
- Breast pumps
- Surgical microscope
- Ultrasonic nebulizers
- Sphygmomanometers
- Surgical table
- Surgical lights.
- Temperature monitor
- Aspirators
- X-ray diagnostic equipment
- Lensometer
- keratometer
- LifeGuard30

3. Regulations for Medical Device and the Role of Guidance Documents in Europe.

3.1 Introduction:

Before the introduction of the medical device directives nearly 20 years ago, European regulation of medical devices was a patchwork of differing requirements. No two countries had the same system for regulating medical devices. Some countries had published regulations for certain types of medical products, such as sterile medical devices; others maintained lists of devices that were regulated based on perceived risk or national experience; certain countries classified some devices as medicinal products while subjecting others to specific device regulations. In yet other countries, medical devices were not subject to a regulatory regime or were regulated under voluntary systems of control. These differences represented a significant barrier to trade, which also affected other industrial sectors.

At that time, many will agree that the strongest point of reference for a comprehensive system of regulating medical devices rested with the United States (US) Food and Drug Administration (FDA). The US Medical Device Amendments of 1976 and the establishment of the Bureau of Medical Devices, later merged with the Bureau of Radiological Health to become the Center for Devices and Radiological Health, allowed FDA to provide a specific set of requirements for medical devices, which differed in important ways from the manner in which it regulated pharmaceuticals and other products.

The US system was certainly known to European regulators. Subsequently, the European Commission pressured countries to stop the development of their own systems for regulating medical devices, because European harmonisation efforts were underway. Other contacts between the United States and Europe included the Tripartite Subcommittee for Medical Devices, which fostered a mutual awareness of US and UK device regulatory systems. The Tripartite Subcommittee consisted of senior officials of the medical device authorities of the United States, United Kingdom and Canada and produced through its Toxicology Subgroup, the Tripartite Biocompatibility Guidance for Medical Devices of 1987, to

which FDA still refers today. In spite of this close contact, Europe chose to adopt a system for regulating medical devices that differed in significant ways from the United States or other regulatory regimes.

As a result of considerable effort by a number of interested parties, including industry segments, medical devices were included in the products covered by Europe's **"New Approach"** to technical harmonisation. This approach, introduced by a European Council resolution in **1985,** addressed a persistent and frustrating problem in Europe unofficially termed Eurosclerosis. This unfortunate condition meant that by the time European directives containing very detailed technical provisions were adopted, they were already obsolete.

To counter this, the **New Approach directives** referenced a list of essential requirements that become legally binding when transposed into national laws and regulations. The detailed technical provisions are provided in harmonised standards adopted and updated by European standards organisations CEN and CENELEC. Although these standards are voluntary, they confer a presumption of conformity with the relevant essential requirements. Products that are in compliance with the directives are then able to circulate throughout the European Economic Area.

The **medical device directives** are "**New Approach directives**".

- The Active Implantable Medical Devices Directive (**90/385/EEC**) (**AIMDD**) was adopted on 20 June 1990 and became mandatory on 1 January 1995.
- The In Vitro Diagnostic Medical Devices Directive (**98/79/EC**) (**IVDD**) was adopted on 27 October 1998 and became mandatory on 7 December 2003.
- The Medical Devices Directive (**93/42/EEC**) (**MDD**) was adopted on 14 June 1993 and became mandatory on 15 June 1998.

Medical devices that comply with the relevant directive, as transposed by each European country into national laws and regulations, can be sold throughout Europe, which addresses the previous dramatic lack of medical device harmonisation in the region. Most readers will be aware that some differences persist from country to country, most notably national language and registration requirements, but the situation is markedly improved from 20 years ago.

3.2 Guidance Documents:

"Guidance documents" are the strongest documented consensus of how directives or specific parts of a directive are interpreted. And many of the entities involved in the medical device industry in Europe have designated groups that issue these guidance documents. A simple way to think about guidance is as a set of instructions or directions, just as instructions for use are required for certain devices, guidance documents further explain the legislation.

a) Major Players in the Regulation of Medical Devices in Europe

Numerous entities play a role in assessing, evaluating and modifying regulations for medical devices in Europe; hence, many entities issue guidance documents. As you might imagine, there are many organizations and committees dealing with various issues that are important to specific device categories. However, certain groups exert significant influence.

Let's start with a succinct legislative primer: The European Commission is involved in proposing legislation. In each member state, the competent authorities all have national rules and regulations in addition to the transposed Medical Device Directive (MDD). In addition, notified bodies, such as BSI and TÜV, play an active role in the medical device industry.

Similar to the hierarchy that existed for standards, there exists some semblance of a hierarchy for guidance; such documents from the EU Commission are the **most** significant, and MEDDEV guidance documents are more significant than NB-MED guidelines. And, similar to vertical and horizontal standards, there are "vertical" and "horizontal" guidance documents.

b) The Major Guidance Documents.

- **EU Commission Guidance** - The European Commission was granted the "right of initiative" in the legislative process to propose legislation that is ratified by the European Parliament and Council. In this capacity, the EU Commission also publishes guidance to provide explanations to the directives. As an example, the EU Commission published EU Guidelines on the application of the Directive **89/336/EEC** on the approximation of the laws of the member states relating to electromagnetic compatibility. The guidance was developed to explain the "requirements for compliance with the provisions of the EMC Directive." Even more significant, the EU Commission has provided guidance on the "New Approach Standardisation in the Internal Market"- this is an extensive repository of resources.

- **MEDDEV Guidance Documents** - The EU Commission established the Medical Device Expert Group (MDEG). It is composed of delegates from member state competent authorities and other EU well-known organizations including EUCOMED, EDMA, CEN, CENELEC, NB-MED and EAAR. The MDEG is most well known for the guidance documents it publishes, MEDDEV Guidance Documents. These items reflect the consensus position of its members on such issues as the demarcation between the MDD and AIMDD Directive, definition of an accessory, classification of devices, translation procedures and much more. The opinion of this group is not legally binding but is considered the "highest" of guidelines in the industry.
  The MDEG meets regularly to discuss common issues and discusses the drafting of new guidance documents. More than 10 sub-groups of the MDEG contribute; some of them include the Market Surveillance Operation Group; Vigilance Expert Group; and New & Emerging Medical Device Technologies Working Group. Currently, 28 MEDDEVs have been issued, and they are all available on the EU Commission Europa Web site. Let's discuss them in more detail.

- **NB-MED Guidance Documents** - The EU Commission and individual countries formed the Notified Body Operations Group (NBOG) in 2000 to address concerns about the inconsistent performance of notified bodies in medical devices and the competent authorities responsible for them. Essentially, the NBOG identifies and communicates "best practices" for notified bodies and reports on their progress at the semi-annual meeting of the Competent Authorities and the MDEG. One member of the NBOG

usually produces a written guidance, which is then circulated to the other members for comment.

c) Competent Authority Issued Guidance Documents

Competent authorities and the National Ministries of Health, in each member state, enforce the medical device directives. Each country has transposed these directives into their national law; therefore, competent authorities also can describe their opinions in guidance documents. Such guidance may be applicable if a manufacturer is distributing its device in a specific member state. As an example, in Ireland, the Medical Devices Department of the Irish Medicines Board issues pertinent guidance. In December, the group issued a guidance document titled, Guide for Manufacturers of System and Procedure Packs Regarding Legislative Requirements.
It is important to know that when this transposition occurs, differences can occur from country to country. Individual competent authorities may have differing interpretations on the meaning of what was originally approved, and additional differences can occur due to simple translation errors.

3.3 Medical Device Directive:

The **Medical Device Directive** (Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ No L 169/1 of 1993-07-12) is intended to harmonise the laws relating to medical devices within the European Union. The MD Directive is a 'New Approach' Directive and consequently in order for a manufacturer to legally place a medical device on the European market the requirements of the MD Directive have to be met. Manufacturers' products meeting 'harmonised standards' have a presumption of conformity to the Directive. Products conforming with the MD Directive must have a **CE mark** applied. The Directive was most recently reviewed and amended by the 2007/47/EC and a number of changes were made. Compliance with the revised directive became mandatory on March 21, 2010.

The **CE marking** (also known as **CE mark**) is a mandatory conformance mark on many products placed on the single market in the European Economic Area (EEA). The **CE marking** certifies that a product has met EU consumer safety, health or environmental requirements. CE stands for *conformité européenne*, French for "European conformity". By affixing the CE marking to a product, the manufacturer – on his sole responsibility – declares that it meets EU safety, health and environmental requirements.

CE mark:

Existing in its present form since 1993, the CE marking is a key indicator of a product's compliance with EU legislation and enables the free movement of products within the European market. By affixing the CE marking on a product, a manufacturer is declaring, on his sole responsibility, conformity with all of the legal requirements to achieve CE marking and therefore ensuring validity for that product to be sold throughout the European Economic Area. This also applies to products made in third countries which are sold in the EEA.

a) The main goals of the CE Marking

• To indicate a product's conformity with the **"essential requirements"** (e.g. safety, health, environmental protection requirements) of the applicable directive(s) – or, if stipulated in the directive(s), had it examined by a notified conformity assessment body.
• To allow products to be "placed on the market"
• To ensure the "free movement of goods"
• To allow the "withdrawal of non-conforming products" by customs and enforcement authorities

b) Countries requiring the CE Marking

The CE marking is mandatory for certain product groups in the European Economic Area (EEA), consisting of the 27 Member States of the EU and EFTA countries Iceland, Norway and Liechtenstein. It is also obligatory for all products made in third countries (non-member states) which are sold in the EEA. In that case, the importer has to make sure that the manufacturer outside the EU has taken the necessary steps that allow him to affix the CE marking.
It is still not required within the member countries of the Central European Free Trade Agreement (CEFTA), although some of them (Republic of Macedonia, Croatia, Serbia, Montenegro) are official candidates for membership to the European Union, and are already adopting many of its standards within their legislation (like most of the former Central European countries that were members of CEFTA before joining the EU).

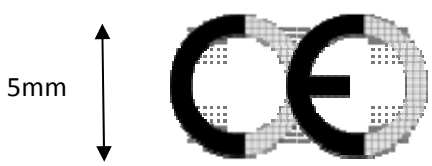
c) Rules underlying CE marking

There are certain rules underlying the procedure to affix the marking:

- Products that are subject to certain EC directives providing for CE marking, have to be affixed with the CE marking before they can be placed on the market
- Manufacturers have to check on their sole responsibility, which EU directives they need to apply for their products
- The product may only be placed on the market if it complies with the provisions of all applicable directives and if the conformity assessment procedure has been carried out accordingly
- The manufacturer draws up an EC declaration of conformity and affixes the CE marking on the product
- If stipulated in the directive(s), an authorized third party (Notified Body) must be involved in the conformity assessment procedure
- If the CE marking is affixed on a product, it can only bear additional markings under the condition that they are of different significance, do not overlap with the CE marking and are not neither confusing and not nor impairing the legibility and visibility of the CE marking

d) Characteristics of the CE marking

The CE conformity marking shall consist of the initials 'CE' taking the following form:



- The size of the CE marking must be at least 5 mm, if enlarged or reduced its proportions have to be kept and respected.
- If the appearance and workmanship of a product do not allow for the CE marking to be affixed on the product itself, the marking has to be affixed to its packaging or accompanying documents
- If a directive requires the involvement of a Notified Body in the conformity assessment procedure, its identification number has to be put behind the CE marking. This is done under the responsibility of the Notified Body.
- This minimum dimension may be waived for small-scale devices.

e) Confusing CE marks

Some products have a CE symbol that has been alleged to stand for China Export and is confusingly very similar to the E.U.'s CE mark. The two letters are close together, not spaced as in the European conformance mark.

European conformance CE mark

"China Export" CE symbol

Some products may be conforming but not displaying the logotype correctly and others may illegally put the correct mark on non-conforming items, or on an item without the required accompanying certificate of conformity

3.4 Declaration of Conformity:

A Declaration of Conformity is a written declaration containing directive specific information that the manufacturer can enclose in the packaging with each product shipped. The master copy must be kept available for reference by the relevant authorities for 10 years after the final production date.

File Components:

- Declaration of Conformity
- Name and address of responsible person
- Description (essential characteristics) of the apparatus
- Numbers and titles of standards applied
- Declaration that the product conforms with the protective requirements of the Directive
- Signature of (or on behalf of) manufacturer or authorized representative
- Date of issue.

3.5 Notified Bodies:

Notified Bodies: are a vital element of the European regulatory system, a public or private organisation that has been accredited to **validate the compliance of the device to the European Directive**, as they are responsible **for assessing technical documentation** and issuing certificates needed for the CE marking process. They need to be competent to carry out these critical tasks, yet not all Notified Bodies have equivalent resources and expertise. Measures are being taken to improve this situation; the publication of best practices guides by the Notified Bodies Operations Group set up by the European Commission and member states is one example. Not all member states are equally effective in overseeing the Notified Bodies operating within their territories. If a manufacturer contracts with a Notified Body that is unable to perform as needed, many parties are potentially adversely affected, not least of which are the patients and users of the devices concerned. The quality of Notified Bodies needs to be better ensured and the variability in competence minimised.

3.6 Medical Device Essential Requirements and Regulations.

a) How are medical devices regulated in Europe?

The three Directives are based on the European Commission's New Approach which is designed to protect consumers (in these instance patients) and to allow the free movement of goods. The new Approach Directives are based on the following principles; harmonization is limited to essential requirements, only products fulfilling the essential requirements may be placed on the market. The application of harmonized standards or other specifications remains voluntary and manufacturers are free to choose any technical solution that provides compliance with the essential requirements.
The system is best understood by considering the operation of the Medical Devices Directive which is the core of the legislation. It defines three categories of device, graded accordingly to the risk assessment. The **essential requirements** (Annex I of the Directive 93/42/EEC) are the standards which have been met by the manufacturer for quality systems for the design, production release marketing of the product and its individual risk assessment. The level of control, supervision and the content of data to support the product depend on the categorization.
In the European system, manufacturers of devices of **high-risk devices** (**class II and III**), as well as devices of class I with either measuring function or sterility requirements, must submit to the regulator (competent authority):

(1) a Declaration of Conformity to the appropriate EC Directives, and
(2) details of the conformity assessment procedure followed.

In addition, for higher risk class devices that require design examination or type examination, the corresponding EC-Certificates issued by a notified body must also be submitted to the competent authority.
Other medical devices of **low risk** (**class I**) are exempt from pre-market submissions, although they must follow the essential principles of safety and performance in their design, construction and labeling requirements.
The Notified Bodies check the development and the designs of the device. They also review the clinical studies, which have been undertaken, monitor the quality control procedures and the production of the device. Once the device has been granted a CE mark in one Member State, it can be marketed in all the other European Member States without further controls and no further evaluations. This is significantly

different from the position for medicines. Thus if a German Notified Body approves the device, then the manufacturer can market it immediately in the UK and any other EU country.

b) Data requirements and format of the application dossier

Each application for consultation shall be submitted to the EMEA using the relevant application form, that can be found on the EMEA website and containing the information described in this document. Guidance on data requirements and format of the application dossier can be found in Appendix 1. For its preparation the EMEA has taken as basis the MEDDEV guidance 2.1/3 rev 2, July 2001 and supplemented this with guidance of EudraLex Notice to Applicants Volume 2B (Presentation and content of the dossier – CTD). In addition, references to specific guidance available for plasma-derived medicinal products, biological/biotechnological products and new chemical entities are given.
For ancillary human blood derivatives, the notified body has to provide information to the EMEA regarding the "context"3 that the human blood derivative will be used in, in order to ensure that the EMEA can give an opinion on the quality and safety of the substance and at the same time assess its usefulness within that context and reach a conclusion on the risk/benefit ratio for its incorporation in the medical device.
For medicinal substances, with ancillary action that are incorporated in a medical device, the safety, quality and usefulness will be verified, taking account of the intended purpose of the device, by analogy with the appropriate methods specified in Directive 75/318/EEC (this reference has to be understood as **Annex I** to Directive 2001/83/EC as amended).
According to MEDDEV guidance 2.1/3 rev 2, July 2001, the aspect of "usefulness" relates to the rationale for using the medicinal substance in relation to the specific intended purpose of the device. It refers to the suitability of the medicinal substance to achieve its intended action, and whether the potential inherent risks (aspects of "safety") due to the medicinal substance are justified in relation to the benefit to be obtained within the intended purpose of the device.

C) Summary of the Essential Requirements Medical device Directive 93/42/EEC.

Manufacturers of devices or their authorised representatives must:

- Review the classification rules to confirm that their products fall within their Class
- Check that their products meet the Essential Requirements (Annex I of the Directive);
- prepare relevant **technical documentation**
- draw up the “EC Declaration of Conformity” before applying the CE marking to their devices;
- implement and maintain corrective action and vigilance procedures.
- obtain notified body approval for sterility or metrology aspects of their devices, where applicable
- make available relevant documentation on request for inspection by the Competent Authority
- register with the Competent Authority.
- notify the Competent Authority, in advance, of any proposals to carry out a clinical investigation to demonstrate safety and performance of a device as required by the Regulations .

d) Technical Documentation

What is a Technical file and what information should it contain?

A technical file is required by the primary directives to document the conformity assessment and the product's design. The technical file shall be compiled by the manufacturer or authorized representative and contain design documentation, manufacturing, test reports and operation information to show conformity as required by the directives.

File Components:

- Declaration of Conformity (and/or certificate for regulated products)
- The name and address of the manufacturer and identification of the products
- European agent's name and address, if applicable
- List of harmonized standards followed and/or the solutions adopted to satisfy the ERs
- Description of the product (model, name, etc.…)
- Operating instructions
- Test report(s)
- Design details, description of operation, components list, test rationale, circuits and diagrams –including items necessary to understand the solutions adopted to satisfy the ERs
- Technical Construction File (TCF) – This is a special technical file for regulated products, high-risk machines (Annex IV machinery), and occasionally for EMC (large equipment, etc.), where the use of a Notified or Competent Body is mandatory.

4. Medical Device Classification in Europe

4.1 Purpose and philosophy Of Medical Device Classification

It is not feasible economically nor justifiable in practice to subject all medical devices to the most rigorous conformity assessment procedures available. A graduated system of control is more appropriate. In such a system, the level of control corresponds to the level of potential hazard inherent in the type of device concerned. A medical device classification system is therefore needed, in order to apply to medical devices an appropriate conformity assessment procedure.

In order to ensure that conformity assessment under the Medical Device Directive functions effectively, manufacturers should be able to determine the classification of their product as early as possible in device development. It was therefore decided to set up a system of classification rules within the Directive, so that each manufacturer could classify its own devices.

The classification of medical devices is a '**risk based'** system based on the vulnerability of the human body taking account of the potential risks associated with the devices.

These are referred to as the 'classification rules' and are set out in Annex IX of Directive 93/42/EEC. They correspond, to a large extent, to the classification rules established by the Global Harmonization Task Force (GHTF) in the guidance document GHTF/SG1/N15:20063.

In addition there may be devices that cannot be classified by the existing rules because of their unusual nature or situations where the classification would result in the wrong level of conformity assessment in light of the hazard represented by the device.

4.2 How to carry out classification

The manufacturer should first decide if the product concerned is a medical device as defined in Directive 93/42/EEC or an accessory to such a medical device, if it is not excluded from the scope of this Directive and if it therefore comes within the scope of this Directive.

Basic definitions

The classification rules are based on different criteria such as:

- The **duration** of contact with the patient,
- The degree of **invasiveness** and
- The part of the **body** affected by the use of the device.

Intended purpose is defined in Article 1 paragraph 2(g) of Directive 93/42/EEC.
The other terms are defined in chapter I section 1 of Annex IX of Directive 93/42/EEC.

1) Intended purpose:

"Intended purpose" means the use for which the device is intended according to the data supplied by the manufacturer on the labelling, in the instructions and/or in promotional materials.

2) Time:

a) Duration

Transient: Normally intended for continuous use for less than 60 minutes.
Short term: Normally intended for continuous use for not more than 30 days.
Long term: Normally intended for continuous use for more than 30 days.
In certain instances the duration of effect for a product needs to be considered as the duration of use. For instance, application of a topical cream to the skin may only take seconds to apply but the cream may remain in situ for many hours. The duration of use should therefore not be considered as the time taken to apply the product but rather the duration for which the product achieves its intended purpose.

b) Concept of continuous use

In calculating the duration referred to in Section 1.1 of Chapter I of Annex IX to Directive 93/42/EEC, continuous use means "an uninterrupted actual use of the device for the intended purpose. However where usage of a device is discontinued in order for the device to be replaced immediately by the same or an identical device this shall be considered as an extension of the continuous use of the device" (Section 2.6 of Chapter II of Annex IX to Directive 93/42/EEC).
For example, a scalpel may be used on the same patient throughout an operation that may last for several hours. The uninterrupted use for an intended purpose, i.e. cutting tissue, will normally not last for more than a few seconds at a time. Therefore a scalpel is a transient use device. However where usage of a device is discontinued in order for the device to be replaced immediately by the same or an identical device (e.g. replacement of a ureteric catheter) this shall be considered an extension of the continuous use of the device.
If it cannot be demonstrated that components of the device is totally eliminated in the interval between uses, this is also considered as an immediate replacement.

3) Invasiveness:

- Invasive devices A device which, in whole or in part, penetrates inside the body, either through a body orifice or through the surface of the body.
- Body orifice Any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma.
- Surgically invasive device An invasive device which penetrates inside the body through the surface of the body, with the aid of or in the context of a surgical operation.

For the purposes of this Directive devices other than those referred to in the previous subparagraph and which produce penetration other than through an established body orifice, shall be treated as surgically invasive devices.
The term surgical operation used in this definition includes all clinical interventional procedures in which a device is placed into the body through the surface in the context of a surgical operation or other clinical procedure.

In this context it should be noted the following:
►A surgically created stoma used in urostomy, colostomy and ileostomy or permanent tracheostomy is considered to be a body orifice. Therefore devices introduced into such a stoma are not surgically invasive. A surgically created opening to allow access to the circulatory system in contrast should not be considered to be such a "body orifice". Devices introduced into such an opening are surgically invasive.
►A device that administers energy to the body should not be considered as invasive if only energy penetrates the body and not the device itself. Energy as such is not a device and therefore it cannot be classified. Only the device generating the energy must be classified. However, if a device administers a substance, whether this substance is a medicine or a medical device, such a substance must be assessed in its own right (e.g. substances administeredby a jet injector).
Any device which, in whole or in part, penetrates inside the body, either through a natural body orifice or through the surface of the body is an invasive device. A surgically invasive device always implies that it enters through an artificially created opening. This can be a large opening, such as a surgical incision, or it can be a pinprick opening created by a needle. Therefore surgical gloves and needles used with syringes are surgically invasive.
The concept of surgically invasive should be understood as covering also liquids that are in invasive contact with organs, tissue or other parts of the body if the access for such liquids is through a surgically created opening.

- Reusable surgical instrument Instrument intended for surgical use by cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without connection to any active medical device and which can be reused after appropriate procedures have been carried out (Section 1.3 of Annex IX of Directive 93/42/EEC).
- Implantable device Any device which is intended:
  - to be totally introduced into the human body or,
  - to replace an epithelial surface or the surface of the eye, by surgical intervention which is intended to remain in place after the procedure.

Any device intended to be partially introduced into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.
One of the key elements in defining an implantable device is the concept of "procedure". Thus an implantable device must remain in the patient after the procedure. A "procedure" must be understood in this context to include the surgical procedure during which the implant is placed into the body and the immediate post-operative care that is associated with the procedure. The "procedure" does not extend to the conclusion of the therapeutic treatment, e.g. the removal of an
implant must be considered to be another "procedure". Thus a plate used to reduce a fracture of the bone is an implant even if it is taken out after the fracture has healed. In this case the placing of the plate and its explantation are two different surgical procedures.
Some partially implanted devices are deemed to be implants. For instance, if an operation is carried out specifically to place an infusion port into the body, then such an infusion port would remain for at least 30 days after the procedure and consequently be an implant. However, a non-tunnelled central venous catheter which is intended for use for temporary vascular access and intended to be removed after 7 – 10 days is not a long-term implantable device. Nor would a suture used for skin wound closure that is taken out prior to 30 days be considered an implant.

- Critical anatomical locations For the purposes of the Directive 93/42/EEC, **'central circulatory system'** means the following vessels:

arteriae pulmonales, aorta ascendens, arcus aorta, aorta descendens to the bifurcatio aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachiocephalicus, venae cordis, venae pulmonales, vena cava superior, vena cava inferior.
For the purposes of the Directive 93/42/EEC the **'central nervous system'** means brain, meninges and spinal cord.

4) Active medical devices:

Any medical device operation of which depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy. Medical devices intended to transmit energy, substances or other elements between an active medical device and the patient, without any significant change, are not considered to be active medical devices. Stand alone software is considered to be an active medical device.
The concept "act by converting energy" includes conversion of energy in the device and/or conversion at the interface between the device and the tissues or in the tissues.

The concept of "significant changes" includes changes in the nature, level and density of energy (see Rule 9). This means that for instance an electrode is not an active device under this classification system as long as the energy input is intended to be the same as the energy output. For instance, resistance in a wire that causes minor changes between input and output cannot be considered to constitute "significant change". However, electrodes used in electrosurgery for cutting tissues or cauterisation are active devices because their operation depends on energy provided by a generator and their action is achieved by conversion of energy at the interface between the device and the tissue or in the tissue. Electrodes intended for E.C.G. or E.E.G are normally not active devices because they do not normally act by conversion of energy.

However, it should be understood that an electrode, which is an accessory of an active implant, is covered under the relevant Directive for active implants. Further information on this issue can be found in "Guidelines relating to the application of the Council Directive 90/385/EEC on active implantable medical devices5.

The application of energy from the human body does not make a device "active" unless that energy is stored within the device for subsequent release. For instance, energy generated by human muscle and applied to the plunger of a syringe (thus causing a substance to be delivered to a patient) does not make this syringe an "active device". However, if a drug delivery system depends upon manual winding to preload a spring which is subsequently released to deliver a
substance, then the device incorporating the spring is an "active device".

Medical devices using prestored gases and/or vacuum as a power source are regarded as active devices, e.g. gas mixers with anaesthesia machines and gas powered suction pumps.

Heating/cooling pads intended only to release stored thermal energy are not active devices because they do not act by conversion of energy. However, heating/cooling pads which act by chemical action (e.g. endothermic or exothermic reaction) are active devices as they are converting chemical energy into heat energy and or vice versa.

Radioactive sources that are intended to deliver ionising radiation are regarded as active medical devices, unless they are radiopharmaceuticals as defined in article 1 of Directive 2001/83/EC or radioactive implants as defined in article 1 of Directive 90/385/EEC.

5) Devices with a measuring function:

Information on devices with a measuring function can be found in MEDDEV 2.1/56

6) Procedure pack:

Procedure packs per Article 12 of Directive 93/42/EEC normally do not require classification as each device in the procedure pack keeps its own CE marking and classification.

However, in cases where the procedure pack incorporates devices which do not bear a CE marking, or where the chosen combination of devices is not compatible in view of their original intended use, the system or procedure pack shall be treated as a device in its own right and as such be subjected to the relevant procedure pursuant to Article 11 of Directive 93/42/EEC.

For a procedure pack that is a device in its own right, the classification is normally determined by the intended use. In those cases where the intended use of the procedure pack is not specific enough to determine the classification, the classification of the pack is at the level of the highest classified device included in the pack, where applicable taking into account the new intended use of the device.

4.3 Application of the classification rules

In terms of further interpretation of the classification rules, the following should be considered:

- It is the intended purpose that determines the class of the device and not the particular technical characteristics of the device, unless these have a direct bearing on the intended purpose. e.g. incorporation of an ancillary substance, tissue of animal origin etc.
- It is the intended and not the accidental use of the device that determines the class of the device. For instance a suture organizer, that is intended to keep order of suture threads used in open heart surgery, should not be considered as an invasive device if in the normal use it can be kept outside the patient. Similarly, if a medical practitioner uses the device in a manner not intended by the manufacturer, this does not change the class of the device for the purpose of conformity assessment. However, if the normal clinical use of the device changes in time with evolving clinical practice such that the intended purpose and classification of the device changes this should be addressed by the manufacturer and the conformity of the device assessed for the new intended purpose.
- It is the intended purpose assigned by the manufacturer to the device that determines the class of the device and not the class assigned to other similar products. For instance two sutures that have the same composition may well have different intended purposes.
- As an alternative to classifying the system as a whole, the determination of the class of a particular device may be made with respect to the simplest configuration that can still be considered, in view of its proper functional features, as a device in its own right. A device that is part of a system, e.g. a tube in an extra corporeal circulation set, may be classed as a device in its own right rather than classifying the system as a whole. The device, however, must be CE marked in its own right as a separate device in such instances.
- Similarly combination devices with parts that have different functional purposes may be analysed separately with respect to each of these parts. For instance, a drainage device will have an invasive tube and a non-invasive collection device. These components may be classified separately, provided that they are also CE marked separately.
- Accessories are classified in their own right separately from the device with which they are used (Annex IX Section 2.2 of Directive 93/42/EEC).
- If a given device can be classified according to several rules, then the highest possible class applies. For instance, a wound dressing incorporating collagen is covered by rules 4 (Class I, Class IIa or Class IIb depending on intended use) and 17 (Class III). All rules must be considered, for instance if an active device is also surgically invasive, the relevant rules for surgically invasive devices must also be considered.
- If the device is not intended to be used solely or principally in a specific part of the body, it must be considered and classified on the basis of the most critical specified use. Classification of the device will have to be determined on the basis of claims contained in the information provided with the device.

The manufacturer must be sufficiently specific in that regard. If the manufacturer wants to avoid the particular higher classification, then it must clearly define on the labelling the intended purpose in such a way that the device falls into the lower class. The manufacturer must provide as a minimum requirement either appropriate positive or negative indications for use.

- For a device to be "specifically intended" for the purpose referenced in a particular classification rule, the manufacturer must clearly indicate that the device is intended for such a specific purpose in the

information accompanying the device. Otherwise it is deemed to have the intended use which is principally used and accepted in general medical practice.
- Multi-application equipment such as laser printers and identification cameras, which may be used in combination with medical devices, are not medical devices unless their manufacturer places them on the market with specific intended purpose as medical devices.
- Due to its complexity, classification of standalone software will be covered in a specific guidance document.

4.4 How to use the rules

The manufacturer must take into consideration all the rules in order to establish the proper classification for its device. It is quite conceivable for instance that one of the general rules that are not specific to active devices, nevertheless applies to such a device. All the device characteristics must be taken into consideration.
The characteristic or combination of characteristics in accordance with the intended purpose of the device that rates the highest class determines the class for the device as a whole.
By derogation to the classification rules set out in Annex IX of Directive 93/42/EEC, the manufacturers must also take account of additional Directives which may affect the classification of their device or the conformity route to be followed, e.g. 14

- Directive 2003/12/EC7 on the reclassification of breast implants in the framework of Directive 93/42/EEC concerning medical devices.
- Directive 2005/50/EC8 on the reclassification of hip, knee and shoulder joint replacements in the framework of Council Directive 93/42/EEC concerning medical devices.
- Directive 2003/32/EC9 introducing detailed specifications as regards the requirements laid down in Council Directive 93/ 42/EEC with respect to medical devices manufactured utilising tissues of animal origin.

4.5 Practical example

A simple wound drainage device has three components that must be taken into consideration: the cannula, the tubing and the collector unit. If the device is sold without a cannula, then the classification of the cannula does not need to be taken into account. It is assumed here that the device is used for short term duration, i.e. that uninterrupted intended use is more than 60 minutes and less than 30 days. It is furthermore assumed that the collected liquids are not intended to be re infused into the body nor reprocessed for eventual re infusion and that the device is not intended to be connected to a powered suction system.
Intended uses Rule Class
Surgically invasive cannula to reach a wound site in the pleural cavity to drain the cavity IIa
Non-invasive tubing to evacuate body liquids towards the collector. I
Non-invasive collector to receive the body liquids I

The clear conclusion here is that the manufacturer would have a choice of applying Class II A to the whole device or carrying out separate conformity assessment procedures for the cannula on one hand and the tubing and collector on the other hand.

In case the manufacturer is unsure how its devices should be classified, it should first consult a Notified Body.
In case doubts remain or there is a disagreement with the Notified Body, the relevant Competent Authority (i.e. the Competent Authority to which the notified body
is subject) should be approached in accordance with Article 9 of Directive 93/42/EEC.
In addition, Directive 93/42/EEC provides Community wide mechanisms, including a committee procedure, to address problems related to classification.
Complex classification issues may be referred to the 'Borderline and Classification Medical Devices Expert Group' for resolution. Consensus positions on classification reached by this Expert Group are published for reference in the Manual on Borderline and Classification10.
In addition, MEDDEV 2.1/3 rev 311 provides with useful information relating to devices incorporating, as an integral part, a substance which, if used separately, can
be considered to be a medicinal product or a human blood derivative, and which is liable to act on the human body with action ancillary to that of the devices.

4.6 Explanations of individual rules

The explanations are given in the following manner. This section begins with a graphical summary of the rules, as a preface to subsections on the individual rules.
Each subsection starts with a general explanation of the rule followed by a tabular presentation of the rule and examples of devices to which it applies. Any special terms used are explained and practical issues related to the rule are clarified. It must be emphasised that even if a particular device type is given as an example, this does not mean that such devices are in all cases in the class indicated by the example. It is always possible that some manufacturer will assign to such a device an entirely different intended use than what was used in the context of the example.

4.7 Graphical summary – medical devices classification guidance chart for initial identification of probable device class

Note: Always confirm definitive classification by reading all rules in detail, and utilise additional assistance in this guidelines document as provided in the form of general explanations of rules and examples of devices.

SUBJECTS
Non invasive devices – Rules 1, 2, 3, 4
Invasive devices – Rules 5, 6, 7, 8
Active devices – Rules 9, 10, 11, 12
Special rules – Rules 13, 14, 15, 16, 17, 18

4.8 General explanation of rules /Practical issues / examples

- **Rule 1 - Devices that either do not touch the patient or contact intact skin only General explanation of the rule**

This is a fallback rule applying to all devices that are not covered by a more specific rule.

This is a rule that applies in general to devices that come into contact only with intact skin or that do not touch the patient.

RULE 1	**EXAMPLES**
All non-invasive devices are in Class I, unless one of the rules set out hereinafter applies.	- Body liquid collection devices intended to be used in such a way that a return flow is unlikely (*e.g.* to collect body wastes such as urine collection bottles, ostomy pouches, incontinence pads or collectors used with wound drainage devices). They may be connected to the patient by means of catheters and tubing - Devices used to immobilise body parts and/or to apply force or compression on them (*e.g.* non-sterile dressings used to aid the healing of a sprain, plaster of Paris, cervical collars, gravity traction devices, compression hosiery) - Devices intended in general for external patient support (*e.g.* hospital beds, patient hoists, walking aids, wheelchairs, stretchers, dental patient chairs) - Corrective glasses and frames - Stethoscopes for diagnosis. - Eye occlusion plasters - Incision drapes - Conductive gels - Non-invasive electrodes (electrodes for EEG or ECG) - Image intensifying screens - Permanent magnets for removal of ocular debris

Practical issues of classification

Some non-invasive devices are indirectly in contact with the body and can influence internal physiological processes by storing, channelling or treating blood, other body liquids or liquids which are returned or infused into the body or by generating energy that is delivered to the body. These must be excluded from the application of this Rule and be handled by another rule because of the hazards inherent in such indirect influence on the body.

- **Rule 2 - Channeling or storing for eventual administration General explanation of the rule**

These types of devices must be considered separately from the non-contact devices of rule 1 because they may be indirectly invasive. They channel or store substances that will eventually be administered to the body. Typically these devices are used in transfusion, infusion, extracorporeal circulation and delivery of anaesthetic gases and oxygen.

In some cases devices covered under this rule are very simple gravity activated delivery devices.

RULE 2	EXAMPLES
All non-invasive devices intended for channelling or storing blood, body liquids or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are in Class IIa: - if they may be connected to an active medical device in Class IIa or a higher class,	- Devices intended to be used as channels in active drug delivery systems, *e.g.* tubing intended for use with an infusion pump - Devices used for channelling, *e.g.* antistatic tubing for anaesthesia, anaesthesia breathing circuits, pressure indicator, pressure limiting devices - Syringes for infusion pumps
- if they are intended for use for storing or channelling blood or other body liquids or for storing organs, parts of organs or body tissues	- Devices intended to channel blood (*e.g.* in transfusion, extracorporeal circulation) - Devices intended for temporary storage and transport of organs for transplantation (*i.e.* containers, bags and similar products) - Devices intended for long term storage of biological substances and tissues such as corneas, sperm, human embryos, etc. (*i.e.* containers, bags and similar products) - Fridges specifically intended for storing blood , tissues etc
- in all other cases they are in Class I. -	Devices that provide a simple channelling function, with gravity providing the force to transport the liquid, *e.g.* administration sets for infusion - Devices intended to be used for a temporary containment or storage function, *e.g.* cups and spoons specifically intended for administering medicines - Syringes without needles

Practical issues of classification

Blood bags are covered as an exception under a separate rule (see Rule 18).

If a device, *e.g.* tubing, can be used for a purpose that would cause it to be connected to an active device such a device will be automatically in Class IIa, unless the manufacturer clearly state that it should not be connected to an active device of Class IIa or higher.

Explanation of special concepts

Note 1: "May be connected to an active device". Such a connection is deemed to exist between a non-active device and an active device where the non-active device forms a link in the transfer of the substance between the patient and the active device and the safety and performance of one of the devices is influenced by the other device. For instance, this applies to tubing in an extracorporeal circulation system which is downstream from a blood pump and in the same blood flow circuit, but not directly in contact with the pump.

- **Rule 3 – Non-invasive devices that modify biological or chemical composition of blood, body liquids or other liquids intended for infusion into the body**

General explanation of the rule

These types of devices must be considered separately from the non-contact devices of Rule 1 because they are indirectly invasive. They modify substances that will eventually be infused into the body. This rule covers mostly the more sophisticated elements of extracorporeal circulation sets, dialysis systems and autotransfusion systems as well as devices for extracorporeal treatment of body fluids which may or may not be immediately reintroduced into the body, including, where the patient is not in a closed loop with the device.

RULE 3	EXAMPLES
All non-invasive devices intended for modifying the biological or chemical composition of blood, other body liquids or other liquids intended for infusion into the body are in Class IIb,	- Devices intended to remove undesirable substances out of the blood by exchange of solutes such as hemodialysers - Devices intended to separate cells by physical means, *e.g.* gradient medium for sperm separation - Haemodialysis concentrates
unless the treatment consists of filtration, centrifugation or exchange of gas or heat, in which case they are in Class IIa.	- Particulate filtration of blood in an extracorporeal circulation system. These are used to remove particles and emboli from the blood - Centrifugation of blood to prepare it for transfusion or autotransfusion - Removal of carbon dioxide from the blood and/or adding oxygen - Warming or cooling the blood in an extracorporeal circulation system

Practical issues of classification

These devices are normally used in conjunction with an active medical device covered under Rule 9 or Rule 11.
Filtration and centrifugation should be understood in the context of this rule as exclusively mechanical methods.

- **Rule 4 - Non-invasive devices which come into contact with injured skin**

General explanation of the rule

This rule is intended to primarily cover wound dressings independently of the depth of the wound. The traditional types of products, such as those used as a mechanical barrier, are well understood and do not result in any great hazard. There have also been rapid technological developments in this area, with the emergence of new types of wound dressings for which non-traditional claims are made, *e.g.* management of the micro-environment of a wound to enhance its natural healing mechanism.
More ambitious claims relate to the mechanism of healing by secondary intent, such as influencing the underlying mechanisms of granulation or epithelial formation or preventing contraction of the wound.
Some devices used on breached dermis may even have a life-sustaining or lifesaving purpose, *e.g.* when there is full thickness destruction of the skin over a large area and/or systemic effect.
Dressings containing medicinal products which act ancillary to the dressing fall within Class III under Rule 13.

RULE 4	EXAMPLES
All non-invasive devices which come into contact with injured skin: - are in Class I if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates,	- Wound dressings, such as: absorbent pads, island dressings, cotton wool, wound strips, adhesive bandages (sticking plasters, band-aid) and gauze dressings which act as a barrier, maintain wound position or absorb exudates from the wound
- are in Class IIb if they are intended to be used principally with wounds which have breached the dermis and can only heal by secondary intent	- Are principally intended to be used with severe wounds that have substantially and extensively breached the dermis, and where the healing process can only be by secondary intent such as: - dressings for chronic extensive ulcerated wounds - dressings for severe burns having breached the dermis and covering an extensive area - dressings for severe decubitis wounds - dressings incorporating means of augmenting tissue and providing a temporary skin substitute
- are in Class IIa in all other cases, including devices principally intended to manage the micro-environment of a wound.	- Have specific properties intended to assist the healing process by controlling the level of moisture at the wound during the healing process and to generally regulate the environment in terms of humidity and temperature, levels of oxygen and other gases and pH values or by influencing the process by other physical means - These devices may specify particular additional healing properties whilst not being intended for extensive wounds requiring healing by secondary intent. - Adhesives for topical use - Polymer film dressings - Hydrogel dressings - Non-medicated impregnated gauze dressings

Practical issues of classification

Products covered under this rule are extremely claim sensitive, *e.g.* a polymeric film dressing would be in Class IIa if the intended use is to manage the micro-environment of the wound or in Class I if its intended use is limited to retaining an invasive cannula at the wound site. Consequently it is impossible to say *a priori* that a particular type of dressing is in a given class without knowing its intended use as defined by the manufacturer. However, a claim that the device is interactive or active with respect to the wound healing process usually implies that the device is in Class IIb.

Most dressings that are intended for a use that is in Class IIa or IIb, also perform functions that are in Class I, *e.g.* that of a mechanical barrier. Such devices are nevertheless classed according to the intended use in the higher class.

For such devices incorporating a medicinal product or a human blood derivative see Rule 13 or animal tissues or derivatives rendered non-viable see Rule 17.

Explanation of special concepts

- Breached dermis: the wound exposes at least partly the subcutaneous tissue.
- Secondary intent: the wound heals by first being filled with granulation tissue, subsequently the epithelium grows back over the granulation tissue and the wound contracts. In contrast primary intent implies that the edges of the wound are close enough or pulled together, *e.g.* by suturing, to allow the wound to heal.
- A skin might be considered as "injured" either because of pathological (*e.g.* diabetic ulcers) or external factors (*e.g.* burns)

- **Rule 5 - Devices invasive with respect to body orifices /General explanation of the rule**

Invasiveness with respect to the body orifices (ear, mouth, nose, eye, anus, urethra and vagina) must be considered separately from invasiveness that penetrates through a cut in the body surfaces (surgical invasiveness). For short term use, a further distinction must be made between invasiveness with respect to the less vulnerable anterior parts of the ear, mouth and nose and the other anatomical sites that can be accessed through natural body orifices.
Surgically created stoma, which for example allows the evacuation of urine or faeces, should also be considered as a body orifice.
Devices covered by this rule tend to be diagnostic and therapeutic instruments used in particular specialities (ENT, ophthalmology, dentistry, proctology, urology and gynaecology).

RULE 5	**EXAMPLES**
All invasive devices with respect to body orifices, other than surgically invasive devices and which are not intended for connection to an active medical device or which are intended for connection to an active medical device in Class I:	
- are in Class I if they are intended for transient use,	- Handheld mirrors used in dentistry to aid in dental diagnosis and surgery - Dental impression materials - Tubes used for pumping the stomach - Impression trays - Enema devices - Examination gloves - Urinary catheters intended for transient use - Prostatic balloon dilation catheters
- are in Class IIa if they are intended for short term use	- Short term corrective contact lenses - Tracheal tubes - Stents - Vaginal pessaries - Indwelling urinary catheters intended for short term use
except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in a nasal	- Dressings for nose bleeds - Materials for manufacturing dentures

cavity , in which case they are in Class I,	
- are in Class IIb if they are intended for long term use,	- Urethral stents - Long term corrective contact lenses - Tracheal cannulae - Urinary catheters intended for long term use
except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in a nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are in Class IIa.	- Orthodontic wires - Fixed dental prostheses - Fissures sealants
All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to an active medical device in Class IIa or a higher class, are in Class IIa.	- Tracheostomy or tracheal tubes connected to a ventilator - Blood oxygen analysers placed under the eye-lid - Powered nasal irrigators - Nasopharyngeal airways - Some enteral feeding tubes - Fibre optics in endoscopes connected to surgical lasers - Suction catheters or tubes for stomach drainage - Dental aspirator tips

- **Rule 6 - Surgically invasive devices intended for transient use (< 60 minutes*)***

General explanation of the rule

This rule primarily covers three major groups of devices: devices that are used to create a conduit through the skin (needles, cannulae, etc.), surgical instruments (scalpels, saws, etc.) and various types of catheters, suckers, etc.

RULE 6	**EXAMPLES**
All surgically invasive1 devices intended for transient use are in Class IIa unless they are:	- Needles used for suturing - Needles of syringes - Lancets - Suckers - Single use scalpels and single use scalpel blades - Support devices in ophthalmic surgery - Staplers - Surgical swabs - Drill bits connected to active devices - Surgical gloves - Etchants - Tester of artificial heart valves - Heart valve occluders, sizers and holders - Swabs to sample exudates - Single use aortic punches (see note 2)
- intended specifically to control, diagnose, monitor or correct a defect 2 of the heart or of the central circulatory system1 through direct contact with these parts of the body, in which case they are in Class III 3	- Cardiovascular catheters (*e.g.* angioplasty balloon catheters, stent delivery catheters/systems), including related guidewires, related introducers and dedicated4 disposable cardiovascular surgical instruments *e.g.*

	electrophysiological catheters, electrodes for electrophysiological diagnosis and ablation - Catheters containing or incorporating sealed radioisotopes, where the radioactive isotope is not intended to be released into the body, if used in the central circulatory system - Distal protection devices
- reusable surgical instruments1, in which case they are in Class I3	- Scalpels and scalpel handles - Reamers - Drill bits - Saws, that are not intended for connection to an active device - Retractors forceps, excavators and chisels - Sternum retractors for transient use
- intended specifically for use in direct contact with the central nervous system, in which case they are in Class III	- Neuro-endoscopes - Brain spatulas - Direct stimulation canulae - Spinal cord retractors - spinal needles
- intended to supply energy in the form of ionizing radiation in which case they are in Class IIb,	- Catheters containing or incorporating sealed radioisotopes, where the radioactive isotope as such is not intended to be released into the body, if used in the circulatory system, excluding the central circulatory system
- intended to have a biological5 effect or to be wholly or mainly absorbed6 in which case they are in Class IIb,	
- intended to administer medicines by means of a delivery system, if this is done in a manner that is potentially hazardous7 taking account of the mode of application, in which case they are Class IIb.	- Devices for repeated self-application where dosage levels and the nature of the medicinal product are critical, *e.g.* insulin pens

Explanations of special concepts

Note 1: Terms such as "surgically invasive device", "central circulatory system", “central nervous system” and "reusable surgical instruments" are defined in Section I of Annex IX of Directive 93/42/EEC. In particular surgical instruments connected to an active device are not considered to be “reusable surgical instruments”.

Note 2*:* The expression "correct a defect" does not cover devices that are used accessorily in heart surgery procedures, *e.g.* clamps, aortic punch instruments. The first indent of this rule does not apply to aortic punches and similar cutting instruments which perform a similar function to a scalpel.

Note 3: Surgical instruments which are not specifically intended for purposes described in the first indent, and irrespective of the site of application, are in class IIa, if they are intended for single use and in class I if they are reusable.

Note 4: Dedicated means that the intended purpose of the device or accessory is to specifically control, diagnose, monitor or correct a defect of the heart or of the central circulatory system.

Note 5: Biological effect: All materials and devices have the potential to affect tissues following use in a surgically invasive procedure. A material is considered to have a biological effect if it actively and

intentionally induces, alters or prevents a response from the tissues that is mediated by specific reactions at a molecular level. Such a device may be described as bioactive.
Note 6: Wholly or mainly absorbed: The term absorption refers to the degradation of a material within the body and the metabolic elimination of the resulting degradation products from the body.
Note *7:* The concept of "potentially hazardous manner" is related to the characteristics of the device and not the competence of the user.

- **Rule 7 - Surgically invasive devices intended for short-term use *(>60 minutes, <30 days)*/General explanation of the rule**

These are mostly devices used in the context of surgery or post-operative care (*e.g.* clamps, drains), infusion devices (cannulae, needles) and catheters of various types.

RULE 7	**EXAMPLES**
All surgically invasive devices intended for short term use are in Class IIaunless they are intended:	- Clamps - Infusion cannulae - Skin closure devices - Temporary filling materials - Tissue stabilisers2 used in cardiac surgery
- either specifically to control**,** diagnose, monitor or correct a defect2 of the heart or of the central circulatory system through direct contact with these parts of the body, in which case they are in Class III,	- Cardiovascular catheters - Cardiac output probes - Temporary pacemaker leads - Thoracic catheters intended to drain the heart, including the pericardium - Carotid artery shunts - Ablation catheter
- or specifically for use in direct contact with the central nervous system, in which case they are in Class III,	- Neurological catheters - Cortical electrodes
- or to supply energy in the form of ionising radiation in which case they are in Class IIb,	- Brachytherapy devices
- intended to have a biological effect or to be wholly or mainly absorbed in which case they are in Class III,	- Absorbable sutures - Biological adhesives
- or to undergo chemical change in the body, except if the devices are placed in the teeth, or to administer medicines1, in which case they are Class IIb.	- Adhesives

Practical issues of classification

Note 1: Administration of medicines is more than just channelling, it implies also storage and/or influencing the volume and rate of the medicine delivered. Implanted capsules for the slow release of medicines are medicines and not medical devices.
Note 2: The expression “correct a defect” does not cover devices that are used accessorily in heart surgery, *e.g.* tissue stabilisers.

- **Rule 8 - Implantable devices and long-term surgically invasive devices (> 30 days) / General explanation of the rule**

These are mostly implants in the orthopaedic, dental, ophthalmic and cardiovascular fields as well as soft tissue implants such as implants used in plastic surgery.

RULE 8	**EXAMPLES**
All implantable devices and long-term surgically invasive devices are in Class IIb unless they are intended:	- Prosthetic joint replacements not covered by Directive 2005/50/EC - Ligaments - Shunts - Stents and valves (*e.g*. pulmonary) - Nails and plates - Intra-ocular lenses - Internal closure devices.(including vascular closure devices2) - Tissue augmentation implants - Peripheral vascular catheters - Peripheral vascular grafts and stents - Penile implants - Non-absorbable sutures, bone cements and maxillo-facial implants, visco-elastic surgical devices intended specifically for ophthalmic anterior segment surgery 1
- to be placed in the *teeth3*, in which case they are in Class IIa,	- Bridges and crowns - Dental filling materials and pins - Dental alloys, ceramics and polymers
- to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are Class III,	- Prosthetic heart valves - Aneurysm clips - Vascular prosthesis and stents - Central vascular catheters - Spinal stents - CNS electrodes - Cardiovascular sutures - Permanent and retrievable vena cava filters - Septal occlusion devices - Intra-aortic balloon pumps - External left ventricular assisting devices
- to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class III,	- Absorbable sutures - Adhesives and implantable devices claimed to be bioactive through the attachment of surface coatings such as phosphorylcholine
- or to undergo chemical *change4* in the body, except if the devices are placed in the teeth, or to administer medicines, in which case they are in Class III.	- Rechargeable non-active drug delivery systems
- Directive 2003/12/EC introduced a derogation from this rule, reclassifying breast implants in Class III	- Breast implants
Directive 2005/50/EC introduced a derogation from this rule, reclassifying hip, knee and shoulder joint replacements in Class III	- Total hip, knee and shoulder joint replacements systems and components of systems12

Practical issues of classification

Note 1: These products are implants because in normal conditions a significant amount of the substance remains at the surgical site after the procedure. If these devices contain animal tissues or derivatives of animal tissues, they are covered by Rule 17.
Note 2: For closure of arteriotomies in the peripheral vascular system. (please refer to definition of central circulatory system)
Note *3*: Implants without bioactive coatings intended to secure teeth or prostheses to the maxillary or mandibular bones are in Class IIb following the general rule. Hydroxyapatite
is considered as having biological effect only if so claimed and demonstrated by the manufacturer.
Note 4: The clause about chemical change under this rule does not apply to products such as bone cements where the chemical change takes place during the placement and does not continue in long term.

- **Rule 9 - Active therapeutic devices intended to administer or exchange energy / General explanation of the rule**

Devices classified by this rul*e* are mostly electrical equipment used in surgery such as lasers and surgical generators. In addition there are devices for specialised treatment such as radiation treatment. Another category consists of stimulation devices, although not all of them can be considered as delivering dangerous levels of energy considering the tissue involved.

RULE 9	**EXAMPLES**
All active therapeutic devices intended to administer or exchange energy are in Class IIa	Electrical and/or magnetic and electromagnetic energy - Muscle stimulators - External bone growth stimulators - TENS devices - Eye electromagnets - Electrical acupuncture Thermal energy - Cryosurgery equipment. - Heat exchangers**,** except the types described below Mechanical energy - Powered dermatomes - Powered drills - Dental hand pieces. Light - Phototherapy for skin treatment and for neonatal care Sound - Hearing aids Ultrasound - Equipment for physiotherapy
unless their characteristics are such that they may administer or exchange Kinetic energy energy to and from the human body in a potentially hazardous way1, taking account of the nature, the density and the site of application of the energy, in which case they are in Class IIb.	Kinetic energy - Lung ventilators Thermal energy - Incubators for babies - Warming blankets - Blood warmers - Electrically powered heat exchangers (for example, those used with patients incapable of

	reacting, communicating and/or who are without a sense of feeling) Electrical energy - High-frequency electrosurgical generators, and electrocautery equipment, including their electrodes - External pacemakers and defibrillators - Electroconvulsive therapy equipment. Coherent light - Surgical lasers Ultrasound - Lithotriptors, surgical ultrasound devices Ionizing radiation - Radioactive sources for afterloading therapy - Therapeutic cyclotrons and linear accelerators - Therapeutic X-ray sources
All active devices intended to control or monitor the performance of active therapeutic devices in Class IIb or intended to influence directly the performance of such devices are in Class IIb.	- External feedback systems for active therapeutic devices - Afterloading control devices

Explanation of special concepts

Note 1: The decision as to whether a medical device administers or exchanges energy to and from the human body in a potentially hazardous way should take into account the following factors. The concept of "potentially hazardous" is dependent on the type of technology involved and the intended application of the device to the patient and not on the measures adopted by the manufacturer in view of good design management (*e.g.* use of technical standards, risk analysis). For instance all devices intended to emit ionizing radiation, all lung ventilators and lithotriptors should be in Class IIb. However, the manufacturer's obligation to comply with design requirements and solutions adopted, such as use of standards, exist independently from the classification system.

- **Rule 10 - Active devices for diagnosis**

General explanation of the rule

This primarily covers a whole range of widely used equipment in various fields, *e.g.* ultrasound diagnosis, capture of physiological signals and therapeutic and diagnostic radiology.

RULE 10	**EXAMPLES**
Active devices intended for diagnosis are in Class IIa: - if they are intended to supply energy which will be absorbed by the human body, except for devices used to illuminate the patient's body, in the visible spectrum,	- Magnetic resonance equipment. - Pulp testers. - Evoked response stimulators - Diagnostic ultrasound
- if they are intended to image *in vivo* distribution of radiopharmaceuticals,	- Gamma cameras - Positron emission tomography and single photon emission computer tomography
- if they are intended to allow direct diagnosis or monitoring of vital physiological processes1,	- Electrocardiographs - Electroencephalographs - Cardioscopes with or without pacing pulse indicators2

	- Electronic thermometers - Electronic stethoscopes - Electronic blood pressure measuring equipment.
unless they are specifically intended for monitoring of vital physiological parameters, where the nature of variations is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of CNS in which case they are in Class IIb.	- Intensive care monitoring and alarm devices (*e.g.* blood pressure, temperature, oxygen saturation) - Biological sensors - Blood gas analysers used in open heart surgery - Cardioscopes - Apnoea monitors, including apnoea monitors in home care
Active devices intended to emit ionizing radiation and intended for diagnostic and therapeutic interventional radiology*3* including devices which control or monitor*4* such devices, or which directly influence their performance, are in Class IIb.	- Diagnostic X-ray sources

Examples of special concepts:

Note 1: Vital physiological processes and parameters include, for example respiration, heart rate, cerebral functions, blood gases, blood pressure and body temperature.
Medical devices intended to be used for continuous surveillance of vital physiological processes in anaesthesia, intensive care or emergency care are in Class IIb, whilst medical devices intended to be used to obtain readings of vital physiological signals in routine check ups and in self-monitoring are in Class IIa. A thermal imaging device intended to monitor blood flow is not considered to be a temperature measuring device.
Note 2*:* Devices specifically intended to monitor AIMDs fall under the AIMD Directive.
Note 3: Therapeutic interventional radiology refers to diagnosis being carried out during surgical procedures.
Note 4: This refers to active devices for the control, monitoring or influencing of the emission of ionizing and not to the subsequent processing, recording or viewing of the resulting image.

- **Rule 11 - Active devices intended to administer and/or remove medicines, body liquids or other substances to or from the body**

General explanation of the rule

This rule is intended to primarily cover drug delivery systems and anaesthesia equipment.

RULE 11	**EXAMPLES**
All active devices intended to administer and/or remove medicines, body liquids or other substances to or from the body are in Class IIa,	- Suction equipment - Feeding pumps - Jet injectors for vaccination - Nebulisers to be used on conscious and spontaneously breathing patients where failure to deliver the appropriate dosage characteristics is not potentially hazardous
unless this is done in a manner: - that is potentially hazardous, taking account of the	- Infusion pumps - Ventilators

nature of the substances involved, of the part of the body concerned and of the mode of application, in which case they are in Class IIb.	- Anaesthesia machines - Anaesthetic vaporisers - Dialysis equipment - Blood pumps for heart-lung machines - Hyperbaric chambers - Pressure regulators for medical gases - Medical gas mixers - Moisture exchangers in breathing circuits if used on unconscious or non-spontaneously breathing patients - Nebulisers where the failure to deliver the appropriate dosage characteristics could be hazardous

- **Rule 12 - All other active devices**

General explanation of the rule

This is a fallback rule to cover all active devices not covered by the previous rules.

RULE 12	**EXAMPLES**
All other active devices are in Class I	- Active diagnostic devices intended to illuminate the patient's body in the visible spectrum such as examination lights or to optically view the body such as surgical microscopes - Devices intended in general for external patient support (*e.g.* hospital beds, patient hoists, wheelchairs, dental patient chairs) - Active diagnostic devices intended for thermography - Dental curing lights

Special rules:

- **Rule 13 - Devices incorporating, as an integral part, a medicinal product or a human blood derivative (See MEDDEV. 2.1/3 for further guidance)**

General explanation of the rule

This rule is intended to cover combination devices that contain a medicinal substance incorporated into the device for the purpose of assisting the functioning of that device.

However this rule does not cover those devices incorporating substances which under other circumstances may be considered as medicinal substances, but which are incorporated into the device exclusively for the purpose at maintaining certain characteristics of the device and which are not liable to act on the body. The primary function of the device does not rely on the pharmacological, metabolic or immunological effect of the medicine. If the latter is the case, the product is a medicinal product rather than a device and not covered by this Directive.

RULE 13	**EXAMPLES**
All devices incorporating, as an integral part*1*, a substance which, if used separately, can be considered to be a medicinal product as defined in Article 1 of the Directive 2001/83/EC, and which is liable to act on the	- Antibiotic bone cements - Condoms with spermicide - Heparin coated catheters - Endodontic materials with antibiotics

human body with action ancillary to that of the devices, are in Class III	- Ophthalmic irrigation solutions principally intended for irrigation, which contain components which support the metabolism of the endothelial cells of the cornea - Dressings incorporating an antimicrobial agent where the purpose of such an agent is to provide ancillary action on the wound - Contraceptive intrauterine devices (IUDs) containing copper or silver - Drug eluting stents, *e.g.* coronary, pulmonary
All devices incorporating as an integral part, a human blood derivative are in Class III	- Surgical sealants containing human serum albumin

Note 1: "Integral part" means that the device and the medicinal substance are physically or chemically combined at the time of administration (*i.e.* use, implantation, application etc) to the patient.

- **Rule 14 - Devices used for contraception or prevention of sexually transmitted diseases / General explanation of the rule**

These intended uses relate to special cases of human vulnerability that cannot be covered by the normal criteria of time, invasiveness and organic function.
Although this rule covers two very different device applications, some devices may perform both functions, *e.g.* condoms. Devices intended to prevent the sexual transmission of the HIV are also covered by this rule.

RULE 14	**EXAMPLES**
All devices used for contraception or the prevention of the transmission of sexually transmitted diseases are in Class IIb,	- Condoms - Contraceptive diaphragms
unless they are implantable or long term invasive devices, in which case they are in Class III.	- Contraceptive intrauterine devices (IUDs)1

Note 1: Intrauterine contraceptives whose primary purpose is to release progestogens are not medical devices (see Article 1.3 2nd paragraph of this Directive).

- **Rule 15 - Specific disinfecting, cleaning and rinsing devices / General explanation of the rule**

This rule is principally intended to cover various contact lens fluids. It also covers substances and other equipment used principally in a medical environment to disinfect medical devices.

RULE 15	**EXAMPLES**
All devices intended specifically to be used for disinfecting, cleaning, rinsing or, when appropriate hydrating contact lenses are in Class IIb.	- Contact lens solutions - Comfort solutions

All devices intended specifically to be used for disinfecting medical devices are in Class IIa	- Disinfectants specifically intended for non-invasive medical devices and equipment such as sterilizers specifically intended to sterilize medical devices in a medical environment and washer disinfectors - Washers-disinfectors intended specifically for disinfecting non-invasive medical devices
unless they are specifically to be used for disinfecting invasive devices in which case they are in Class IIb.	- Denture disinfecting products - Washers-disinfectors for endoscopes - Disinfectants for the fluid pathways of haemodialysis equipment - Disinfectants for ocular prosthesis, intraosseous transcutaneous amputation prosthesis, surgical equipment and invasive dental equipment
This rule does not apply to products that are intended to clean medical devices other than contact lenses by means of physical action1.	

Practical issues of classification

Note 1: This rule does not apply to mechanical means of cleaning of devices, such as brushes and ultrasound. Such products will only fall under this Directive if they are specifically intended for use with medical devices.

- **Rule 16 - Devices to record X-ray diagnostic images**

RULE 16	**EXAMPLES**
Devices specifically intended for recording of X-ray diagnostic images are in Class IIa.	- X-ray films - Photostimulable phosphor plates

Note: This refers to primary recording media such as X-ray films and not to media used for subsequent reproduction.

- **Rule 17 - Devices utilising animal tissues or derivatives**

Explanation of the rule

This rule covers devices that contain or are made of animal tissues that have been rendered non-viable or derivatives from such tissues also being non-viable, i.e. where there is no longer any capacity for cellular metabolic activity. Devices containing viable animal tissues and/or any human tissues or derivatives are excluded from the scope of this Directive.

Further information on this issue can be found in MEDDEV 2.11/1 rev.213.
The manufacture of some devices may use industrial raw materials which contain small amounts of tallow or tallow derivatives (*e.g.* stearates in polymers). Such substances are not considered as derivatives of animal tissues for the purpose of this rule which therefore does not apply.

RULE 17	EXAMPLES
All devices manufactured utilizing animal tissues or derivatives1 rendered nonviable are Class III except where such devices are intended to come into contact with intact skin2 only.	- Biological heart valves - Porcine xenograft dressings - Implants and dressings made from collagen - Devices utilising hyaluronic acid of animal origin

Practical classification issues

Devices made of non-viable animal tissue that comes into contact with intact skin only (*e.g.* leather components of orthopaedic appliances) are in Class I in accordance to Rule 1.

Note 1: Derivatives are products that are processed from animal tissues and exclude substances such as milk, silk, beeswax, hair, lanolin

Note 2: Intact skin includes the skin around an established stoma unless the skin is breached

- **Rule 18 - Blood bags**

General explanation of the rule

This is a special rule that covers only blood bags.

RULE 18	EXAMPLES
By derogation from other rules, blood bags are in Class IIb.	- Blood bags (including those containing or coated with an anticoagulant). Where blood bags have a function greater than for storing purposes and include systems for preservation other than anti-coagulants then other rules (*e.g.* rule 13) may apply

Note: Blood bags are described in the European Pharmacopoeia in the monograph on "Containers for Blood and Blood Components".

5. Clinical Evaluation of Medical Devices:

According to Clause 1.1, Annex X of the amending MDD 2007/47/EC, medical device manufacturers in Europe must provide a formal document, referred to as a Clinical Evaluation, irrespective of the classification of the medical device in question. The clinical evaluation document will become an obligatory document that must be provided by the medical device manufacturer in the course of his conformity assessment. Therefore, clinical evaluation has to be part of the technical documentation for the respective device (Clause 1.1b.) and must be actively kept updated and consider the postmarketing results obtained after placing the product on the market (Clause 1.1.c). In addition, the amending MDD states that clinical investigations are, in particular, expected for implant devices and for Class III devices (Clause 1.1a, Annex X).

In Clauses 1.1 and 1.1a of Annex X it becomes clear that a manufacturer can use his own clinical data for the evaluation or he can make use of comparable medical devices. However, in the latter case, the

manufacturer must actively document and justify the equivalence of the medical device to be evaluated with the predicate device he uses for comparison.
Typically, a product can be assumed to be equivalent if it has the same technological characteristics (geometry and surface properties), is made of comparable material, has the same chemical composition, is subjected to comparable manufacturing processes (including sterilisation process) and is used for the same purpose (intended use including nature and duration of body contact). From this list it becomes obvious that the documentation of equivalence may sometimes be difficult.
Clause 1.1.a of Annex X states that clinical investigations become a mandatory prerequisite for the clinical evaluation of implantable and Class III devices, and particular justification is required if a manufacturer uses existing clinical data, that is, clinical data that were obtained with a comparable medical device (predicate device). This requirement goes far beyond those of the former medical device Directives.

5.1 MEDDEV Guidance for clinical evaluation:

With regard to the clinical evaluation of medical devices (literature route/clinical investigation route), the following MEDDEV documents have been issued:

- MEDDEV 2.7.1. Evaluation of Clinical Data: A Guide for Manufacturers and Notified Bodies (April 2003)
- MEDDEV 2.12-2 Guideline on Postmarket Clinical Follow-Up (May 2004).

Two other guidelines are also available, issued by the European Notified Bodies Co-Ordination Medical Devices Group:

- NB-MED/2.7/Rec3 Evaluation of Clinical Data. Chapter 2.7. Clinical Investigations, Clinical Evaluation (revised 11.5.1999)
- NB-MED/2.7/Rec1 Guidance on Clinicals. Chapter 2.7. Guidance on when a clinical investigation is needed for CE marking (revised 20.4.1998).

Sources of data
With regard to clinical data to be evaluated, MEDDEV 2.7.1, accepts the following sources:

- Results from clinical investigations with the manufacturer's investigational device
- Results from clinical investigations with CE-marked predicate devices
- Published data from clinical studies or other clinical results with comparable medical devices
- Postmarketing surveillance data with the device in question or with comparable devices

If the manufacturer makes use of clinical data that were not obtained with the medical device in question, the level of comparability must be described and justified. With regard to postmarketing surveillance data, the report should specify an appropriate reporting period and should state the number of sold devices, the total number of complaints and the total number and nature of clinically relevant complaints/notified adverse reactions.
An abbreviated CV of the author(s) should be attached to the clinical evaluation report. At the end of the clinical evaluation report, all search runs that were conducted, including the received search results, should be attached. With regard to the selected and evaluated literature, at least the abstracts or better, complete copies of the respective documents should be attached to the clinical evaluation report.

5.2Clinical investigation of medical devices:

If an initial clinical evaluation concludes that an innovative or substantially modified medical device cannot be fully evaluated regarding its clinical effectiveness and/or safety, the medical device manufacturer will need to perform a clinical investigation to generate appropriate clinical data. In unclear cases, the Notified Bodies' recommendation NB-MED/2.7/Rec1 can give advice.

According to this guideline, a clinical study should be performed

- where a completely new device is proposed for the market, whose components, features and/or method of action are previously unknown
- where an existing device is modified and the modification might significantly affect the clinical safety and performance
- where a previously established device is proposed for a new indication
- where a device incorporates new materials, previously unknown, coming into contact with the human body or existing materials applied in a location not previously exposed to that material, and for which there is no convincing prior experience, or that the device will be used for a significantly longer time.

If a clinical investigation is required, the amending MDD (and the former MDD and AIMDD) gives a brief list of requirements with which a sponsor (medical device manufacturer or other organisation initiating a clinical investigation) must comply. For the MDD, this is specified in Annex X of Article 15 and for the AIMDD, it is in Annex 7 of Article 10.

5.3 EN ISO 14155 Parts 1 and 2

EN ISO 14155[2] was developed under the former MDD and AIMDD to describe the procedures that need to be followed in a clinical investigation. This standard is intended "to be applied worldwide to clinical investigations of medical devices to fulfill the technical aspects of the various national, regional and international regulatory requirements."

Core elements:

Part 1

- Ethical considerations
  EN ISO 14155 Part 1 reinforces the importance of ethical considerations in a clinical trial. So the rights, safety and wellbeing of study subjects shall be protected consistent with the ethical principles laid down in **the Declaration of Helsinki.**
- General requirements that need to be complied, personal responsibilities with detailed assignments and a final report after completion of the clinical trials.

Part 2:

- Clinical Investigation Plan (CIP) is the most important document to be prepared to ensure a scientifically sound and administratively correct conduct of a clinical investigation.(this part of the standard provides detailed requirements for this document and introduces a normative and scientific approach to the preparation of a CIP, formerly known as the protocol or clinical protocol.)

In general the CIP must include:

  - all relevant information on the investigational device, the sponsor, involved clinical institutions, clinical investigators, monitoring arrangements, data and quality management and must be approved in writing by all involved parties.

- summarise the current literature, justify the planned study design and disclose any preclinical investigations, previous clinical experience and possible risks associated with the use or administration of the investigational device.
- justify the clinical endpoints and their success and failure criteria.
- Inclusion and exclusion criteria for the study population must be listed, the methods and timing for assessing, recording and analysing study variables must be described, and a (statistical) justification must be provided for the planned number of subjects to be included in the study.
- methods and the analytical procedures to be used.

- Addresses the justification for the study, its design and its population.
- Any deviation from the clinical protocol must be documented in the course of the clinical study. If applicable, modifications to the plan may be implemented by officially amending the clinical investigation plan; these amendments must be approved in writing by all involved parties.
- Finally, the case report form (CRF) must be prepared, mirroring the clinical investigation plan, to allow a complete documentation of the study information to be recorded. CRF pages must be identifiable by version number and date and must be allocatable to the respective study subject at any time.

6. Medical Device Regulation in the United States:

6.1 Introduction and Definitions:

The Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act define a medical device in as **"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related articles, including any component, part, or accessory, which is:**

- Recognized by the official National Formulary, or the United States
- Pharmacopoeia (USP), 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 a man or other animals.
- Intended to affect the structure or any function of the body of a man or other animals, and which does not achieve any of its principal intended purposes through chemical action within or on the body of a man or other animals and which is not dependent upon being metabolized for the achievement of its principal intended uses."

Foreign establishments engaged in the manufacture, preparation, propagation, compounding, or processing of a device that is imported, or offered for import, into the U.S. must register their establishments and provide the FDA with the name of the U.S. agent representing their establishment. Foreign establishments must also continue to file device listing forms for medical devices they are exporting to the U.S. FDA is also authorized to enter into cooperative agreements with foreign countries to ensure that non-compliant products are refused entry into the U.S.

The importation of medical devices into the U.S. is subject to the laws of the FFD & C Act.(Federal Food, Drug, and Cosmetic Act) They are:

- Sections 481-521 of the Tariff Act (TA) of 1930, as amended (19 U.S.C. 1521), enforced by the U.S. Customs Service of the Department of Treasury which sets the entry requirements for all imports into the U.S.
- Section 510(I) and (k) Registration of Procedures for Drugs and Devices
- Section 519 Records and Reports on Devices Section 801(a), (b), and (c) of the Federal Food, Drug, and Cosmetic (FFD&C) Act (21U.S.C. 381 (a), (b), and (c)) which contains special requirements for the import of
- Medical devices and section 536 which contains special requirements for the import of radiation-emitting electronic products.
- Section 801(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381 (d)) which permits the importation of medical device component parts or accessories or other articles of devices so long as the imported item is further processed or incorporated into a product that will be exported. If the imported item is not exported, it must be destroyed.

Section 481-521

The major responsibility of the U.S. Customs Service is to administer the Tariff Act of 1930 as amended. Primary duties include assessment and collection of all duties, taxes, and fees on imported merchandise; administration and review of import entry forms; the enforcement of U.S. Customs and related laws; and administration of certain navigation laws and treaties. Currently, there is a working agreement between FDA and U.S. Customs for the cooperative enforcement of Section 801 of the FFD &C Act. Most cooperative action centers on violations of the FFD & C Act, particularly noncompliance with FDA import requirements, or when FDA determines it necessary to sample imported devices to assure their safety and effectiveness.

The first process includes the importer or filer submitting the necessary entry information to the local U.S. Customs district office. For those entries not filed electronically, a paper entry consisting of the commercial invoice, Customs entry forms CF3461/3461ALT and/or CF7501 or documentation that would need to be provided by the importer or filer. Most importers ask that domestic customhouse brokers complete these forms and make the submissions on their behalf. However, this does not always result in the immediate release into U.S. commercial channels. Furthermore, submitting these forms does not release the importer from responsibility to assure FDA that the premarketing or other requirements have been met. When an entry is filed with U.S. Customs, a copy of the entry is also provided to the local FDA district office.

Section 510(I) and (k) Registration of Procedures of Drugs and Devices

The FDA district office then determines if the product complies with FDA requirements. For devices intended for commercial distribution in the U.S., this includes assuring that the importer or original distributor is registered, the foreign manufacturer has registered and listed their establishments and devices and provided FDA with the name of the U.S. agent representing their establishment, that the device is compliant with the Quality Systems (QS) regulation and is properly labeled. The device has been given clearance or approval for marketing following the submission of a 510(k) premarket notification [or is exempt] of a PMA. If the FDA district office determines that the device, manufacturer, or importer has not complied with FDA import requirements, the device will be detained at the port of entry and the importer will be given a "Notice of Detention and Hearing." At this point,

the importer, the foreign manufacturer, or the device itself must be brought into compliance before the device is released.

Section 801

FDA may examine certain devices to assure their safety and effectiveness. When this occurs, FDA will issue a "Notice" to the "importer of a record," who may or may not be the initial distributor on a form titled "Notice of FDA Action." Sampling may involve examining the product at the port of entry or physical collection of a statistical portion of the lot for analysis by an FDA laboratory If there is a problem, or if the sample is determined to be out of compliance with required specifications, the device will be detained and the "importer of record" will be issued a "Notice of FDA Action" indicating that the article is being detained due to the appearance of a violation under the FFD&C Act. Under certain conditions, the "importer of record" of a device that has been detained, is given an opportunity to submit application for authorization to bring the device into compliance with the Act. If FDA permits reconditioning, another sample may be collected and analyzed after reconditioning. If the device is then determined to be in compliance, it will be released. If the "importer of record" fails to properly recondition the device, or FDA does not permit reconditioning, the "importer of record" must either export or destroy that particular lot.
Failure to do so within 90-days may result in issuance of a Customs Redelivery Notice and an assessment for liquidated damages for up to 3 times the value of the lot.

Section 519 Operational and Administrative Systems for Import Support (OASIS)

The FDA computerized import system, known as the Operational and Administrative System for Import Support (OASIS), became fully operational in all district offices in November 1997 to expedite and support a "paperless" import of goods into the U.S. The OASIS program is an electronic interface between FDA and the Customs Service's Automated Commercial System (ACS). OASIS is an on-line interactive and automated system, which replaced the existing process of reviewing the paperwork for import entries manually. This computer-generated system supports FDA's ability to effectively regulate imported products. Through the use of OASIS, FDA is focusing on high risk, suspect, or known problem products while allowing the lower risk products into domestic commerce more efficiently. This system will expedite the flow of international commerce and the needs of the importing community. OASIS enables Customhouse filers to transmit their entry data to FA electronically at the same time they are transmitting their required electronic data to the U.S. Customs Service. Within 15 minutes of keying in the data, the filer receives a computerized response stating whether the entry requires further FDA review, or if it can move immediately into domestic commerce.

6.2 US Classification

The Food and Drug Administration has recognized **three classes** of medical devices based on the level of control necessary to assure the safety and effectiveness of the device. The classification procedures are described in the Code of Federal Regulations, Title 21, part 860 (usually known as 21 CFR 860).
Title 21 of the Code of Federal Regulations : is the portion of the Code of Federal Regulations that governs food and drugs within the United States for the Food and Drug Administration (FDA), the Drug Enforcement Administration (DEA), and the Office of National Drug Control Policy (ONDCP).
It is divided into three chapters:

- Chapter I — Food and Drug Administration
- Chapter II — Drug Enforcement Administration
- Chapter III — Office of National Drug Control Policy

Section 58 Good Lab the 800 series are for medical devices:

- 803 Medical Device Reporting
- 814 Premarket Approval of Medical Devices
- 820 *et seq.* Quality system regulations (analogous to cGMP, but structured like ISO)
- 860 *et seq.* Listing of specific approved devices and how they are classified
- Good oratory Practices (GLP) for nonclinical studies

Medical devices vary widely in their complexity and their degree of risk or benefits. They do not all need the same degree of regulation. **Thus, U.S. FDA places all medical devices into one of three regulatory classes based on the level of control necessary to assure safety and effectiveness of the device.**

These classes are:

- 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 Code of Federal Regulations (CFR) Parts 862 through 892. There are approximately 1,700 device classifications within 16 medical specialties. Of the 1,700 classified devices, 45% are Class I, 47% are Class II and 8% are Class III.

CLASS I - GENERAL CONTROLS

Class I devices are subject to the least regulatory control. They present

- minimal potential for harm to the user and
- are often simpler in design than Class II or Class III devices.

Class I devices are subject to "General Controls" as are Class II and Class III devices.

General controls include:

1. Establishment registration (use FDA Form 2891) of companies which are required to register under 21 CFR part 807.20, such as manufacturers, distributors, repackagers and relabelers, and foreign firms.
2. Medical device listing (use FDA Form 2892) with FDA of devices to be marketed.
3. Manufacturing devices in accordance with the Quality Systems regulation (GMP's) in 21 CFR Part 820.
4. Labeling devices in accordance with labeling regulations in 21 CFR Part 801 or 809.
5. Submission of a premarket notification 510(k) before marketing a device.

Examples of Class I devices include elastic bandages, examination gloves, and hand-held surgical instruments.

Most Class I devices are exempt from the premarket notification and/or the Quality System regulation.

CLASS II - SPECIAL CONTROLS

Class II devices are those for which

- general controls alone are insufficient to assure safety and effectiveness,
- and existing methods are available to provide such assurances.

- In addition to complying with general controls, Class II devices are also subject to special controls.

Special controls may include special labeling requirements, mandatory and voluntary performance standards and postmarket surveillance.
Examples of Class II devices include powered wheelchairs, infusion pumps, and surgical drapes.
Class II devices are usually not exempt from the premarket notification or the Quality System regulation.

CLASS III - PREMARKET APPROVAL

Class III is the most stringent regulatory category for devices. Class III devices are those for which

- Insufficient information exists to assure safety and effectiveness solely through general or special controls.
- 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.

Premarket approval is the required process of scientific review to ensure the safety and effectiveness of Class III devices. Not all Class III devices require an approved premarket approval application for marketing. Class III devices which are equivalent to devices legally marketed before May 28, 1976 may be marketed through the premarket notification [510(k)] process until FDA has published a requirement for manufacturers of that device type to submit premarket approval data.

SECTIONS RELATED TO DEVICE CLASSIFICATION

Section 206 and 207 include provisions for the classification of Class II and Class III devices.

- Section 206 contains requirements that exempt certain Class I and II devices from Premarket Notification.
- Section 207 contains a requirement that allows for classification of new, low risk, Class III devices. These provisions are addressed in the Premarket Notification (Section 206) and Premarket Approval (Section 207) of the FFD&C Act.

6.3 ESTABLISHMENT REGISTRATION AND MEDICAL DEVICE LISTING

Section 510 of the FFD&C Act requires both domestic and foreign manufacturers to list their devices with the FDA if the devices are in commercial distribution in the U.S. Devices are listed by their classification name on form FDA 2892. The proprietary and common or usual name of the device(s) must be submitted to FDA upon request. In addition, manufacturers must maintain a historical listing file of labelling and advertisements in accordance with Title 21 Code of Federal Regulations (CFR) 807.31.
In many other countries the term "registration" means the process by which the government clears or approves a product for marketing. In the U.S., however, neither registration nor listing constitutes FDA clearance or approval for marketing or commercial distribution. Unless the device is exempt, a premarket notification submission [510(k)] or a premarket approval application (PMA) is required before commercial distribution

6.4 PERFORMANCE/EFFECTIVENESS REQUIREMENTS:

a. PREMARKET NOTIFICATION - 510(k)

The faster marketing process is premarket notification or 510(k). The 510(k) applicant must demonstrate to FDA that their device is substantially equivalent to a legally marketed device that is, one that was marketed before May 28, 1976 or one that was marketed after that date that was found substantially equivalent through the 510(k) process.

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

- has the same intended use; and
- has the same technological characteristics as the legally marketed device,
- or
- has different technological characteristics, and submitted information:
  - 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.

All 510(k) applications must include descriptive information, labelling, and may require performance and effectiveness testing depending upon the devices technological characteristics and risk associated with its application.

Performance and effectiveness information may include mechanical bench testing, biocompatibility testing, animal testing and clinical evaluation. Devices in contact with the human body must be biocompatible and most implanted and life-supporting devices require clinical evaluation in support of a 510(k) application.

If the device is determined by FDA to be substantially equivalent then the device may be marketed. If FDA determines the device is not substantially equivalent, the manufacturer may resubmit another 510(k) with new data, file a petition to reclassify the device, or submit a premarket approval (PMA) application.

b. PREMARKET APPROVAL

The most stringent marketing application required by FDA is premarket approval or PMA. The PMA application must contain sufficient information to reasonably assure FDA of the safety and effectiveness of the device. This requires valid scientific data to demonstrate that the device is safe and effective for its intended use. In most cases, this includes well-controlled clinical studies; full reports of safety and effectiveness and data regarding the manufacturing of the device. Clinical studies to support the premarket approval application must be done in accordance with the Investigational Device Exemption (IDE) regulation.

The PMA review process consists of an administrative/filing review, scientific and regulatory review, advisory committee review/recommendation, and final documentation and notification of approval. An approved Premarket Approval Application is, in effect, a private license granted to the applicant for marketing a particular device.

About 1% of the medical devices in commercial distribution have gone through the PMA process. Class III devices marketed through the 510(k) process are preamendment devices for which FDA has not yet required the premarket approval application. FDA has been receiving approximately 50 premarket approval submissions per year.

The performance and effectiveness of medical devices marketed through the 510(k) process must only be demonstrated to the extent of substantial equivalence. That is, it must be as safe and as effective as a

similar device already marketed. The performance and effectiveness of devices marketed through the PMA process must demonstrate that the device is reasonably safe and effective. These devices must demonstrate, on their own merit, safety and effectiveness through valid scientific evidence.

c. PRODUCT DEVELOPMENT PROTOCOL

As part of its reengineering initiative, the Food and Drug Administration, Center for Devices and Radiological Health is proposing to implement the statutory authority for Product Development Protocol (PDP). Section 515 (f) of the Federal Food, Drug, and Cosmetic Act provides this alternative process to the premarket approval process (PMA) for Class III devices. This alternative process, (PDP), was not implemented during the early years of the device program because it was considered potentially complex and there was a need to focus attention on implementing the core provisions of the Medical Device Amendments of 1076 such as the IDE, PMA, 510(k), GMP, and problem reporting requirements.

A reengineering team comprised of FDA staff, industry and other non-government representatives have focused their efforts on a proposal with the following goals:

a. provide a process that will allow FDA to effectively regulate Class III products from initial development to marketing to eventual replacement by more advanced products,
b. reduce the FDA resources required to review and approve new Class III devices,
c. Reduce the total time to get a new class III device to market, and 4. no reduction in the overall assurance of safety and effectiveness as compared with the PMA process. The process will be designed to facilitate use of expertise outside FDA and will provide a clear development path "road map" for products to the market.

d. CLINICAL DATA (International and Domestic)

Clinical data may be required in support of premarket notification [510(k)] submissions and in most cases in support of a premarket approval (PMA) application.

Clinical data is required in less than 10% of all 510(k) submissions. The sole purpose of clinical data in a 510(k) would be to demonstrate equivalence in performance to another device. FDA does not intend the data, in a 510(k), to determine the device's absolute safety and effectiveness, but to validate that it is equivalent or better, in terms of its safety and effectiveness, than another device with the same intended use.

The need for performance testing depends on what is needed to demonstrate equivalence and on the complexity of the device.

For example, it is likely that little or no clinical data would be needed to determine equivalence of a laparoscopic surgical instrument. In contrast, considerable data would be necessary to judge the equivalence of an implantable cardiac pacemaker.

Clinical data is, however, required in a premarket approval application. The PMA applicant must provide a cogent demonstration of the safety and effectiveness for all diagnostic and/or therapeutic medical claims for the device based on laboratory, animal and clinical data.

Regardless of the type of marketing application, the clinical data must be based on sound scientific principles to demonstrate the endpoint of substantial equivalence or safety and effectiveness.

These principles consist of a proper study design, including: controls and adequate number of patients, monitoring of the study to assure protocol is followed by the investigators, and proper analysis of results.

All clinical studies performed in the U.S. in support of a 510(k) or PMA must be conducted in accordance with the Investigational Device Exemption (IDE) regulation. This required the manufacturer to obtain approval of the study before it begins, informed consent provided to each patient, and proper monitoring during the conduct of the study.
A PMA based solely on foreign clinical data and otherwise meeting the criteria for approval under this part may be approved if:

- the foreign data are applicable to the United States population, medical practice, and
- requirements for informed consent in conformance with the Declaration of Helsinki;
  - the studies have been performed by clinical investigators of recognized competence; and
  - the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA can validate the data through an on-site inspection or other appropriate means.
  - Applicants who seek approval based solely on foreign data can meet with FDA officials in a "presubmission" meeting.

e. PRE-IDE PROCESS

In order to facilitate the initiation of clinical trials under the IDE regulation, the Food and Drug Administration (FDA) encourages sponsors to begin communicating with the ODE reviewing division prior to the submission of the original IDE application. This communication may take the form of a "Pre-IDE" meeting and/or a "Pre-IDE" submission.

f. PRE-IDE MEETINGS

Two types of pre-IDE meetings are possible: meetings in which FDA provides "informal guidance" and meetings where FDA provides "formal guidance" as provided for in Section 201 of the FDA Modernization Act of 1997.

"Informal Guidance" Meetings

Sponsors are encouraged to meet with the ODE reviewing division before the IDE application is submitted for review so that the reviewing division can provide any advice/guidance which can be used in the development of supporting pre-clinical data or the investigational plan for incorporation into the IDE application.

"Formal Guidance" Meetings

A sponsor or applicant may submit a written request for a meeting to reach an agreement with FDA regarding FDA's review of an investigational plan (including a clinical protocol). As required by the statute, this meeting should take place no later than 30 days after receipt of the request. The written request should include a detailed description of the device, a detailed description of the proposed conditions of use of the device, a proposed plan (including a clinical protocol) for determining whether there is a reasonable assurance of effectiveness, and, if available, information regarding the expected performance of the device.
If an agreement is reached between FDA and the sponsor or applicant regarding the parameters of an investigational plan (including a clinical protocol), the terms of the agreement should be put in writing and made part of the administrative record by FDA.
Detailed procedures for implementing this new requirement will be issued in the near future
CLINICAL STUDY SITES LOCATED OUTSIDE THE UNITED STATES FDA does not have jurisdiction over clinical study sites located outside the U.S. As a result, sponsors may proceed at these sites using their own discretion. FDA, however, encourages sponsors to follow a uniform protocol at

the domestic and foreign investigational sites. Although FDA does not have jurisdiction over clinical study sites located outside the U.S., FDA may accept, in support of a premarket approval application (PMA), the data generated from such sites. If the foreign clinical study was not conducted pursuant to the IDE regulation, the PMA regulation requires that the PMA applicant verify in the marketing application that the data generated from the foreign study site(s) are valid and that the investigators at the foreign sites conducted the studies in accordance with the "Declaration of Helsinki" and explain why the country's standards afforded greater protection to the human subjects.

g. GOOD MANUFACTURING PRACTICES

The current Good Manufacturing Practices (GMP) requirements set forth in the Quality System (QS) regulation are promulgated under section 520 of the Federal Food, Drug and Cosmetic (FFD&CAct). They require that domestic or foreign manufacturers have a quality system for the design and production of medical devices intended for commercial distribution in the United States. The regulation requires that various specifications and controls be established for devices;

- that devices be designed under a quality system to meet these specifications;
- that devices be manufactured under a quality system;
- that finished devices meet these specifications;
- that devices be correctly installed, checked and serviced;
- that quality data be analyzed to identify and correct quality problems;
- and that complaints be processed.

Thus, the QS regulation helps assure that medical devices are safe and effective for their intended use. The Food and Drug Administration (FDA) monitors device problem data and inspects the operations and records of device developers and manufacturers to determine compliance with the GMP requirements in the QS regulation.

The QS regulation is in Title 21, Code of Federal Regulations (CFR), Part 820. This regulation covers quality management and organization, device design, buildings, equipment, purchase and handling of components, production and process controls, packaging and labeling control, device evaluation, distribution, installation, complaint handling, servicing, and records. The preamble describes the public comments received during the development of the QS regulation and describes the FDA Commissioner's resolution of the comments. Thus, the preamble contains valuable insight into the meaning and intent of the QS regulation.

The Medical Device Quality Systems Manual: A Small Entity Compliance Guide, First Edition details the requirements of the new QS regulation and provides detailed guidance in the following areas:

1. Obtaining information on GMP requirements;
2. determining the appropriate quality system needed to control the design, production and distribution of the proposed device;
3. Designing products and processes;
4. Training employees;
5. Acquiring adequate facilities;
6. Purchasing and installing processing equipment;
7. Drafting the device master record;
8. Noting how to change the device master records;
9. Procuring components and materials;
10. Producing devices;

11. Labelling devices;
12. Evaluating finished devices;
13. Packaging devices;
14. Distributing devices;
15. Processing complaints and analyzing service and repair data;
16. Servicing devices;
17. Auditing and correcting deficiencies in the quality system; and
18. Preparing for an FDA inspection.

h. POSTMARKET SURVEILLANCE/TRACKING

The Safe Medical Devices Act of 1990 (SMDA) amended the Federal Food, Drug and Cosmetic (FFD&C) Act increasing FDA's postmarketing regulation of medical devices. The two additional postmarketing activities include Postmarket Surveillance Studies and Device Tracking. Although the device criteria for postmarket surveillance and tracking are similar and the devices overlap, the intents are clearly twofold; postmarket surveillance is an early warning system after the initial marketing of a device while tracking is a system for locating potentially serious devices whether in distribution or with the user.

i. POSTMARKET SURVEILLANCE STUDIES

FDA may order manufacturers to conduct postmarket surveillance studies to gather safety and efficacy data for certain Class II and Class III devices. This requirement applies to any Class II and Class III device:

- the failure of which would be reasonably likely to have serious adverse health consequences; or
- which is intended to be implanted in the human body for more than one year; or
- which is intended to be a life sustaining or life supporting device used outside a device user facility.

Manufacturers must, within 30 days of receiving an order to conduct a postmarket surveillance study from FDA, submit, for approval, a plan for the required surveillance. The FDA may order a study for up to 36 months. Any longer period has to be mutually agreed upon by the manufacturer and FDA. If no agreement or a longer time period can be reached, then a dispute resolution process is to be followed.

After receiving the manufacturer's proposed plan, FDA has 60 days to determine if the person designated to conduct the surveillance is qualified and experienced, and if the plan will collect useful data that can reveal unforeseen adverse events or other information necessary to protect the public health.

j. DEVICE TRACKING

FDA has the discretion to order manufacturers of certain types of Class II or Class III devices to initiate a program to track their medical devices down to the patient level. The types of devices subject to a tracking order may include any Class II or Class III device:

- the failure of which would be reasonably likely to have serious adverse health consequences, or
- which is intended to be implanted in the human body for more than one year, or
- which is intended to be a life-sustaining or life-supporting device used outside a device user facility.

In addition, patients receiving a tracked device may refuse to release, or refuse permission to release, their name, address, social security number, or other identifying information for thepurpose of tracking.

k. MEDICAL DEVICE REPORTING

Since December 13, 1984, manufacturers and importers of medical devices have been required to comply with the Medical Device Reporting (MDR) regulation. The MDR requirements were changed in 1990, 1992, 1995 and again in 1997. Under the current provisions of the MDR regulation, which are found in 21 CFR Part 803, domestic and foreign medical device manufacturers and importers of medical devices are subject to the requirements.

The Food and Drug Administration (FDA) requires manufacturers and importers to report to FDA whenever the firm becomes aware of information that reasonably suggests that one of its marketed devices

(1) has or may have caused or contributed to a death or serious injury, or

(2) has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The Medical Device Reporting (MDR) regulation is a mechanism for FDA and manufacturers to identify and monitor significant adverse events involving medical devices so that problems may be detected and corrected in a timely manner.

The MDR regulation requires manufacturers of medical devices to report a device-related death, serious injury, or malfunction to FDA whenever they become aware of information that reasonably suggests that a reportable event occurred (one of their devices has or may have caused or contributed to the event).

Manufacturers must submit baseline reports that provide basic device identification information including:

1. brand name,
2. device family designation,
3. model number,
4. catalog number, and
5. any other device identification number.

Baseline reports also contain other important information about the device including:

- regulatory basis for marketing the device,
- shelf life or expected life of the device, and
- date device was first marketed and when marketing stopped, if applicable

l. MEDWATCH

The MDR reporting program is one component of the total FDA adverse event and product problem reporting system. This system was renamed, “MedWatch – The FDA Medical Products Reporting Program” and was launched on June 6, 1993. The MedWatch program integrates onto a single reporting form, all of the adverse event and product problem reporting information required by the various FDA regulations. The program has both voluntary and mandatory components.

The voluntary component encourages health care professionals to report serious adverse events and product problems involving devices, drugs, biologics, special nutritional products and other products directly to the FDA. The mandatory component covers the adverse event and product problem reporting requirements currently in place for manufacturers of drugs, biologics and medical device manufacturers, distributors and user facilities

m. PERFORMANCE STANDARDS

Under Section 514 of the FFD&C Act, FDA is authorized to develop and establish mandatory performance standards for Class II devices. Such standards may be developed by FDA or by outside organizations which offer to develop standards for FDA's consideration, or may be an existing standard that FDA adapts as its mandatory standard. If an FDA performance standard exists for a device, that device must conform to the standard before it can be legally marketed in the U.S. Regulations establishing a performance standard promulgated under Section 514 would not be effective before 1 year after the date of publication in the Federal Register, unless an earlier date is necessary for the protection of the public health and safety. Performance standards under Section 514 presently exist for Electrode Lead Wires and Patient Cables (21 CFR 898). There are standards for radiological devices, but they are not under Section 514.

n. RADIATION STANDARDS

In addition to performance standards that may be promulgated for medical devices under the FFD&C Act, CDRH may promulgate performance standards for radiation-emitting electronic products. So far, CDRH has developed performance standards for the following products:

- **Television Receivers** – This standard became effective January 15, 1970, and has been recodified in 21 CFR 1020.10. It applies to television receivers designed to receive and display a television picture, and includes electronic viewfinders on TV cameras, TV projectors, and TV monitors used with x-ray and other systems.
- **Diagnostic X-ray Equipment** – This standard became effective August 1, 1974, and has been recodified in 21 CFR 1020.30 through 1020.33, with subsequent amendments.
- It applies to complete diagnostic x-ray systems, as well as major components, including tube-housing assemblies, x-ray controls, high voltage x-ray generator, fluoroscopic imaging assemblies, x-ray tables, cradles, film changers, cassette holders, and beamlimiting devices.
- **Cabinet X-ray Systems** – This standard became effective April 10, 1976, and has been recodified in 21 CFR 1020.40. In addition to baggage inspection systems, it applies to other x-ray machines enclosed freestanding cabinets.
- **Laser Products** – This standard became effective August 1, 1976, and has been recodified in 21 CFR 1040.10 and 1040.11, with subsequent amendments. It applies to all lasers and products containing lasers. Specific requirements for medical lasers are in 21 CFR 1040.11(a).
- **Sunlamp Products and Ultraviolet Lamps Intended for Use in Sunlamp Products**

This standard became effective on May 7, 1980 and was amended September 8, 1986. It applies to all sunlamp products and ultraviolet lamps intended to induce suntanning

Ultrasonic Therapy Products – This standard became effective February 17, 1979, and has been recodified in 21 CFR 1050.10. It applies to any device intended to generate and emit ultrasonic radiation for therapeutic purposes at frequencies above 16 kilohertz, or any generator or applicator designed or specifically designated for use in such a device.

o. LABELLING

The labeling of medical devices and in vitro diagnostic products are governed by two U.S. Federal laws:

- Fair Packaging and Labeling Act (FPLA)

- Federal Food, Drug and Cosmetic (FFD&C)Act

Most of the provisions of the FPLA and the FFD&C Act are codified in the following parts of Title 21 of the U.S. Code of Federal Regulations (CFR):

- 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 FFD&C Act is the primary law under which the FDA takes action against non-complying regulated devices, such as adulterated, misbranded (mislabeled) devices. Section 201 of the FFD&C Act defines the terms "label" and "labeling" as they apply to medical devices and draws a distinction between the two terms. Certain provisions apply specifically to the "label" of the device, others are related to its "labeling". "Labeling" is a very broad term and deals with labels on the device as well as descriptive and informational literature that accompanies the device.

The FFD&C Act defines **"label"** as:

A "display of written, printed, or graphic matter upon the immediate container of any article…".
"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."

General device labeling requirements consist of:

- Name, address and qualifier for manufacturer, packager or distributors;
- Intended use/directions for use;
- Prominence of labels;
- Over-the-counter (OTC) devices;
- Prescription devices;
- Labeling in English;
- Warning and caution statements; and
- Specific labeling for certain devices.

There are no requirements for FDA to review a device's label and/or labeling to confirm compliance with the labeling regulations.

The device label and/or labeling is reviewed with the premarket notification or premarket approval submission, but strictly for indication for use statements and the demonstration of substantial equivalence and/or safety and effectiveness of the device.

When labeling does not meet the FDA regulations in 21 CFR Part 801, the device is considered to be misbranded. The following activities would cause a device to be misbranded:

- Its labeling is false or misleading in any particular, including promotion for unapproved uses;
- It is in package form and its label fails to contain the name and place of business of
- the manufacturer, packer, or distributor; and an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count;
- Any required wording is not prominently displayed as compared with other wording on the device, or is not clearly stated;

- Its label does not bear adequate directions for use including warnings against use in certain pathological conditions; or by children where its use may be dangerous to health; or against unsafe dosage, or methods, or duration of administration or application;
- It is dangerous to health when used in the dosage or manner or with the frequency or duration prescribed, recommended or suggested in the labeling; or
- It does not comply with the color additives provisions listed under Section 706 of the Act.

Compliance with the labeling regulations is enforced during postmarked activities such as GMP inspections of the facility.

p. MARKING-COUNTRY OF ORIGIN

Laws enforced by the U.S. Customs Service require that each imported article be legibly and conspicuously marked in English with the name of the country of origin. Exceptions to this rule are: articles which are merely in transit through the U.S.; articles which are otherwise specifically exempted from marking requirements. Certain articles may also require special marking.

q. PROCEDURES FOR THE EXPORT OF MEDICAL DEVICES FROM THE U.S.

Chapter VIII of the Federal Food, Drug and Cosmetic (FFD&C) Act addresses FDA regulation of the import and export of foods, drugs, cosmetics, biologics, medical devices, and radiation emitting electronic products. Sections 801 and 802 of Chapter VIII list the specific rules governing the import and the establishment of an Office of International Relations to act as FDA liaison with foreign governments.

7. Medical Device Regulation in the Jordan:

7.1 Medical device Regulations in Jordan by the JFDA:

Article (1) this is called the **Foundations of Import and Circulation of Medical supplies**, including Disinfectants (the principles of handling medical supplies, including antiseptics and disinfectants) and works by date of publication in the Official Journal.

Article (2) For the purposes of the application of these principles based tariffs as set out in Article (2) of the Act, plus the following:

- **Medical entailing:**

each device, means or substance or device or class, whether used alone or associated with others, including the software necessary for its use, prepared by the manufacturer to be used for a person in order to achieve any of the following goals :

1. diagnosis, prevention, surveillance, treatment, disease reduction
2. diagnosis, surveillance, mitigation and / or compensation for any injury or disability.
3. disclosure, compensation, or amendment from / to the anatomical situation
4. Planning pregnancy :

And which does not achieve the objective of the manual in / on the human body by means of pharmacological or immunological or representative food, but can help to be done with this mean, and this is what sets it apart from medicine

Accessories

are tools prepared by the manufacturer for use with medical supplies in particular.

Category

group involved which entails a medical underneath in terms of safety / dangerous to use and divided into:

- Category 1
- Category 2 A
- Category 2 B
- Category 3
- Category of effective medical supplies which are grown in the body (Active Implants)
  As categorized in the:
  Medical Devices Directive 93/42
  Active Implantable MDD 90/385/EEC
- **Laboratory:** The Drug Control Laboratory
- **Committee: Committee for Medical supplies, including disinfectants and antiseptic (responsible authority)**

Article (3)

A. Is to allow the import and circulation of medical supplies, except as provided in (b) below, after approval by the Director-General or his deputy by the conditions set forth in Annex No. (1) and Annex No. (3) and annex (4).
B. Are importing and circulation of medical supplies of pharmaceutical form and those containing drugs with the prior approval of the Committee according to the conditions contained in Annex No. (1) and Annex No. (3) and annex (4).
C. Are imported detergents and antiseptics by Supplement No. (2) and Annex No. (3) and Annex No. (4).
D. Prohibits the import of medical supplies used or refurbished for all health sectors in the Kingdom.

Article (4)

A. The Committee shall examine the requests to allow the import of the material in item (b, c) of Article (3) contributions to the Foundation by importers and a decision about them during a maximum period of thirty working days from the date of application
B. The applicant's right to object to the Commission's decision of refusal within a maximum period of thirty working days from the date of notification of the decision in writing.
C. The Committee shall examine the objections and make a decision about them within a period of thirty working days from the date of submission of the institution.

Article (5)

The Director-General on the recommendation of the Committee to take a reasoned decision to ban the import or distribution, or stop to stop selling or prevent the sale or cancellation of prior approvals or retrieve medical supplies, disinfectants and antiseptics.

Article (6)

Must be taken the Committee's approval on any changes to the medical supplies, disinfectants and antiseptics, contrary to what has been previously approved by it.

Article (7)

Director General shall issue special instructions for the inspection of manufacturers and institutions, import and trading and distribution of medical supplies, disinfectants, sterilizers and supplies, disinfectants and antiseptics used in places such as hospitals and other .

Article (8)

To the Director-General introduced the controversial issues that may arise from the application of these principles to the Committee for decision and decision

Article (9)

May not be for customs officials to allow clearance of any consignment of medical supplies, disinfectants, detergents or any of their raw materials to local industry, but after approval of the Director-General or his deputy

Article (10)

should not be advertised on any accessory or medical disinfectant or sterilized in any of the print media or radio, or any of the other means only after approval of the Director-General on the recommendation of the Committee and with the exception of publication in medical journals specialized.

Article (11)

To hospitals, clinics and health centers, or any other authority concerned to inform the institution of any severe damage (serious) or deaths associated with the use of any accessory or medical disinfectant or sterilizer.

7.2 Medical Device Requirement for registration

Technical file including:

1. Notarized CE or FDA certificate (EC Declaration of Conformity certificate) or Free Sale Certificate " FSC " for the product in the country of origin.
2. If the product has only a FSC and does not have a CE or FDA , then in addition to point number 1 above we have to submit another FSC for the product in one of the following countries (Switzerland , Australia, Canada, Japan , Norway).
3. Certificate of analysis for samples that have same batch number will be analyze, titled with trade name and has mfd & exp date.
4. Certificate of analysis for standards or other materials needs for analysis.
5. Safety material data sheets for standards
6. Composition for active & not active materials with quantities.
7. Finished product specifications last version.
8. Method of analysis for all tests under specifications can be applied in lab and calculations.
9. Stability data contains storage condition & validity
10. Chromatograms HPLC and GC for sample, standards and degradations
11. Chromatograms HPLC and GC for sample, standards and degradations products.
12. Outer pack in independent language.

- Samples must be signed from the medical device department with a form contains same batch number, trade name, size, company and number of samples.
- The file takes 10 days to review all requirements in the check list.
- The company takes the check list and provides the R&D division with the requirements that have been missed in two days (Sunday& Tuesday)

- If the file is completed with all The requirements, each sample takes a serial number with a letter R for registration and apply the analysis
- All requirements found in check list

Check List

اسم المستحضر وشكله الصيدلاني : .....

التركيز : .....

١-	الكتب والمراسلات الخاصة بالمستحضر	
٢ -	شهادات التحليل	
٣-	شهادة تحليل (Standard)	
٤-	شهادة التركيب (Composition)	
٥ -	مواصفات المستحضر النهائية (Finished Product Specification)	
٦-	طرق التحليل (Method of Analysis)	
٧ -	خلاصة دراسة الثبات	
٨-	العبوة الخارجية تحمل رمز الدواء (Bar Code)	
٩ -	النشرة الداخلية	

توقيع الفني المسؤول

(المستودع / الشركة)

توقيع الفني المسؤول

(مختبر الرقابة الدوائية)

Check List

THE FILE CAN ENTER BY:
DATE:

FILE NO.:

QUALITY CONTROL LABORATORY

PRODUCT NAME:…….. STORE NAME:……

NO. OF SAMPLES:…….. NO.OF FILES:……

NO.OF STANDARD:…….. PHONE NO:……

REICIVING DATE:…….. REVISION DATE:……

1. CERTIFICATE OF ANALYSIS CONTAINING;

☐ THE SAME BATCH NO. AS SAMPLES ☐ MFG DATE ☐ EXPIRY DATE

2. FINISHED PRODUCT SPECIFICATIONS:

☐ AT SHELF LIFE/DECLARATION ☐ TITLED WITH THE TRADE NAME

3. REFERENCE STANDARD:

☐ CERTIFICATE OF ANALYSIS ☐ REFERANCE STD ☐ SAFFETY DATA SHEET

A…… NO.:……

B…… STORE AT:……..

4. WORKING STANDARD:

☐ CERTIFICATE OF ANALYSIS ☐ WORKING STD ☐ SAFETY DATA SHEET

A…….. NO.:……

B…… STORE AT:……..

5. LAST VERSION OF METHODS OF ANALYSIS IN DETAILS AS IN SPECS.:

☐ COMPLETE ☐ NOT COMPLETE

1: ……..

2: ……..

3: ……..

4: ……..

5: ……..

6. CALCULATIONS NEEDED:

☐ DISSOLUTION ☐ ASSAY ☐ RELATED/IMPURITIES ☐ OTHERS

7. CHROMATOGRAMS AT INITIAL/ ZERO TIME:

☐ ASSAY ☐ STANDARDS ☐ RELATED SAMPLE/IMPURITIES ☐ DISSOLUTION

8. COMPOSITION OF THE PRODUCT:

☐ AVAILABLE ☐ NOT AVAILABLE

PREPARED & PRINTED BY:
Huda Qurani & Hiba Bassam Abdel Rahim

THE FILE CAN ENTER BY: FILE NO.:

DATE:

9. STABILITY CONCLUSION;

☐ VALIDITY ☐ STORAGE CONDITIONS

10. SAMPLES:

BROUGHT:..... NEEDED:.....

EXPIRY DATE:..... STORAGE CONDITIONS:.....

11. RELATED SUBSTANCES/IMPURITIES:

NO.	NAME OF THE MATERIAL NEEDED	QUANTITY	SAFTY DATA SHEET

12. COLUMNS:

NAME OF THE COLUMN NEEDED	THE TEST NEEDED FOR	PAGE NO.

13. ANY OTHER CHIMICALS NOT AVAILABLE IN LAB.

1: WE ALWAYS NEED PLACEBO AND SYSTEM SUITABILITY.

2: .....

3: .....

4: .....

1) ENTERING SAMPLE/FILE FOR STUDY:

AGENT NAME:..... SIGNATURE:..... DATE: .....

2) FILE STUDY:

ANALYST NAME:..... SIGNATURE:..... DATE:

CHECKED BY:..... SIGNATURE:..... DATE:

3) RECEIVING COPY OF CHECKLIST

AGENT NAME:..... SIGNATURE:..... DATE:

4) ENTERING SAMPLE/FILE FOR ANALYSIS

APPROVED BY:..... SIGNATURE:..... DATE:

Telephone no. of the drug store: Fax no.:

PREPARED & PRINTED BY:
Huda Qurani & Hiba Bassam Abdel Rahim

8. Medical Device Regulation in Kingdom of Saudi Arabia:

Explanatory Memorandum

Saudi Food and Drug Authority (SFDA) was established under the Council of Ministers resolution no. (1) Issued on 10/3/2003, as an independent Authority reporting to the Council of Ministers. The SFDA **aims** to "ensure the safety of food, safety, quality and effectiveness of drug, and the safety, quality, effectiveness and performance of medical devices according to their intended purpose. Regulating medical devices, in vitro- diagnostic devices, prescription eye glasses, contact lenses and their solutions, are among the responsibilities of SFDA in accordance with its law issued by the royal decree No.(M/6) issued on 13/2/2007.

As a result the SFDA launched a comprehensive marketing authorisation program intended to safeguard public health as it relates to medical devices. The program comprises **two major steps.**

a) Establish an overall profile of the medical devices presently on the Kingdom of Saudi Arabia (KSA) market.

b) Develop, adopt and apply a **Medical Devices Interim Regulation (MDIR)**, complemented by Implementing Rules, thereby ensuring legal certainty that only medical devices that have been authorised by one of the Founding Members of the Global Harmonization Task Force (GHTF) have access to the KSA market.

The Medical Device Interim Regulation applies to the following parties and products:

A) Manufacturers, authorised representatives, importers and distributors.

B) All Medical Devices and their accessories that will be supplied to the KSA market.

C) Contact lenses and laser surgical equipment for cosmetic rather than medical purposes, and their accessories.

The SFDA also adopt and publish guidelines to ensure a coherent and uniform application of some provisions of the Implementing Rules (the contents of MDIR):

1) Implementing Rule on Designation and Oversight of Conformity Assessment Bodies (MDS- IR1)

This implementing rule specifies and completes the provisions of chapter SEVEN of the MDIR the SFDA may designate third-party organisations, known as Conformity Assessment Bodies (CABs), to assist it in carrying out the duties specified in Chapters TWO and SIX of the MDIR

2) Implementing Rule on Establishment Registration (MDS-IR2)

This Implementing Rule specifies and completes the provisions of Chapters THREE and FOUR of the MDIR. Local manufactures, authorised representatives, importers and distributers involved in the supply of medical devices, authorised by the SFDA in application of the MDIR shall register their establishments with the SFDA's Medical Device National Registry (MDNR). They shall submit the information specified in Article 8 of Implementing Rule MDS – IR2 before they place such medical devices on the KSA market. SFDA will assign an establishment National Registry Number to each registrant.

3) Implementing Rule on Medical Devices Listing (MDS-IR3)

This Implementing Rule specifies and completes the provisions of Chapters THREE and FOUR of the MDIR. Local manufacturers, authorised representatives, importers and distributers involved in the supply of SFDA authorised medical devices shall list the devices they intend to place on the Saudi market with the SFDA's Medical Device National Registry (MDNR). They shall submit the information specified in Article 8 of Implementing Rule MDS-IR3 when they supply such medical devices to the KSA market. SFDA will assign a Listing National Registry Number to each medical device listed in the database.

4) Implementing Rule on Establishment Licensing (MDS-IR4)

This Implementing Rule specifies and completes the provisions of Chapter FIVE of the MDIR. Organizations involved in the importation and/or the distribution of SFDA authorised medical devices into or within the KSA shall have an establishment license for each activity issued by the SFDA before supplying devices. They shall submit the information specified in respectively Articles 7 and 12 of Implementing Rule MDS-IR4 in due time. SFDA will issue the applicant with an establishment license for its requested activity (ies), when it is satisfied that the relevant requirements have been met.

5) Implementing Rule on Licensing of Authorised Representatives (MDS-IR5)

This Implementing Rule specifies and completes the provisions of Chapter SIX of the MDIR. Manufacturers not established in the KSA shall designate an organization authorised by it to act on his behalf in the KSA. This authorised representative shall introduce an application with the SFDA and declare to perform the activities specified in Article 6 of Implementing Rule MDS-IR5. SFDA will issue the authorised representative with an establishment License, when it is satisfied that the relevant requirements have been met.

6) Implementing Rule on the Validation of Documents to be provided to the SFDA by Manufacturers for Marketing Authorisation (MDS-IR6)

This Implementing Rule specifies and completes the provisions of Chapters TWO and SIX of the MDIR. Manufacturers wishing to supply a Medical Device in the KSA shall provide the SFDA with documentation that demonstrates that the device is authorised to be placed on the market in one of the GHTF Founding Member jurisdictions and that it complies with the specific Saudi requirements specified in the MDIR and Article 5 of Implementing Rule MDS-IR6. SFDA shall issue a marketing authorisation in writing to the manufacturer, when it is satisfied that the relevant requirements have been met.

7) Implementing Rule on Post-Marketing Surveillance (MDS-IR7).

This Implementing Rule specifies and completes the provisions of Chapters EIGHT and TEN of the MDIR. SFDA shall take all appropriate measures, within its power, to ensure that SFDA authorised medical devices are subject to post-marketing surveillance, comprising device adverse event management (Chapter TWO) and market control (Chapter THREE). All parties concerned shall be made aware of their responsibilities and obligations.

8)Implementing Rule on Safeguard Procedures (MDS-IR8)

This Implementing Rule specifies and completes the provisions of Chapter NINE of the MDIR.
SFDA requires that measures are taken to remove any threat to public health that may be caused by medical devices available on the KSA market which do not comply with the MDIR and its relevant Implementation Rules. Where appropriate, SFDA shall take safeguard actions against these devices and inform the authorising GHTF Competent Authorities concerned.