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EMC guideline for the design of an artificial pancreas.

Current and required standards and tests.

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Electronic Engineering Thesis

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Abstract

The goal of this thesis is to cover the different important points to commercialize an implantable artificial pancreas. All the medical devices must obtain the marking CE in order to commercialize them. This is an official marking that needs all electrical and electronic products in the European Union. Thus this thesis will explain how to obtain the marking CE to commercialize an artificial pancreas.

The artificial pancreas is an implantable medical device, because it is introduced in the body and destined to remain after the operation. In addition it is active because it depends on a power supply not generated by the human body. In conclusion an artificial pancreas, as all the implantable medical devices, is regulated by the directive 90/385/ECC.

Later the thesis has a guideline to implement the artificial pancreas complying the EMC normative. This guideline is divided in two, one for the implementation of the power supply and one for the implementation of the control system.

Finally the thesis will explain the different tests that the artificial pancreas will need to pass in order to get the CE marking. In this point it is important to mention that the artificial pancreas must comply several harmonized normatives. These harmonized standards are:

- Electromagnetic compatibility EN 60601-1-2

- Electric security EN 60601-1
- Biocompatibility EN ISO 10993-1

The thesis will explain these normative, but it will consider with special care the EMC normative. The thesis will deal with special details the subjects about the electromagnetic compatibility because of their vital importance. Thus the different EMC tests are explained.

The important necessity of standards is observed because they assure the compatibility of the artificial pancreas with other equipment and systems. Fortunately exists specifics standards for most of the electronical devices, although an universal normative is missed. Nevertheless the directive 90/385/ECC is a great step and supposes the free active implantable product circulation in the European market, this already supposes a great advance in the normalization of sanitary products.

* Note: The student had a workload of 21 ECTS credits for this work, therefore the present work is valid for the Master's thesis and a course in Electromagnetic Compatibility.

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Firstly, my best regards to the project manager Mr. Esa Häkkinen and to the coordinator Alberto García. Thanks for all your help and understanding you provided me through this project, it was a pleasure working with you.

I want to dedicate this thesis to my parents, Pedro de León and Pepita Cotolí. I want also to say thanks to my parents for helping me to come to Finland. Thanks daddies to support to your son all these years.

Also I want to dedicate this thesis to my uncles and to my granny. I want in addition to congratulate them being the best family of the world.

Also say thanks to the research team and my best friends Jordi, Yazan, Esteban, Loïc and my brothers for all the fun and the great moments we had together and for always being there behind me to back me up in good and hard times. I hold all of you in my heart.

Finally I want to dedicate a few lines to my grandpa. I am writing these words and I feel that whatever I write is not enough for my grandpa, Arcadio Cotolí. Anyway I want to say: “Thanks grandpa for all the moments that we have lived together. Thanks to share your life with me. Thanks to teach me how to live. Thanks to be my grandpa. Thanks for everything. See you some day”.

Pedro Pablo de León Cotolí
Helsinki, August 2005

List of Most Important Abbreviations

AIMDD	Active Implantable Medical Devices
AC	Alternating Current
AE	Auxiliary Equipment
CDN	Coupling-Decoupling Network
CE marking	European Conformity
CISPR	International Special Committee On Radio Interference
DC	Direct Current
EC	European Community
EM Clamp	ElectroMagnetic Clamp
EMC	ElectroMagnetic Compatibility
EMI	ElectroMagnetic Interference
ESD	ElectroStatic Discharge
EU	European Union
EUT	Equipment Under Test
GRP	Reference Ground Plane
IC	Integrated Circuit
LISN	Line Impedance Stabilization Network
MDD	Medical Device Directive
OATS	Open Area Test Site
PCB	Printed Circuit Board
RF	Radio Frequency
UUT	Unit Under Test
VDE	Verband Deutscher Elektrotechniker (GERMANY)

Table of contents

1. Introduction

This thesis is a part of an Artificial Pancreas Project. It is important to mention that this project is very important and useful due to there are many people suffering from diabetes.

Diabetes is a sickness that affects ability of your body to produce or use insulin. Insulin is a hormone. When your body turns the food you eat into energy (also called sugar or glucose), insulin is released to help transport this energy to the cells. Insulin acts as a key. Its chemical message tells the cell to open and receive glucose. If you produce little or no insulin, or are insulin resistant, too much sugar remains in your blood. Blood glucose levels are more elevated than normal for persons with diabetes.

The goal of this thesis is to cover the different important points to commercialize an implantable artificial pancreas. But firstly, this thesis explains briefly the problem of the diabetes. Also it explains briefly the whole of the Artificial Pancreas Project.

After, this thesis covers the subject about how do get the CE marking, this marking is indispensable to commercialize the artificial pancreas. In this chapter it will explain the harmonized standards and Directives that the artificial pancreas needs.

Later the thesis presents a guideline to design the artificial pancreas in order to comply the EMC normative

And finally this thesis explains the different tests that the artificial pancreas will need pass to get the CE marking and thus to commercialize it. In this point it is important to mention that the artificial pancreas must comply several harmonized normatives. The thesis explains these normative, but it considers with special care the EMC normative.

2. Background

2.1 Diabetes Definition [26]

Diabetes Mellitus is a common illness. It is estimated that nearly 180 million people worldwide suffer from diabetes and its frequency is dramatically rising all over the world. Insulin is a hormone that lowers glucose levels in the blood. Glucose (a form of sugar) is the main source of fuel for our bodies. It comes from foods containing carbohydrate.

Diabetes Mellitus develops when the pancreas (the organ responsible for producing insulin) is either unable to make insulin, or the insulin is unable to work effectively. Without insulin doing its job, glucose builds up in the blood leading to high blood glucose levels causing health problems.

There are two main types of diabetes. The main aim of its treatment to achieve blood glucose and blood pressure levels as near to the normal values as possible. This, together with a healthy lifestyle, will help to improve wellbeing and protect against long-term damage to the eyes, kidneys, nerves, heart and major arteries.

2.2 Two main types of diabetes [26]

2.2.1 Type 1

When you are affected with Type 1 diabetes, your pancreas does not produce insulin. Type 1 diabetes is also called juvenile diabetes, since it is often diagnosed in children or teens. This type accounts for 5-10% of people with diabetes.

2.2.2 Type 2.

Type 2 diabetes occurs when the body does not produce enough insulin, or when the cells are unable to use insulin properly, which is called insulin resistance. Type 2 diabetes is commonly called “adult-onset diabetes” since it is diagnosed later in life, generally after the age of 45. 90-95% of people with diabetes have this type. In recent years Type 2 diabetes has been diagnosed in younger people, including children, more frequently than in the past.

2.3 Malfunction in Glucose Metabolism [14]

In a normal body, carbohydrates (sugars and starches) are broken down in the intestines to simple sugars (mostly glucose), which then circulate in the blood, entering cells, where they are used to generate energy. Diabetics respond inappropriately to carbohydrate metabolism, and glucose can not enter the cells normally.

Insulin (a hormone that is made in the pancreas and released into the bloodstream and carried throughout the body) enables the organs to take sugar from the blood and use it for energy. If body cells become resistant to effect of insulin or if there is not enough insulin, sugar stays in the blood and accumulates, causing high blood sugar. At the same time, cells starve because there is no insulin to help move sugar into the cells.

Diabetes is diagnosed by measuring blood sugar levels. This can begin with a urine test sampled for glucose because excess sugar in the blood spills over into the urine. Further testing involves taking blood samples after an overnight fast. Standard fasting blood glucose levels are between 3.89 mmol/l and 5.83 mmol/l; a fasting blood glucose measurement superior than 7 mmol/l on two separate occasions indicates diabetes.

Diabetes can result in many complications, including nerve damage, foot and leg ulcers, and eye problems that can lead to blindness. Diabetics also are at greater risk for heart disease, stroke, narrowing of the arteries, and kidney failure. But evidence shows that the better the patient controls his or her blood sugar levels, the greater the chances that the disease's serious complications can be reduced.

2.4 Shot of insulin

The first insulin for diabetes was derived from the pancreas of cows and pigs. Today, chemically synthesized human insulin is the most often used. It is prepared from bacteria with DNA technology. Human insulin is not necessarily an advantage over animal insulin, and most doctors do not recommend that patients on animal insulin automatically switch to human insulin. But if they do switch, dosages may change. Human insulin is favourite for those patients who take insulin intermittently.

2.5 Diabetes Statistics

In 2004, according to the World Health Organization, more than 150 million people worldwide suffer from diabetes. Its incidence is increasing rapidly, and it is estimated that by the year 2025 this number will double in Africa, the Eastern Mediterranean and Middle East, and South-East Asia, and rise by 20% in Europe, 50% in North America, 85% in South and Central America and 75% in the Western Pacific.

Diabetes occurs throughout the world, but is more common (especially Type II) in the more developed countries. The greatest increase in prevalence rate is, however, expected to occur in Asia and Africa, where most of the diabetic patients will be seen by 2025. The increase in incidence of diabetes in the developing countries follows the trend of urbanization and life style changes.

Diabetes is in the top 10, and perhaps the top 5, of the most significant diseases in the developed world, and is gaining in significance. For at least 20 years, diabetes rates in North America have been increasing substantially. In 2002 there were about 18.2 million diabetics in the United States alone. The Centers for Disease Control has termed the change an epidemic. The National Diabetes Information Clearinghouse estimates that diabetes costs $132,000 millions in the United States alone every year. [28]

3. Quick Overview of the Project Team and the Solution Approach for the Whole Artificial Pancreas Project [11]

The closed-loop system for controlling the blood glucose level that had been developed at Helsinki Polytechnic Stadia is composed of three main blocks. The closed-loop system has the implantable device, the external system communicator and the external charger of the super-capacitor.

The implantable device has a glucose sensor, a microcontroller, an insulin reservoir and pump, a glucagon reservoir and pump, a super capacitor with a loading system, and a RF transmitter. The glucose sensor detects the amount of glucose in the blood of the patient. This information is sent to the microcontroller which processes it and calculates the dosage of the insulin or glucagon. Then, the insulin pump delivers the right amount of insulin or glucagon in the peritoneal cavity. The reservoirs will have a mechanism to be safely refilled by means of injections. For instance, if the reservoir has been vacuumed from air, the negative inner pressure will absorb the medicine automatically. Otherwise, during the injection, the air within the reservoir should be evacuated. Moreover, the microcontroller also runs the software needed to control the RF transmission system. All this system will be powered by a super-capacitor. Also, there will be a loading system that will recharge this super-capacitor externally.

The external system communicator uses an RF system to interact with the implantable part of the device. It will provide the patient with important information about the status of the system. Especially if there is a system failure, this external system communicator will immediately inform the patient with a suitable alarm. As well, this communicator will be used to update the software running on the microcontroller.

The third part is an external induction system to charge the internal super-capacitor. The patient will have to recharge the super-capacitor periodically using this device. Simply by placing this charger on the skin of the patient, the super-capacitor will get reloaded. The charger produces a magnetic field that is converted into electricity, due to induction, by the internal part of the charger. This electricity refills the super-capacitor that will be the energy source of the internal system. Figure 3.1 depicts a block diagram of the system.

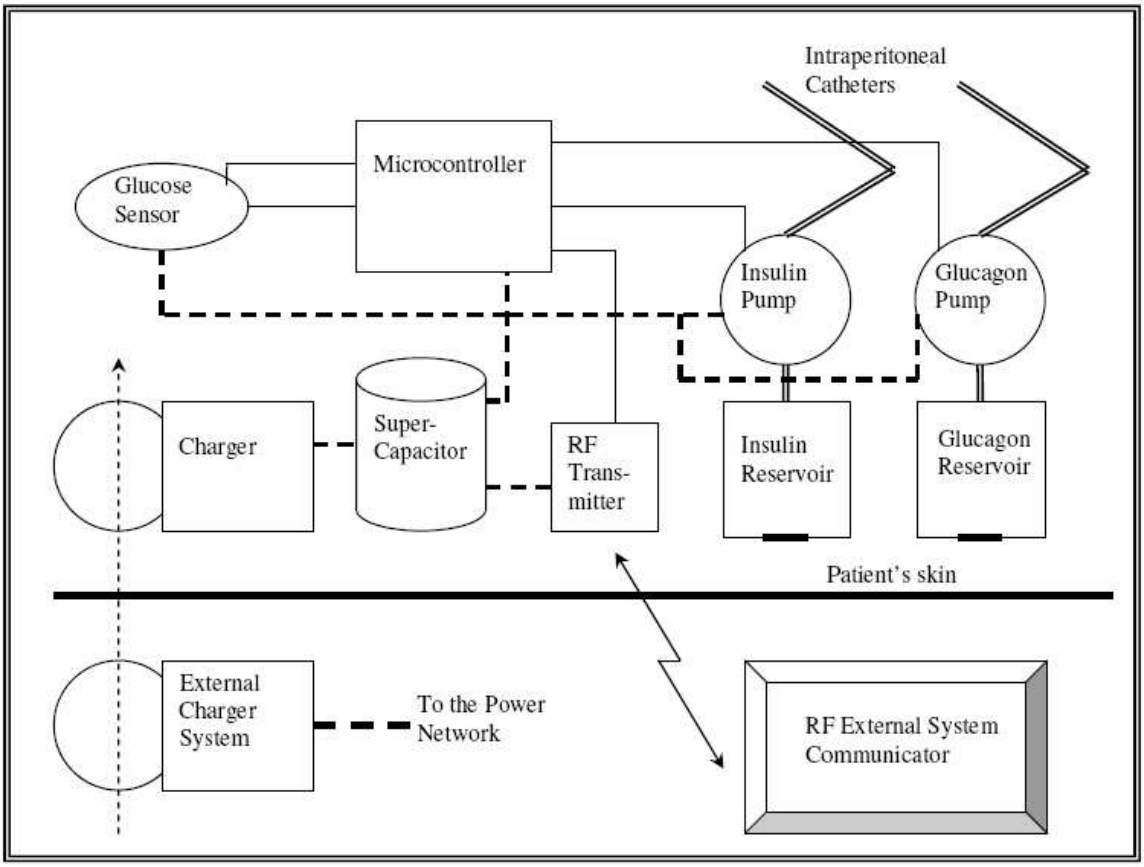

Figure 3.1 – Block Diagram of the Artificial Pancreas Project. The MCU is driven by the power from the super-capacitor, it reads the blood sugar level from the sensor and controls the pumps, and also it sends data to the RF transmitter

Table 3.1 gives a description of each person responsibilities and tasks.

Name of Team Member	Field of work in the Project
Mr. Esa Häkkinen	- Project management. - Invention of a Blood Glucose Sensor.
Alberto Garcia	- Coordination between the manager and the researchers.
Yazan Jarrar	- Microcontroller interfacing and Software programming.
Jordi Martinez & Esteban Sancho	- Modeling the behavior of blood glucose levels in diabetic persons.
Pablo De Leon	- Research on medical standardization.
Henri Niinivirta	- Research on insulin types and Glucagon. - Providing the team with his practical experience.
Gijs Mulder	- Research on sensor technologies
Victor Garcia-Rojo	- Research on implantable pumps and reservoirs
Leon Verbruggen & Ronald v/d Heiligenberg	- Research on Wireless Power Supply

Table 3.1 – Short Description of the team members' responsibilities

4. How to obtain CE marking for an artificial pancreas [4]

4.1 Introduction

There are several steps to be taken in order to comply with the European legislation and to be entitled to affix the CE-marking to an artificial pancreas or whatever medical device. In this chapter, the thesis discusses in detail the necessary steps to obtain the CE-marking. This guideline explains how do affix the CE-marking to an artificial pancreas, thus following those steps, the process of CE-marking will become clear.

The "new approach" Directives regulate national technical legislation. They lay down binding rules that manufacturers must comply before placing their products on the market.

This document outlines the specific issues for an artificial pancreas, thus I will follow the *Directive 90*/385/EEC: Active implantable medical devices (AIMDD).

It is very important to mention that an artificial pancreas is covered directly by the *Active Implantable Medical Devices Directive (90/385/EEC).*

4.2 Steps to apply the CE-marking

In the process of CE-marking the manufacturer must comply several steps. These steps are enumerated in the table1.1.

Step 1	Chose applicable Directives to your product
Step 2	Check which standards are applicable to your product
Step 3	Check essential requirements
Step 4	Draw up a Technical File
Step 5	Test the product
Step 6	Draw up an EC Declaration of Conformity
Step 7	Draw up a file in which the production process is described
Step 8	Affix the CE Marking to the product

Table 1.1 – Steps to apply the CE-marking

4.3 Step 1. Chose applicable Directive(s) to your product

Firstly applicable directives to the product, in this case an artificial pancreas, must be found out,. Next, the manufacturer must determine which of these directives to apply to the product. For this, the scope of the Directive must be known.

Generally, directives are available by internet free of charge.

The table 1.2 shows most of all Directives.

Directive referente	Subject of directive
89/106/EEC	Construction products
89/336/EEC	Electromagnetic compatibility
96/57/EC	Energy efficiency requirements for household electric refrigerators, freezers and combinations
94/9/EC	Equipment and protective systems in potentially explosive atmospheres
73/23/EEC	Low voltage equipment
98/37/EC	Machinery safety
90/385/EEC	Medical devices: Active implantable
93/42/EEC	Medical devices: General
98/79/EC	Medical devices: In vitro diagnostic
90/384/EEC	Non-automatic weighing instruments
89/686/EEC	Personal protective equipment
97/23/EC	Pressure equipment
87/404/EEC	Simple pressure vessels
88/378/EEC	Toys safety

1.2 Table – Directives and Standards

4.3.1 The Medical Devices Directive

Medical devices have become an increasingly important health care area in relation to their impact on health and health care expenditure. The sector covers some 8000 types of products, ranging from simple bandages and spectacles, through life maintaining implantable devices, equipment to screen and diagnose disease and health conditions, to the most sophisticated diagnostic imaging and minimal invasive surgery equipment. The European Union's involvement concerns mainly the regulatory framework for market access, international trade relations and regulatory convergence, and the competitiveness of industry.

The full text of the Active Implantable Medical Device Directive may be accessed in the appendix A of this thesis.

This directive has been amended by Directive 93/68/EEC. See Directive 93/68/EEC, Article 9, related to the amendment of Directive 90/385/EEC. You can find the full text of this directive in the appendix B of this thesis.

4.3.2 Scope and exclusions of the medical devices directive

The scope of the directives reveals if a product is described by the directive. Some products may be subject to more than one directive.

An explanation of the directive and the demarcation with other directives may be seen on the following guidelines developed by the European Union (EU):

- Field of application of directive "active implantable medical devices"
  This guideline is located in the appendix C of this thesis.

- Treatment of computers used to program implantable pulse generators
  This guideline is located in the appendix D of this thesis.

- Interface with other directives – Medical devices/medicinal products
  This guideline is located in the appendix E of this thesis.

- Medical devices with a measuring function
  This guideline is located in the appendix F of this thesis.

Medical devices and electromagnetic compatibility

The Directive 90/385/EEC on active implantable medical devices (AIMDD) is a "specific directive" with regard to Directive 89/336/EEC relating to electromagnetic compatibility- (see: Article 1(5) AIMDD. The aforementioned medical devices directives cover all aspects related to electromagnetic compatibility (immunity and electromagnetic interference) of medical devices (see AIMDD, Annex I, section 8). Thus, in all cases when the AIMDD directive is applied, there is no need to apply the Directive 89/336/EEC with regard to EMC aspects.

4.4 Step 2. Check which standards are applicable to your product

The next step in the process is the point of how to comply with the Directives that apply to your product. Since the Directives only set the essential requirements, it is the responsibility of the manufacturer to find a way to comply with these requirements. Although the manufacturer is free to choose how to comply with the essential requirements, standards help for correct implementation. When some standards have been approved by the European Commission, they become called “harmonised standards”, and give *a* presumption of conformity. This means that complying with the standard equals the complying with the requirements in the directive.

Standards give detailed technical information on implementing the EU requirements. However, not all standards have been harmonised yet. Only standards that have their reference published in the Official Journal of the EU are called ‘harmonised standards’. Complying with these standards means that the authorities presume compliance with the Directives.

Standards are developed within a European network of participating interested parties, organised through the national standardisation bodies. The EU Commission gives mandates for the development of European standards. The EU Commission publishes the reference of the harmonised standards in the EU Official Journal, giving compliance to these standards the so-called "presumption of conformity". This means that, if a product complies with the relevant standards, it complies with the directives involved.

Combined with input from all members, a standard can be harmonised by the European standardisation bodies. All these bodies sell standards, both harmonised and national standards. We can and should check the websites for “European sites on standardisation”. These websites often provide online facilities for ordering standards and checking the latest ones.

This step of checking the relevant standards is crucial for CE-marking. The manufacturer should pay attention to applying the relevant, applicable standards.

The application of standards appears in the technical file, showing a complete list of standards used and a file of requirements met and verified, and the test results where appropriate.

The artificial pancreas needs to pass the next harmonized standards:

- Electromagnetic compatibility EN 60601-1-2
- Electric security EN 60601-1
- Biocompatibility EN ISO 10993-1

4.4.1 How to find harmonised standards

The EU is in the process of harmonising the standards that are used in all the individual EU countries. A compilation of the references of standards that have been published in the Official Journal of the European Union is available by internet [30].

4.5 Step 3. Check essential requirements

The essential requirements for the design and manufacture of medical devices ensure the protection of the health and safety of patients, users and third parties. These requirements stipulate that the principles of safety should be integral to the design of the product and that the product should be suitable for its intended purpose. The essential requirements are defined in Annex I of the MDD.

4.6 Step 4. Draw up a technical file

The technical documentation is a very important part of the conformity process in all Directives. This file should contain the documentation on how the conformity has been achieved. If the directive requires a verification of the file, for example when the product has to be submitted to an EC type approval, this file will be checked together with the product or separately.
This technical file can also be used for verification purposed by the competent market surveillance authorities in the EU-Member States. This may happen when there is a serious reason to doubt the compliance to the health and safety requirements or in case of an accident with the product. The file should be kept available at the manufacturer for 10 years.

Besides general information like name and address of the manufacturer, identification of the product, drawings and overviews of the product, all relevant detailed information on the design, construction and testing must be included. This includes the risk assessment, certificates, applied standards, a description of the preventive measures and a copy of the user manual are part of the file.

It is recommended to make a file per type of product. Also, if new products appear regularly, a ‘standard’ technical construction file may be helpful.

The technical documentation must be kept at the disposal of the national authorities for inspection purposes for at least ten years from the last date of manufacture of the product. The technical documentation may be kept on electronic support, provided that it is easily accessible for inspection. Where the manufacturer is not established in the EU and he has no

authorized representative in the EU, this obligation lies with the importer or the person responsible for placing the product on the Community market.

4.7 Step 5. Test the product

This step means to test the product (prototype) according to the specifications in the technical file, and, if required in the relevant Directive(s), submit a model of the product to an EC type approval by a notified body.

All testing carried out by the manufacturer, a laboratory, test house or notified body, will be included in the technical file. Since it is not always possible or feasible to test onsite, the technical file may be completed as far as the description of the product (artificial pancreas in or case) and the (intended) compliance with the relevant Directives and standards.

The flow chart shown in the figure 4.1 shows the process of the called “conformity assessment”. It is recommended to keep in main this flow chart, because of it summarizes perfectly all the process to obtain the CE marking for the artificial pancreas.

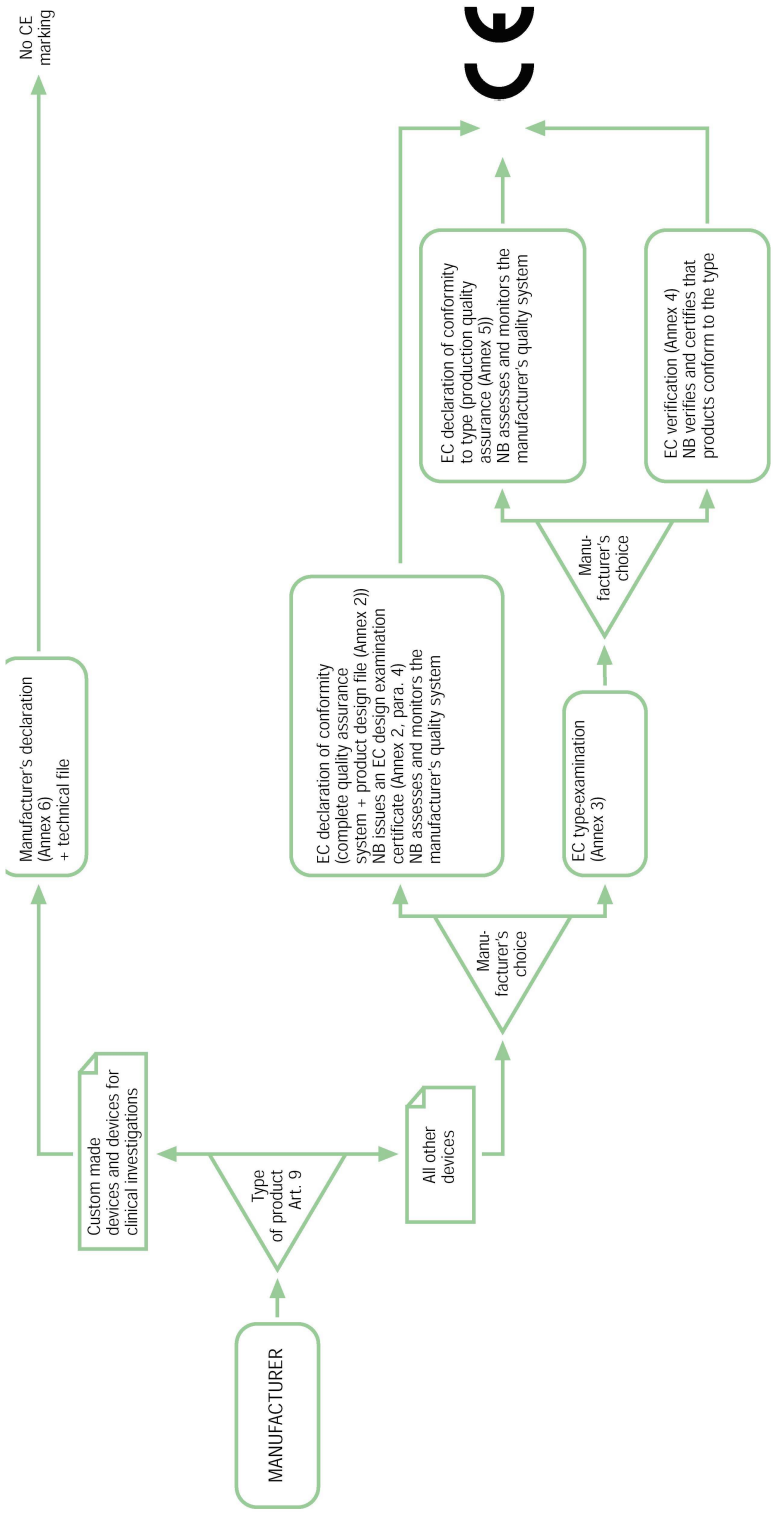

Figure 4.1 – The flowchart shows different ways or routes to obtain the CE marking of a certain product.

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The EC-type examination is the procedure that the product (prototype) is tested and certified. A model of the product, or a range if various types are tested at the same time, is sent to a notified body.

The EC-type examination is described in directive 90/385/EEC, Annex 3.

4.8 Step 6. Draw up an EC Declaration of Conformity

To ensure that each product will be the same as the model that has been approved, the production process must be described.

With the EC Declaration of Conformity, the manufacturer officially declares that the product complies with essential requirement of the applicable Directives. The manufacturer also declares that, if this product has been submitted to an EC type approval, each product is in conformity with the model that has been approved, and, if required, the relevant quality assurance procedure

The conformity assessment is described in Directive 90/385/EEC, Article 9:

1) In the case of devices other than those which are custom-made or intended for clinical investigations, the manufacturer must, in order to affix the CE mark, chose between these ways:

    - Follow the procedure relating to the EC declaration of conformity set out in Annex 2 (Complete quality assurance system).
    - Follow the procedure relating to EC type-examination set out in Annex 3, coupled with:

    a) The procedure relating to EC verification set out in Annex 4, or
    b) The procedure relating to the EC declaration of conformity to type set out in Annex 5 (Assurance of production quality).

2) In the case of custom-made devices, the manufacturer must draw up the declaration provided for in Annex 6 (Statement concerning devices intended for special purposes) before placing each device on the market.

3) Where appropriate, the procedures provided for in Annexes 3, 4 and 6 may be discharged by the manufacturer's authorized representative established in the Community.

4) The records and correspondence relating to the procedures referred to in paragraphs 1, 2 and 3 shall be in an official language of the Member State in which the said procedures will be carried out and/or in a language acceptable to the notified body.

The declaration of conformity will be written generally in the language of the country of the Union in which it has been elaborated and, when it must accompany the product, we will add a translation to one of the languages of the use country.

All Declaration of Conformity must include the next data:

- Name and direction of the manufacturer or its representative established in the European Union.
- Description of the product (marks, model, etc.).
- Pertinent dispositions to which the product adjusts (Directors again Approach).
- Reference to the harmonized norms used (also is possible to include other norms or engineering specifications that have been used).
- Name of the Notified Organisms that have taken part in the evaluation of the conformity of the product.
- Number of certificate "EC" of type, in necessary case.
- When one is an importer or drug dealer, name and trade name of this one.
- Identification of the signatory (name, last name and position).
- Date.

For devices intended for clinical investigations, see Directive 90/385/EEC, article 10.

For a list of Notified Bodies, see: “Notified bodies for AIMDD (90/385/EEC)”, in the appendix G of this thesis.

The conformity of the product is declared with the essential requirements of the Directives of application, and in case of the procedure of certification followed an examination "EC" of type has been made, the conformity to the product with the model will be declared in addition object of examination "EC" of type.

Due to the importance of the declaration of conformity and the technical documentation, is precise to maintain them updated, and the changes in the product have to be properly reflected, reason why they will have to update so that they do not contain inadequate or incomplete information (examples: new name or designation of the product, modification of the predicted use or change in the list of norms with which conformity is declared).

4.9 Step 7. Draw up a file in which the production process is described

This step consists in to draw up a file in which the production process is described, and, if required in the relevant directive(s), submit the production process to a quality control procedure as described in the directive(s).

Since just a model is submitted to the EC-type approval as described in many directives, hundreds or thousands of products may be manufactured over the years, and these do not need additional testing as long as they are still manufactured according to the type that has been submitted and approved.

To ensure that each product will be the same as the prototype that has been approved, the production process must be described. For many directives, this is an obligation, but apart from complying with the law, a sound process description may help preventing defective products to emerge and to cause damage, possibly resulting in product liability.

The description of the production process may be assessed and certified. Some directives require this process for different categories of products.

As each group of products demands different requirements – medical products for instance need more checks than machinery – each Directive uses a different set of quality process requirements.

4.10 Step 8. Affix the CE marking

The CE marking must be affixed visibly, legibly and indelibly to the product or to its data plate, depending on the directive.

However, where this is not possible or not warranted on account of the nature of the product, it must be affixed to the packaging, if any, and to the accompanying documents, where the directive concerned provides for such documents.

For products under manufacturer self-assessment, the CE marking is affixed on the product without third party intervention. When there is a third party intervention, the manufacturer will affix the CE marking as well. Only when the notified body participates in the control of the production phase, the manufacturer will affix the CE marking plus the number of the notified body.

The shape and size of the CE marking is as follows:

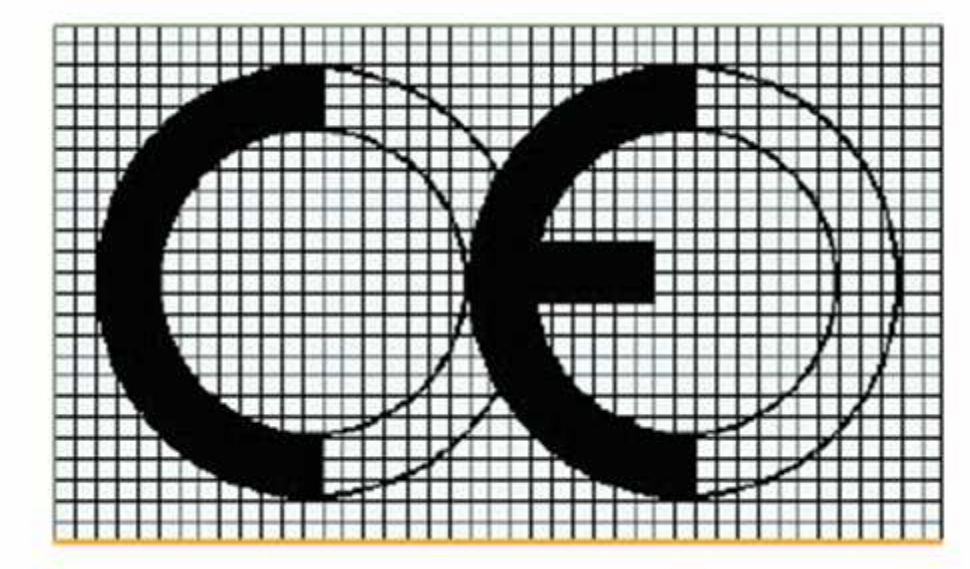


Figure 4.2 – The CE conformity marking consists of the initials 'CE' taking the form shown in the figure. If the CE marking is reduced or enlarged the proportions given in the above graduated drawing must be respected. The various components of the CE marking must have substantially the same vertical dimension, which may not be less than 5 mm.

Please note that products (equipment prototypes) to be shown at trade fairs do not have to conform with the requirements of the Directive, as long as appropriate safety measures are taken, and information is provided as to declare the non-conformity of the product involved.

4.11 Discussion

It can be noticed that the most important to get the CE marking for the artificial pancreas it is to find an appropriate Directive

It is very important to mention that an artificial pancreas is covered directly by the *Active Implantable Medical Devices Directive (90/385/EEC).* This is obvious because an artificial pancreas in an active implantable medical device. The artificial pancreas is active because it uses a source of electrical energy or any source of power other than that directly generated by the human body or gravity. Also the artificial pancreas is implantable because it is intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain there after the procedure.

5. EMC GUIDELINES

This chapter is a guideline for the manufacturer of the artificial pancreas. A guideline for helping the manufacturer to implement the artificial pancreas in order to comply the EMC norms.

This chapter is divided in two guidelines, one chapter for the implementation of the power supply and another one for the implementation of the control of the artificial pancreas.

5.1 Design EMC of power supply

5.1.1 Introduction

This lesson will analyze the problem of the interferences in switching power supplies. This lesson is a guideline to design switching power supplies without EMC problems.

Switching power supplies are very usual in the modern electronic equipment because of these have a relative low weight and double or triple efficiency than linear power supplies.

Switching power supplies work in a permanent transient state, switching currents through diverse branches of the circuit and generating harmonic, local overvoltage, surges of current, high dv/dt and di/dt that, like consequence, it generates interferences (EMI) that affect to the own power supply, to the receivers connected to the same one, to the circuits charged by the power supply and to the circuits susceptible to receive the disturbances by radiation.

Thus, the power supply can generate conducted EMI on their input/output terminals, although with the suitable filters and a good internal design can be attenuated to pass the norms of electromagnetic compatibility (EMC). Power supplies also generate radiated EMI, because its power circuit works in switching regime, generating practically rectangular waveform. The work frequency depends on the type of power supply, but it can usually vary, according to the application, between 5 and 200 kHz, although at the moment there is a tendency to increase it. In many cases intensities of several tens of amperes are switched in times about 1 us, originating important interferences between 30 KHz and 150 MHz.

Thus, EMI generated by power supplies can have mainly these forms: EMI conducted through input/output terminals, EMI conducted through the shield and radiated EMI.

Although not so important, problem EMI to the inverse can exist, that is, some parts of the circuit of a power supply can electromagnetically be susceptible (EMS) to their own generation of EMI or external disturbances.

5.1.2 EMI Behaviour of the components of a switching power supply

Switching transistor and EMI.

Power supplies use bipolar and MOSFET transistors as switches due to the advantages of their easy blockade forced. These diodes must work with minimum losses and this demand to have capacity to block high tensions with low leakage current, capacity to support to high currents with a small fall of tension in the conduction state and rapidity of switching to avoid losses and to allow working to high frequencies. But the rapidity of switching implies high di/dt and dv/dt, with the consequent generation of interferences.

Therefore, a kind of incompatibility exists between minimization of losses, that demands short times of commutation, and generation of EMI cause of fast commutations increase interferences to high frequencies.

Diodes behaviour and EMI

A diode behaves like an important generator of interferences at the moment of the commutation. It is due to the existence of an abrupt variation of current (high di/dt) and, therefore, of magnetic field. The amplitude of these interferences is proportional to the recovered load Qr, as it is shown in the figure 5.1. Spectrum of frequencies of these interferences depends on the form in which the diode is blocked.

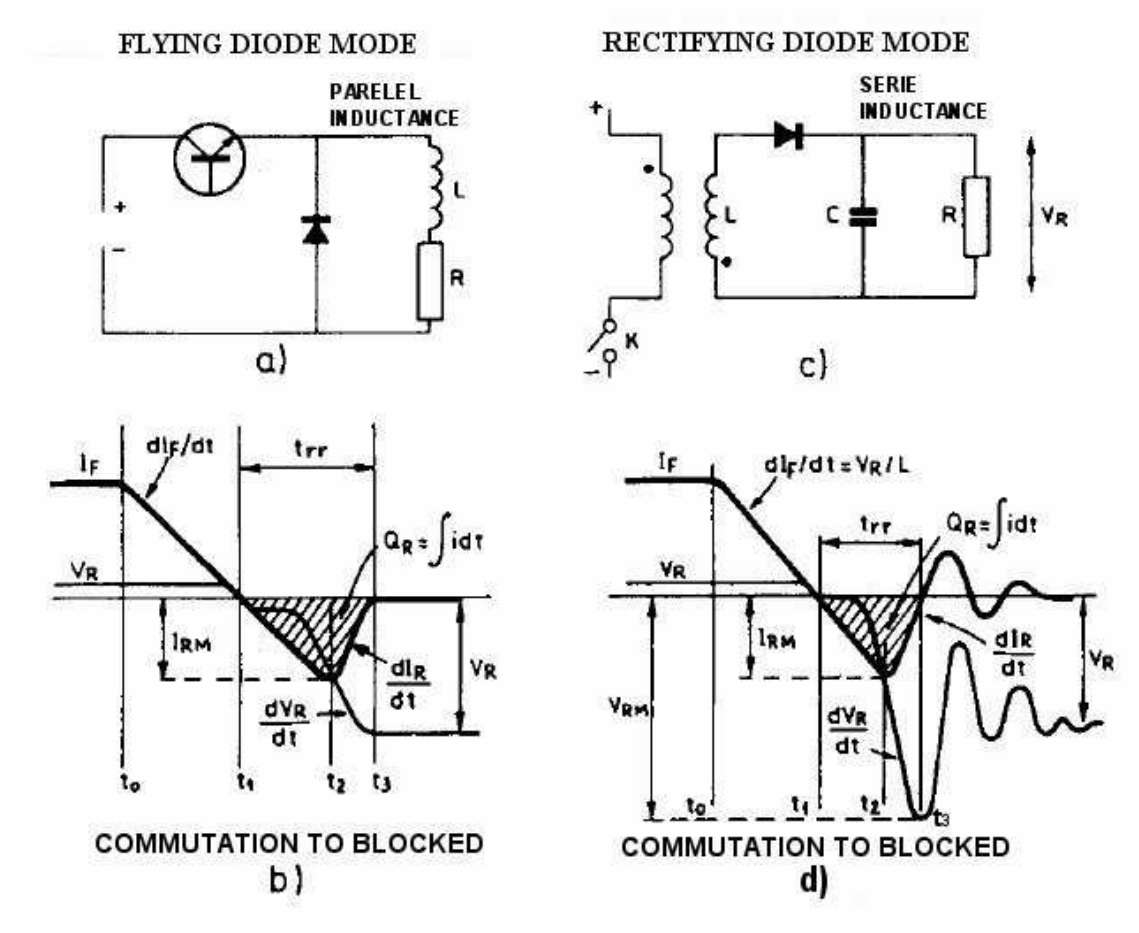


Figure 5.1
(a) The operation of the flying diode has the inductance in parallel when it is blocked. (b) Diagram of operation of the flying diode. I_F = forward intensity, V_R = inverse tension and Q_R = recovered load. (c) The operation of the rectifying diode as the inductance in series. (d) Diagram of operation of the diode in rectifying way. Here the oscillation of tension stands out.

If we replace an ordinary diode by a fast one, the amplitude of the commutation interferences decreases considerably. In the case of a fast diode of smooth recovery we have to consider that EMI level is very low for superior frequencies to [π / (t2-t1)].

In some diodes, especially low tension diodes, they have high parasitic capacity and a low resistance of damping, can be observed oscillations due to the crossing of energy between the inductance of the circuit and the parasitic capacity of the diode. High tension diodes are less prone to these oscillations.

These oscillations do not have to be confused with the phenomenon “snap off recovery”, which generates much interferences.

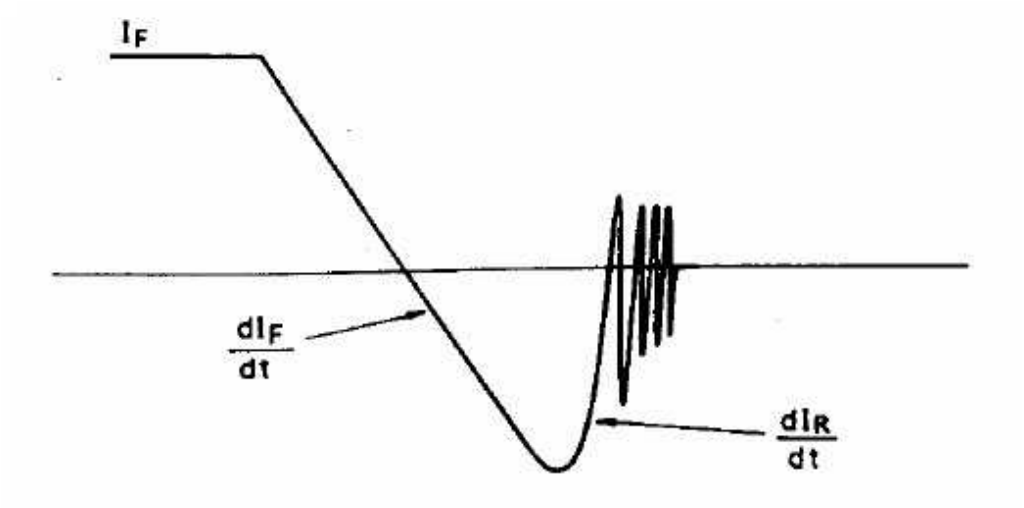


Figure 5.2 – Interferences generated by the phenomenon snap off recovery

Most of the present diodes are of smooth recovery, which means that the slope of variation of the current dI_F/dt is controlled, thus the phenomenon "snap off recovery" does not happen. But in some applications, depending on the circuit and the inductance, oscillations can exist, especially with low tension diodes and smooth recovery diodes. In order to avoid these oscillations, figure 5.3 shows some circuits of damping.

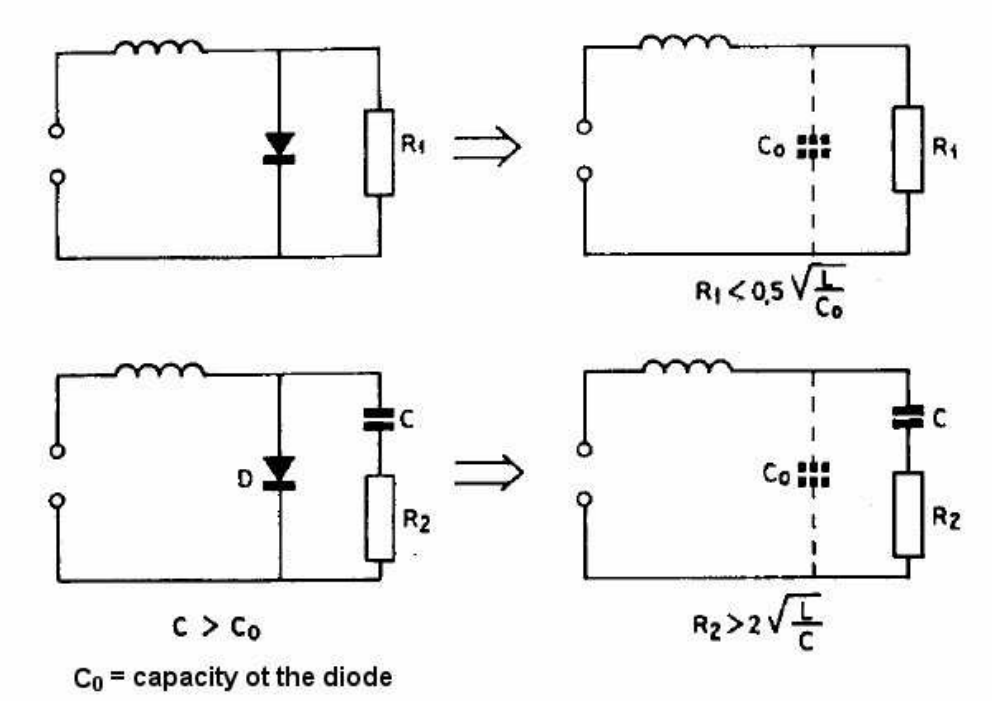


Figure 5.3 – Circuits of damping to eliminate possible oscillations in some applications.

Transformers of switching power supplies and EMI

We will talk at this moment about the transformers used in the switching power supplies, we have to mention about them that EMI can spread through the capacities between windings and between windings and the nucleus. The nucleus would have to be connected to ground if it is possible and the primary winding placed adjacent to the nucleus, retaining the currents of EMI within the loop of the primary circuit.

The parasitic capacities between the primary and secondary windings, with values about 100 pF, are the greatest cause of propagation of EMI. Faraday Screens are used between the windings to avoid the capacitive coupling. A ring in short circuit is used around the transformer to not radiate the commutation surges.

5.1.3 Generation of interferences in the commuted sources

From the point of view of the electromagnetic compatibility, the initial question that we have to worry when we want to design a commuted power supply is: what electrical circuits are able to produce high levels of electromagnetic interferences? The answer is easy: the circuits where the capacities are loaded and unloaded fastly, because they cause fast variations of current (di/dt), and also the circuits where inductances are commuted because they cause fast variations of tension (dv/dt).

In addition, the area of the loops facilitates the coupling of the magnetic fields and the parasitic capacities facilitate the coupling of the electric fields. These capacities predominate between the windings of the transformers, between space between the semiconductors and their dissipaters, between the dissipaters and electric ground and between the terminals of the different components.

The effects previously mentioned can be seen illustrated in the example of the figure 5.4.

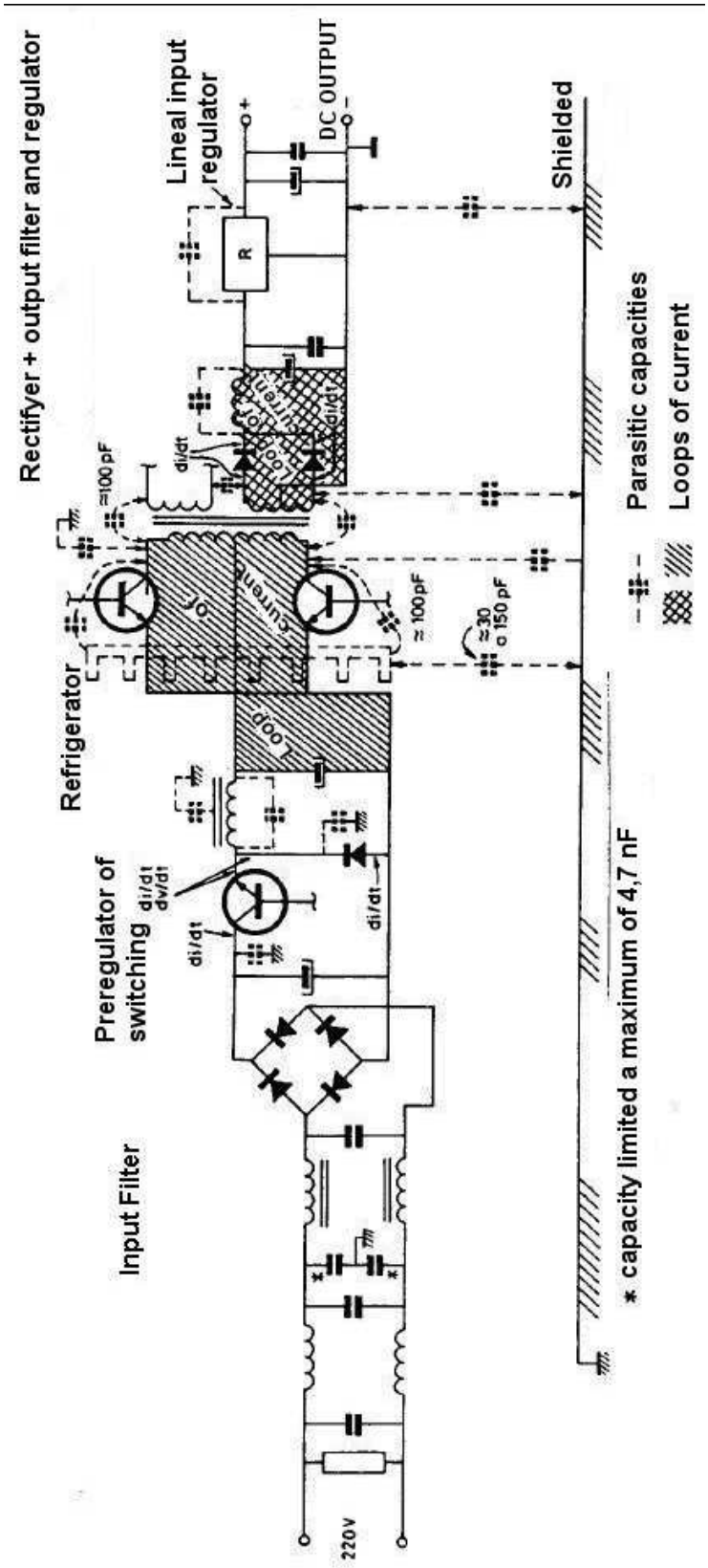


Figure 5.4 - Source of interference in a switching power supply. Emphasize between them di/dt, dv/dt, loops of current and capacitive coupling due to parasitic capacities.

Inductive transitory and the general effects of the magnetic fields that are annulled abruptly can arrive at megahertz, depending on the inductances and the effective capacities that are in the road of the current produced by the field that is annulled. The resistance of the conductor controls the damping that, as well, controls the surrounding of its spectrum.

When commuted power supplies are designed with integrated circuits (CI), the reduction of the size and the increase of density of integration affect the level of electromagnetic compatibility (EMC), due to the coupling by conduction in common mode and to which it is from the magnetic fields and electrical. The use of more and more small discrete components has like result greater spurious capacities because of a greater packing density. These deteriorate the level of EMC because of the interactions of electric field.

5.1.4 Suppression techniques of dv/dt and di/dt

A fundamental norm to reduce to the surges of tension and the high dv/dt is to eliminate or to reduce all the parasitic inductances that exist in the circuits of power. With a careful selection of the material of the nucleus and a good design of the transformer it is possible to be reduced the level of the surges tension and surges intensity.

The time of ascent of the current depends on the form of the magnetic curve of hysteresis of the material (curve B-H). If the saturation is reached abruptly or there are abrupt changes of magnetic flux, the amplitude of the surges will increase. The time of reduction of the current depends on the speed of commutation of the transistors and on reactances of the circuit.

The figure 5.5 sample some circuits developed for the protection against transitory of tension. The presented techniques of suppression consist on connection of diodes and capacities between the collectors and the emitters of the commutation transistors or the disposition of diodes in the tips of the inductive load. RC networks in tips of the windings of feedback or in tips of the secondary of the transformer also reduce dv/dt. Finally, the use of capacities placed between the collectors or from the bases to the positive tension can be advisable.

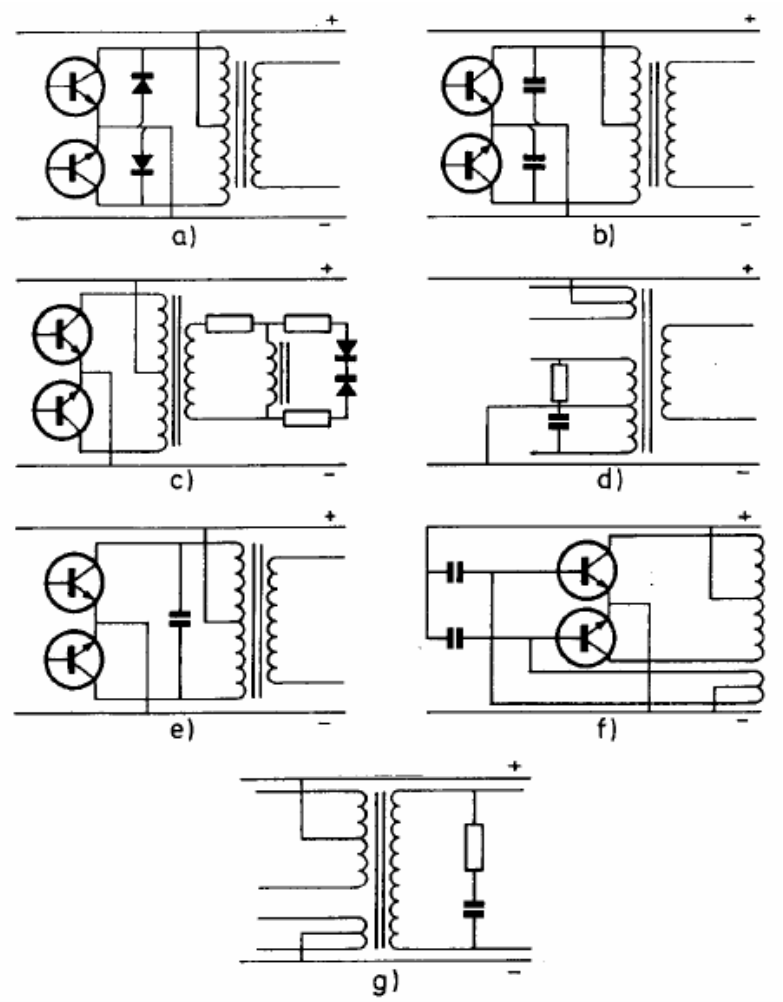


Figure 5.5 – Several circuits for the protection before transitory of tension.

Generally, to eliminate or to reduce the great variations of intensity (di/dt) we must insert series inductances and to reduce the capacities. EMI generated by current of pulsating entrance (di/dt) can interfere to other systems through the network, also this EMI could damage the control circuit of the converter. This is because EMI can start up falsely their transistors and make that the entrance is not the necessary clean DC current of EMI or even cause a short circuit.

Mainly we avoid di/dt by means of a small inductance placed in series in the point where it is desired to reduce di/dt, but considering that it can cause in some cases oscillations due to the resonant circuits.

5.1.5 Radiation in power supplies.

In switching power supplies, the electric fields due to the high impedances of their generators (high dv/dt) easily are attenuated by their housing or metal cover. Nevertheless, it is more difficult to attenuate the magnetic fields caused by the high di/dt due to the very low impedance of the near field.

Unfortunately the main generators of EMI that couple the interferences in the housing are components that are warmed up. Due to transistors, rectifiers of power, transformers and inductances, are damaged or destroyed if they are not cooled suitably, normally they are placed on the housing next to a refrigerator. This assembly facilitates coupling that allow to the intensities of EMI spread by the housing. These intensities cause that EMI appears in all the entrances and exits.

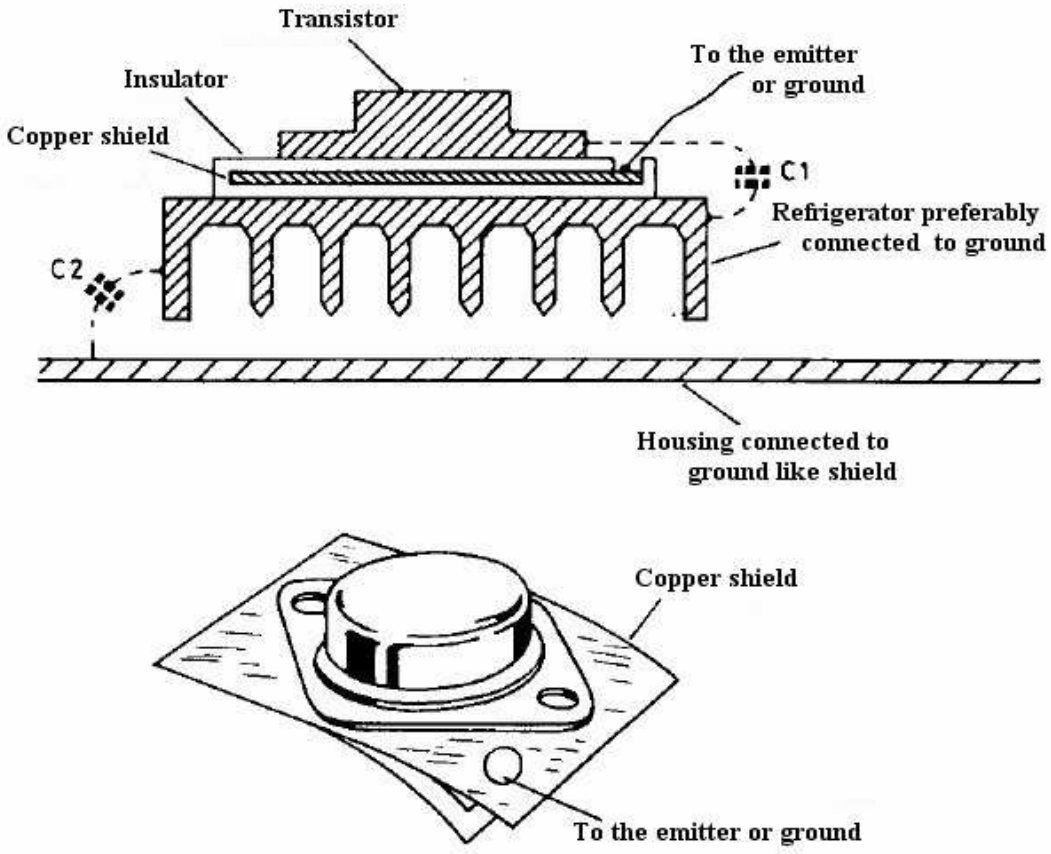


Figure 5.6 - Capacities between a TO-3 transistor, a mica insulator and the refrigerator. Electrostatic screen between the transistor and the refrigerator.

These voluminous and warm EMI generators must be placed in the switching power supply of such form that they are cooled, and they do not radiate to the sensible points.

5.1.6 Techniques for placing of components.

When the disposition of the components of the switching power supply is planned is necessary to remember:

- Lines with transitory di/dt and dv/dt must be as short as possible to reduce to the effective area of the interference transmitter and the parasitic capacities.

- Conductors of entrance and exit must be as far as is practical of the electrostatic and electromagnetic interferences generator.

- To simplify the road of commuted current to avoid to create ground loops and thus to minimize the introduction of additional surges of interference.

- To place shields between the generating source of interference and the sensible conductors of input and output. This shield can be of mumetal, iron, aluminium or cooper.

- Minimize the capacitive coupling to the chassis.

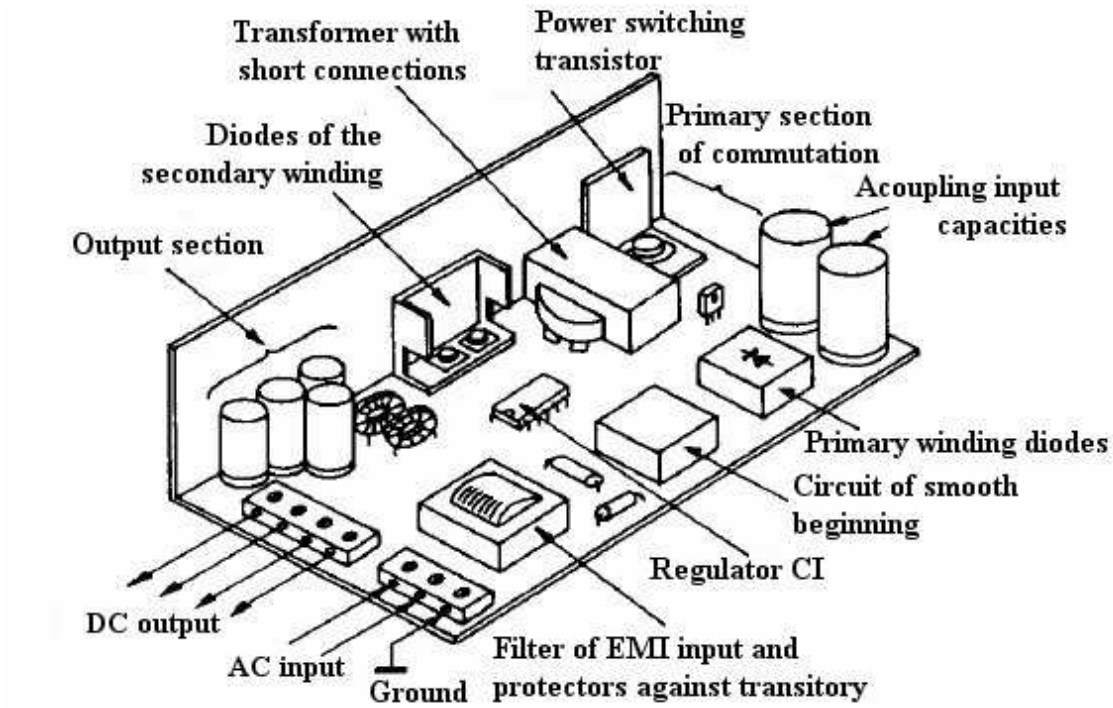


Figure 5.7 - Good location of components in a power supply

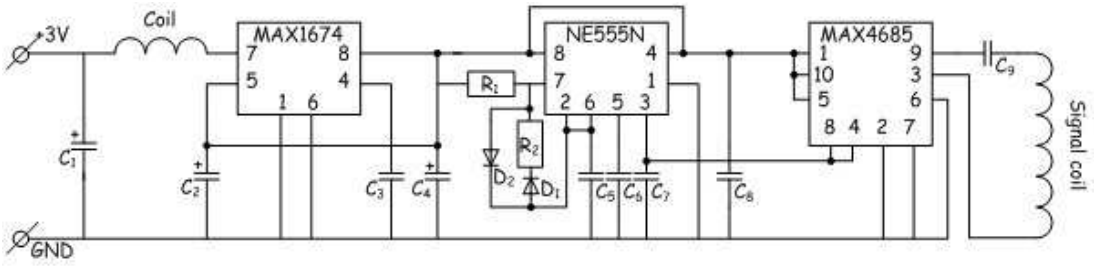


Figure 5.8 – Schematic diagram of the power supply used in the Artificial Pancreas Project

5.2 EMC design of electronic subsystems

5.2.1 Interferences in electronic subsystems

Generally many electronic subsystems are built on printed circuit boards (PCB´s). This subject dedicates an important part to the design of this type of boards but from the EMC point of view.

Like any electronic circuit, a PCB has different levels of design. On the one hand, it is possible to distinguish the electrical design that establishes, aside of the route of the paths, its thickness according to the current that circulates through them, size of pads, the minimum distance between paths (clearance) in agreement with the required isolation, routing of the paths, etc.

To design a PCB from the EMC point of view includes the following objectives:

- Control of PCB emissions.
- PCB immunity to internal and external disturbances.
- Signal integrity.
- ESD immunity.
- CE marking of the PCB.

The paths of components interconnection are a source of emission and reception of interferences.

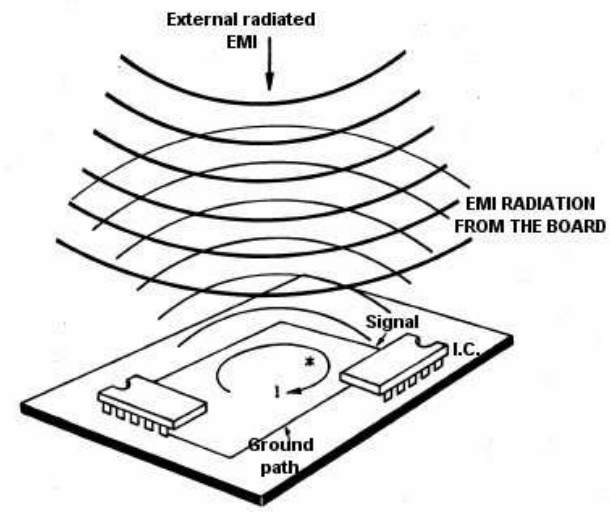


Figure 5.9 – EMI radiation in a PCB

Also, due to the parasitic inductances, these can alter the right operation of circuits that share paths (especially paths of supply and ground).

Also, noise can exist in differential mode and in common mode.

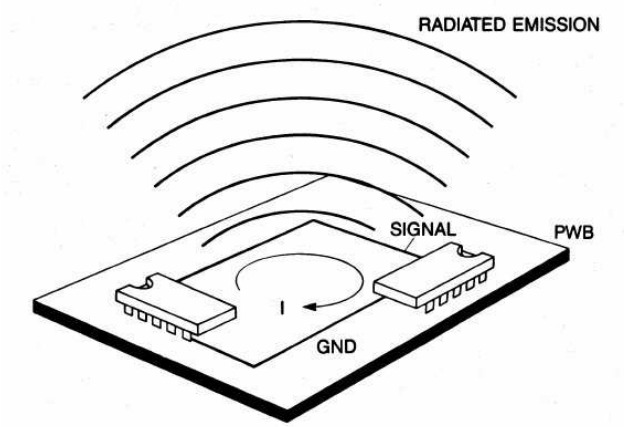


Figure 5.10 – Differential-mode radiation from printed wiring board (PWB).

The following table shows to the maximum area of the loop in a PCB for an emission of electric field in differential mode of 30 dBµV/m.

Logic family	t_r/t_f ns	ΔI mA	Loop area (cm^2) to the clock frequency			
			4 MHz	10 MHz	30 MHz	100 MHz
4.000B CMOS a 5 V	40	6	1.000	400	-	-
74HC	6	20	45	18	6	-
74LS	6	50	18	7,2	2,4	-
74ALS	3,5	50	10	4	1,4	0,4
74AC	3	80	5,5	2,2	0,75	0,25
74F	3	80	5,5	2,2	0,75	0,25
74AS	1,4	120	2	0,8	0,3	0,15

Loop area for 30 dBµV/m 30 MHz - 230 MHz, 37 dBµV/m 230 MHz - 1000 MHz to10 m

Table 5.1 – Loop area for 30 dBµV/m

The following table illustrates the maxim length of paths allowed for an emission of electric field in common mode of 30 of dBµV/m.

Logic family	t_r/t_f ns	ΔI mA	Path length (cm) to the clock frequency			
			4 MHz	10 MHz	30 MHz	100 MHz
4.000B CMOS a 5V	40	6	180	75	-	-
74HC	6	20	8,5	3,2	1	-
74LS	6	50	3,25	1,3	0,45	-
74ALS	3,5	50	1,9	0,75	0,25	0,08
74AC	3	80	1,0	0,4	0,14	0,05
74F	3	80	1,0	0,4	0,14	0,05
74AS	1,4	120	0,4	0,15	0,05	-

Allowed path length for 30 dBμV/m 30 MHz - 230 MHz, 37 dBμV/m 230 MHz - 1000 MHz to 10 m; cable length = 1 m; structure: paths of 0,5 mm paralel with a separation of 0,5 mm (2,8 nH/cm)

Table 5.2 – Allowed path name length

5.2.2 Printed circuit board crosstalk

As it has been commented previously, an electronic subsystem is and emitter and a receiver of interferences. The interferences can basically be of two types:

- Internal interferences, they are internally generated by the different circuits within the PCB.
- External interferences, they are generated by the connection the PCB to the outer surroundings, like connection cables, displays, switch of control, etc.

Crosstalk is the disturbance that takes place in a continuous path due to an inductive and/or capacitive coupling between two or more paths.

Generally in a PCB, the crosstalk is the superposition of the inductive and capacitive coupling that takes place in the conductors.
Without differentiating between inductive or capacitive coupling, the rules to reduce crosstalk in the paths of a PCB are the following:

- Reduce the dielectric constant ξr of PCB's fibre.
- Reduce the common length of paths.
- Increase the distance between paths.
- When both previous points cannot be fulfilled, there is considered to implement a path of guard between the paths and connected to ground.
- Control the relation length/separation of parallel paths.
- Reduce the value of the disturbing tension, although in digital circuits it is determined by the logical family and it is constant excluding in family CMOS series 4000.

- Is preferable to place the signal paths immediately over its paths of return or ground plane instead of a coplanar disposition (in the same face).
- Never draw up paths of logic circuits, specially the fastest, with paths of analogical circuits specially the very susceptible ones (ones with low level of signal).
- To reduce PCB's thickness in order to reduce the distance between the paths and their ground plane.
- To work at the possible lowest frequency that satisfies the functional exigencies with the specifications.

Crosstalk in logic families

A study about the crosstalk generated by the logics families has been carried out. The different studied modes of operation are:

- Positive and negative flanks in the disturber path with logical states 1 and 0 in the receiver path.
- Disposition 1: Logical flow in the same direction in the two paths (disturber: input-output, receiver: input-output).
- Disposition 2: Opposed logical flow in the two paths (disturber: input-output, receiver: output - input).

A series of diagrams Z+/Z- are generated. These diagrams mark the danger areas (irregular lines or surfaces) where the crosstalk can cause logical errors. Z+ is the impedance of the path for signals in common mode and Z- is the impedance of the path for signals in differential mode.

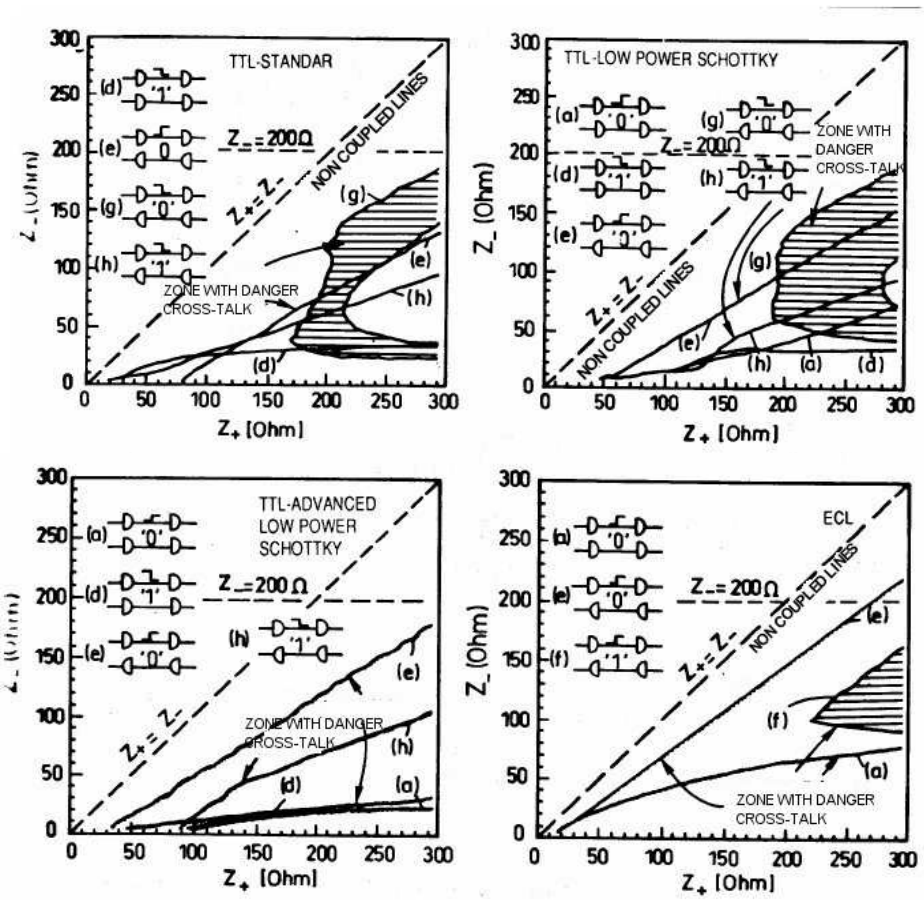


Figure 5.11 – Diagrams Z+/Z- to study the cross-talk

The figure 5.11 is interpreted like it follows (for example for the logic TTL-Low Power Schottky):

- In the case ‘a’ we have a disturber path with ascending flank and the receiver path has a logical state 0 and the logical direction of the signals is the same. There is dangerous crosstalk for values underneath the curve ‘a’ and over it there is no crosstalk risk.

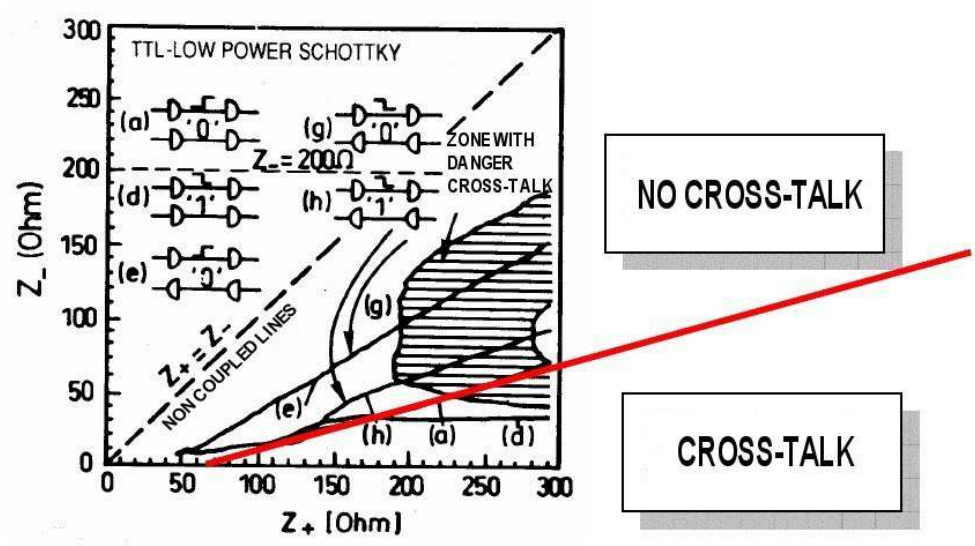


Figure 5.12 – Diagram Z-/Z+ for the logic TTL-Low Power Schottky

Introducing the variable k1 ($k1 = \frac{Z_-}{Z_+}$) a dangerous crosstalk is not observed if it is fulfilled:

$$Z_- > k1 \bullet Z_+$$

For a configuration of logical flows with the same direction.

- In the case 'e' we have the same situation but the logical directions are opposed.

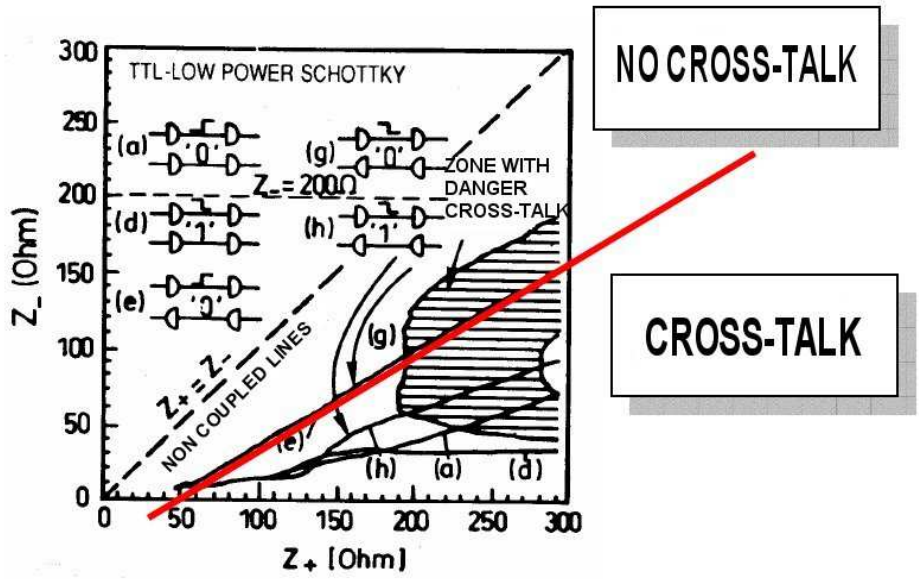


Figure 5.13 – Diagram Z-/Z+ for the logic TTL-Low Power Schottky

Introducing the variable $k2 = \frac{Z_-}{Z_+} k2(\ )$ a dangerous crosstalk is not observed if it is fulfilled:

$$Z_- > k2 \bullet Z_+$$

For a configuration of logical flows with opposite direction:

When k1 and k2 are smaller, that means that the risk of crosstalk is smaller. Thus if k1 = k2 = 0, it implies that there is no crosstalk. On the curves it is observed that crosstalk does not exist for any logical family for superior values to k1=k2=1. The following table is obtained from the previous curves.

Z –, Z + < 200 Ω	k 1	k2
TTL STANDARD	0,3	0,5
LS - TTL	0,2	0,5
ALS-TTL	0,2	0,6
ECL	0,55	0,75
CMOS 4000	0	0

Table 5.3 – Border values of k1 and k2 without critic cross-talk

The table 5.3 indicates at a level of summary of the previous curves, the limit values of k1 and k2. From the previous values, the crosstalk is not critical. The figure 5.14 shows to the entailment of the values k1 and k2 with the dimensions of the paths.

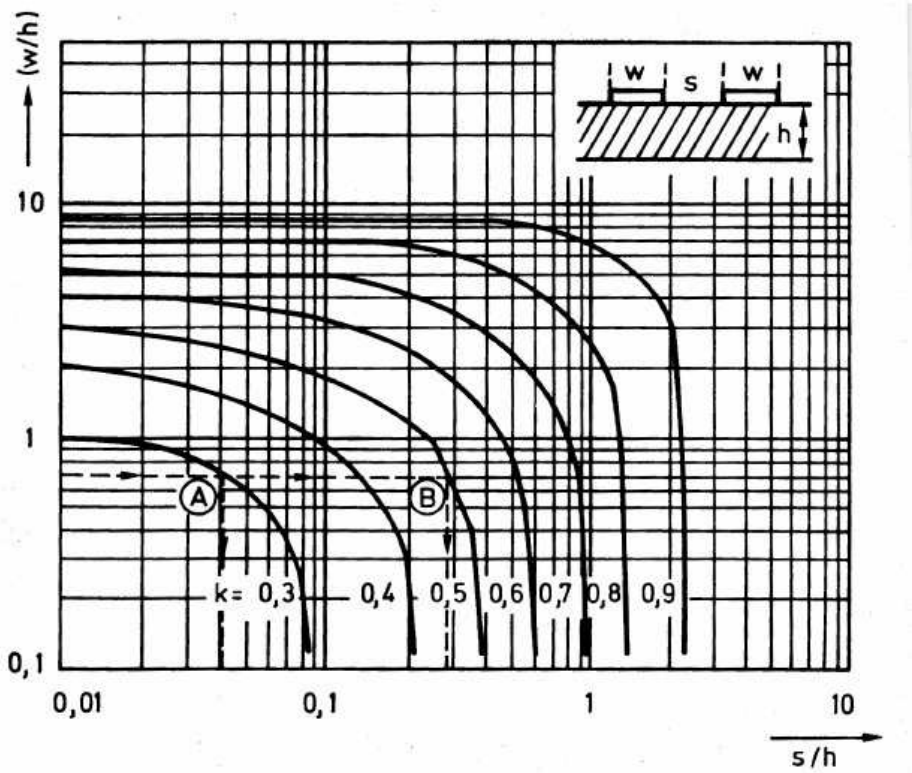


Figure 5.14 – Relation of k1 and k2 with the size of the paths

The figure 5.14 is used like it follows: Well-known for example the width of the paths (w) and the height to the ground plane (h) for a fixed logical family (the parameters k1 and k2 are known from previous 5.3), the minimum necessary separation is determined, that means the relation s/h whose vertical line cut to the horizontal line (w/h) in a point in which the value of k is superior to the minimum value in the table 5.3. Thus, for example we suppose a PCB with:

h = 1,5 mm
w = 1 mm
Logic TTL standard

⇒ w/h = 1/1,5 = 0,7

We have to find out the minimum separation that does not cause crosstalk. In the case of flows in the same direction k1 = 0,3 and for flows of different direction k2 = 0,5 (from the table 5.3). Thus it gives values of a separation $s = relation \times h$, thus s = 0.04 x 1.5 = 0.06 mm for the case of flows in opposite directions and s = 0.29 x 1.5 = 0.44 mm for flows in the same direction.

Therefore the minimum distance of separation will have to be of approximately 0,5mm.

The consequences of the aforementioned are the following:

- Logical family CMOS 4000 is practically insensitive to the interference.
- The paths that have opposite logical flows are more sensitive to the interference that the paths have logical flows in the same direction.
- Is advisable to have a connected path to ground in the paths that have different logical flows.
- Approaching the ground plane to the paths (diminution of the impedance in common mode) is possible to reduce the danger of crosstalk with equal or greater effectiveness than moving away the paths.

5.2.3 Radiated interferences in printed circuit boards

Generally circuits that switch are source of interferences. If in addition big loops exist, these become effective antennas and the disturbance becomes an electromagnetic wave that it spreads to other circuits by air.

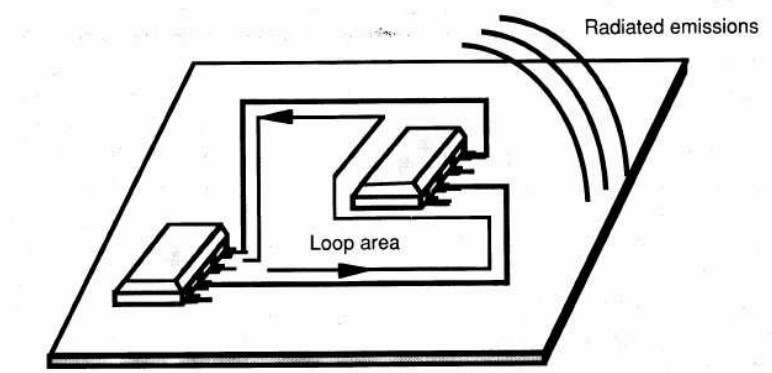


Figure 5.15 – Loop area between components

The figure 5.16 shows the spectrum of emission of a printed circuit board.

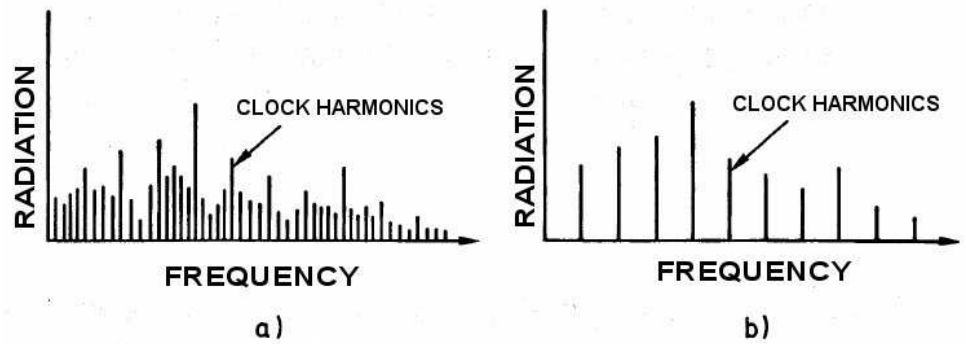


Figure 5.16 – (a) Spectrum of emission of a printed circuit board working all its circuits. (b) Spectrum of emission of a printed circuit board working only the circuits related to the main clock

The figure 5.17 shows to the bands frequencies normally used in applications.

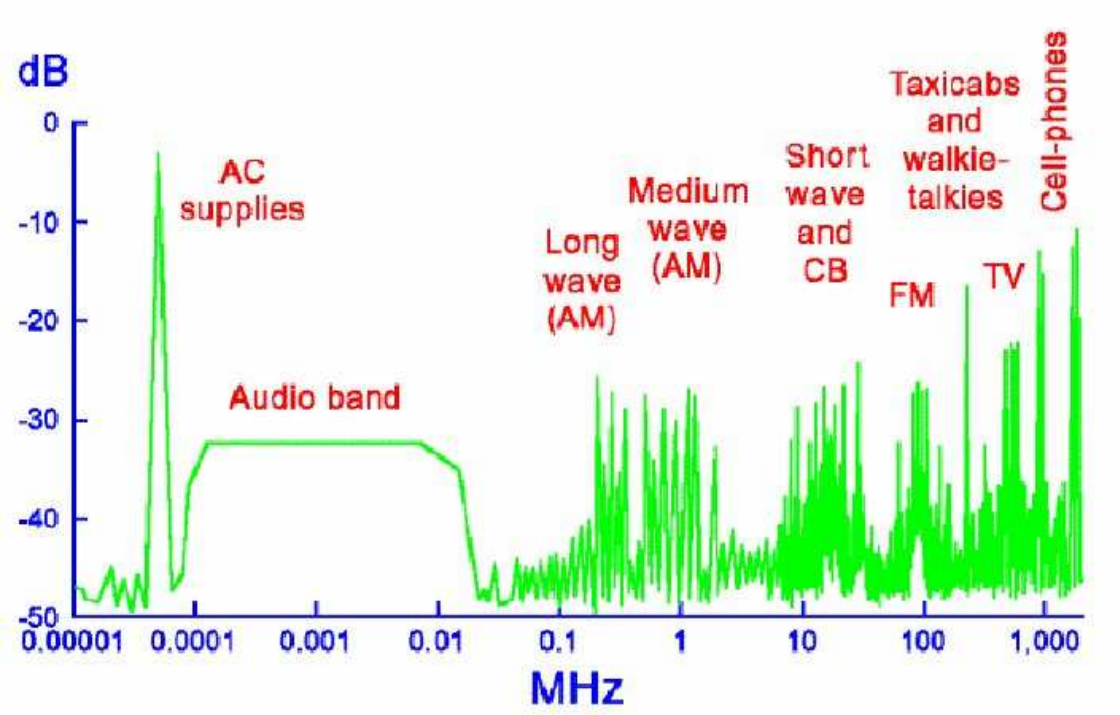


Figure 5.17– Frequencies we use in different applications

The figure 5.18 illustrates how the previous frequency band can be altered by the emission of interferences due to electronic circuits.

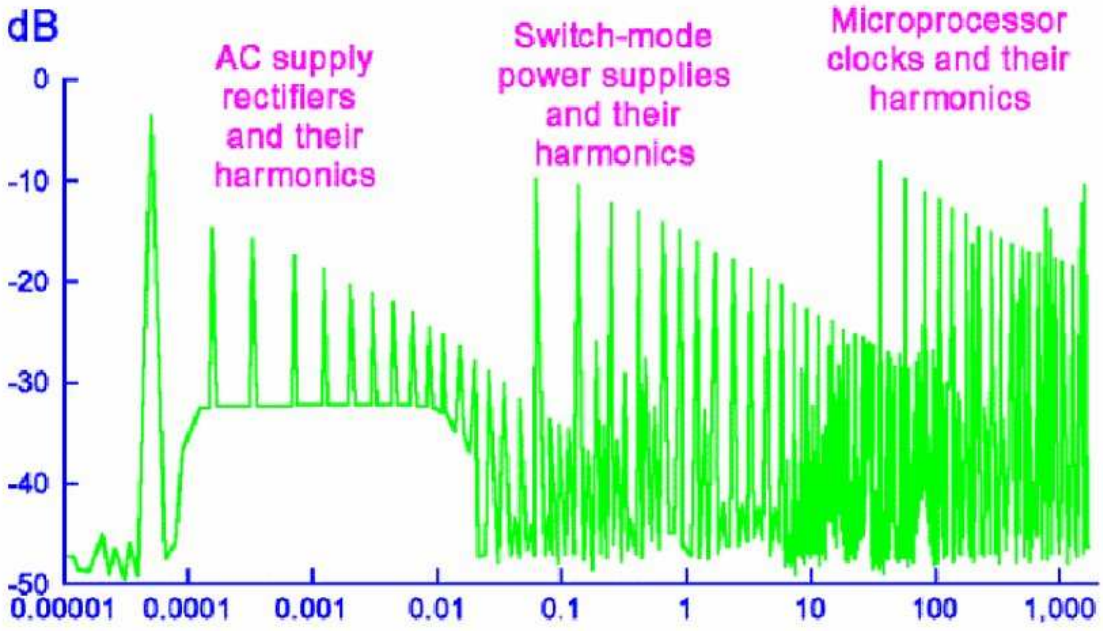


Figure 5.18 - Band of frequencies of different applications altered by interferences

The methods normally used to diminish the emission of radiated interferences are:

- Good design of ground.
- Use a ground plane or a grid of ground. If it is feasible, to place the signals between ground planes. The ideal disposition is to place the signal paths between ground planes.
- To be wide as much as can the ground lines: the most opaque it is the PCB to the light, better.
- To have many ground points in each connector of the PCB.
- To classify the ground on diverse types: EMI ground, electrical ground, analogical ground, digital ground, main supply ground.
- To use with families logics of high speed boards multilayer. The rule of 5/5 indicates when we have to use a board multilayer and when we do not have to use it. This establishes "When the frequency of the clock is higher than 5 MHz or when the times of commutation are superior to 5 nseg is necessary to use multilayer boards."
- Good decoupling of the power supplies by means of capacitors next to the I.C.
- To make a good location of the components of the PCB to avoid long routes of the current (long paths).
- To use braided cables shielded to interconnect "backplanes", along with buffers and balances receivers of lines.
- To use correct terminations in the I.C. to avoid reflections. Remember that a path really behaves like a transmission line.
- Whenever it is possible to use the slowest logical family.
- Not use skirting board of I.C., but if you have to use it, use skirting board of low profile.
- To use I.C. encapsulated in superficial assembly, since they reduce to half the area of emission of radiated interferences.
- The clock lines must be the shortest possible, also you should shield it with lines of ground around it.
- All connections I/O must be centralized in the PBC, connecting their grounds to an only point of the ground of the circuit.
- Do not use techniques of autorouting in the design of PCB´s for the critics lines, since they can form big emitting loops of interferences.

5.2.4 Printed circuit board design

As it has been commented previously, the objectives of EMC design for a PCB are the following:

- Integrity of the signal. If there is no integrity of the signal, the circuits can work wrongly.
- Control of emissions
- Immunity.

The steps for the design of a PCB are the following:

- Accomplishment of a schematic very defined
- To decide if the PCB is of two layers or multilayer
- Architecture of PCB´s

  - Partitions of PCB
  - Ground and supplies
  - Isolations
  - Disposition of components.
  - Layout of paths.

- Interfaces
  - Interfaces between the PCB and the outer.
  - Interfaces between the diverse zones of the PCB.
  - Techniques of suppression.

- Technical of distribution of ground and decoupling.
  - Techniques of decoupling
  - Resonances

- Terminations

5.2.4.1 Accomplishment of a defined schematic

Before beginning the design of a PBC is imperative distinguishing clearly the internal circuits to the PCB and the connections with the outer. For this, it is necessary to show in schematic the different functional areas (sensitive supplies, analogical circuits, nonsensitive analogical circuits, highly disturbing digital circuits, nondisturbing digital circuits, electromechanical components etc) and to mark them by means of discontinuous lines in the schematic to indicate that they are from EMC point of view different circuits.
On the other hand, also it is important to know how the PCB is going to place in the total system. The PCB designs are in two dimensions, but it can happen that when locating the PCB in the final system, in its neighbourhoods highly conductors disturbing cross and consequently, even if the PCB from EMC point of view was well designed, in the total system it has an operation badly.

5.2.4.2 To decide if the PCB is of two layers or multilayer

The decision can be of technical or economic character. The PCB of two layers is cheap whereas PCB multilayer is more expensive. Nevertheless, from the point of view EMC a multilayer is preferable than a bilayer and normally it is applied at the time of the technical decision the previously commented rule 5/5 and that it establishes that *if the frequency is superior to 5 MHz or the times of commutation are superior to 5 nseg, from the technical point of view we must use a multilayer.*

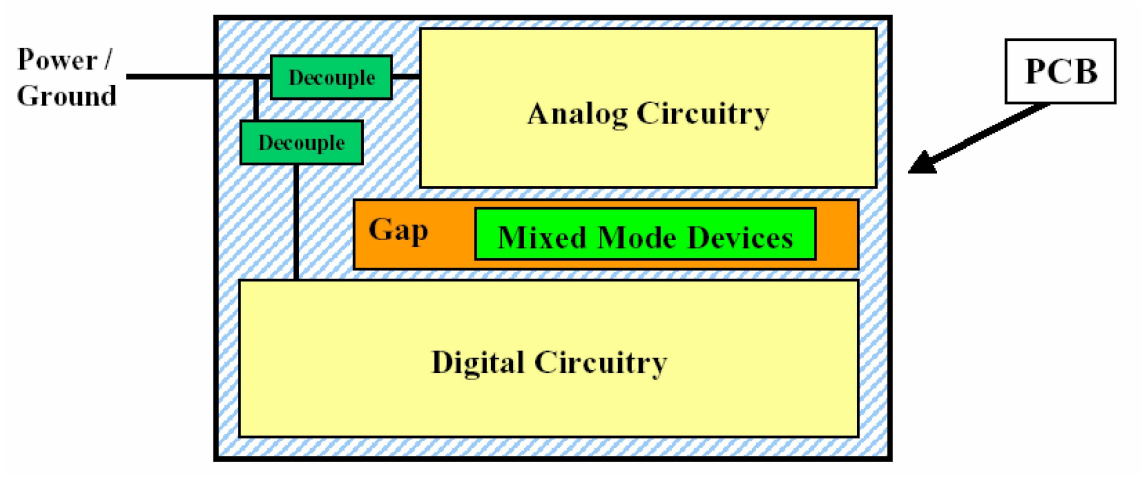
In small series, where there is no an enormous pressure of costs, the multilayer PCB can generally be used. In large series the use of a bilayer PCB for economic reasons can be imperative.

5.2.4.3 Architecture of PCB´s

Partition of the PCB

Once decided the previous point, it is necessary to make a partition of the circuit in zones in agreement with the different functional parts (analogical section, digital section....). The partition of a PCB means the physical separation of the same one in different functional blocks according to its EMI characteristics (zone noisy (or dirty) high speed, of potentially aggressive circuits and clean or small noisy zone, of sensitive circuits and potential victims etc.). The partition also can be made by supply tensions of the different functional blocks. Also it can be made partitions of ground planes in agreement with the block functional and all of them connected finally to a common point if there is only one reference for the circuits.

The figure 5.19 shows examples of partition of a PCB in different functional blocks.



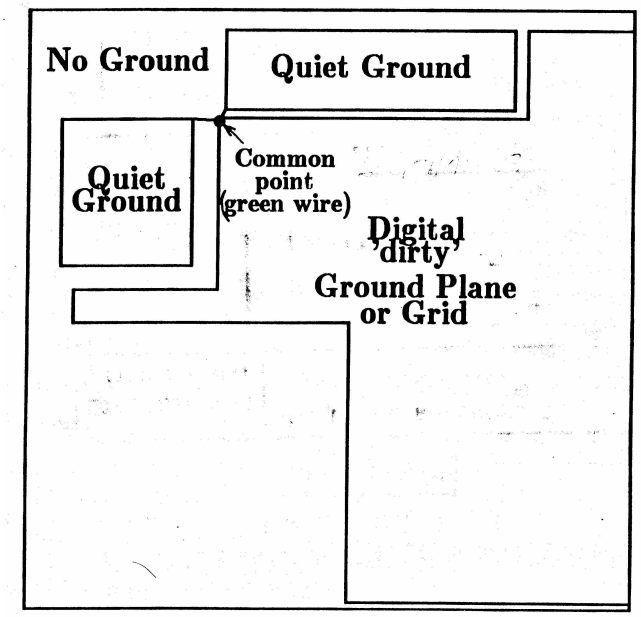


Figure 5.19 – Two examples of partition of a PCB

The figures from 5.20 to 5.25 show typical partitions of a PCB.

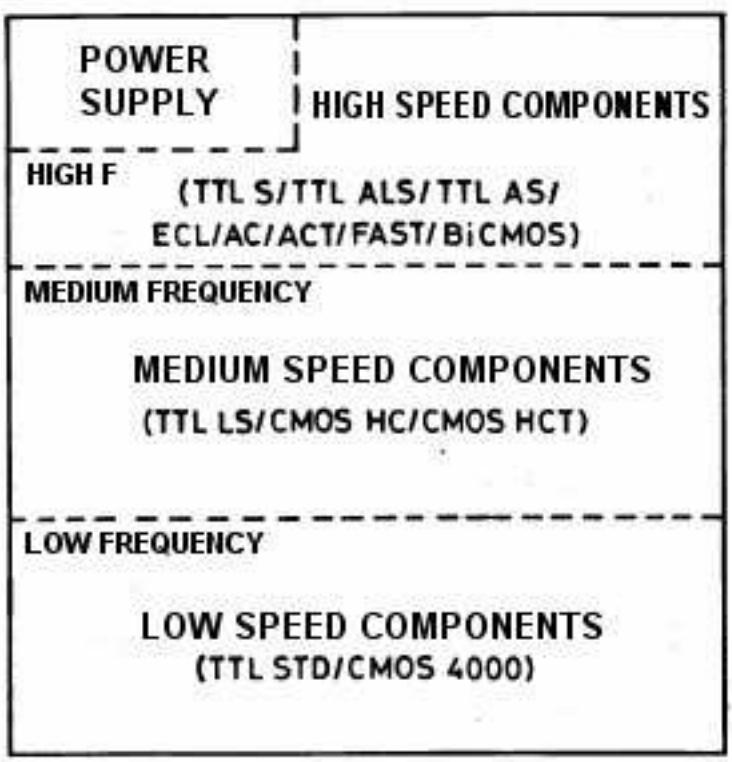


Figure 5.20 - PCB partition in a circuit with an only board

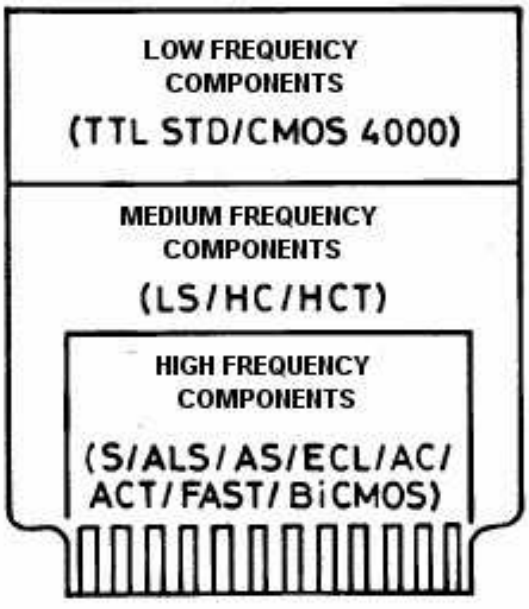


Figure 5.21 - PCB partition in a circuit with a configuration multiboard with the components of high frequency next to the connector of the bus

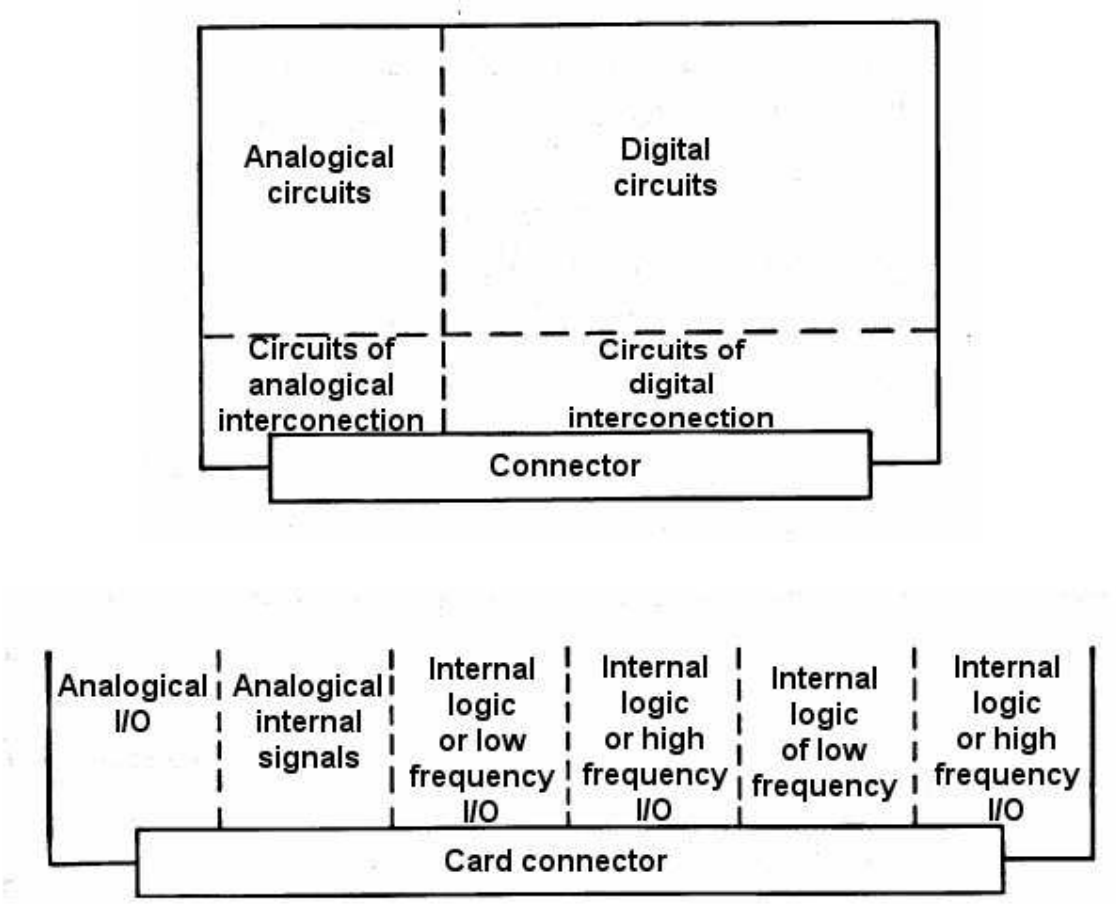


Figure 5.22 - PCB partition in a PCB with analogical and digital circuits

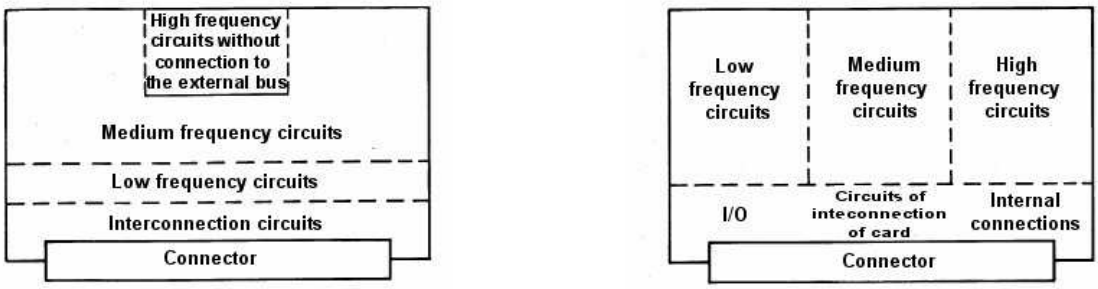


Figure 5.23 - PCB partition in a PCB with different frequencies from work

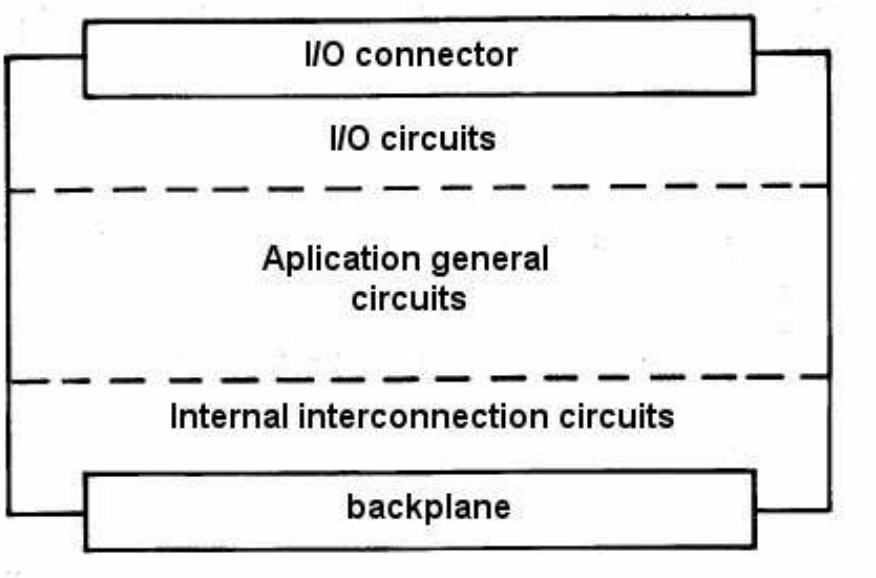


Figure 5.24 - PCB partition in a PCB with connector I/O and connector backplane

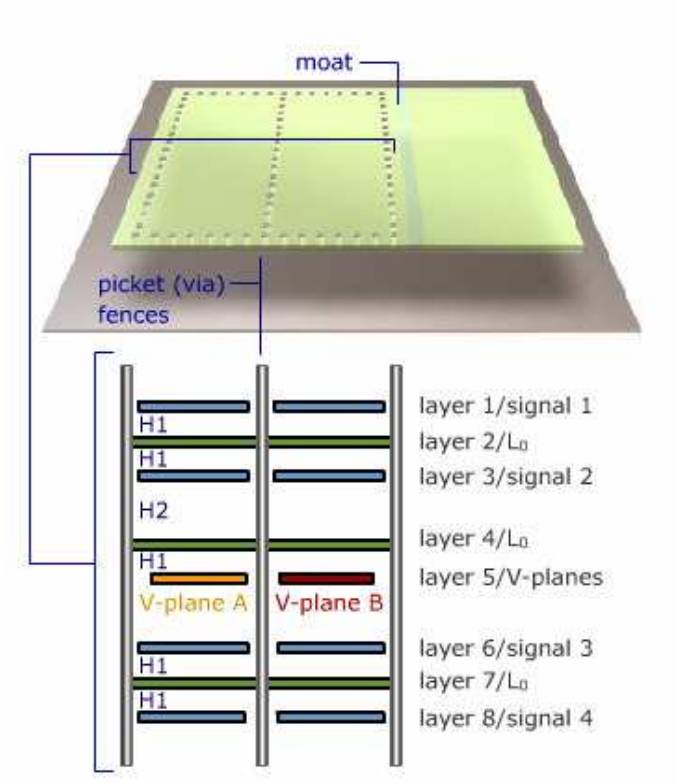


Figure 5.25 - PCB partition in a PCB multilayer, in which the ground planes are shared.

Grounds and supplies

Once the partition of the different functional blocks is made, it is necessary to make the decision about how the supplies and grounds of the PCB are

going to be. In other words, a common supply (nonisolated of the different required supplies) or independent and isolated supplies. It entails to the distribution of the ground plane, in other words, only one ground plane or a ground plane divided in agreement with the made functional partitions. In general, there is no a unique answer to the problem and there are cases in that only one ground plane has benefits superior than the case of a divided ground plane.

The figure 5.26 shows, on the one hand, a circuit with common ground plane for the analogical and digital zone and, on the other hand, the same circuit but with separated ground plane for the analogical and digital zone.

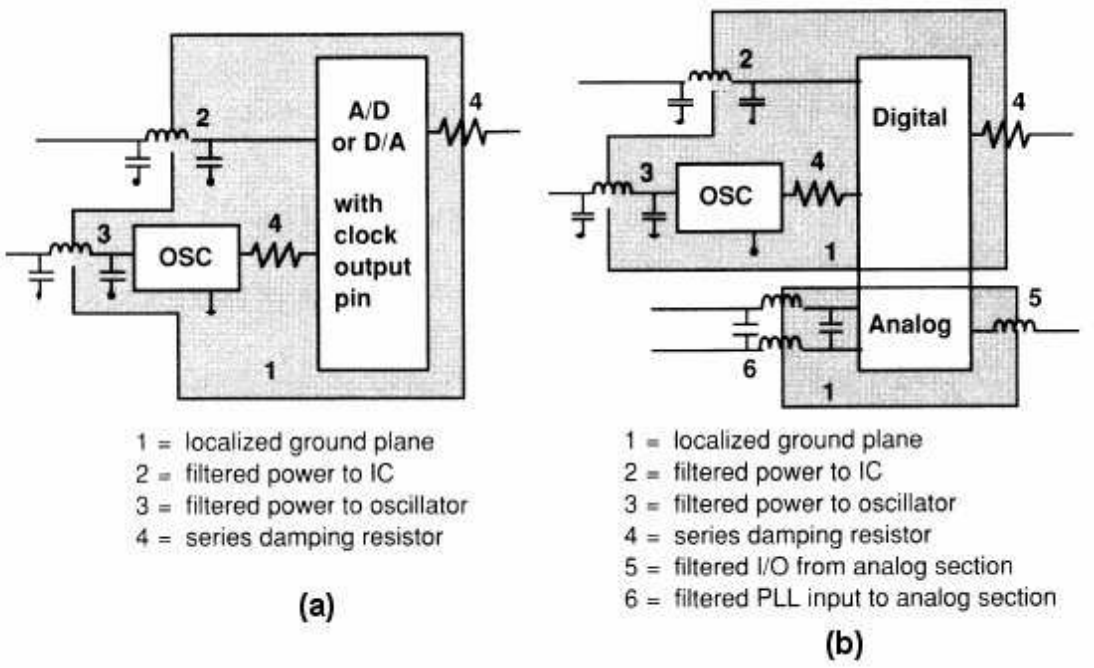


Figure 5.26 – (a) Localized ground plane with a common digital and analogical ground (b)Localized ground plane with separate digital-to-analogical ground structure

If there is electrical ESD security reasons, the diverse zones must be referred to a common electrical ground.

The 5.27 shows the disposition of vias in the chassis ground.

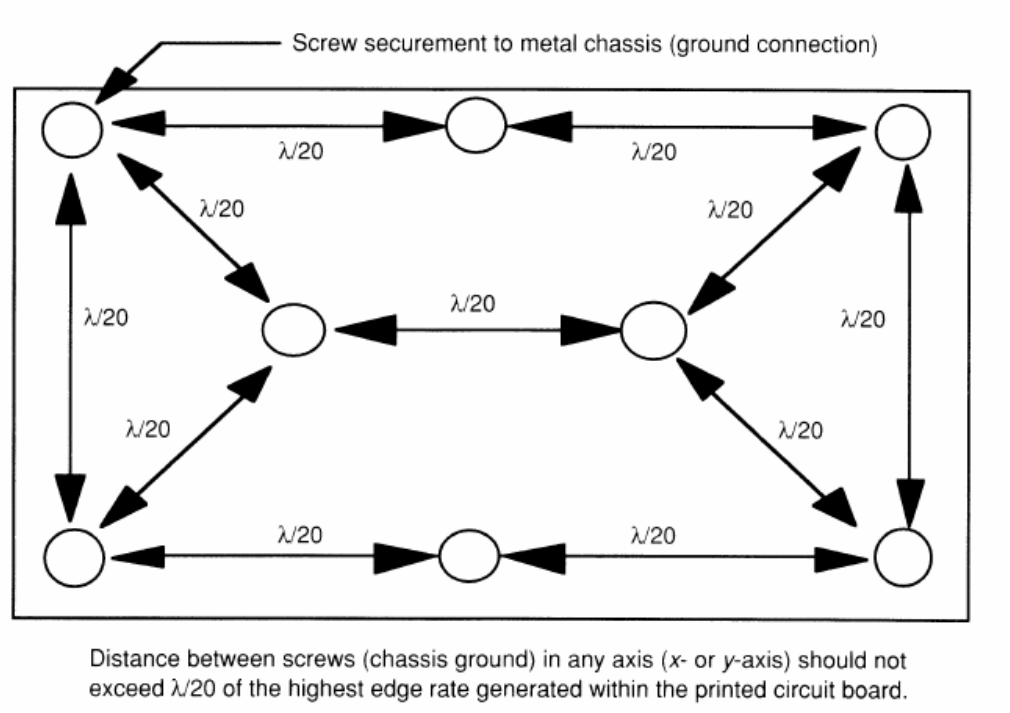


Figure 5.27 - Location of vias in the chassis ground

The figure 5.28 shows a partition with multipoint ground to chassis.

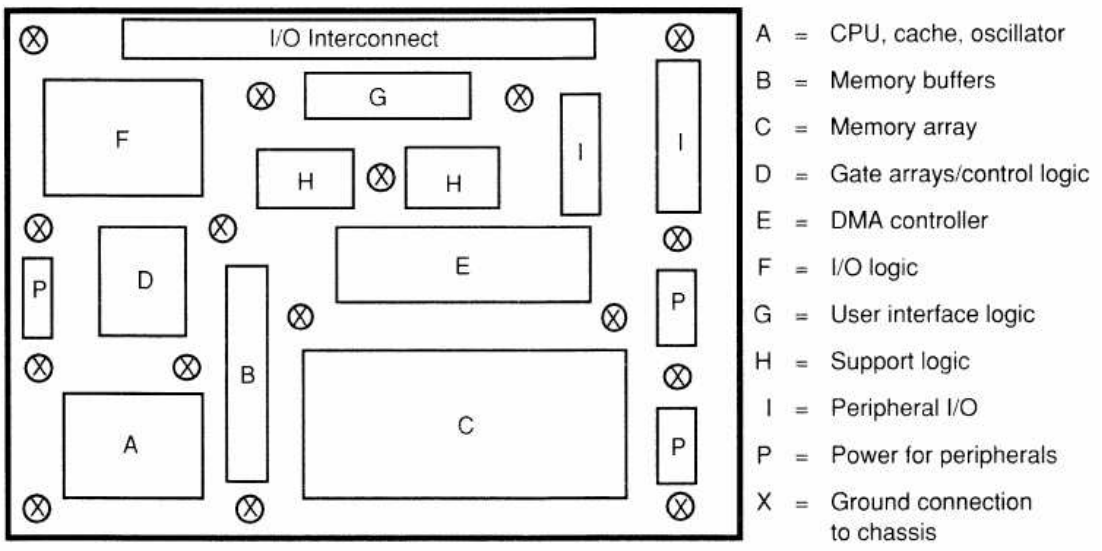
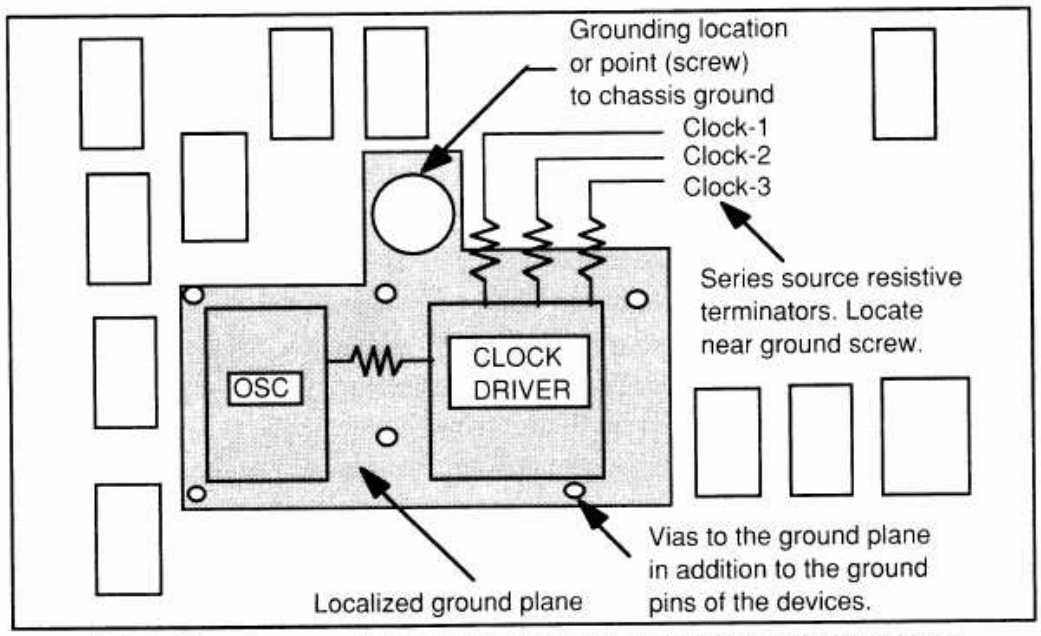


Figure 5.28 – Multipoint grounding – implementation with aspect ratio

Other examples of partition of grounds planes are ground plane located for certain fast components, like oscillators and clock drivers, as it is shown in the figure 5.29.



Note 1: Do not run any traces on layer 1 through the localized ground plane.
Note 2: If two microstrip layers exist, do not route any traces on layer two of the localized ground plane (route keep-out area).
Note 3: The localized ground plane is a solid copper plane without solder mask bonded to the main ground plane(s) by vias "and" bonded to the ground stitch location by a screw or equivalent method.

Figure 5.29– Localized ground plane

The previous examples are simple examples that they show:

- Whenever it is possible to separate the supply systems of each functional section of the PCB
- Generally the use of only one ground plane instead of different ground planes is preferable in agreement with the partitions. Nevertheless this in practice is difficult to generalize and there are circuits in which a partition of grounds in agreement with the functional partition offers better results than only one ground plane and in other circuits happen the opposite.

Isolation between zones

Isolation means that the different functional grounds are isolated to each other at level of RF.
The ideal situation between the zones is isolation, being fulfilled:

- The diverse zones must be loose of the others leaving small channels free of components.
- Each zone must have its own supply and ground.

The isolated zones are zones with absence of Cu around them using a separation from one to another one of about 5 mm like minimum. Only the necessary signals for the communication of a zone with the other one are

allowed to cross between two zones. Each zone has their own supply and ground and the communication signals are isolated between zones by means of opotoacopladores, transformers, etc. The previous configuration, being from EMC point of view the optimal situation, it is not from the point of view of costs, due to the use of independent supplies, optoacopladores, etc.

Considerations about the ground planes

Generally to frequencies superior to 1 MHz, paths, cables, etc… cannot provide a stable reference. As practice rule the inductance of a path of a PCB represents an inductance of 1nH/mm. It is equivalent to say that, for example, a ground path of 10 mm represents an impedance of 6.3Ω to 100 MHz and 63 Ω to 1 GHz. For that reason, only ground plane can provide a relatively stable reference to high frequencies.
The previous thinking is also used for the supply lines of power reason why the paths are not effective to high frequencies and also planes of distribution of supply are required. Ground plane and supply plane must be very next to the I.C. to which are referenced.
Perforations between different layers of the PCB introduce additional inductances as it can be seen in the figure 5.30.

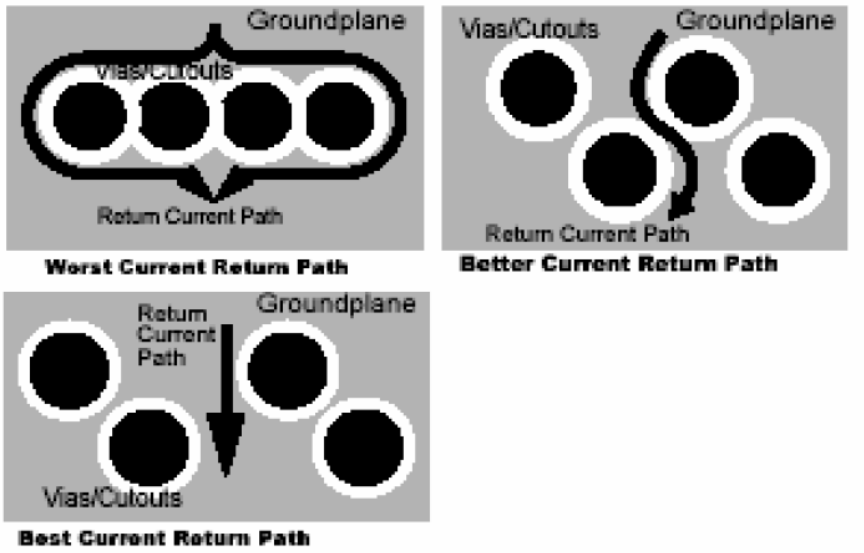


Figure 5.30– Different disposition of vias/cutouts

In order to avoid the previous situation, the ground must surround all the discontinuities due to perforations as it is indicated in the figure 5.31.

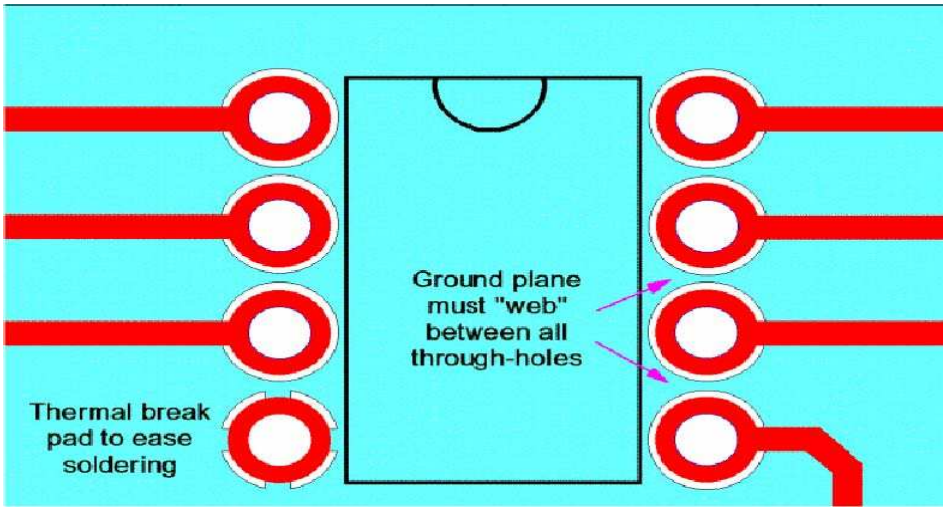
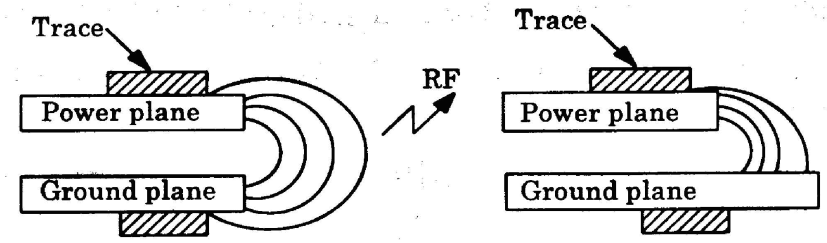


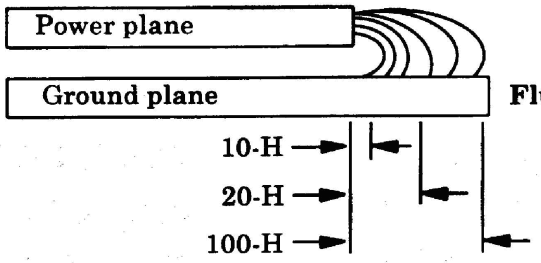
Figure 5.31 - Ground plane must surround al though-holes

Another important point to consider when ground planes are designed is the rule 20H that establishes that the power distribution plane must be inferior in dimensions to the other planes at least 20 times the distance between planes.



RF currents fringing between the power and ground planes at the edge of the board.
RF emissions occur.

RF currents do not fringe from edge of board. RF currents have a return plane to couple to.
RF emissions do not occur.



Flux Boundary Display

At 10-H, impedance change of the planes is first observed
At 20-H, we reach the 70% flux boundary
At 100-H, we approach the 98% flux boundary

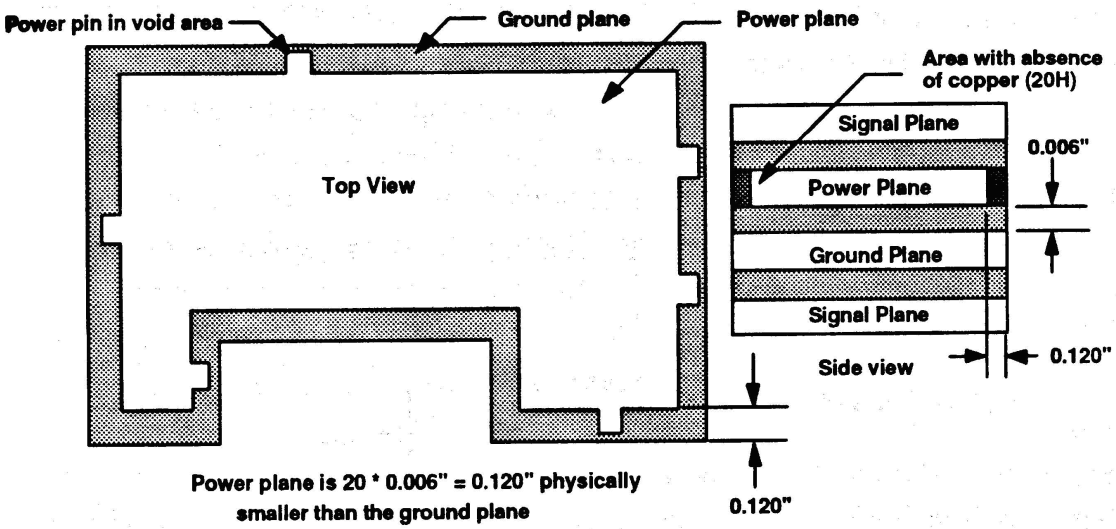


Figure 5.32 – Implementing the 20H rule

The figure 5.33 shows to the distribution of analogical and digital supplies and grounds according with 20H rule.

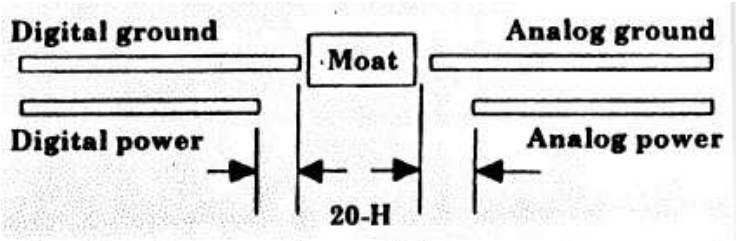


Figure 5.33 – 20-H rule implementation

Disposition of components and layout of paths

Once the segregation of the circuit is made, it is necessary to locate the components within each zone. The noisiest components in a zone must be placed in the center of the zone. Such components are clocks and distribution of these, I.C. of digital buses, microcontroller, transistors in commutation and rectifiers of high frequency, shocks, transformers and radiators.

The most sensitive components must be located in the center of their zone. Such components are analogical I.C., amplifiers of low level.

Related to the paths layout, the following rules must be followed:

- Distributions of clock (very aggressive signals) must draw up in only one layer of the PCB in a plane very next to ground. These paths must be as shortest as possible.
- Digital buses and high speed I/O must draw up after, similarly to the paths of distribution of the clock.
- Paths with very susceptible signals, as originating from transducers or sensors of very low level of signal must draw up with the previous criteria but logically in their area.
- All the other types of analogical, digital and power signals must be drawn up according to their level of disturbance or sensitivity.
- The paths of clocks and data bus are very aggressive and they do not have to be allowed to place them in the proximity of sensitive areas.
- Also the distributions of supply and ground lead signals of high frequency and must be defined well their area and we do not have to allow intermix them with sensitive zones.
- The components of interface between zones like converters A/D, transformers, latches of data bus, filters, and insulators must be located in the border between zones.
- When the techniques described are not sufficient to provide the sufficient immunity is necessary to use suppression techniques such as:
    - Filtered in common mode and/or differential mode.
    - Galvanic isolation by means of optoacopladores or transformers.
    - Communication protocols.

- Techniques of balance.
- Use of EMI connectors when the external disturbances are elevated.
- Shield of areas.

Figure 5.34 – Different types of EMI filters

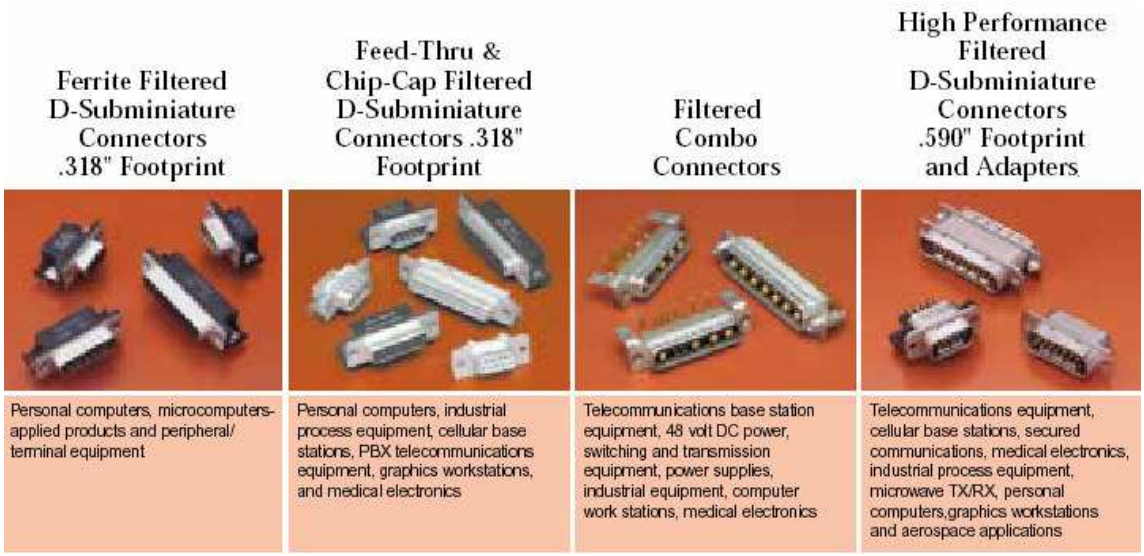


Figure 5.35 – Different types of EMI connectors

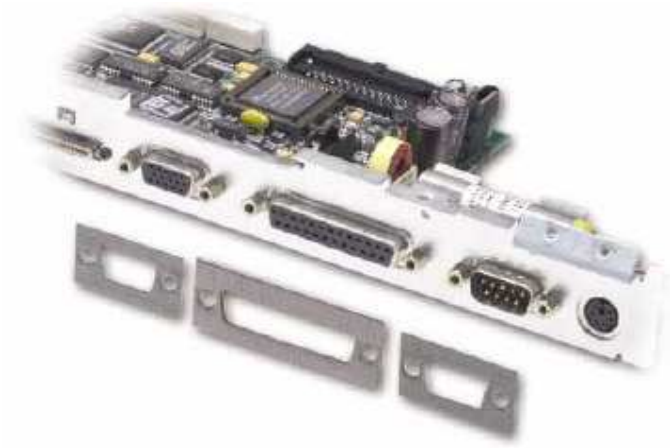


Figure 5.36 - Gaskets for connectors

5.2.4.4 Distribution of supplies and decoupling

An important aspect, once the previously commented partitions and architecture of ground planes and supplies are made, is a correct distribution of the supplies and grounds and specially a good system of filtrate of the supplies in order to diminish the galvanic noise and emissions of interferences radiated by long-hauls of currents in loops.

The result of long-hauls of the pulsating current is like it has commented radiation and over voltages that can cause the badly operation of the circuits.

The figure 5.37 shows the deformation of the signal due to the parasitic inductance loading the parasitic capacity of the following integrated circuit.

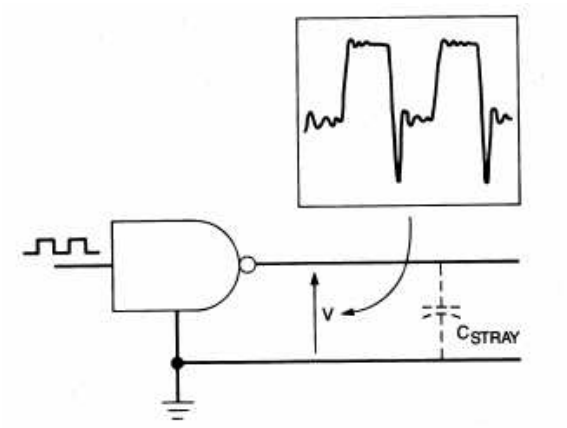


Figure 5.37 - Deformation of signal due to a parasitic inductance

For that reason, it is necessary to diminish the routes of the pulsating current. That's why the method normally used is the use of high frequency capacitor, able to give to the current demanded by the I.C. momentarily. That is; the capacitor plays the role of power supply for the pulsating current that demands the I.C. In other words, the mission of a decoupling

capacitor is to provide to each I.C. a power supply with practically null impedance (what from the practical point of view is impedance smaller than 1Ω or even smaller than 0.1 Ω in the operation rank, 150 kHz to 1 GHz).

If we want that the filtrate system or decoupling to be effective, the decoupling capacitor must be located as closer as possible from supply terminals of the I.C.

In order to diminish the parasitic resonances there are two very important aspects:

- Capacitor technology to be used.
- Type of capacitor

The figure 5.38 shows ranks of frequencies of use of the different technologies capacitors.

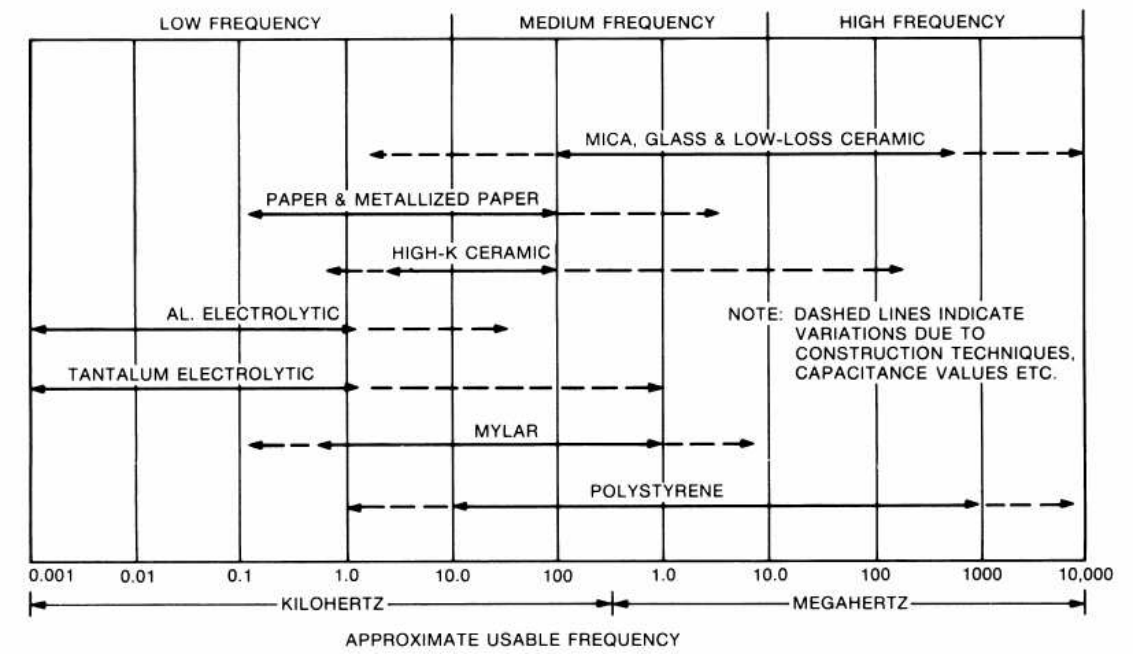


Figure 5.38 – Approximate usable frequency ranges for various types of capacitors

The figure 5.39 shows the impedance of several types of decoupling capacitors in series with an inductance of 30 nH (equivalent to its connections).

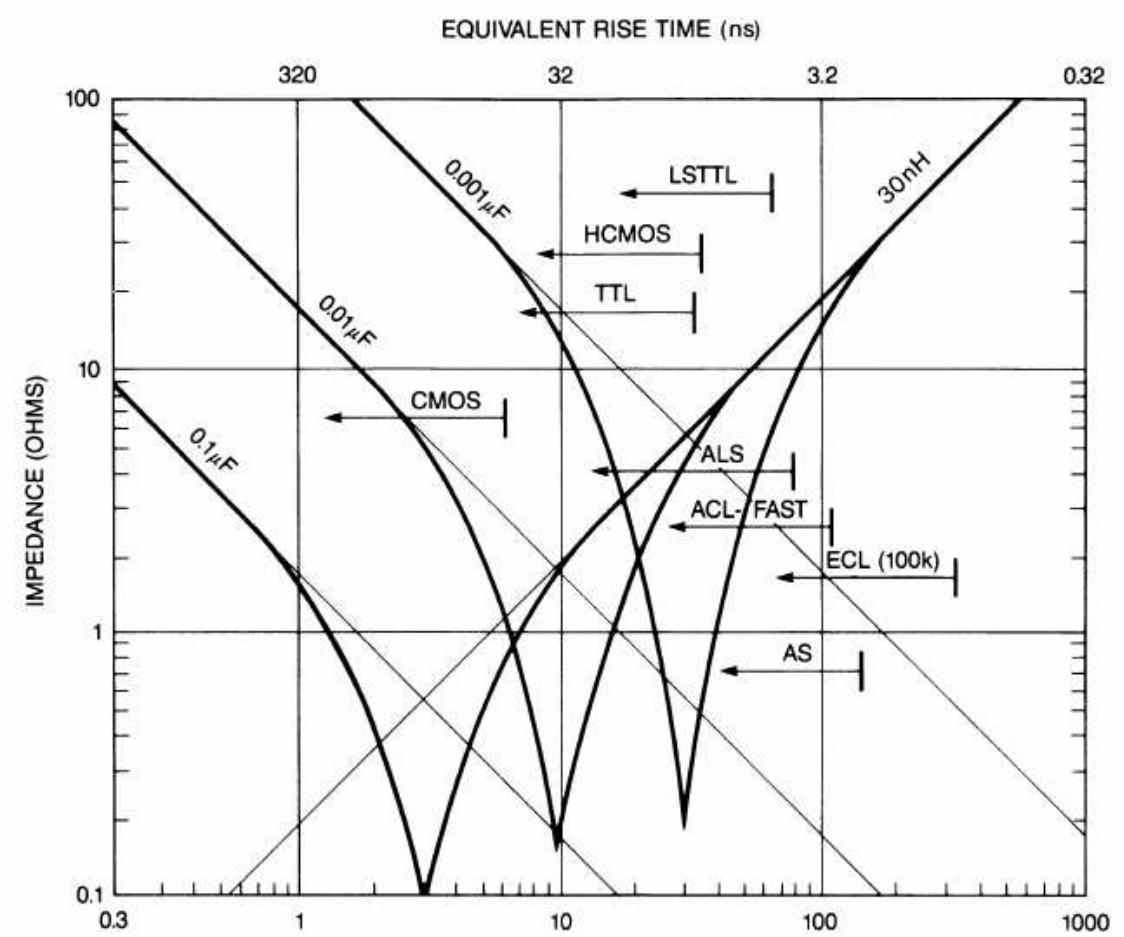


Figure 5.39 – Impedance of various value decoupling capacitors in series with 30 nH of inductance

When the habitual capacitors do not give the demanded benefits, it is necessary to use another type of capacitors (more expensive), concretely capacitors of three terminals SMD of type feedthrough.

The figure 5.40 shows how these capacitors are placed in the PCB.

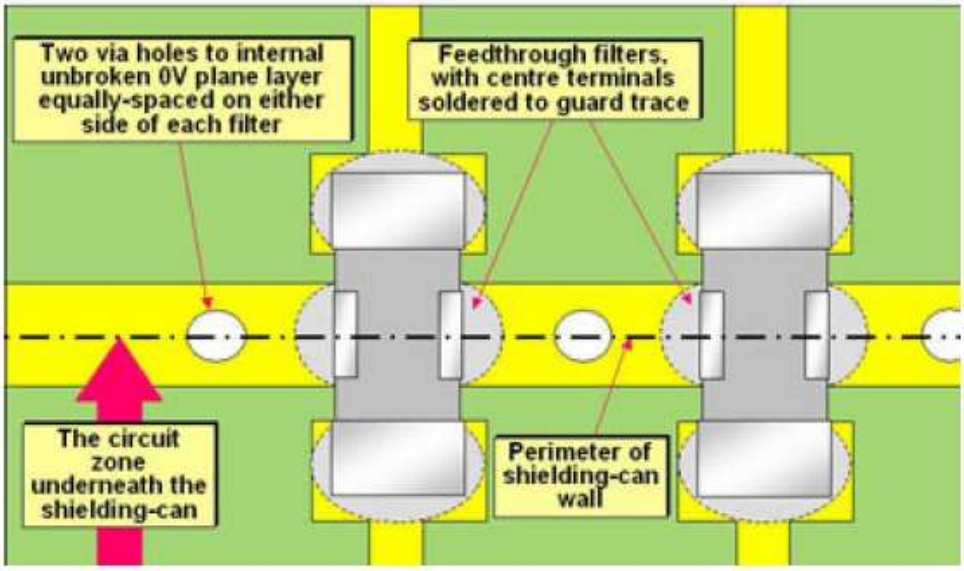


Figure5.40 – Feedthrough soldered to guard trace

In the figure 5.41, the comparison of this type of condensers with ground connection and without it can be observed.

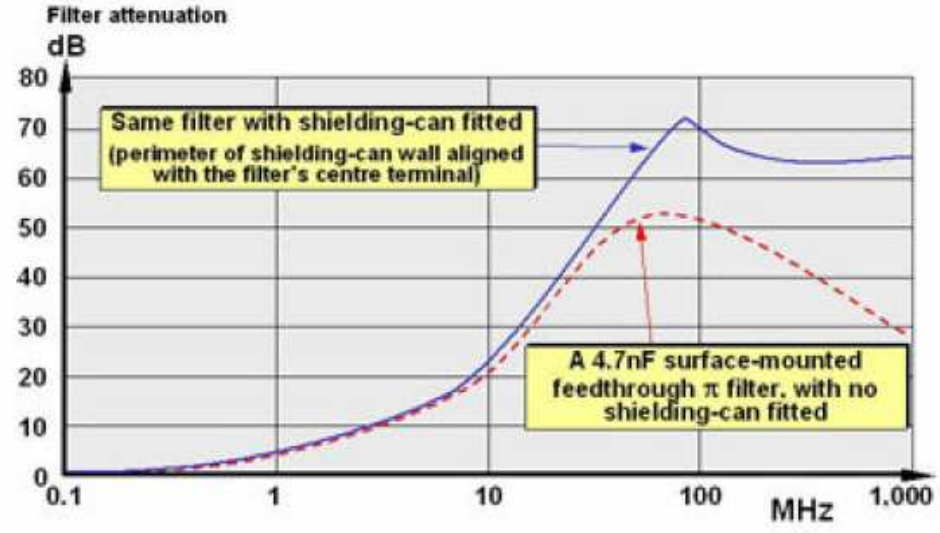


Figure 5.41 – The effect of a shielding can on the performance of a feedthrough filter

Another type of used capacitors are laminar capacitors integrated in the I.C., they can be seen in the figure 5.42.

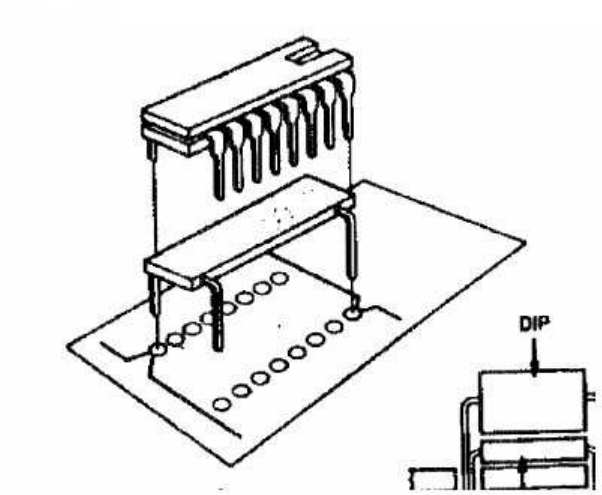


Figure 5.42 – Example of laminar capacitor integrated in the I.C.

In both cases, the point is to obtain a larger frequency of resonance than by means of habitual capacitors.

On the other hand, in a PCB with ground plane, perfect plane capacitor is inherently generated between the ground plane and supply plane. The figure 5.43 shows the contribution to the current of commutation of the diverse capacitors existing in the input of a I.C.

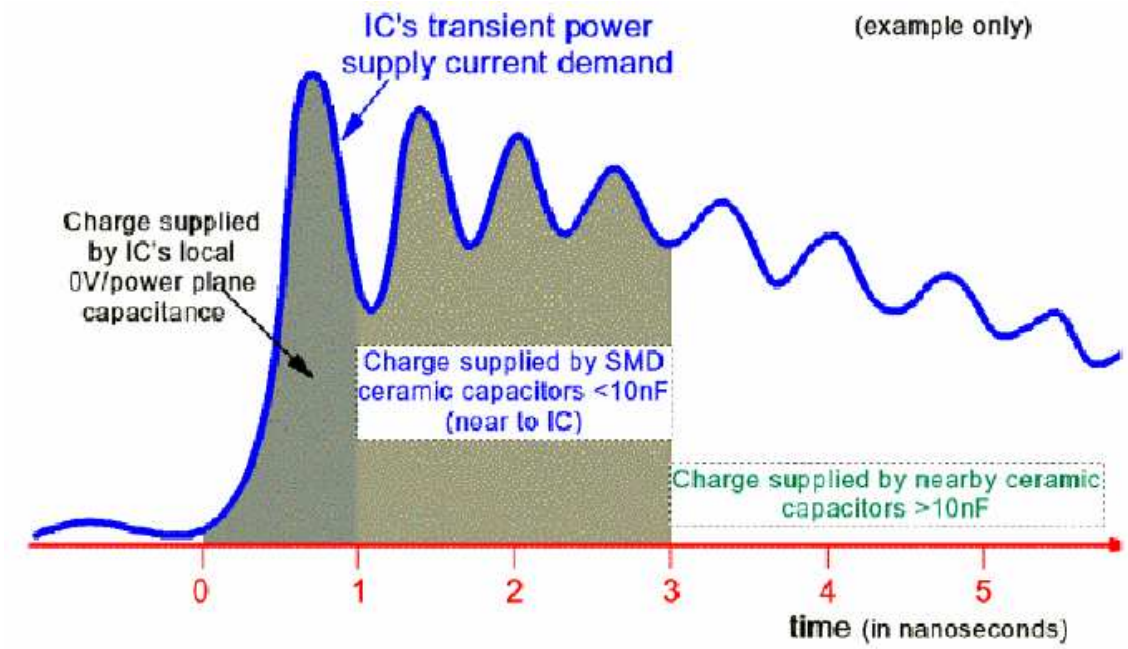


Figure 5.43 – A time domain view of a good power supply decoupling

It is observed that in first nseg, the current is given by the capacitor generated between the ground plane and the one of supply. Next the capacitors SMD very next to the C.I give the necessary current. After the ceramic capacitors will give the current and finally the electrolytic capacitors provide the current to recharge to the condensers previously

mentioned from the 20 nseg. On the other hand, we do not have to think that due to the capacitor decoupling it will be more difficult to reduce the emissions of interferences with more efficiency.

5.2.4.5 Shield of the PCB

When the levels of required interferences or immunity are very elevated is no another remedy that to shield the PCB or certain areas of the same one. The figures 5.44 and 5.45 respectively show a partition of a PCB without and with a shielded zone.

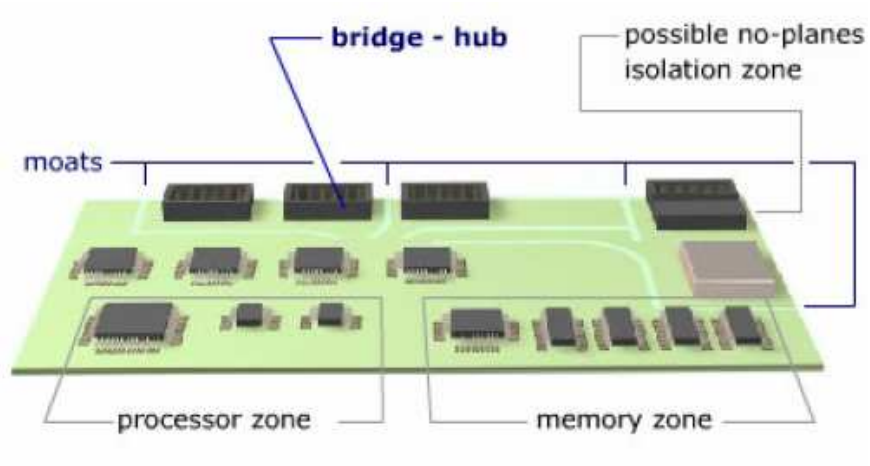


Figure 5.44 - Partition of a PCB without shielded zone

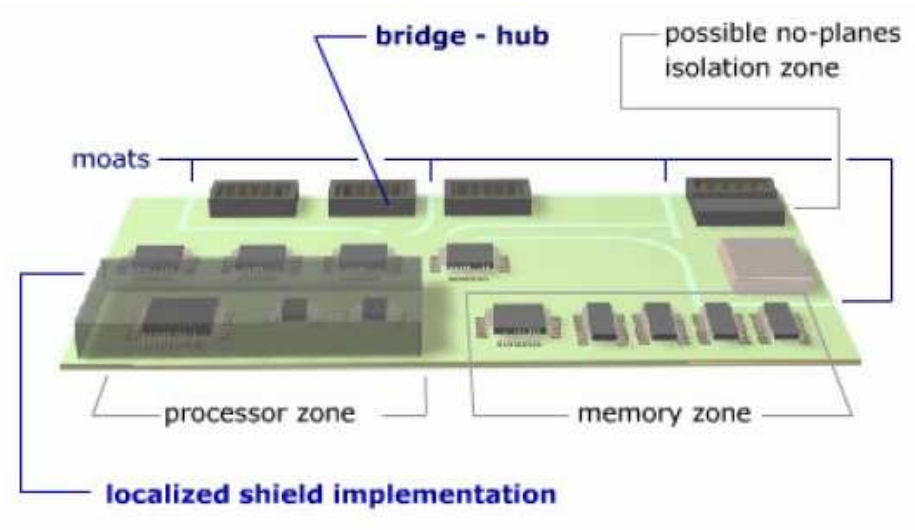


Figure 5.45 - Partition of a PCB with shielded zone

The figure 5.46 shows a cross-sectional section of a PCB partially shielded.

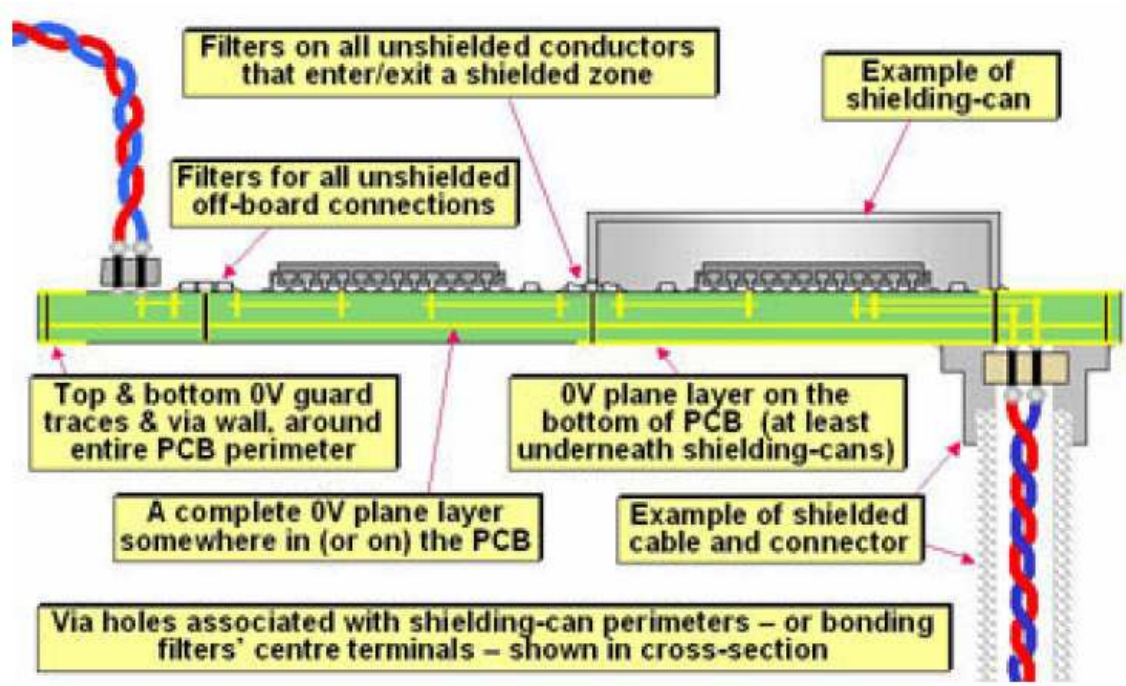


Figure 5.46 – Cross-section of a partially shielded PCB with both shielded and unshielded cable interconnections.

In the figure 5.47 a configuration of a PCB simultaneously with shield and filtrate is shown.

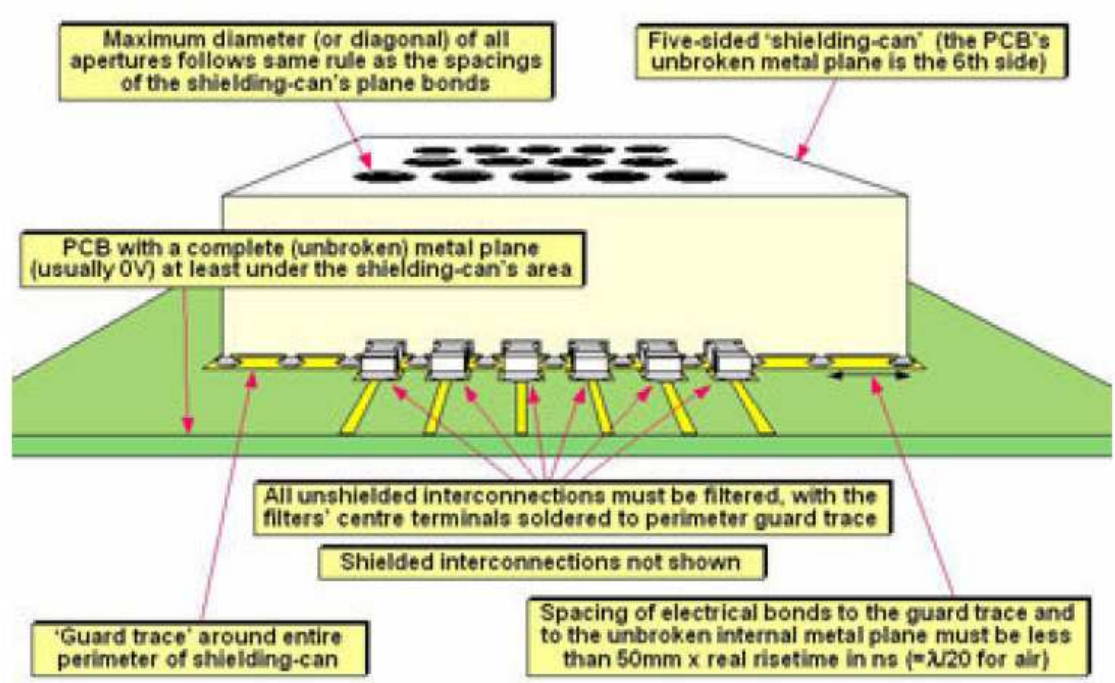


Figure 5.47 – Overview of PCB-level shielding and filtering

The connection of the shield to ground can be seen in a multilayer or with shield in the two faces.

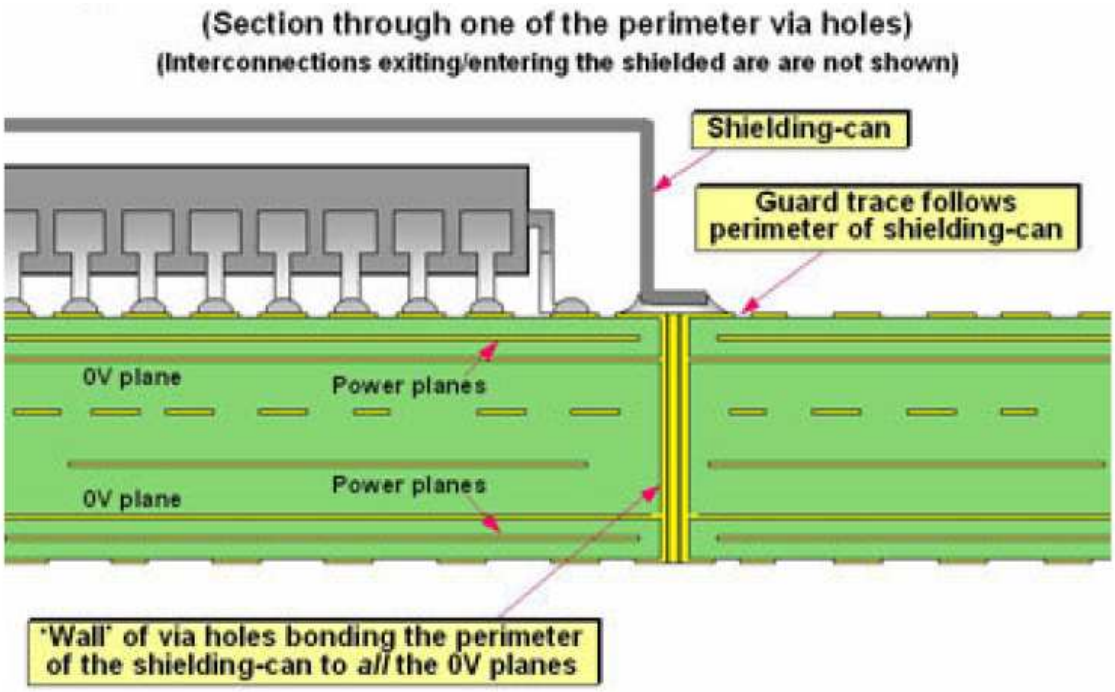


Figure 5.48 – Cross-section of part of a shielded PCB zone

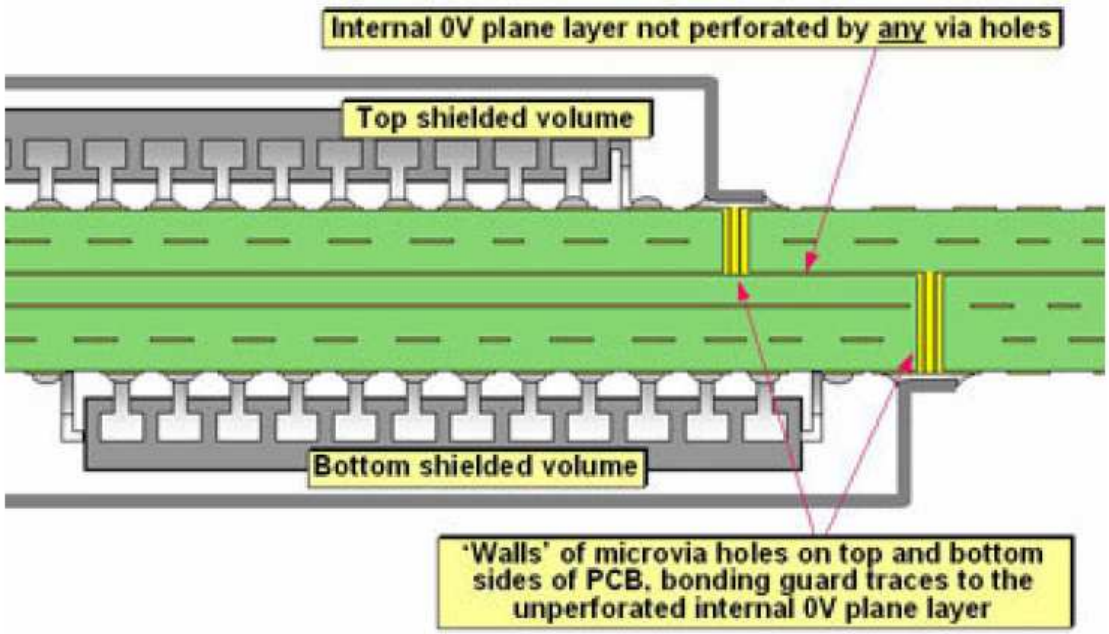


Figure 5.49 – Example of double-sided shielding using microvia PCB technology

Also the shield can be obtained using the radiator if it exists.

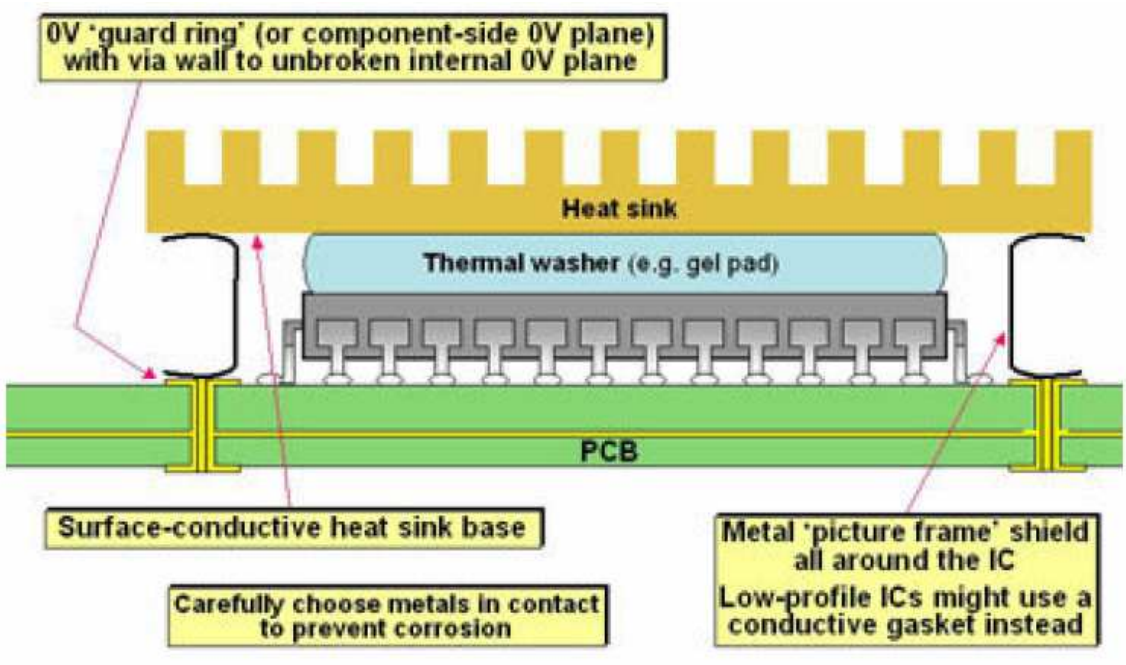


Figure 5.50 – Example of heatsink combined with shielding

The figure 5.51 shows a real example of a PCB with shielded zones.

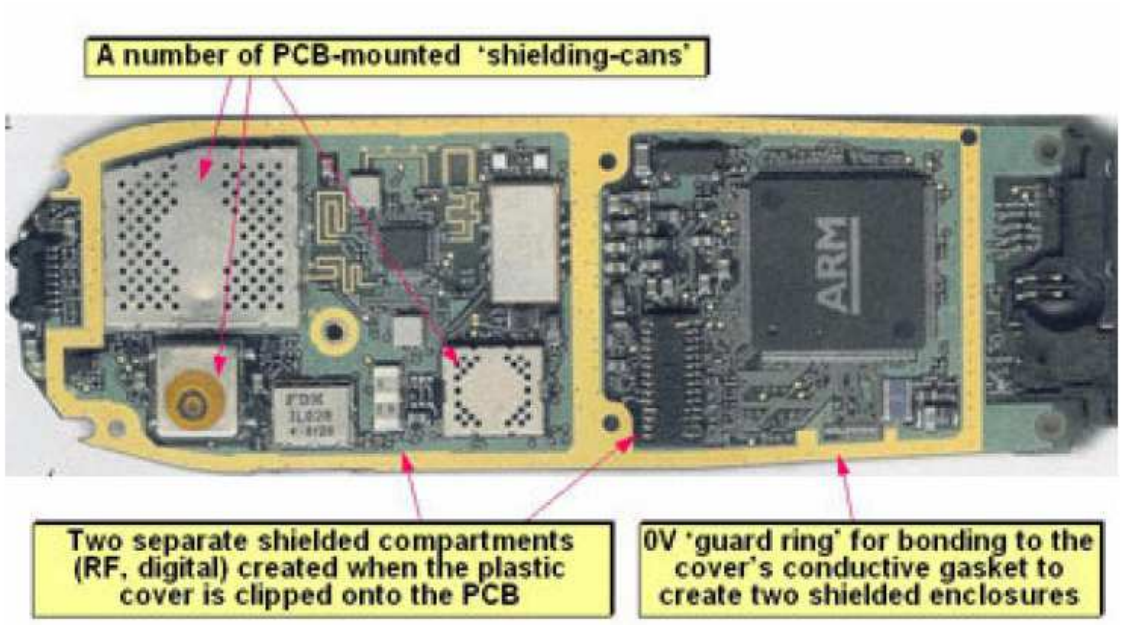


Figure 5.51 – Example of PCB-level shielding in a cellphone

5.2.4.6 Terminations

To high frequencies, as it has commented previously, a path of a PCB behaves like a line of transmission.

The table 5.4 shows the distance for a behaviour like line of transmission of the paths of a PCB.

Logic family	t_r/t_f ns	Length critical line
4.000B CMOS a 5V	40	65,6 cm
74HC	6	53,34 cm
74LS	6	53,34 cm
74ALS	3,5	30,48cm
74AC	3	25,4 cm
74F	3	25,4 cm
74AS	1,4	12,7 cm

Length line calculated for a dielectric constant = 4,5 (epoxi vitrificado FR4), t_{PD} = 5,58 bs/m.

Table 5.4 - Distance for a behaviour like line of transmission of the paths of a PCB

There are two types PCB paths:

- Microstrip paths.
- Stripline paths.

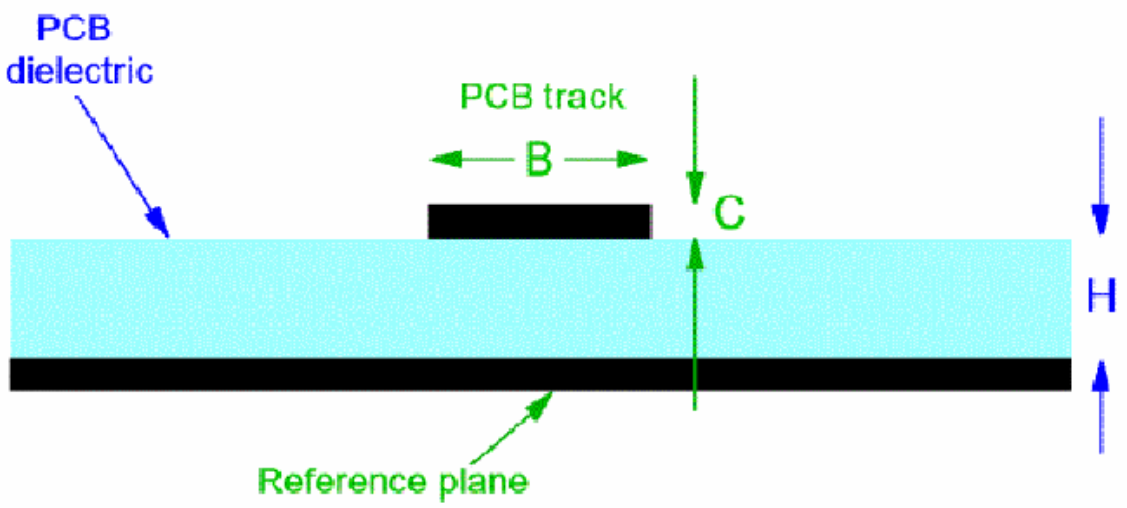


Figure 5.52– A surface microstrip

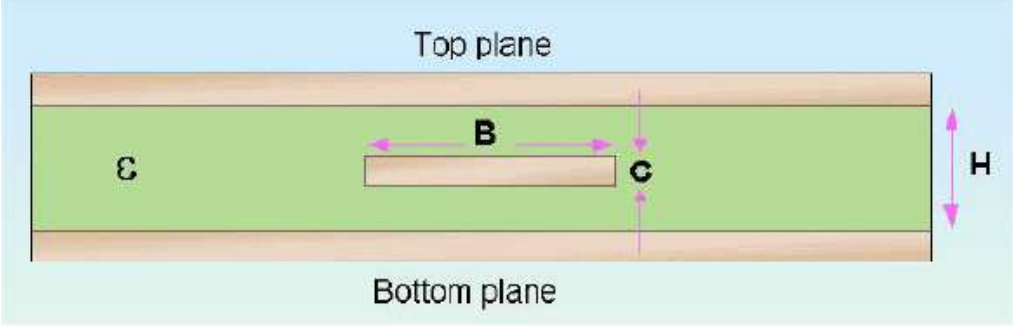


Figure 5.53 – A symmetrical stripline

The impedances features of the paths are:

Microstrip

$$Z0 = \frac{87}{\sqrt{\xi r + 1{,}41}} \bullet \ln \frac{5{,}98 \bullet H}{0{,}8 \bullet B + C}$$

Stripline

$$Z0 = \frac{60}{\sqrt{\xi r}} \bullet \ln \frac{1{,}9 \bullet H}{0{,}8 \bullet B + C}$$

From the electronic point of view, the behaviour of a path is like a resonant circuit L-C of multiple sections, producing oscillations and surges nonwished. Generally terminations of high impedance, as it is the case of the input impedance of input of I.C., produce strong reflections that are translated in parasitic oscillations in the path. For that reason, it is necessary to finish the paths conveniently. The figure 5.54 shows the typical terminations normally used in practice.

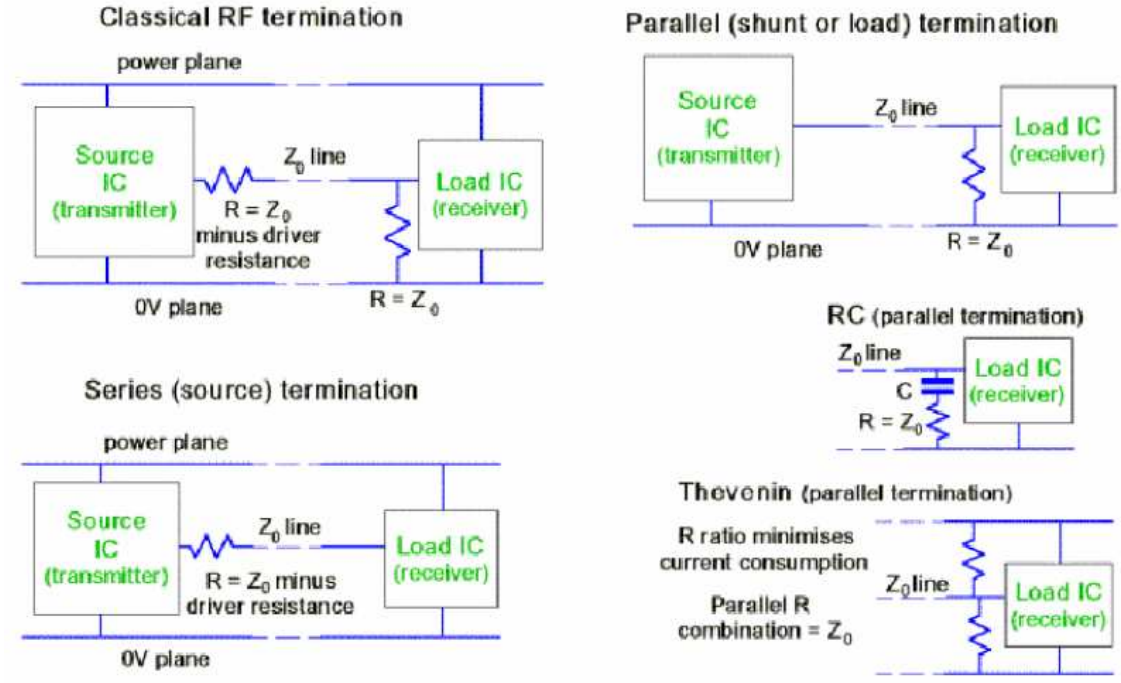


Figure 5.54 – Various transmission line termination methods

5.2.4.7 Interface between the outside and the interior of a PCB

Unavoidably a PCB must communicate with the outer world, normally through cables. The interconnection between outer and inner world of PCB (I/O) must be designed very carefully since generally the outer world (long cables, etc) is very aggressive and if we do not have the correct techniques of suppression of interferences, even if we have taken care of the layout of paths, described previously, the outer levels of noise propagate in the interior of the PCB causing disturbances nonwished and they can lead to the badly operation of the circuits contained in the PCB.
The figure 5.55 shows a typical partition of a PCB including connection I/O.

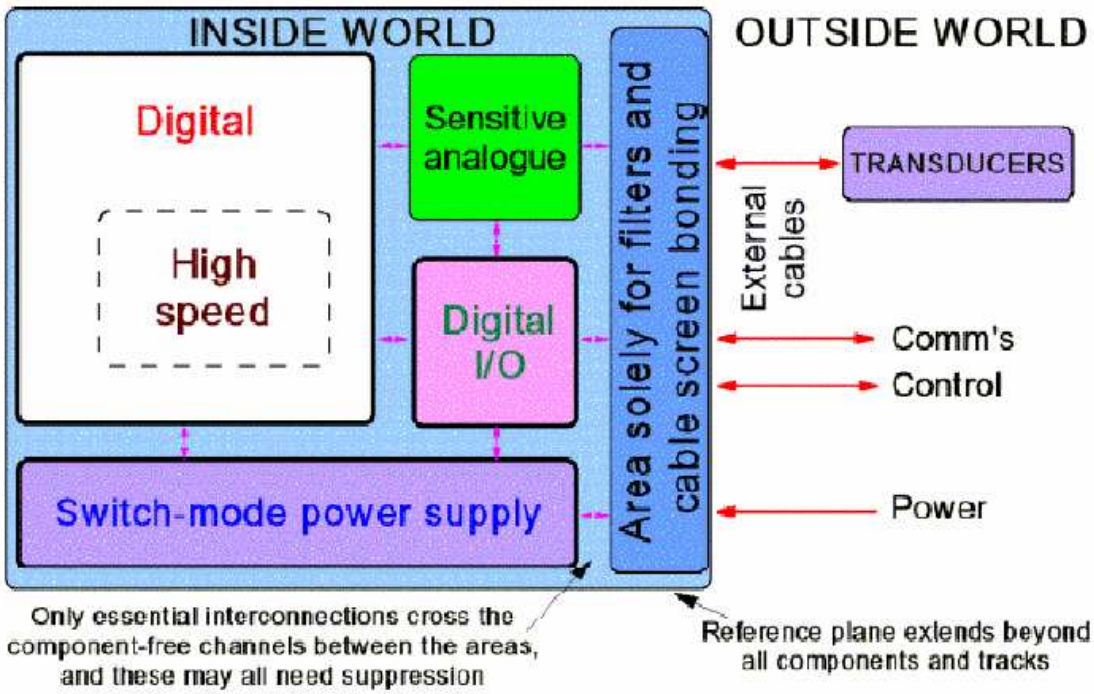


Figure 5.55 – Example of circuit segregation for a single-PCB product

External space to the PCB (external connections of sensors, interlocks etc) it is formed normally by conductors or cables that unite the outer world to the interior of the PCB. Generally the conductors or cables are effective antennas to pick up noise and consequently this one must be isolated of the PCB. Another important aspect is that only one PCB has better EMC features than the same circuit in several PCB´s.
The union zone between outer and inner world of the PCB must contain only optoacopladores, transformers of isolation, filters, transitory suppressors but never I.C.

Connection rules between the outside and interior of the PCB

- To prance the conductors of signal in form of twisted pairs with its returns, with the intention of displaying the smaller possible area to the inductive connections.
- To screen the cables with object to avoid the capacitive coupling, connecting the screen to ground.
- For screening before magnetic fields, the screen of the shielded cable must be connected to ground in its two ends. Nevertheless, due to the ground loop that is generated, there only can be obtained a limited protection before this type of fields.
- To finish correctly the lines of transmission that form the cables.
- If is possible in I/O to use tensions higher than the one of supply of the main circuit to apply to a resistive splitter filter.
- Think that an inverser I.C. is more susceptible to a positive tip when its input is at logical level 0 and vice versa.
- It is so important to not leave a pin of input of any C.I to the air, mainly if this is MOS due to its high impedance of input. In this case the nonused pins must be connected directly to ground or the positive.
- No used output must be left to the air.
- The inputs do not have to exceed the supply tension neither to lower of the ground level: in order to avoid it to put in the input look diodes.
- The 20 values that can go up to around mA RMS or 100 see function of the used logical family is due to limit the intensity of lines I/O one mA of tip. For it usually they are used a resistance series of about 100 Ω.
- Ferrite is very effective to a large extent to reduce noise in common way due by the great curls of mass that normally form.
- Never mix conductors of power, control, supply.
- Eliminate the current loops or to diminish its areas.
- Filter all the cables that cross zones EMI, is with filters R-C or L-C.
- The crossings of the wiring between a line with interference and a sensitive line is due to do, as far as possible, always to 90º.
- Per each 10 sideburns of a connector dedicate one to ground.
- In case of using flat cables, it is advisable intercalary ground lines between those of signal.

5.2.4.8 Summary of rules of design of PCB´s

- Not to draw up clock paths of high speed next to sensitive paths like interruptions, reset, analogical digital tracks I/O to and in general all the control lines of a microprocessor. In order to resolve this problem, draw up clock paths with a ground path protection next.
- The positive must be drawn up next to the ground paths or in a plane of feeding in multilayered PCB.

- It is simpler the design of a PBC multilayer that one of double layer, but this one last one has an inferior cost.
- In the schematic, make functional partitions and/or by tensions of supply. To make those partitions in the PCB.
- Use separated supplies for the diverse partitions of the circuit, with the purpose of avoiding the galvanic noise between zones, as much with respect to the supply as to its return (mass).
- To reduce the magnetic connections, reduce the area of all those curls that can form and capture EMI. The mass planes help remarkably in the reduction of mass curls but they require a multilayered PCB.
- To design carefully the signal tracks. The key is to maintain a good isolation between the sensitive lines of signal and the lines of high level of tension and/or current. Isolated lines to mass can be used so that they act there of screens where a line of signal and feeding must pass parallel.
- To control the impedances characteristic and the completions of the tracks. This is critical in tracks of high frequency where there is to consider so much the delay of propagation as well as the reflections of the signal.
- Take care the maximum levels accepted by each technology, Transitory ultrashort over the 30 V can destroy or degrade the I.C.
- The ground and supply paths in a PCB of two layers must have minimum a width of 1 mm to do the PCB the most opaque possible, vista to backlighting, prioritising the track of mass as opposed to the one of feeding.

6. Test of the artificial pancreas

6.1 Test equipment

Next the most important equipment, used in the tests of the artificial pancreas, is explained.

LISN

"LISNs are used to measure the RF conducted back down the mains lead from the unit under test (UUT). Many standards refer to a LISN as an artificial mains V-network of 50ohm/50uH as specified by CISPR16. All standard Laplace LISNs are fully compliant with this requirement in all respects for the frequency band B, 150KHz to 30MHz. Each standard LISN includes a mains RF low pass filter to reject any noise already on the mains and an effective voltage transient limiter to protect any sensitive analyzer or receiver against high energy spikes. Note that these LISNs may be used on low voltage and/or DC connections provided that the current rating is not exceeded" [19].

Figure 6.1 - CISPR16, single phase, 16 amp LISN

Spectrum analyzer

A spectrum analyzer is a device used to examine at the spectral composition of some electrical, acoustic or optical waveform.

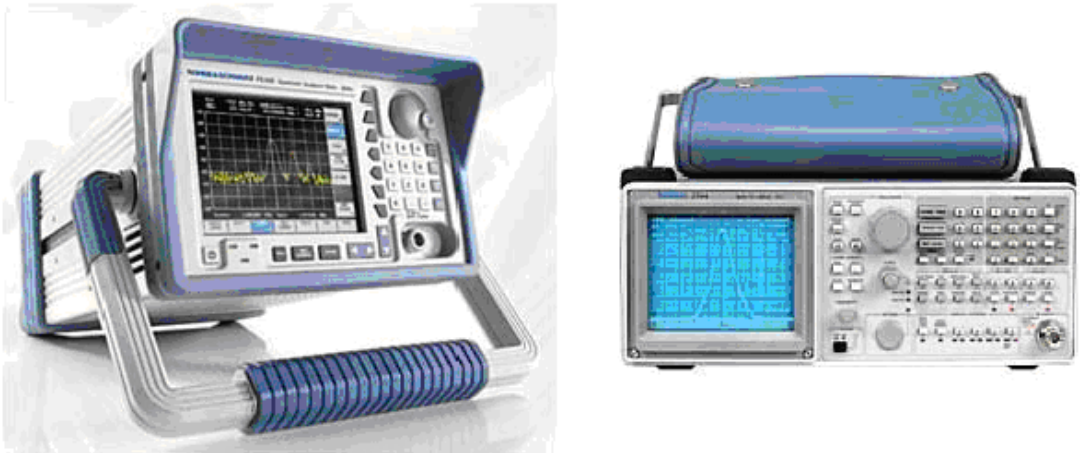


Figure 6.2 – Front view of the spectrum analyzer of EMI according to CISPR

Signal generator

Signal generator is an electronic instrument used for the production of electromagnetic or acoustic signals with certain desired characteristics. It is useful in testing and calibration.

Figure 6.3 - Front view of two signal generator

Amplifier

Amplifier is a device used to increase the strength of a signal. An electronic device that takes in an original signal and gives it more power and provides it as an output.

Field probe

Field probe is used to measure the radio-frequency (RF) fields.

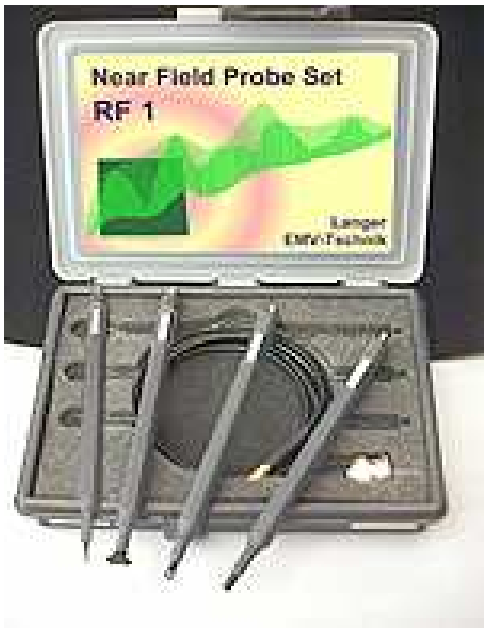


Figure 6.4 – Near field probe set

Antenna

Antenna is a conductive physical device designed to radiate RF energy from a transmitter, or to capture RF energy for application to a receiver.

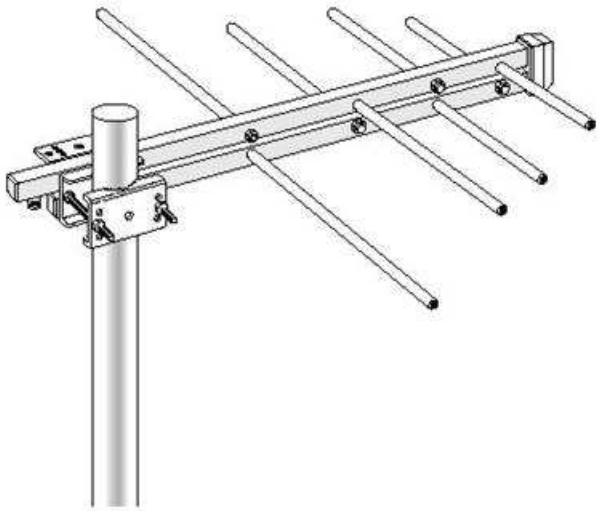


Figure 6.5 - Antenna, Log Periodic (B)

Coupling / Decoupling Networks (CDN's)

CDN is designed specifically to meet the conducted RF immunity testing conditions specified in EN61000-4-6: 1996.

The Coupling-Decoupling Network (CDN) is designed to couple the disturbance signal directly to the EUT cable while at the same time preventing it from passing towards the AE (associated or auxiliary equipment).

Figure 6.6 - Commercial CDN

EM Clamp

The EM-clamp is a clamping device that subjects the cable under test to both capacitive and inductive coupling of the RF stress.

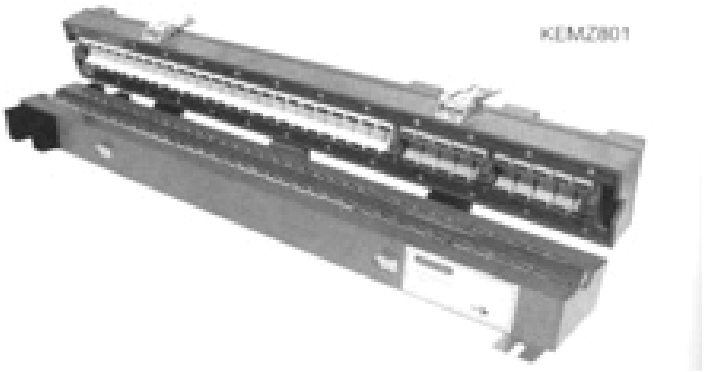


Figure 6.7 – Front view of a commercial EM clamp

ElectroStatic discharge simulator (ESD simulator)

The figure 6.8 shows a commercial ESD simulator.

Figure 6.8 - Commercial ESD simulator

6.2 Electromagnetic Compatibility Testing. Standard EN 60601-1-2

6.2.1 Electrostatic discharge (ESD). Standard EN 61000-4-2 [19]

Object

The main goal of this test is to evaluate the performance of the EUT (Equipment Under Test) when it is subject to electrostatic discharges of ± 4 kV using the direct contact method, and/or ± 8 kV using the through air method.

Procedure

The test is made on a reference ground plane. The EUT and its interface cables are isolated from the ground plane by a distance of 0.5 millimeters (Figure 6.9). Discharges are made to all the places of the EUT which are normally accessible to the operator. At least four test points are selected for every side. The voltage level is set initially at 2 kV, and increased to a maximum level of 4 kV for contact discharges and 8 kV for air discharges. Fifty discharges for each polarity are tested to each test point with a minimum time interval of 1 second between discharges.

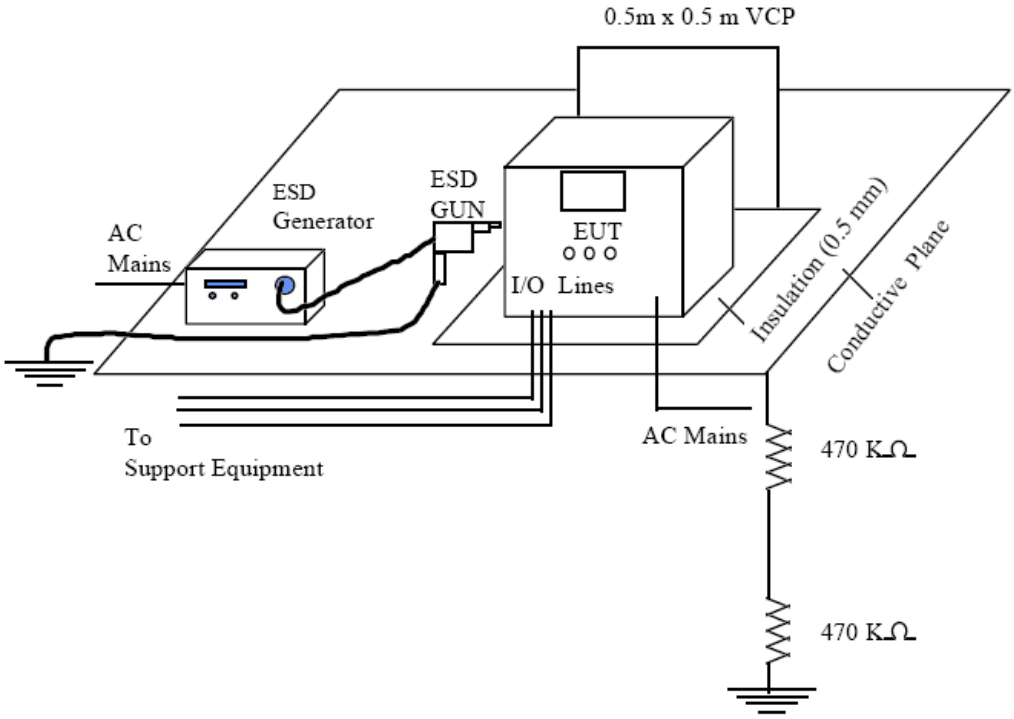


Figure 6.9 – Location of all the devices for EN 61000-4-2 test

The favourite method of discharge is direct contact injection. This method is made on all metallic surfaces. If an electrostatic discharge event is inaccessible by using the direct contact method, then air method of discharge is used.

Extra discharges are performed in close proximity to the EUT for simulating charged objects next to the EUT. These discharges are performed to a vertical coupling plate around all sides of the EUT and its interface cables.
About 200 single discharges are performed to the ground plane, with a minimum time interval of 1 second between discharges.

Test Equipment
The following test equipment is used for this test:

- ESD simulator

Climatic Conditions
The climatic conditions must fulfil with certain requirements during testing.

	Requirement
Ambient temperature	15°C to 35°C
Humidity	30% to 60%
Pressure	86 kPa to 106 kPa

Table 6.1 – Requirements of the climatic conditions for EN 60601-1-2 test

Confidence of Results and Deviations from Test Method
Confidence of results is obtained by exceeding the requirement for minimum number of discharge locations and by increasing the test voltage level to 105% of specification.

6.2.2 Electrical Fast Transient. Standard EN 61000-4-4 [19]

Object
The main goal of this test is to evaluate the behaviour of the EUT when subjected to electrical fast transients of ± 1.0 kV on the power lines and ± 0.5 kV on the signal lines and I/O lines.

Procedure
Testing is made on a reference ground plane. The EUT and its interface cables are isolated from the ground plane by a distance of 0.8 meters (Figure 6.10). The interference signal is coupled to the power lines through an internal capacitive coupling network in the interference generator. The transients are applied to the power lines at ± 1.0 kV in several coupling configurations including L1 to Ground, L2 to Ground and L1/L2 to Ground, while monitoring the EUT for performance. Transients are applied for a minimum of one minute for each test configuration.

In addition to the power lines, the signal is also applied to all signal lines greater than 3 meters in length. This is done with the use of a capacitive coupling clamp (Figure 6.10). The interference signal is applied directly to the clamp while the signal cables under test are placed in the clamp. This provides a means of capacitively coupling the interference signal to the cables without a direct electrical connection. The interference level is set at ± 0.5 kV, while monitoring the EUT for performance.

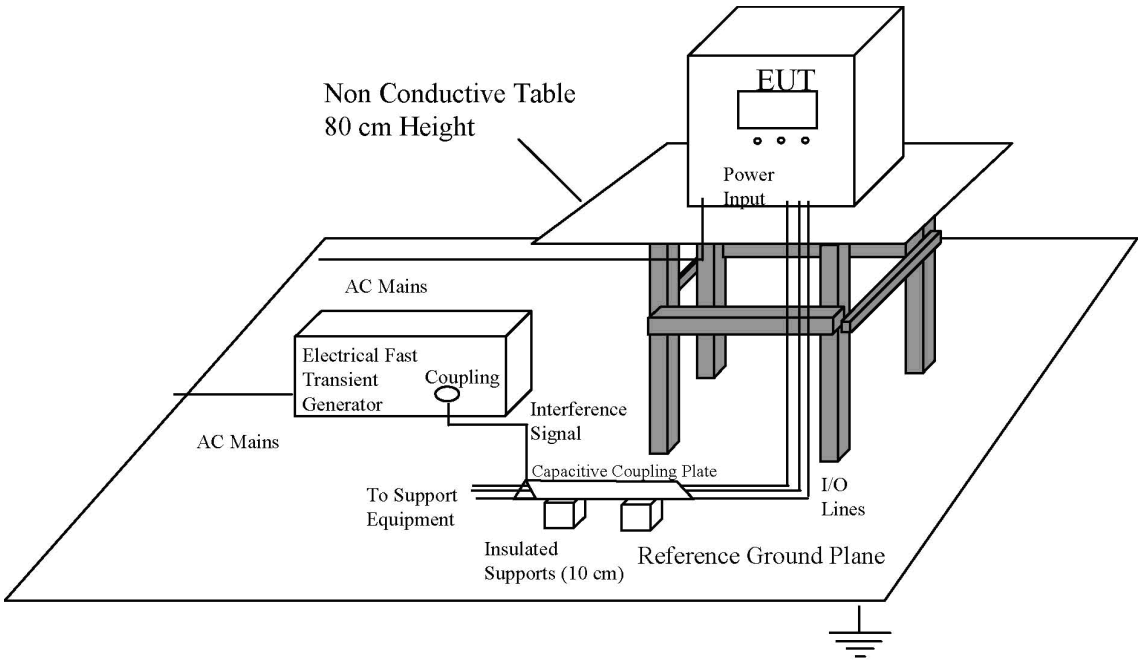


Figure 6.10 – Location of all the devices for EN 61000-4-4 test

Test Equipment
The following test equipment was used for this test:

- Fast Transient Burst Generator
- I/O and Signal Line Clamp (Amplifier Research)

Climatic Conditions

The climatic conditions must comply with certain requirements during testing.

	Requirement
Ambient temperature	15°C to 35°C
Humidity	25% to 75%
Pressure	86 kPa to 106 kPa

Table 6.2 – Requirements of the climatic conditions for EN 60601-1-4 test

Confidence of Results and Deviations from Test Method

Confidence of results is obtained by extending test duration from one (1) minute per configuration to a minimum of three (3) minutes per configuration.

6.2.3 Conducted RF immunity. Standard EN 61000-4-5

Object
The main goal of this test is to determine the behaviour of the EUT when subjected to a surge injected in the supply lines or in I/O signal lines.
.
Procedure
For EUT power supply:
The surge is to be applied to the EUT power supply terminals via the capacitive coupling network. Decoupling networks are required in order to avoid possible adverse effects on equipment not under test that may be powered by the same lines, and to provide sufficient decoupling impedance to the surge wave. The power cord between the EUT and the coupling/decoupling networks shall be 2 meters in length (or shorter).

For test applied to unshielded unsymmetrically operated interconnection lines of EUT:
The surge is applied to the lines via the capacitive coupling network. The coupling/decoupling networks shall not influence the specified functional conditions of the EUT. The interconnection line between the EUT and the coupling/decoupling shall be 2 meters in length (or shorter).

For test applied to unshielded unsymmetrically operated interconnection telecommunication lines of EUT:
The surge is applied to the lines via gas arrestors coupling. Test levels below the ignition point of the coupling arrestor cannot be specified. The interconnection line between the EUT and the coupling/decoupling shall be 2 meters in length (or shorter).

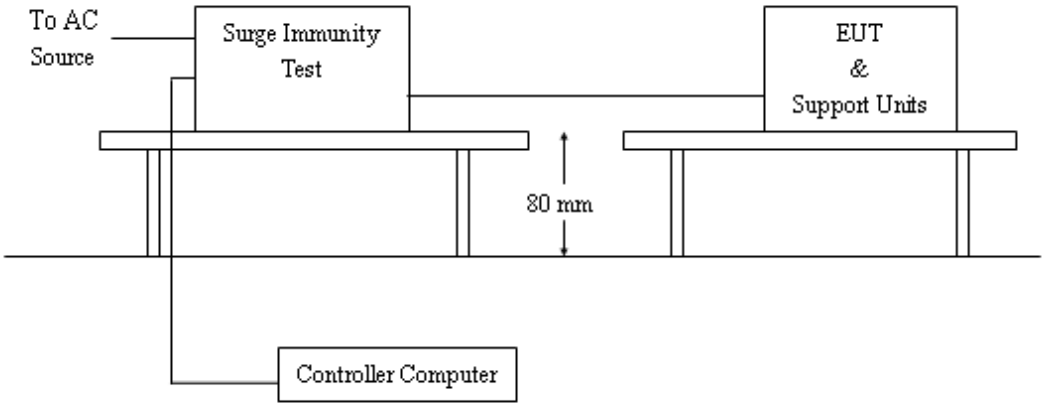


Figure 6.11 – Location of all the devices for EN 61000-4-5 test

Confidence of Results and Deviations from Test Method
Confidence of results is obtained by increasing the test voltage level to 105% of specification.

Test Equipment

The following test equipment is used for this test:

- Surge combination wave
- Surge coupler/decoupler
- External coupler/decoupler for telecom lines
- I/O signal line coupler/decoupler
- Surge cable
- Surge adapter

6.2.4 Radiated RF immunity. Standard EN 61000-4-3 [19]

Object

The main goal of this test is to estimate the behaviour of the EUT when subjected to an electric field of 10 V/m from 80 MHz to 1000 MHz with 80% amplitude modulation at 1 kHz.

Procedure

The test must be made in a shielded anechoic chamber. A calibration of the field is made to validate the uniform test area. The “uniform area” is a vertical plane in which e-field variations are adequately small. This uniform area size is 1.5m x 1.5m. An isotropic field strength probe is placed within the empty room connected to the field strength monitor over a fiber optic cable. The signal level to the radiating system is adjusted until the required field intensity is indicated. The frequency range is swept from 80 MHz to 1000 MHz. The voltage or power required at the output terminals of the amplifier to establish the specified field is monitored and recorded. The number of points to be tested to demonstrate uniformity is 16, at 0.5 steps. A field is then verified uniform when its magnitude does not vary over the defined area by greater than -0 dB, + 6 dB of nominal value, over 75%.

The EUT is placed in the center of the chamber (on a wooden table), and a broadband transmitting antenna is placed 3 meters away (see Figure 6.12). The EUT support equipment is located outside of the shielded chamber. Cable connections from inside to outside of the chamber are made through feed through connectors. EUT connections to its support equipment are made through an access hole in the shielded chamber.

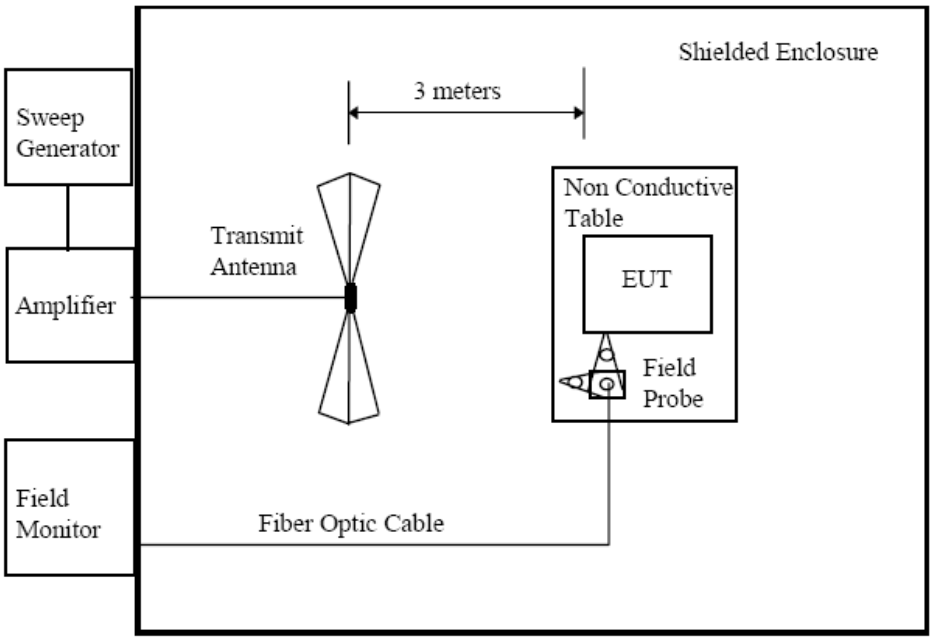


Figure 6.12 – Location of all the devices for EN 61000-4-3 test

The frequency is then swept across the entire range of interest at the required field strength while monitoring the EUT for performance. The sweep is repeated for both horizontal and vertical polarizations of the antenna and again, for all sides of the EUT in succession.

Test Equipment
The following test equipment is used for this test:

- Signal Generator
- Isotropic Field Monitor
- Field Probe
- Amplifier (50W)
- Antenna, Log Periodic (B)

Confidence of Results and Deviations from Test Method
Confidence of results is obtained by ensuring the frequency sweep rate is slow/fast enough to detect a product failure and by increasing the test voltage level to 105% of specification.

6.2.5 Conducted RF immunity. Standard EN 61000-4-6

Object
The main goal of this test is to determine the immunity level before interferences of coupled close fields through supply lines and signal lines.

Procedure
The EUT is located on an insulating stand 10cm over a ground plane. There is one single cable for input and one BNC coaxial for output. The input cable is coupled via a switchable impedance to the case. The minimum series impedance is given by a 3R3 low inductance resistor and the voltage across this is passed to the output BNC connector through a 47R matching resistor, and thence via the external cable and CDN-S1 to the measuring instrument. The internal circuit is shown in Figure 6.13.

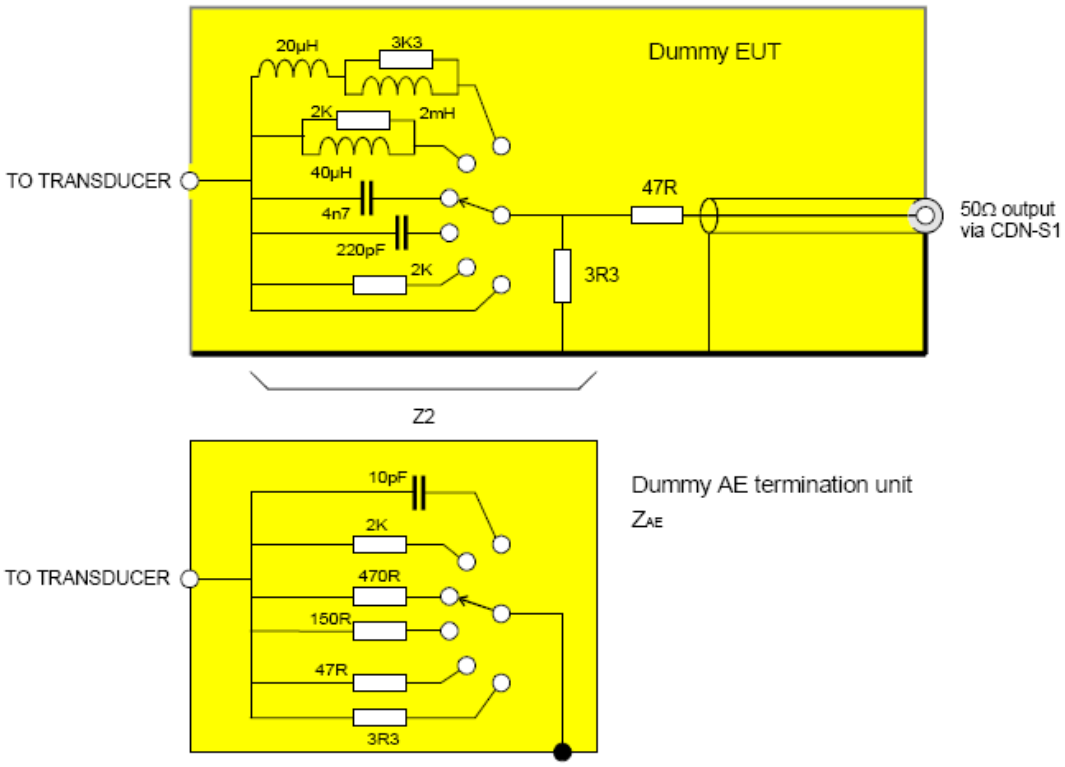


Figure 6.13 – Internal circuit for EN 61000-4-6 test

Figure 6.13 also shows the switched impedance which is used to give a reproducible but selectable common mode impedance ZAE at the AE position.

The general setup follows the instructions given in IEC 61000-4-6 as far as possible. These instructions include:

- use of a metal ground plane, with the dummy EUT at a height of 0.1m and more than 0.5m from other metallic objects

- the distance from the EUT input connector to the transducer set to between 10cm and 30cm
- the height of the cable from the EUT input connector to the transducer set to between 3cm and 5cm
- the distance from the transducer (current probe or EM-clamp) to the dummy AE should be less than 0.3m “where possible”; it is set to 0.1m, 0.5m or 1m (not applicable for the CDN)
- the height of the cable from the transducer (current probe or EM-clamp) to the dummy AE set to between 3cm and 5cm
- the non-tested cable is the coaxial line from the output port, which should be terminated in a separate CDN to give a 150W common mode impedance; a CDN-S1 is used, and the cable is invariant, and set to 4cm height and 20cm length (the middle of the required range)

Variations were made between the extreme values for the EUT and AE cable layout. The wire used for the input (cable under test) was a combination of lengths of 16/0.2 stranded insulated copper. For the output connection to the CDN-S1, the cable was standard 50W RG58C/U.

A general view of the setup is shown in Figure 6.14.

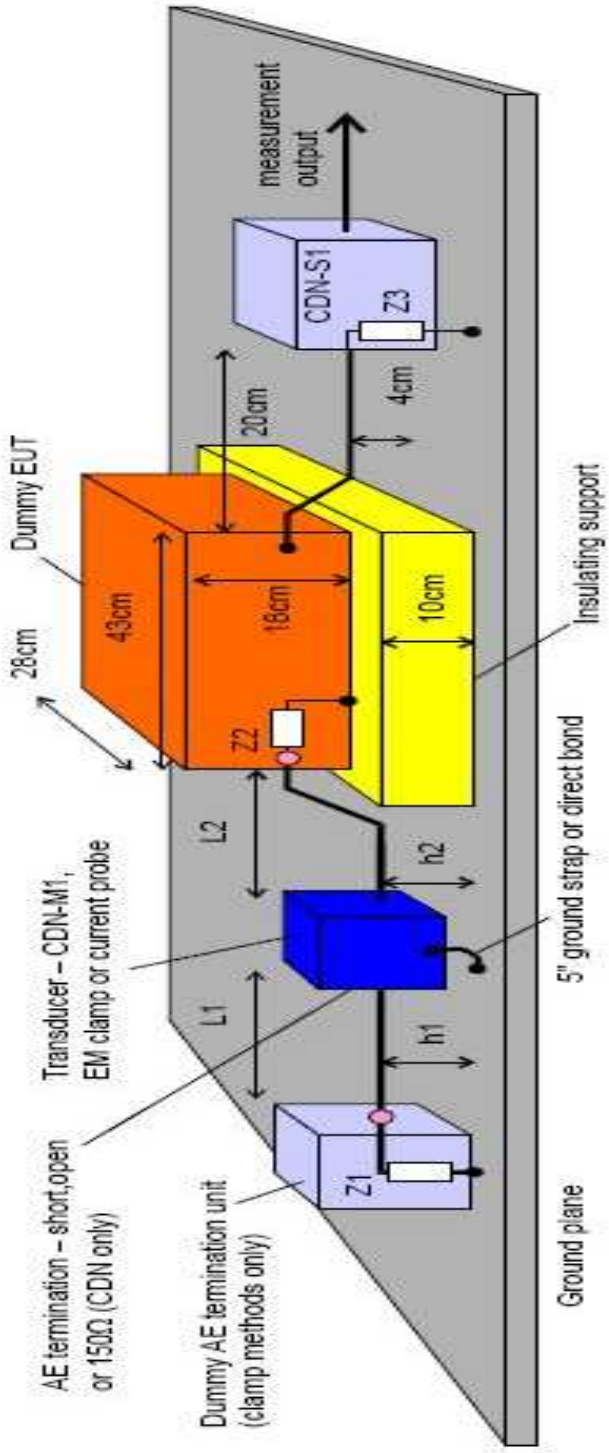


Figure 6.14 – Location of all the devices for EN 61000-4-6 test

Test equipment

- Spectrum Analyser
- Amplifier
- Test CDN
- Current Probe
- EM Clamp

Confidence of Results and Deviations from Test Method

Confidence of results is obtained by increasing the test voltage level to 105% of specification.

6.2.6 Power frequency H-field immunity. Standard EN 61000-4-8

Object
The main goal of this test is to determine the immunity of the EUT to low frequency magnetic fields.

Procedure
The equipment is configured and connected to satisfy its functional requirements. It shall be placed on the Reference Ground Plane (GRP) with the interposition of a 0.1m-thick insulating support.
The equipment cabinets shall be connected to the safety earth directly on the GRP via the earth terminal of the EUT.
The power supply, input and output circuits shall be connected to the sources of power supply, control and signal.
The cables supplied or recommended by the equipment manufacturer shall be used. 1 meter of all cables used shall be exposed to the magnetic field.

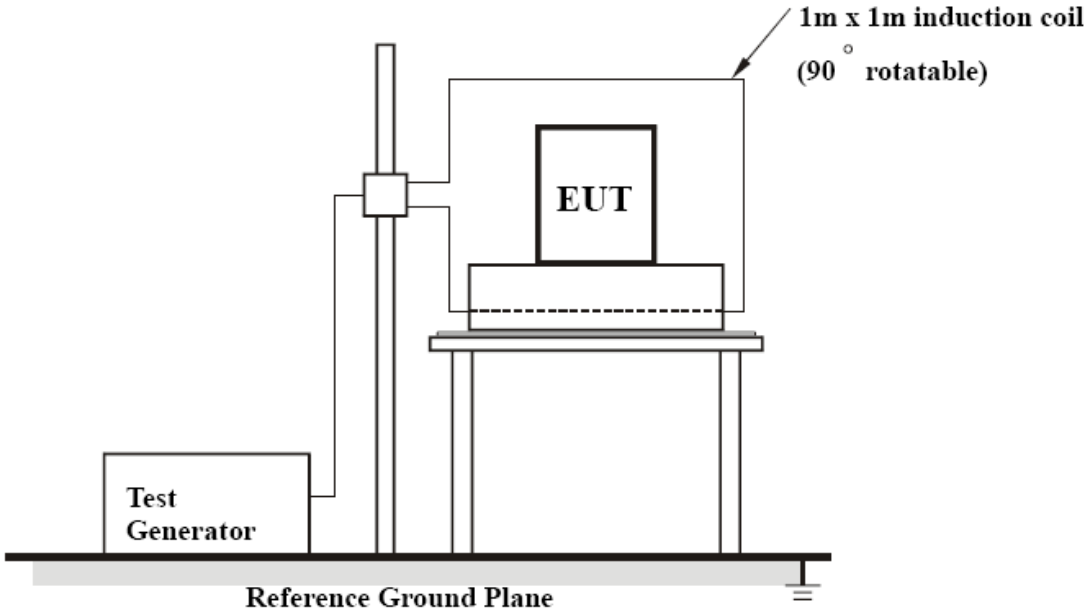


Figure 6.15 – Location of all the devices for EN 61000-4-8 test

Confidence of Results and Deviations from Test Method
Confidence of results is obtained by increasing the test voltage level to 105% of specification.

Test Equipment
The following test equipment is used for this test:

- Magnetic field tester
- Field meter

6.2.7 Conducted emissions. Standard EN 55011

Object
The main goal of this test is the measurement of the level of symmetrical and asymmetric disturbances conducted by power supply cable and signal cable.

Procedure
Measurement of EMI tensions of the cables, by means of an adapter of standard impedance, it is known as LISN (Line Impedance Stabilizing Network) and a standard measurer. The frequency range covered by these measures is from 30 KHz to 1MHz.

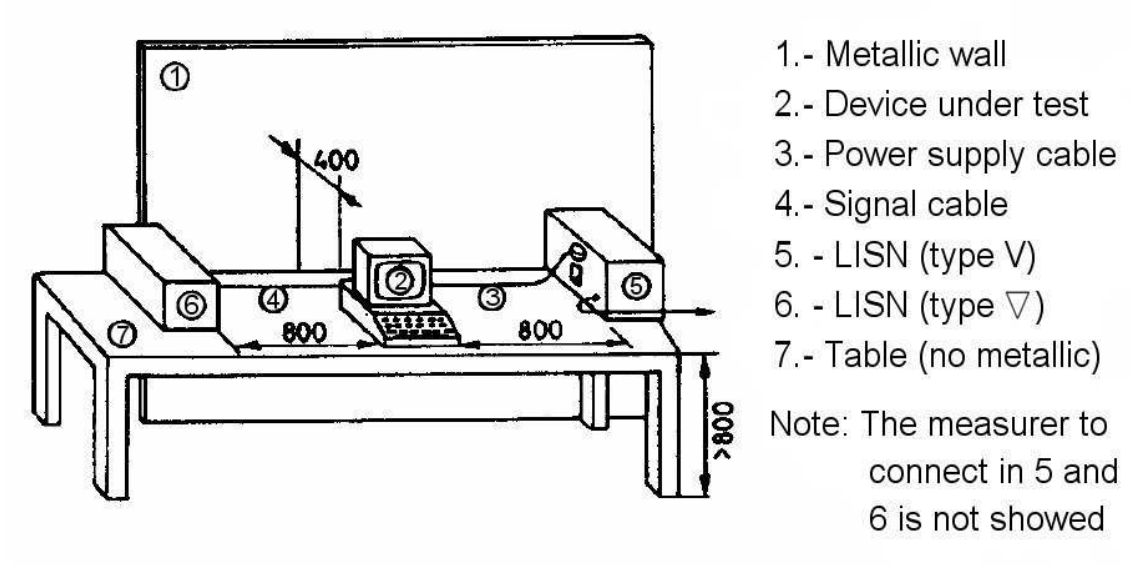


Figure 6.16 - Example of disposition for test of conducted EMI.

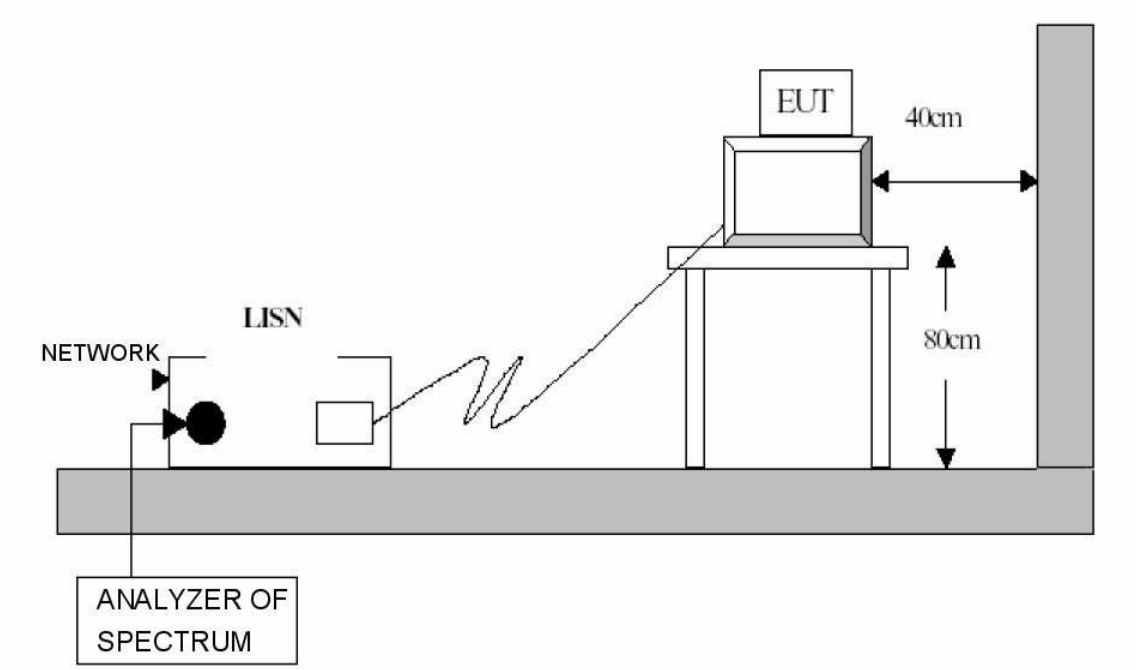


Figure 6.17 - Correct disposition for a test of conducted EMI

For precertification tests, these must be made according to the specifications that generally define a location with a ground plane in the floor and free of interferences (it is mean shielded).

Confidence of results and deviations from test method
Confidence of results is obtained by increasing the test voltage level to 105% of specification.

Test equipment
The following test equipment is used for this test:

- LISN
- Analyzer of spectrum

6.2.8 Radiated E-field emissions. Standard EN 55011

Object
The main goal of this test is the measurement of the level of disturbance radiated by chassis, supply cable and signal cable from different distances (generally 3, 10 and 30 m).

Procedure
For frequencies between 10 kHz and 30 MHz the measurement of the magnetic field is demanded and for frequencies between 30 MHz and 1 GHz the measurement of the electromagnetic field is demanded. The EMI signal is caught with the appropriate antennas, looking for the direction of maxim disturbance, later the signal caught is applied to the standard measurer. The tests must be made in an atmosphere free of external interferences and obstacles that can produce reflections of the electromagnetic field.

For supply cables the measurement of the power of the radiated electromagnetic field is also demanded. The measurement is made by means of absorption transducers, connected to the standard measurer. The disposition of the equipment under test and the measuring equipment must be as the figure 6.18.

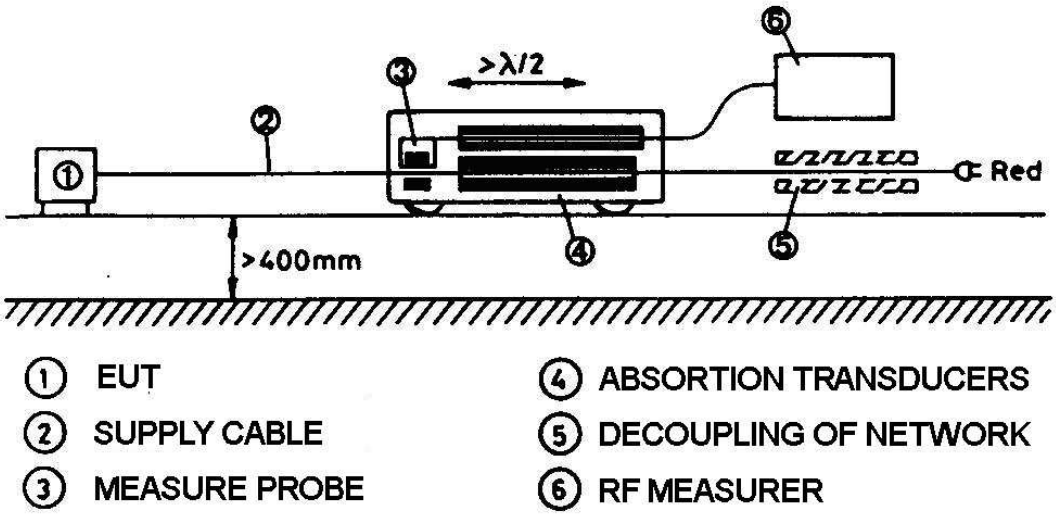


Figure 6.18 - Disposition for the measurement of the power radiated by cables (30 MHz -1 GHz)

For the tests of radiation, the disposition of the equipment under test and the instruments of measurement must be as is showed by the figure 6.19, where the space marked by the ellipse must be free of external disturbing elements and the floor must be flat and conductor. International Special Committee On Radio Interference (CISPR) norms and Verband Deutscher Elektrotechniker (VDE) admit the accomplishment of tests in free locations

or shielded chambers, denominated anechoic chambers as it is showed in the figure schematically.

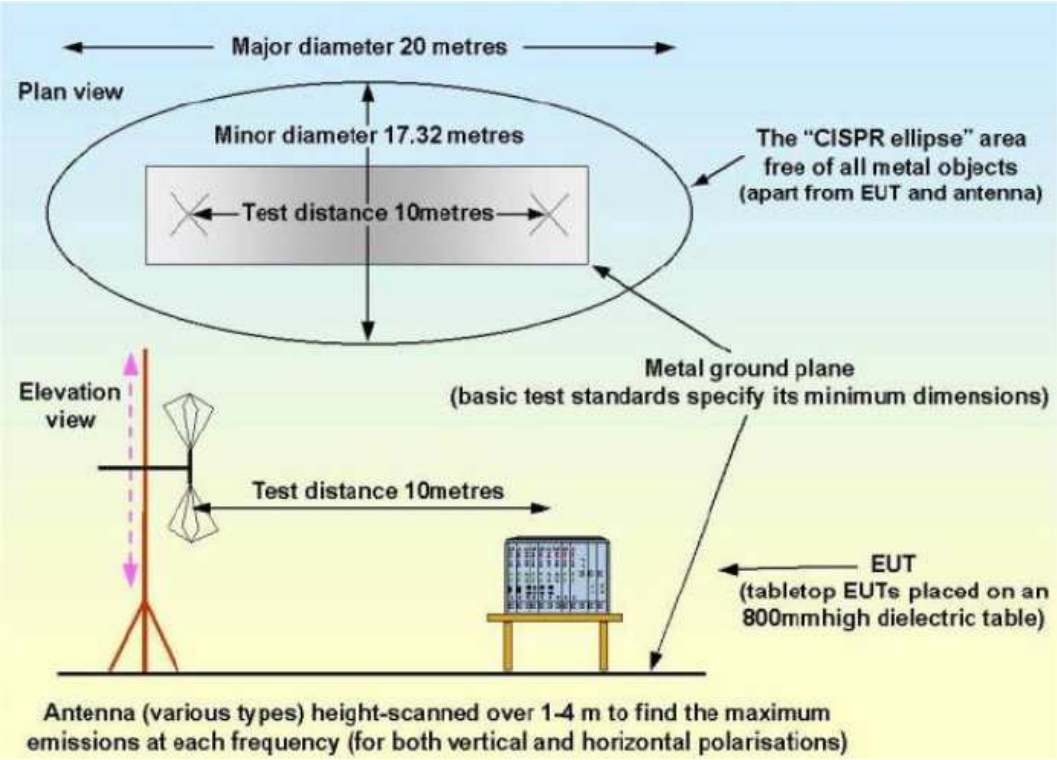


Figure 6.19 – General Open Area Test Site (OATS) requirements in EN 55022

For precertification tests, these must be made according to the specifications that generally define a location with a ground plane in the floor and free of interferences (it is mean shielded).

Test Equipment

The following test equipment is used for this test:

- Signal Generator
- Isotropic Field Monitor
- Field Probe
- Amplifier (50W)
- Antenna, Log Periodic (B)

6.2.9 Testing and Certification Equipment and Services

The table 6.1 shows companies that offer electromagnetic compatibility testing services.

COMPANY	WEBSITE OF CONTACT
Baumer Electric Ltd.	http://www.devicelink.com/company/euro/b/b0142.html
Consultants Europe B.V.	http://www.devicelink.com/company/euro/s/s0228.html
Eurocat Institute for Certification and Testing, Darmstadt, Germany	http://www.devicelink.com/company/euro/e/e0115.html
IMST GmbH, Kamp-Lintfort, Germany	http://www.devicelink.com/company/euro/co/230/23035.html
International Electrotechnical Commission	http://www.devicelink.com/company/euro/i/i0035.html
Intertek ETL Semko	http://www.devicelink.com/company/euro/i/i0069.html
Intertek Semko AB	http://www.devicelink.com/company/euro/s/s0033.html
MET Laboratories Inc.	http://www.devicelink.com/company/euro/m/m0077.html
Mikron Assembly Technology	http://www.devicelink.com/company/euro/m/m0105.html
Montena emc S.A., Rossens	http://www.devicelink.com/company/euro/m/m0142.html
PartnerTech AB	http://www.devicelink.com/company/euro/p/p0013.html
Pemstar Inc.	http://www.devicelink.com/company/euro/co/185/18553.html
PMR Ltd.	http://www.devicelink.com/company/euro/co/224/22452.html
RWTÜV Systems GmbH	http://www.devicelink.com/company/euro/r/r0064.html
TÜV Rheinland Product Safety GmbH	http://www.devicelink.com/company/euro/t/t0074.html

Table 6.1 – Companies for Electromagnetic Compatibility Testing Services

6.3 Electrical Safety Tests. Standard EN 60601-1

This chapter explains what exactly electrical safety testing (EST) is and low the various tests are performed. Electrical Safety Testing verifies product safety under simulated fault and/or material stress conditions. The objective is to test the artificial pancreas to its limitations to make sure that it can resist the electrical conditions it will be subjected to on the job.

The harmonized standard 60601-1 includes dielectric strength, leakage current and protection earth verification type tests. The dielectric strength test may be referred to as dielectric withstand, dielectric breakdown or high potential but the process is the same: using a high voltage, stress the insulation beyond what it would encounter in normal (specified) use. Leakage current tests detect the amount of leakage present to a patient or operator when the medical device is energized and if that amount is at a secure level. The most crucial safety test is verifying the product's protective earth connection. This is performed using a ground continuity test. Although not required by IEC 60601-1, an insulation resistance test measures the strength of insulation within a product and it is a very frequent electrical safety production test.

The essential electrical safety tests are:

- Protective earth verification:
    - Ground continuity test
    - Ground bond test
- Dielectric strength:
    - AC high potential test
    - DC high potential test
- High resistance:
    - Insulation resistance test
- Leakage current:
    - Earth leakage, touch/chassis (enclosure),
    - Patient leakage & patient auxiliary leakage

The appendix H contains an explanation of the previous test.

6.4 Biocompatibility Safety Tests. Standard EN ISO 10993-1

This chapter outlines the tests about biological safety and biocompatibility that the artificial pancreas must pass. These tests should be conducted on final product. ISO 10993-1 recommends that the rationale for selection and/or waiving of tests be justified and documented. For regulatory clearance purposes, tests should be carried out under controlled laboratory conditions in compliance with Good Laboratory Practices (GLP).

Next individual tests included in the ISO 10993/EN 30993 standard are enumerated:

- Cytotoxicity
- Sensitization
- Skin Irritation
- Intracutaneous Reactivity
- Acute Systemic Toxicity
- Genotoxicity
- Implantation
- Hemocompatibility
- Subchronic and Chronic Toxicity
- Carcinogenicity

Appendix I provides a description of the individual tests previously mentioned.

7. Discussions

Directive 90/385/ECC provides a good understanding of the security and the requirements of EMC applicable to the artificial pancreas. Anyway expert people in this field and the manufacturers advised to approach accredited test laboratories to consult about regulatory requirements and product testing. Knowledgeable people are available to lead the manufacturers through the entire approval process.

The need for specifications that insure compatibility among equipment and systems it is noticed. Therefore, it is well-recognized that the artificial pancreas must operate as intended and also not interfere with the operation of other equipment. Exists specifics standards for the artificial pancreas, although still an universal normative is missed. Nevertheless the directive 90/385/ECC is a great step and supposes the free active implantable product circulation in the European market, this already supposes a great advance in the normalization of sanitary products.

Personally I believe that the pancreas artificial can be realized, and a few years hence the pancreas will be finally realized and developed. But I am conscious that a long way and many hours of investigation leave to develop a competent artificial pancreas that fulfills the specific standards.

8. Conclusions

Diabetes that yet has no cure is dangerous, and millions of people are suffering from it and its further complications. The current state of the art in controlling diabetes is good but it is painful, needs too much care to provide good regulation for the blood glucose levels. In order to solve that it is important to develop a painless automated control system. This automated control system will provide better regulation in the blood glucose levels. Also this system will make less probably diabetes complications. In summary, the artificial pancreas will substantially improve the quality of life of the patient.

The work presented in this thesis is part of Artificial Pancreas Project. This thesis covers the different important points to commercialize an implantable artificial pancreas. The thesis also, covers the different tests that the artificial pancreas must comply in order to get the CE marking.

Thanks to the Directive 90/385/EEC, free active implantables product circulation in the European market is going to mean a great advance in the normalization and quality of Sanitary products. In the field of the medicine it lacked a unification of criteria that included all the actors of the sanitary scene: manufacturer, distributor, doctor, operator and patient because the security and effectiveness of products cannot guarantee it only one of such. Productive years of transition will come and will sweep products of doubtful scientific base of the sanitary market. The specifications of the product must be very clear to choose all the correct and necessary tests.

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APPENDIX A

ACTIVE IMPLANTABLE DIRECTIVE (90/385/EEC)

ACTIVE IMPLANTABLE DIRECTIVE (90/385/EEC)

COUNCIL DIRECTIVE

of 20 June 1990

on the approximation of the laws of the Member States relating to active implantable medical devices.

(90/385/EEC)

The Council of the European Communites,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 100a thereof,

Having regard to the proposal from the Commission,
A cooperation with the European Parliament,
Having regard to the opinion of the Economic and Social Committee,

Whereas in each Member State active implantable medical devices must give patients, users and other persons a high level of protection and achieve the intended level of performance when implanted in human beings;
Whereas several Member States have sought to ensure that level of safety by mandatory specifications relating both to the technical safety features and the ispection procedures for such devices; whereas those specifications differ from one Member State to another;

Whereas national provisions ensuring that safety level should be harmonized in order to guarantee the free movement of active implantable medical devices without lowering existing and justified levels of safety in the Member States;
Whereas harmonized measures must be distinguished from measures taken by Member States to manage the financing of public health and sickness insurance schemes directly or indirectly concerning such devices; whereas, therefore, such provisions do not affect the right of Member States to implement the abvementioned measures in compliance with Community law;

Whereas maintaining or improving the level of protection achieved in Member States constitues one of this Directive's essential objectives as defined by the essential requirements;
Whereas rules governing active implantable medical devices can be confined to those provisions needed to safisfy the essential requirements, whereas, because they are essential, these requirements must replace corresponding national provisions;

Whereas, in order to facilitate proof of conformity with these essential requirements and to permit monitoring of that conformity, it is desiderable to have Europe-wide harmonized standards in respect of the prevention of risks in connection with the

design, manufacture and packaging of active implantable medical devices; whereas such standards harmonized at European level are drawn up by private-law bodies and must retain in their status as non-mandatory texts; whereas, to that end, the European Committee for Standardization (CEN) and the European Committee for Electrotechnical Standardization (Cenelec) are recognized as being the competent bodies to adopt harmonized standards in accordance with the general guidelines for cooperation between the Commission and these two bodies, signed on 13 November 1984; whereas, for the purposes of this Directive, a harmonized standard is a technical specification (European standard or harmonization document) adopted by either or both of these bodies, as instructed by the Commission pursuant to the provisions of Council Directive 83/189/EEC of 28 March 1983 laying down a procedure for the provision of information in the field of technical standards and regulations, as last amended by Directive 88/182/EEC, and under the abovementioned general guidelines;

Whereas evaluation procedures have to be established and accepted by common accord between the Member States in accordance with Community criteria;
Whereas the specific nature of the medical sector makes it advisable to make provision for the notified body and the manufacturer or his agent established in the Community to fix, by common accord, the time limits for completion of the evaluation and verification operations for the conformity of devices,

Has adopted this Directive:

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 1

1. This Directive shall apply active implantable medical devices.

2. For the purpose of this Direcitve, the following definitions shall apply:

a) 'medical device' means any instruments, apparatus appliance, materials or other article, whether used alone or in combination, together with any accessories or software for its proper functioning, intende by the manufacturer to be used for human beings in the:
- diagnosis, prevision, monitoring, treatment or alleviation of disease or injuri,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,
and which does not achieve its principal intended action by pharmacological, chemical, immunological or metabolic means, but which may be assisted in its function by such means;

b) 'active medical device' means any medical device relying for its functioning on a source of electrical energy or any source of power other than that directly generated by the human body or gravity;

c) 'active implantable medical decice' means any active medical device which is intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain after the procedure;

d) 'custom-made device' means any active implantable medical device specifically made in accordance with a medical specialist's written prescription which given, under this responsibility, specific design characteristics and is intended to be used only for an individual named patient;

e) 'device intended for clinical investigation' means any active implantable medical device intended for use by a specialist doctor when conducting investigations in an adequate human clinical environment;

f) 'intended purpose' means the use for which the medical device is intended and for which it is suited according to the data supplied by the manufacturer in the instructions;

g) 'putting into service' means making available to the medical profession for implantation.

3. Where an active implantable medical devices is intended to administer a substance defined as a medicinal product within the meaning of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, as last amended by Directive 87/21/EEC, that substance shall be subject to the system of marketing authorization provided for in that Directive.

4. Where an active implantable medical device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC, that device must be evaluated and authorized in accordance with the provisions of this Directive.

5. This Directive constitutes a specific Directive within the meaning of Article 2 (2) of Council Directive 89/336/EEC of 3 May 1989 on the approximation of the laws of the Member States relating to electromagnetic compatibility.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 2

Member States shall take all necessary steps to ensure that the devices referred to in Article 1 (2) (c) and (b) may be placed on the market and put into service only if they do not compromise the safety and health of patients, users and, where applicable, other persons when properly implanted, maintained and used in accordance with their intended purposes.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 3

The active implantable medical devices referred to in Article 1 (2) (c), (d) and (e), hereinafter to as 'devices' must satisfy the essential requirements set out in Annex 1, which shall apply to them account being taken of the intended purpose of the devices concerned.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 4

1. Member States shall not impede the placing on the market or the putting into service within their territory of devices bearing the CE mark.

2. Member States shall not create any obstacles to:
- devices intended for clinical investigation beings made available to specialist doctors for that purpose if they satisfy the conditions laid down in Article 10 and in Annex 6,
- custom-made devices being placed on the market and put into service if they satisfy the conditions laid down in Annex 6 and are accompanied by the statement referred to in that Annex.
These devices shall not bear the CE mark.

3. At trade fairs, exhibitions, demonstrations, etc., Member States shall not prevent the showing of devices which do not conform to this Directive, provided that a visible sign clearly indicates that such devices do not conform and cannot be put into service until they have been made to comply by the manufacturer or his authorized representative established within the Community.

4. When a device is put into service, Member States may require the information described in sections 13, 14 and 15 of Annex 1 to be in their national language(s).

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 5

Member States shall presume compliance with the essential requirements referred to in Article 3 in respect of devices which are in conformity with the relevant national standards adopted pursuant to the harmonized standards the references of which have been published in the Official Journal of the European Communities; Member States shall publish the references of such national standards.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 6

1. Where a Member State or the Commission considers that the harmonized standards referred to in Article 5 do not entirely meet the essential requirements referred to in Article 3, the Commission or the Member State concerned shall bring the matter before the Standing Committee set up under Directive 83/189/EEC, giving the reasons therefor. The Committee shall deliver an opinion without delay.

In the light of the opinion of the Committee, the Commission shall inform Member States of the measures to be taken with regard to the standards and the publications referred to in Article 5.

2. A Standing Committee, hereinafter referred to as the 'Committee', shall be set up, composed of the representatives of the Member States and chaired by the representative of the Commission. The Committee shall draw up its rules of procedure.
Any matter relating to the implementation and practical application of this Directive may be brought before the Committee, in accordance with the procedure set out below. The representative of the Commission shall submit to the Committee a draft of

the measures to be taken. The Committee shall deliver its opinion according to the urgency of the matter, if necessary by taking a vote.

The opinion shall be recorded in the minutes; in addition, each Member State shall have the right to ask to have its position recorded in the minutes. The Commission shall take utmost account of the opinion delivered by the Committee. It shall inform the Committee of the manner in which its opinion has been taken into account.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 7

1. Where a Member State finds that the devices referred to in Article 1 (2) (c) and (d), correctly put into service and used in accordance with their intended purpose, may compromise the health and/or safety of patients, users or, where applicable, other persons, it shall take all appropriate measures to withdraw such devices from the market or prohibit or restrict their being placed on the market or their being put into service.

The Member State shall immediately inform the Commission of any such measure, indicating the reasons for its decision and, in particular, whether non-compliance with this Directive is due to:
a) failure to meet the essential requirements referred to in Article 3, where the device does not meet in full or in part the standards referred to in Article 5;
b) incorrect applications of those standards;
c) shortcomings in the standards themselves.

2. The Commission shall enter into consultation with the parties concerned as soon as possible as soon as possible. Where, after such consultation, the Commission finds that:
- the measures are justified, it shall immediately so inform the Member State which took the initiative and the other Member States; where the decision referred to in paragraph 1 is attributed to shortcomings in the standards, the Commission shall, after consulting the parties concerned, bring the matter before the Committee referred to in Article 6 (1) within two months if the Member State which has taken the decision intends to maintain it and shall initiative and the manufacturer or his authorized representative established within the Community.

3. Where a device which does not comply bears the CE mark, the competent Member State shall take appropriate action against whomsoever has affixed the mark and shall inform the Commission and the other Member States thereof.

4. The Commission shall ensure that the Member States are kept informed of the progress and outcome of this procedure.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 8

1. Member State shall take the necessary steps to ensure that information brought to their knowledge regarding the incidents mentioned below involving a device is recorded a device is recorded and evaluated in a centralized manner:

a) any deterioration in the characteristics and performance of a device, as well as any inacuracies in the instruction leaflet which micht leas to or might have led to death of a patient of a patient or to a deterioration in his state of health;
b) any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

2. Member States shall, without prejudice to Article 7, forthwith inform the Commission and the other Member States of the incidents referred to in paragraph 1 and of the relevant meadures taken on contemplated.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 9

1. In the case of devices other than those which are custom-made or intended for clinical investigations, the manufacturer must, in order to affix the CE mark, at his own choise:
a) follow the procedure relating to the EC declaration of conformity set out in Annex 2; or
b) follow the procedure relating to EC type-examination set out in Annex 3, coupled with:
i) the procedure relating to EC verification set out in Annex 4, or
ii) the procedure relating to the EC declaration of conformity to type set out in Annex 5.

2. In the case of custom-made devices, the manufacturer must draw up the declaration provided for in Annex 6 before placing each device on the market.

3. Where appropriate, the procedure provided for in Annexes 3, 4 and 6 may be discharged by the manufacturer's authorized representative established in the Community.

4. The records and correspondence relating to the procedures referred to in paragraphs 1, 2 and 3 shall be in an official language of the Member State in which the said procedures will be carried out and/or in a language acceptable to the notified body defined in Article 11.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 10

1. In the case of devices intended for clinical investigations, the manufacturer or his authorized representative established in the Community shall, at least 60 days before the commencement of the investigations, submit the statement referred to in Annex 6 to the competent authorities of the Member State in which the investigations are to be conducted.

2. The manufacturer may commence the relevant clinical investigations at the end of a period of 60 days after notification, unless the competent authorities have notified him within that period of a decision to the contrary, based on considerations of public health or public order.

3. The Member States shall, if necessary, take the appropriate steps to ensure public health and order.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 11

1. Each Member State shall notify the order Member States and the Commission of the bodies which they have designated for carrying out the tasks pertaining to the procedures referred to in Articles 9 and 13, the specific tasks for which each body has been designated and the identifying logo of these bodies, hereinafter referred to as 'notified bodies'.
The Commission shall publish a list of these notified bodies, together with the tasks for which they have been notified, in the Official Journal of the European Communities and shall ensure that the list is kept up to date.

2. Member State shall apply the minimum criteria, set out in Annex 8, for the designation of bodies. Bodies that satisfy the criteria fixed by the relevant harmonized standards shall be presumed to satisfy the relevant minimum criteria.

3. A Member State that has notified a body shall withdraw that notification if it finds that the body no longer meets the criteria referred to in paragraph 2. It shall immediately inform the other Member States and the Commission thereof.

4. The notified body and the manufacturer or his agent established in the Community shall fix, by common accord, the time limits for completion of the evaluation and verification operations referred to in Annexes 2 to 5.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 12

1. Devices other than those which are custom made or intended for clinical investigations considered to meet the essential requirements referred to in Article 3 must bear the EC mark of conformity.

2. The EC mark of conformity, as shown in Annex 9, must appear in a visible, legible and indelible form on the sterile pack and, where appropriate, on the sales packaging, in any, and on the instructions leaflet. It must be accompanied by the logo of the notified body responsible for implementation of the procedures set out in Annexes 2, 4 and 5.

3. The affixing of marks likely to be confused with the EC mark of conformity shall be prohibited.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 13

Where it is established that the EC marks has been wrongly affixed, in particular, in respect of devices:
- that do not conform to the relevant standards referred to in Article 5, should the manufacturer have opted for conformity therewith,
- that do not conform to an approved type,
- that conform to an approved tupe which does not meet the relevant essential requirements,
- regarding which the manufacturer has failed to fulfil his obligations under the relevant EC declaration of conformity,

the notified body shall take appropriate measures and forthwith inform the competent Member State thereof.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 14

Any decision taken pursuant to this Directive and resulting in the refusal of or restrictions on the placing on the market and/or putting into service of a device shall state the exact grounds on which it is based. Such decision shall be notified without delay to the party concerned, who shall at the same time be informed of the remedies available to him under the laws in force in the Member State in question and of the time limits to which such remedies are subject.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 15

Member States shall ensure that all the parties involved in the application of this Directive are bound to observe confidentiality with regard to all informations obtained in carrying out their tasks. This does not affect the obligations of Member States and notified bodies with regard to mutual information and the dissemination of warnings.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 16

1. Before 1 July 1992, Member States shall adopt and publish the laws, regulations and administrative provisions necessary in order to comply with this Directive. They shall forthwith inform the Commission thereof. They shall apply such provisions from 1 January 1993.

2. Member States shall communicate to the Commission the texts of the provisions of national law which they adopt in the field covered by this Directive.

3. Member States shall, for the period up to 31 December 1994, permit the placing on the market and putting into service of devices complying with national rules in force in their territory on 31 December 1992.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ARTICLE 17

This Directive is addressed to the Member States.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 1

Essential Requirements

I. General Requirements

1. The devices must be designed and manufactured in such a way that, when implanted under the conditions and for the purposes laid down, their use does not compromise the clinical conditions or the safety of patients. They must not present any risk to the persons implanting them or, where applicable, to other persons.

2. The devices must achieve the performances intended by the manufacturer, viz. be designed and manufactured in such a way that they are suitable for one or more of the functions referred to in Article 1 (2) (a) as specified by him.

3. The characteristics and performances referred to in sections 1 and 2 must not be adversely affected to such a degree that the clinical condition and safety of the patients or, as appropriate, of other persons are compromised during the lifetime of the device anticipated by the manufacturer, where the device is subjected to stresses which may occur during normal conditions of use.

4. The devices must be designed, manufactured and packed in such a way that their characteristics and performances are not adversely affected in the storage and transport conditions laid down by the manufacturer (temperature, humidity, etc.).

5. Any side effects or undesirable conditions must constitute acceptable risks when weighed against the performance intended.

II. Requirements regarding design and construction

6. The solutions adopted by the manufacturer for the design and constructions of the devices must comply with safety principles taking account of the generally acknowledged state of the art.

7. Implantable devices must be designed, manufactured and packed in a non-reusable pack according to appropriate procedures to ensure they are sterile when placed on the market and, in the storage and transport conditions stipulated by the manufacturer, remain so until the packaging is removed and they are implanted.

8. Devices must be designed and manufactured in such a way as to remove or minimize as far as possible:
- the risk of physical injury in connection with their physical, including dimensional, features,
- risks connected with the use of energy sources with particular reference, where electricity is used, to insulation, leakage currents and overheating of the devices,
- risks connected with reasonably foreseeable environmental conditions such as magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure and acceleration,
- risks connected with medical treatment, in particular those resulting from the use of

defibrillators or high-frequency surgical equipment,
- risks connected with ionizing radiation from radioactive substances included in the device, in compliance with the protection requirements laid down in Directive 80/836/Euratom, as amended by Directives 84/467/Euratom and 84/466/Euratom,
- risks which may arise where maintenance and calibration are impossible, including:
- excessive increase of leakage currents,
- ageing of the materials used,
- excess heat generated by the device,
- decreased accurancy of any measuring or control mechanism.

9. The devices must be designed and manufactured in such a way as to guarantee the characteristics and performance referred to in I. 'General requirements', with particular attention being paid to:
- the choise of materials used, particularly as regards toxicity aspects,
- mutual compatibility between the materials used and biological tissues, cells and body fluids, account being taken of the anticipated use of the device,
- compatibility of the devices with the substances they are intended to administer,
- the quality of the connections, particularly in respect of safety,
- the reliability of the source of energy,
- if appropriate, that they are leakproof,
- proper functioning of the programming and control systems, including software.

10. Where a device incorporates, as an integral part, a substance which, when used separately, is likely to be considered to be a medicinal product as defined in Artilcle 1 of Directive 65/65/EEC, and whose action in combination with the device may result in its bioavailability, the safety, quality and usefulness of the substance, account being taken of the purpose of the device, must be verified by analogy with the appropriate methods specified in Directive 75/318/EEC, as last amended by Directive 89/341/EEC.

11. The devices and, if appropriate, their component parts must be identified to allow any necessary measure to be taken following the discovery of a potential risk in connection with the devices and their component parts.

12. Devices must bear a code by which they and their manufacturer can be unequivocably identified (particularly with regard to the type of device and year of manufacture); it must be possible to read this code, if necessary, without the need for a surgical operation.

13. When a device or its accessories bear instructions required for the operation of the device or indicate operating or adjustment parameters, by means of a visual system, such information must be understandable to the user and , as appropriate, the patient.

14. Every device must bear, legibly and indelibly, the following particulars, where appropriate in the form of generally recognized symbols:

14.1. On the sterile pack:
- the method of sterilization,
- an indication permitting this packaging to be recognized as such,
- the name and address of the manufacturer,

- a description of the device,
- if the device is intended for clinical investigations, the words: 'exclusively for clinical ivestigations',
- if the device is custom-made, the words 'custom-made device'
- a declaration that the implantable device is in a sterile conditions,
- the month and year of manufacture,
- an indication of the time limit for implanting a device safety.

14.2. On the sales packaging:
- the name and address of the manufacturer, - a description of the device,
- the purpose of the device,
- the relevant characteristics for its use,
- if the device is intended for clinical investigations, the words: 'exclusively for clinical investigations',
- if the device is custom-made, the words 'custom-made device',
- a declaration that the implantable device is in a sterile conditions,
- the month and year of manufacture,
- an indication of the time limit for implanting a device safety,
- the conditions for transporting and storing the device.

15. When placed on the market, each device must be accompanied by instructions for use giving the following particulars:
- the year of authorization to affix the CE mark,
- the details referred to in 14.1 and 14.2, with the exception of those referred to in the eight and ninth indents,
- the performances referred to in section 2 and undesirable side effects,
- information allowing the physician to select a suitable device and th corresponding software and accessories,
- information constituting the instructions for use allowing th physician and, where appropriate, the patient to use the device, its accessories and software correctly, as information on the nature, scope and times for operating cotrols and trials and, where appropriate, maintenance measures,
- information allowing, if appropriate, certain risks in connection with implantation of the device to be avoided,
- information regarding the risks of reciprocal interference in connection with the presence of the device during specific investigations or treatment,
- the necessary instructions in the event of the sterile pack being damaged and, where appropriate, details of appropriate methods of resterilization,
- an indication, if appropriate, that a device can be reused only if it is reconditioned under the responsibility of the manufacturer to comply with the essential requirements.

The instruction leaflet must also include details allowing the physician to brief the patient on the contra-indications and the precautions to be taken. These details should cover in particular:
- information allowing the lifetime of the energy source to be established,
- precautions to be taken should changes occur in the device's performance,
- precaution to be taken ad regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, administer.

16. Confirmation that the device satisfies the requirements in respect of characteristics and performance, as referred to in I. 'General requirements', in normal conditions of use, and the evaluation of the side effects or undesiderable effects must be based on clinical data established in accordance with Annex 7.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 2

EC declaration of conformity

(Complete quality assurance system)

1. The manufacturer shall apply the quality system approved for the design, manufacture and final inspection of the products concerned as specified in sections 3 and 4 and shall be subject to EC surveillance as specified in section 5.

2. The declaration of conformity is the procedure by means of which the manufacturer who satisfies the obligations of section 1 ensures and declares that the products concerned meet the provisions of this Directive which apply to them.

The manufacturer shall apply the CE mark in accordance with Article 12 and draw up a written declaration of conformity. This declaration shall cover one or more identified specimens of the product and shall be kept by the manufacturer. The CE mark shall be accompanied by the identifying logo of the notified body responsible.

3. **Quality system**

3.1. The manufacturer shall make an application for evaluation of his quality to a notified body.

The application shall include:
- all the appropriate items of information for the category of products manufacture of which is envisaged,
- the quality-system documentation,
- an undertaking to fulfil the obligations arising from the quality system as approved,
- an undertaking to maintain the approved quality system in such a way that it remains adequate and efficacious,
- an undertaking by the manufacturer to institute and keep up-dated a post-marketing surveillance system. The undertaking shall include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:

i) any deterioration in the characteristics or performances, and any inaccuracies in the instruction leaflet for a device which might lead to or have led to the death of patient or a deterioration in his state of health;
ii) any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

3.2. The application of the quality system must ensure that the products conform to the provisions of this Directive which apply to them at every stage, from design to final controls.

All the elements, requirements and provisions adopted by the manufacturer for his quality system shall be documented in a systematic and orderly manner i the form of written policies and procedures. This quality-system documentation must make possible a uniform interpretation of the quality policies and procedures such as quality programmes, quality plans, quality manuals and quality records.

It shall include in particular an adequate description of:
a) the manufacturer's quality objectives;
b) the organization of the business and in particular:
- the organizational structures, the responsibilities of the managerial staff and their organizational authority where quality of design and manufacture of the products is concerned,
- the methods of monitoring the efficient operation of the quality system and in particular its ability to achieve the desired quality of the design and of the products, including control of products which do not conform; c) the procedures for monitoring and verifying the design of the products and in particular:
- the design specifications, including the standards which will be applied and description of the solutions adopted to fulfil the essential requirements which apply to the products when the standards referred to in Article 5 are not applied in full.
- the techniques of control and verification of the design, the processes and systematic actions which will be used when the products are being designed;

d) the techniques of control and of quality assurance ar the manufacturing stage and in particular:
- the processes and procedures which will be used, particularly as regards sterilization, purchasing and the relevant documents,
- product-identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture;
e) the appropriate tests and trials which will be effected before, during and after production, the frequency with which they will take place, and the test equipment used.

3.3. Without prejudice to Article 13 of this Directive, the notified body shall effect an audit of the quality system to determine whether it meets the requirements referred to in 3.2. It shall presume conformity with these requirements for the quality systems which use the corresponding harmonized standards.

The team entrusted with the evaluation shall include ar least one member who has already had experience of evaluations of the technology concerned. The evaluation procedure shall include an inspection on the manufacturer's premises. The decision shall be notified to the manufacturer after the final inspection. It shall contain the conclusions of the control and a reasoned evaluation.

3.4. The manufacturer shall inform the notified body which has approved the quality system of any plan to alter the quality system. The notified body shall evaluate the proposed modifications and shall verify whether the quality system so modified would meet the requirements referred to in 3.2; it shall notify the manufacturer of its decision. This decision shall contain the conclusion of the control and a reasoned evaluation.

4. **Examination of the design of the product**

4.1. In addition to the obligations incumbent on him under section 3, the manufacturer shall make an application for examination of the design dossier relating to the product which he plants to manufacture and which falls into the category referred to in 3.1.

4.2. The application shall describe, manufacture, and performances of the product in question and shall include the necessary particulars which make it possible to evaluate whether it complies with the requirements of this Directive.

It shall include inter alia:
- the design specifications, including the standards which have been applied,
- the necessary proof of their appropriations, in particular where the standards referred to in Article 5 have not been applied in full. This proof must include the results of the appropriate tests carried out by the manufacturer or carried out under his responsibility,
- a statement as to whether or not the device incorporates, as an integral part, a substance as referred to in section 10 of Annex 1, whose action in combination with the device may result in its biovailability, together with data on the relevant trials conducted,
- the clinical data referred to in Annex 7,
- the draft instruction leaflet.

4.3. The notified body shall examine the application and, where the product complies with the relevant provisions of this Directive, shall issue the applicant with an EC design examination certificate. The notified body may require the application to be supplemented by futher tests or proof so that compliance with the requirements of the Directive may be evaluated. The certificate shall contain the conclusion of the examination, the conditions of its validity, the data needed for identifications of the approved design and, where appropriate, a description of the intended use of the product.

4.4. The applicant shall inform the notified body which issued the EC design must obtain supplementary approval from the notified body which issued the EC design examination certificate where such modifications may affect conformity with the essential requirements of this Directive or the conditions prescribed for the use of the product. This supplementary approval shall be given in the form of an addendum to the EC design examination certificate.

5. **Surveillance**

5.1. The aim of surveillance is to ensure that the manufacturer duly-fulfils the obligations arising from the approved quality system.

5.2. The manufacturer shall authorize the notified body to carry out all necessary inspection and shall supply it with all appropriate information, in particular:
- the quality-system documentation,
- the data stipulated in the part of the quality system relating to design, such as the results of analyses, calculations, tests, etc.,
- the data stipulated in the part of the quality system relating to manufacture, such as reports concerning inspections, tests, standardizations/calibrations and the qualifications of the staff concerned, etc.

5.3. The notified body shall periodically out appropriate inspections and evaluations in order to accertain that the manufacturer is applyring the approved quality system, and shall supply the manufacturer with an evaluation report.

5.4. In addition, the notified body may make unannounced visit to the manufacturer, and shall supply him with an inspection report.

6. The notified body shall communicate to the other notified bodies all relevant information concerning approvals of quality systems, refused and withdrawn.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 3

EC type-examination

1. EC type-examination is the procedure whereby a notified body observes and certifies that a representative sample of the production envisaged satisfies the relevant provisions of this Directive.

2. The application for EC type-examination shall be made by the manufacturer, or by his authorized representative established in the Community, to a notified body.

The application shall include:
- the name and address of the manufacturer and the name and address of the authorized representative if the application in made by the latter,
- a written declaration specifying that an application has not been made to any other notified body,
- the documentation described in section 3 needed to allow an evaluation to be made of the conformity of a representative sample of the production in question, hereinafter referred to as 'type', with the requirements of this Directive.

The applicant shall make a 'type' available to the notified body. The notified body may request other samples as necessary.

3. The documentation must make it possible to understand the design, the manufacture and the performances of the product. The documentation shall contain the following items in particular:
- a general description of the type,
- design drawings, methods of manufacture envisaged, in particular as regards sterilization, and diagrams of parts, sub-assemblies, circuit, etc.,
- the descriptions and explanations necessary for the understanding of the abovementioned drawings and diagrams and of the operation of the product,
- a list of the standards referred to in Article 5, applied in full or in part, and a description of the solutions adopted to satisfy the essential requirements where the standards referred to in Article 5 have not been applied,
- the results of design calculations, investigations and technical tests carried out, etc.,
- a statement as to whether or not the device incorporates, as an integral part, a substance as referred to in section 10 of Annex 1, whose action in combination with the device may result in its bioavailability, together with data on the relevant trials conducted,
- the clinical data referred to in Annex 7,
- the draft instruction leaflet.

4. The notified body shall:

4.1. examine and evaluate the documentation, verify that the type has been manufactured in accordance with that documentation; it shall also record the items which have been designed in accordance with the applicable provisions of the standards referred to in Article 5, as well as the items for which the design is not based on the relevant provisions of the said standards;

4.2. carry our have carried out the appropriate inspection and the tests necessary to verify whether the solutions adopted by the manufacturer satisfy the essential requirements of this Directive where the standards referred to in Article 5 have not been applied;

4.3. carry out or have carried out the appropriate inspections and the tests necessary to verify whether, where the manufacturer has chosen to apply the relevant standards, these have actually been applied;

4.4. agree with the applicant on the place where the necessary inspections and tests will be carried out.

5. Where the type meets the provisions of this Directive, the notified body shall issue an EC type-examination certificate to the applicant. The certificate shall contain the name and address of the manufacturer, the conclusions of the control, the conditions under which the certificate is valid and the information necessary for identification of the type approved. The significant parts of the documentation shall be attached to the certificate and a copy shall be kept by the notified body.

6. The applicant shall inform the notified body which issued the EC type-examination certificate of any modification made to the approval product. Modifications to the approved product must receive further approval from the notified body which issued the EC type-examination certificate where such modifications may affect conformity with the essential requirements or with the conditions of use specified for the product. This new approval shall be issued, where appropriate, in the form of a supplement to the initial EC type-examination certificate.

7. Each notified body shall communicate to the other notified bodies all relevant information on EC-type examination certificates and supplements issued, refused or withdrawn.

8. Other notified bodies obtain a copy of the EC type-examination certificates and/or the supplements to them. The annexes to the certificates shall be made available to the other notified bodies when a reasoned applications is made and after first informing the manufacturer.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 4

EC verification

1. EC verification is the act by which a notified body verifies and certifies that products conform to the type described in the EC type-examination certificate and satisfy the relevant requirements of this Directive.

2. The manufacturer shall, before the start of manufacture, prepare documents defining the manufacturing process, in particular as regards sterilization, together with all the routine, pre-established provisions to be implemented to ensure homogeneity of production and conformity of the products with the type described in the EC type-examination certificate as well as with the relevant requirements of the Directive.

3. The manufacturer shall undertake to institute and keep up-dated a post-marketing surveillamce system. The undertaking shall include an obligation for the menufacturer to notify the component authorities of the following event's immediately on learning of them:
i) any deterioration in the characteristics or performances, and any inaccuracies in the instruction leaflet for a device which might lead to or have led to the death of a patient or a deterioration in his state of health;
ii) any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

4. The notified body shall carry out EC verification by the controls and tests on the products on a statistical basis as specified in 5. The manufacturer must authorize the notified body to evaluate the efficiency of the measures taken pursuant to section 2, by audit where appropriate.

5. **Statistical verification**

5.1. The manufacturer shall present the manufactured products in the form of homogeneous batches.

5.2. A random sample shall be taken from each batch. The products which make up the sample shall be examined individually and appropriate tests, defined in the relevant standard(s) referred to in Article 5, or equivalent tests, shall be carried out to verify the conformity of the products with the type described in the EC type-examination certificate, in order to determine whether the batch is to be accepted or reject.

5.3. Statistical control of products will be based on attributes, entailing a sampling system with the following characteristics:
- a level of quality corresponding to a probibility of acceptance of 95%, with a non-conformity percentage of between 0,29 and 1%,
- a limit quality corresponding to a probability of acceptance of 5%, with a non-conformity percentage of between 3 and 7%.

5.4. If a batch is accepted, the notified body shall draw up a written certificate of conformity. All the products in the batch may be placed on the market, with the

exception of those products in the sample which were found not to conform. If a batch is reject, the notified body which is responsible shall take the appropriate measures to prevent the batch from being placed on the market. If justified on practical grounds, the manufacturer may affix the CE mark during manufacture, under the responsability to the notified body, in accordance with Article 12, accompanied by the identifying logo of the notified body responsible for statistical verification.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 5

EC declaration of conformity to type

(Assurance of production quality)

1. The manufacturer shall apply the quality system approved for the manufacture and shall conduct the final inspection of the products concerned as specified in 3; he shall be subject to the surveillance referred to in section 4.

2. This declaration of conformity is the procedural element whereby the manufacturer who satisfies the obligations of section 1 guarantees and declares that the products concerned conform to the type described in the EC type-examination certificate and meet the provisions of the Directive which apply to them. The manufacturer shall affix the CE mark in accordance with Article 12 and draw up a written declaration of conformity. This declaration shall cover one or more identified specimens of the product and shall be kept by the manufacturer. The CE mark shall be accompanied by the identifying logo of the notified body responsible.

3. **Quality system**

3.1. The manufacturer shall make an application for evaluation of his quality system to a notified body.

The application shall include:
- all appropriate information concerning the products which it is intended to manufacture,
- the quality-system documentation,
- an undertaking to fulfil the obligations arising from the quality system as approved,
- an undertaking to maintain the approved quality system in such a way that it remains adequate and efficacious,
- where appropriate, the technical documentation relating to the approved type and a copy of the EC type-examination certificate,
- an undertaking by the manufacturer to institute and keep up-dated a post-marketing surveillance system. The undertaking shall include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:

i) any deterioration in the characteristics or performance, and any inaccuracies in the instructions leaflet for a device which might lead to or have led to the death of patient or a deterioration in his state of health;
ii) any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

3.2. Application of the quality system must ensure that the products conform to the type described in the EC type-examination certificate.

All the elements, requirements and provisions adopted by the manufacturer for his quality system shall be documented in a systematic and orderly manner in the form of written policies and procedure. This quality-system documentation must make

possible a uniform interpretation of the quality policies and procedures such as quality programmes, quality plans, quality manuals and quality records..

It shall include in particular an adequate description of:

a) the manufacturer's quality objectives;
b) the organization of the business and in particular:
- the organizational structures, the responsibilities of the managerial staff and their organizational authority where manufacture of the products is concerned,
- the methods of monitoring the efficient operation of the quality system and in particular its ability to achieve the desired quality of the design and of the products, including control of products which do not conformity;
c) the techniques of control and of quality assurance at the manufacturing stage and in particular:
- the processes and procedures which will be used, particularly as regards sterilization, purchasing and the relevant documents,
- products identification procedures drawn up and kept up-to-date from drawings, specifications or other relevant documents at every stage of manufacture;
d) the appropriate tests and trials which will be effected before, during and after production, the frequency with which they will take place, and the test equipment used.

3.3. Without prejudice to Article 13, the notified body shall effect an audit of the quality system to determine whether it meets the requirements referred to in 3.2. It shall presume conformity with these requirements for the quality systems which use the corresponding harmonized standards. The team entrusted with the evaluation shall include at least one member who has already had experience of evaluations of the technology concerned. The evaluation procedure shall include an ispection on the manufacturer's premises. The decision shall be notified to the manufacturer after the final inspection. It shall contain the conclusions of the control and reasoned evaluation.

3.4. The manufacturer shall inform the notified body which has approved the quality system of any plan to alter that system. The notified body shall evaluate the proposed modifications and shall very whether the quality system so modified would meet the requirements referred to in 3.2; it shall notify the manufacturer of its decision. This decision shall contain the conclusions of the cotrol and reasoned evaluation.

4. **Surveillance**

4.1. The aim of surveillance is to ensure that the manufacturer duly fulfils the obligations which arise from the approved quality system.

4.2. The manufacturer shall authorize the notified body to carry out all necessary inspections and shall supply it with all appropriate information, in particular:
- the quality-system documentation,
- the data stipulated in the part of the quality system relating to manufacture, such ad reports concerning inspections, tests, standardizations/calibrations and the qualifications of the staff concerned, etc.

4.3. The notified body shall periodically carry out appropriate inspections and evaluations in order to ascertain that the manufacturer is applying the approved quality system, and shall supply the manufacturer with an evaluation report.

4.4. In addition, the notified body may make unannounced visits to the manufacturer, and shall supply him with an ispection report.

5. The notified body shall communicate to the other notified bodies all relevant information concerning approvals of quality systems issued, refused or withdrawn.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 6

Statement concerning devices intended for special purposes

1. The manufacturer or his authorized representative established within the Community shall draw up for custom-made devices or for devices intended for clinical investigations the statement comprising the elements stipulated in section 2.

2. The statment shall comprise the following information:

2.1. For custom-made devices:
- data allowing the device in question to be identified,
- a statement affirming that device is intended for exclusive use by a particular patient, together with his name,
- the name of the doctor who drew up the prescription and, if applicable, the name of the clinic concerned,
- the particular features of the device as described by the medical prescription concerned,
- a statment affirming that the device complies with the essential requirements given in Annex 1 and where applicable, indicating which essential requirements have not been wholly met, together with the grounds.

2.2. For devices intended for clinical investigations covered in Annex 7:
- data allowing the devices in question to be identified,
- an investigation plan giving in particular the purpose, scope and number of the devices concerned,
- the name of the doctor and of the institution responsible for the investigations,
- the place, date of commencement and duration scheduled for the investigations,
- a statment affirming that the device in question complies with the essential requirements apart from the aspects constituting the object of the investigations and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the patient.

3. The manufacturer shall undertake to keep available for the competent national authorities:

3.1. For devices intended for clinical investigations, the documentation shall also contain:
- a general description of the product,
- design drawings, manufacturing methods, in particular as regards sterilization, and diagrams of parts, sub-assemblies, circuits, etc.,
- the descriptions and explanations necessary for the understanding of the said drawings and diagrams and of the operation of the product,
- a list of the standards laid down in Article 5, applied in full or in part, and a description of the solutions adopted to satisfy the essential requirements of the Directive where the standards in Article 5 have not been applied,
- the results of the design calculations, checks and technical tests carried out, etc.,

The manufacturer shall take all necessary measures to see that the manufacturing ensures that the products manufactured conform to the documentation referred to in

3.1 and in the first paragraph of this section. The manufacturer may authorize the evaluation, by audit where necessary, of the effectiveness of these.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 7

Clinical evaluation

1. General provisions

1.1. Adequacy of the clinical data presented, as referred to in section 4.2 of Annex 2, and in section 3 of Annex 3, shall be based, account being taken as appropriate of the relevant harmonized standards, on either:

1.1.1. a collation of currently available relevant scientific literature covering the intended use of the device and the techniques thereof, as well as, if appropriate, a written report making a critical assessment of this collaction; or
1.1.2. the results of all clinical investigations made, including those carried out in accordance with section 2.
1.2. All data must remain confidential unless it is deemed essential that they be divulged.

2. Clinical investigation

2.1. *Purpose*

The purpose of clinical investigation is to:
- verify that, under normal conditions of use, the performance of the device comply with those indicated in section 2 of Annex 1,
- determine any undesirable side effects, under normal conditions of use, and assess whether they are acceptable risks having regard to the intended performance of the device.

2.2. *Ethical consideration*

Clinical investigations shall be made in accordance with the Declaration of Helsinki approved by the 18th World Medical Assembly in Helsinki, Finland, in 1964, and amended by the 29th World Medical Assembly in Tokyo, Japan, in 1975 and the 35th World Medical Assembly in Venice, Italy, in 1983. It is mandatory that all measures relating to the protection of human subjects are carried out in the spirit of the Declaration of Helsenki. This includes every step in the clinical investigation from first consideration of need and justification of the study to publication of results.

2.3. *Methods*

2.3.1. Clinical investigations shall be performed according to an appropriate state of the art plan of investigation defined in such a way as to confirm or refute the manufacture's claims for the device; the investigations shall include an adequate number of observations to guarantee the scientific validity of the conclusions.

2.3.2. The procedures utilized to perform the investigations shall be appropriate to the device under examination.

2.3.3. Clinical investigations shall be performed in circumstances equivalent to those which would be found in normal conditions of use of the device.

2.3.4. All appropriate features, including those involving the safety and performances of the device, and its effects on the patients, shall be examined.

2.3.5. All adverse events shall be fully recorded.

2.3.6. The investigations shall be performed under the responsibility of an appropriately qualified medical specialist, in an appropriate environment. The medical specialist shall have access to the technical data regarding the device.

2.3.7. The written report, signed by the responsible medical specialist, shall comprise a critical evaluation of all the data collected during the clinical investigation.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 8

Minimum criteria to be met when designating inspection bodies to be notified

1. The body, its director and staff responsible for carrying out evaluation and verification operations shall not be the designer, manufacturer, supplier or installer of devices which they control, nor the authorized representative of any of those parties. They may not become directly involved in the design, construction, marketing or maintenance of the devices, nor represent the parties engaged in these activities. This does not preclude the possibility of exchanges of technical information between the manufacturer and the body.

2. The body and its staff must carry out the evaluation and verification operation with the highest degree of professional integrity and technical competence and must be free from all pressures and inducements, particularly financial, which might influence their judgement or the results of the inspection, especially from persons or groups of persons with an interest in the results of verifications.

3. The body must be able to carry out all the tasks in one of Annex 2 to 5 assigned to such a body and for which it has been notified, whether those tasks are carried out by the body itself or under its responsibility. In particular, it must have at its disposal the necessary staff and possess the necessary facilities to enable it to perform properly the technical and administrative tasks connected with evaluation and verification; it must also have access to the equipment necessary for the verifications required.

4. The staff responsible for control operations must have:
- sound vocational training covering all the evaluation and verification operations for which the body has been designated,
- satisfactory knowledge of the requirements of the controls they carry out and adequate experience of such operations,
- the ability required to draw up the certificates, records and reports to demonstrate that the controls have been carried out.

5. The impartiality of inspection staff must be guaranteed. Their remuneration must not depend on the number of controls carried out, nor on the results of such controls.

6. The body must take out liability insurance unless liability is assumed by the State in accordance with national law, or the Member State itself is directly responsible for controls.

7. The staff of the body are bound to observe professional secrecy with regard to all information gained in carrying out their tasks (except vis-à-vis the competent administrative authorities of the State in which their activities are carried out) under this Directive or any provision of national law giving effect to it.

ACTIVE IMPLANTABLES DIRECTIVE (90/385/EEC) - ANNEX 9

CE mark of conformity

APPENDIX B

COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices

COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices

THE COUNCIL OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 100a thereof,

Having regard to the proposal from the Commission (1),

In cooperation with the European Parliament (2),

Having regard to the opinion of the Economic and Social Committee (3),

Whereas measures should be adopted in the context of the internal market; whereas the internal market is an area without internal frontiers in which the free movement of goods, persons, services and capital is ensured;

Whereas the content and scope of the laws, regulations and administrative provisions in force in the Member States with regard to the safety, health protection and performance characteristics of medical devices are different; whereas the certification and inspection procedures for such devices differ from one Member State to another; whereas such disparities constitute barriers to trade within the Community;

Whereas the national provisions for the safety and health protection of patients, users and, where appropriate, other persons, with regard to the use of medical devices should be harmonized in order to guarantee the free movement of such devices within the internal market;

Whereas the harmonized provisions must be distinguished from the measures adopted by the Member States to manage the funding of public health and sickness insurance schemes relating directly or indirectly to such devices; whereas, therefore, the provisions do not affect the ability of the Member States to implement the abovementioned measures provided Community law is complied with;

Whereas medical devices should provide patients, users and third parties with a high level of protection and attain the performance levels attributed to them by the manufacturer; whereas, therefore, the maintenance or improvement of the level of protection attained in the Member States is one of the essential objectives of this Directive;

Whereas certain medical devices are intended to administer medicinal products within the meaning of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (4); whereas, in such cases, the placing on the market of the medical device as a general rule is governed by the present Directive and the placing on the market of the medicinal product is governed by Directive 65/65/EEC; whereas if, however, such a device is placed on the market in such a way that the device and the medicinal product form a single integral unit which is intended exclusively for use in the given combination and which is not reusable, that single-unit product shall be governed by Directive 65/65/EEC; whereas a distinction must be drawn between the abovementioned devices and medical devices incorporating, inter alia, substances which, if used separately, may be considered to be a medicinal substance within the meaning of Directive 65/65/EEC; whereas in such cases, if the substances incorporated in the medical devices are liable to act upon the body with action ancillary to that of the device, the placing of the devices on the market is governed by this Directive; whereas, in this context, the safety, quality and usefulness of the substances must be verified by analogy with the appropriate methods specified in Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products (5);

Whereas the essential requirements and other requirements set out in the Annexes to this Directive, including any reference to 'minimizing' or 'reducing' risk must be interpreted and applied in such a way as to take account of technology and practice existing at the time of design and of technical and economical considerations compatible with a high level of protection of health and safety;
Whereas, in accordance with the principles set out in the Council resolution of 7 May 1985 concerning a new approach to technical harmonization and standardization (6), rules regarding the design and manufacture of medical devices must be confined to the provisions required to meet the essential requirements; whereas, because they are essential, such requirements should replace the corresponding national provisions; whereas the essential requirements should be applied with discretion to take account of the technological level existing at the time of design and of technical and economic considerations compatible with a high level of protection of health and safety;
Whereas Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices (7) is the first case of application of the new approach to the field of medical devices; whereas in the interest of uniform Community rules applicable to all medical devices, this Directive is based largely on the provisions of Directive 90/385/EEC; whereas for the same reasons Directive 90/385/EEC must be amended to insert the general provisions laid down in this Directive;
Whereas the electromagnetic compatibility aspects form an integral part of the safety of medical devices; whereas this Directive should contain specific rules on this subject with regard to Council Directive 89/336/EEC of 3 May 1989 on the approximation of the laws of the Member States relating to electromagnetic compatibility (8);
Whereas this Directive should include requirements regarding the design and manufacture of devices emitting ionizing radiation; whereas this Directive does not affect the authorization required by Council Directive 80/836/Euratom of 15 July 1980 amending the Directives laying down the basic safety standards for the health protection of the general public and workers against the dangers of ionizing radiation (9), nor application of Council Directive 84/466/Euratom of 3 September 1984 laying down basic measures for the radiation protection of persons undergoing medical examination or treatment (10); whereas Council Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work (11) and the specific directives on the same subject should continue to apply;
Whereas, in order to demonstrate conformity with the essential requirements and to enable conformity to be verified, it is desirable to have harmonized European standards to protect against the risks associated with the design, manufacture and packaging of medical devices; whereas such harmonized European standards are drawn up by private-law bodies and should retain their status as non-mandatory texts; whereas, to this end, the European Committee for Standardization (CEN) and the European Committee for Electrotechnical Standardization (Cenelec) are recognized as the competent bodies for the adoption of harmonized standards in accordance with the general guidelines on cooperation between the Commission and these two bodies signed on 13 November 1984;
Whereas, for the purpose of this Directive, a harmonized standard is a technical specification (European standard or harmonization document) adopted, on a mandate from the Commission, by either or both of these bodies in accordance with Council Directive 83/189/EEC of 28 March 1983 laying down a procedure for the provision of

information in the field of technical standards and regulations (12), and pursuant to the abovementioned general guidelines; whereas with regard to possible amendment of the harmonized standards, the Commission should be assisted by the Committee set up pursuant to Directive 83/189/EEC; whereas the measures to be taken must be defined in line with procedure I, as laid down in Council Decision 87/373/EEC (13); whereas, for specific fields, what already exists in the form of European Pharmacopoeia monographs should be incorporated within the framework of this Directive; whereas, therefore, several European Pharmacopoeia monographs may be considered equal to the abovementioned harmonized standards;

Whereas, in Decision 90/683/EEC of 13 December 1990 concerning the modules for the various phases of the conformity assessment procedures which are intended to be used in the technical harmonization directives (14), the Council has laid down harmonized conformity assessment procedures; whereas the application of these modules to medical devices enables the responsibility of manufacturers and notified bodies to be determined during conformity assessment procedures on the basis of the type of devices concerned; whereas the details added to these modules are justified by the nature of the verification required for medical devices;

Whereas it is necessary, essentially for the purpose of the conformity assessment procedures, to group the devices into four product classes; whereas the classification rules are based on the vulnerability of the human body taking account of the potential risks associated with the technical design and manufacture of the devices; whereas the conformity assessment procedures for Class I devices can be carried out, as a general rule, under the sole responsibility of the manufacturers in view of the low level of vulnerability associated with these products; whereas, for Class IIa devices, the intervention of a notified body should be compulsory at the production stage; whereas, for devices falling within Classes IIb and III which constitute a high risk potential, inspection by a notified body is required with regard to the design and manufacture of the devices; whereas Class III is set aside for the most critical devices for which explicit prior authorization with regard to conformity is required for them to be placed on the market;

Whereas in cases where the conformity of the devices can be assessed under the responsibility of the manufacturer the competent authorities must be able, particularly in emergencies, to contact a person responsible for placing the device on the market and established in the Community, whether the manufacturer or another person established in the Community and designated by the manufacturer for the purpose;

Whereas medical devices should, as a general rule, bear the CE mark to indicate their conformity with the provisions of this Directive to enable them to move freely within the Community and to be put into service in accordance with their intended purpose;

Whereas, in the fight against AIDS and in the light of the conclusions of the Council adopted on 16 May 1989 regarding future activities on AIDS prevention and control at Community level (15), medical devices used for protection against the HIV virus must afford a high level of protection; whereas the design and manufacture of such products should be verified by a notified body;

Whereas the classification rules generally enable medical devices to be appropriately classified; whereas, in view of the diverse nature of the devices and technological progress in this field, steps must be taken to include amongst the implementing powers conferred on the Commission the decisions to be taken with regard to the proper classification or reclassification of the devices or, where appropriate, the adjustment of the classification rules themselves; whereas since these issues are

closely connected with the protection of health, it is appropriate that these decisions should come under procedure IIIa, as provided for in Directive 87/373/EEC;
Whereas the confirmation of complicance with the essential requirements may mean that clinical investigations have to be carried out under the responsibility of the manufacturer; whereas, for the purpose of carrying out the clinical investigations, appropriate means have to be specified for the protection of public health and public order;
Whereas the protection of health and the associated controls may be made more effective by means of medical device vigilance systems which are integrated at Community level;
Whereas this Directive covers the medical devices referred to in Council Directive 76/764/EEC of 27 July 1976 on the approximation of the laws of the Member States on clinical mercury-in-glass, maximum reading thermometers (16); whereas the abovementioned Directive must therefore be repealed; whereas for the same reasons Council Directive 84/539/EEC on 17 September 1984 on the approximation of the laws of the Member States relating to electro-medical equipment used in human or veterinary medicine (17) must be amended,
HAS ADOPTED THIS DIRECTIVE:
Article 1
Definitions, scope
1. This Directive shall apply to medical devices and their accessories. For the purposes of this Directive, accessories shall be treated as medical devices in their own right. Both medical devices and accessories shall hereinafter be termed devices.
2. For the purposes of this Directive, the following definitions shall apply:
(a) 'medical device' means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings 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,
and which does 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;
(b) 'accessory' means an article which whilst not being a device is intended specifically by its manufacturer to be used together with a device to enable it to be used in accordance with the use of the device intended by the manufacturer of the device;
(c) 'device used for in vitro diagnosis' means any device which is a reagent, reagent product, kit, instrument, equipment or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of samples derived from the human body with a view to providing information on the physiological state, state of health or disease, or congenital abnormality thereof;
(d) 'custom-made device' means any device specifically made in accordance with a duly qualified medical practitioner's written prescription which gives, under his responsibility, specific design characteristics and is intended for the sole use of a particular patient.

The abovementioned prescription may also be made out by any other person authorized by virtue of his professional qualifications to do so.
Mass-produced devices which need to be adapted to meet the specific requirements of the medical practitioner or any other professional user are not considered to be custom-made devices;
(e) 'device intended for clinical investigation' means any device intended for use by a duly qualified medical practitioner when conducting investigations as referred to in Section 2.1 of Annex X in an adequate human clinical environment.
For the purpose of conducting clinical investigation, any other person who, by virtue of his professional qualifications, is authorized to carry out such investigation shall be accepted as equivalent to a duly qualified medical practitioner;
(f) 'manufacturer' means the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party.
The obligations of this Directive to be met by manufacturers also apply to the natural or legal person who assembles, packages, processes, fully refurbishes and/or labels one or more ready-made products and/or assigns to them their intended purpose as a device with a view to their being placed on the market under his own name. This subparagraph does not apply to the person who, while not a manufacturer within the meaning of the first subparagraph, assembles or adapts devices already on the market to their intended purpose for an individual patient;
(g) '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;
(h) 'placing on the market' means the first making available in return for payment or free of charge of a device other than a device intended for clinical investigation, with a view to distribution and/or use on the Community market, regardless of whether it is new or fully refurbished;
(i) 'putting into service' means the stage at which a device is ready for use on the Community market for the first time for its intended purpose.
3. Where a device is intended to administer a medicinal product within the meaning of Article 1 of Directive 65/65/EEC, that device shall be governed by the present Directive, without prejudice to the provisions of Directive 65/65/EEC with regard to the medicinal product.
If, however, such a device is placed on the market in such a way that the device and the medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single product shall be governed by Directive 65/65/EEC. The relevant essential requirements of Annex I to the present Directive shall apply as far as safety and performance related device features are concerned.
4. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, that device must be assessed and authorized in accordance with this Directive.
5. This Directive does not apply to:
(a) in vitro diagnostic devices;
(b) active implantable devices covered by Directive 90/385/EEC;
(c) medicinal products covered by Directive 65/65/EEC;

(d) cosmetic products covered by Directive 76/768/EEC (18);
(e) human blood, human blood products, human plasma or blood cells of human origin or to devices which incorporate at the time of placing on the market such blood products, plasma or cells;
(f) transplants or tissues or cells of human origin nor to products incorporating or derived from tissues or cells of human origin;
(g) transplants or tissues or cells of animal origin, unless a device is manufactured utilizing animal tissue which is rendered non-viable or non-viable products derived from animal tissue.
6. This Directive does not apply to personal protective equipment covered by Directive 89/686/EEC. In deciding whether a product falls under that Directive or the present Directive, particular account shall be taken of the principal intended purpose of the product.
7. This Directive is a specific Directive within the meaning of Article 2 (2) of Directive 89/336/EEC.
8. This Directive does not affect the application of Directive 80/836/Euratom, nor of Directive 84/466/Euratom.

Article 2

Placing on the market and putting into service

Member States shall take all necessary steps to ensure that devices may be placed on the market and put into service only if they do not compromise the safety and health of patients, users and, where applicable, other persons when properly installed, maintained and used in accordance with their intended purpose.

Article 3

Essential requirements

The devices must meet the essential requirements set out in Annex I which apply to them, taking account of the intended purpose of the devices concerned.

Article 4

Free movement, devices intended for special purposes

1. Member States shall not create any obstacle to the placing on the market or the putting into service within their territory of devices bearing the CE marking provided for in Article 17 which indicate that they have been the subject of an assessment of their conformity in accordance with the provisions of Article 11.
2. Member States shall not create any obstacle to:
- devices intended for clinical investigation being made available to medical practitioners or authorized persons for that purpose if they meet the conditions laid down in Article 15 and in Annex VIII,
- custom-made devices being placed on the market and put into service if they meet the conditions laid down in Article 11 in combination with Annex VIII; Class IIa, IIb and III devices shall be accompanied by the statement referred to in Annex VIII.

These devices shall not bear the CE marking.
3. At trade fairs, exhibitions, demonstrations, etc. Member States shall not create any obstacle to the showing of devices which do not conform to this Directive, provided that a visible sign clearly indicates that such devices cannot be marketed or put into service until they have been made to comply.
4. Member States may require the information, which must be made available to the user and the patient in accordance with Annex I, point 13, to be in their national language(s) or in another Community language, when a device reaches the final user, regardless of whether it is for professional or other use.

5. Where the devices are subject to other Directives concerning other aspects and which also provide for the affixing of the CE marking, the latter shall indicate that the devices also fulfil the provisions of the other Directives.
However, should one or more of these directives allow the manufacturer, during a transitional period, to choose which arrangements to apply, the CE marking shall indicate that the devices fulfil the provisions only of those directives applied by the manufacturer. In this case, the particulars of these directives, as published in the Official Journal of the European Communities, must be given in the documents, notices or instructions required by the directives and accompanying such devices.

Article 5

Reference to standards

1. Member States shall presume compliance with the essential requirements referred to in Article 3 in respect of devices which are in conformity with the relevant national standards adopted pursuant to the harmonized standards the references of which have been publishes in the Official Journal of the European Communities; Member States shall publish the references of such national standards.
2. For the purposes of this Directive, reference to harmonized standards also includes the monographs of the European Pharmacopoeia notably on surgical sutures and on interaction between medicinal products and materials used in devices containing such medicinal products, the references of which have been published in the Official Journal of the European Communities.
3. If a Member State or the Commission considers that the harmonized standards do not entirely meet the essential requirements referred to in Article 3, the measures to be taken by the Member States with regard to these standards and the publication referred to in paragraph 1 of this Article shall be adopted by the procedure defined in Article 6 (2).

Article 6

Committee on Standards and Technical Regulations

1. The Commission shall be assisted by the Committee set up by Article 5 of Directive 83/189/EEC.
2. The representative of the Commission shall submit to the Committee a draft of the measures to be taken. The Committee shall deliver its opinion on the draft within a time limit which the chairman may lay down according to the urgency of the matter, if necessary by taking a vote.
The opinion shall be recorded in the minutes; in addition, each Member State shall have the right to ask to have its position recorded in the minutes.
The Commission shall take the utmost account of the opinion delivered by the Committee. It shall inform the Committee of the manner in which its opinion has been taken into account.

Article 7

Committee on Medical Devices

1. The Commission shall be assisted by the Committee set up by Article 6 (2) of Directive 90/385/EEC.
2. The representative of the Commission shall submit to the Committee a draft of the measures to be taken. The Committee shall deliver its opinion on the draft within a time limit which the chairman may lay down according to the urgency of the matter. The opinion shall be delivered by the majority laid down in Article 148 (2) of the Treaty in the case of decisions which the Council is required to adopt on a proposal from the Commission. The votes of the representatives of the Member States within

the Committee shall be weighted in the manner set out in that Article. The chairman shall not vote.
The Commission shall adopt the measures envisaged if they are in accordance with the opinion of the Committee.
If the measures envisaged are not in accordance with the opinion of the Committee, or if no opinion is delivered, the Commission shall, without delay, submit to the Council a proposal relating to the measures to be taken. The Council shall act by a qualified majority.
If, on the expiry of a period of three months from the date of referral to the Council, the Council has not acted, the proposed measures shall be adopted by the Commission.
4. The Committee may examine any question connected with implementation of this Directive.

Article 8

Safeguard clause

1. Where a Member State ascertains that the devices referred to in Article 4 (1) and (2) second indent, when correctly installed, maintained and used for their intended purpose, may compromise the health and/or safety of patients, users or, where applicable, other persons, it shall take all appropriate interim measures to withdraw such devices from the market or prohibit or restrict their being placed on the market or put into service. The Member State shall immediately inform the Commission of any such measures, indicating the reasons for its decision and, in particular, whether non-compliance with this Directive is due to:
(a) failure to meet the essential requirements referred to in Article 3;
(b) incorrect application of the standards referred to in Article 5, in so far as it is claimed that the standards have been applied;
(c) shortcomings in the standards themselves.
2. The Commission shall enter into consultation with the parties concerned as soon as possible. Where, after such consultation, the Commission finds that:
- the measures are justified, it shall immediately so inform the Member State which took the initiative and the other Member States; where the decision referred to in paragraph 1 is attributed to shortcomings in the standards, the Commission shall, after consulting the parties concerned, bring the matter before the Committee referred to in Article 6 (1) within two months if the Member State which has taken the decision intends to maintain it and shall initiate the procedures referred to in Article 6,
- the measures are unjustified, it shall immediately so inform the Member State which took the initiative and the manufacturer or his authorized representative established within the Community.
3. Where a non-complying device bears the CE marking, the competent Member State shall take appropriate action against whomsoever has affixed the mark and shall inform the Commission and the other Member States thereof.
4. The Commission shall ensure that the Member States are kept informed of the progress and outcome of this procedure.

Article 9

Classification

1. Devices shall be divided into Classes I, IIa, IIb and III. Classification shall be carried out in accordance with Annex IX.
2. In the event of a dispute between the manufacturer and the notified body concerned, resulting from the application of the classification rules, the matter shall be

referred for decision to the competent authority to which the notified body is subject.

3. The classification rules set out in Annex IX may be adapted in accordance with the procedure referred to in Article 7 (2) in the light of technical progress and any information which becomes available under the information system provided for in Article 10.

Article 10

Information on incidents occuring following placing of devices on the market

1. Member States shall take the necessary steps to ensure that any information brought to their knowledge, in accordance with the provisions of this Directive, regarding the incidents mentioned below involving a Class I, IIa, IIb or III device is recorded and evaluated centrally:

(a) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;

(b) any technical or medical reason in relation to the characteristics or performance of a device for the reasons referred to in subparagraph (a), leading to systematic recall of devices of the same type by the manufacturer.

2. Where a Member State requires medical practitioners or the medical institutions to inform the competent authorities of any incidents referred to in paragraph 1, it shall take the necessary steps to ensure that the manufacturer of the device concerned, or his authorized representative established in the Community, is also informed of the incident.

3. After carrying out an assessment, if possible together with the manufacturer, Member States shall, without prejudice to Article 8, immediately inform the Commission and the other Member States of the incidents referred to in paragraph 1 for which relevant measures have been taken or are contemplated.

Article 11

Conformity assessment procedures

1. In the case of devices falling within Class III, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, either:

(a) follow the procedure relating to the EC declaration of conformity set out in Annex II (full quality assurance); or

(b) follow the procedure relating to the EC type-examination set out in Annex III, coupled with:

(i) the procedure relating to the EC verification set out in Annex IV;

or

(ii) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance).

2. In the case of devices falling within Class IIa, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, follow the procedure relating to the EC declaration of conformity set out in Annex VII, coupled with either:

(a) the procedure relating to the EC verification set out in Annex IV;

or

(b) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance);

or

(c) the procedure relating to the EC declaration of conformity set out in Annex VI (product quality assurance).
Instead of applying these procedures, the manufacturer may also follow the procedure referred to in paragraph 3 (a).
3. In the case of devices falling within Class IIb, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, either:
(a) follow the procedure relating to the EC declaration of conformity set out in Annex II (full quality assurance); in this case, point 4 of Annex II is not applicable; or
(b) follow the procedure relating to the EC type-examination set out in Annex III, coupled with:
(i) the procedure relating to the EC verification set out in Annex IV;
or
(ii) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance);
or
(iii) the procedure relating to the EC declaration of conformity set out in Annex VI (product quality assurance).
4. The Commission shall, no later than five years from the date of implementation of this Directive, submit a report to the Council on the operation of the provisions referred to in Article 10 (1), Article 15 (1), in particular in respect of Class I and Class IIa devices, and on the operation of the provisions referred to in Annex II, Section 4.3 second and third subparagraphs and in Annex III, Section 5 second and third subparagraphs to this Directive, accompanied, if necessary, by appropriate proposals.

5. In the case of devices falling within Class I, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, follow the procedure referred to in Annex VII and draw up the EC declaration of conformity required before placing the device on the market.
6. In the case of custom-made devices, the manufacturer shall follow the procedure referred to in Annex VIII and draw up the statement set out in that Annex before placing each device on the market.
Member States may require that the manufacturer shall submit to the competent authority a list of such devices which have been put into service in their territory.
7. During the conformity assessment procedure for a device, the manufacturer and/or the notified body shall take account of the results of any assessment and verification operations which, where appropriate, have been carried out in accordance with this Directive at an intermediate stage of manufacture.
8. The manufacturer may instruct his authorized representative established in the Community to initiate the procedures provided for in Annexes III, IV, VII and VIII.
9. Where the conformity assessment procedure involves the intervention of a notified body, the manufacturer, or his authorized representative established in the Community, may apply to a body of his choice within the framework of the tasks for which the body has been notified.
10. The notified body may require, where duly justified, any information or data, which is necessary for establishing and maintaining the attestation of conformity in view of the chosen procedure.
11. Decisions taken by the notified bodies in accordance with Annexes II and III shall be valid for a maximum of five years and may be extended on application, made at a time agreed in the contract signed by both parties, for further periods of five years.

12. The records and correspondence relating to the procedures referred to in paragraphs 1 to 6 shall be in an official language of the Member State in which the procedures are carried out and/or in another Community language acceptable to the notified body.
13. By derogation from paragraphs 1 to 6, the competent authorities may authorize, on duly justified request, the placing on the market and putting into service, within the territory of the Member State concerned, of individual devices for which the procedures referred to in paragraphs 1 to 6 have not been carried out and the use of which is in the interest of protection of health.

Article 12

Particular procedure for systems and procedure packs

1. By way of derogation from Article 11 this Article shall apply to systems and procedure packs.
2. Any natural or legal person who puts devices bearing the CE marking together within their intended purpose and within the limits of use specified by their manufacturers, in order to place them on the market as a system or procedure pack, shall draw up a declaration by which he states that:
(a) he has verified the mutual compatibility of the devices in accordance with the manufacturers' instructions and has carried out his operations in accordance with these instructions; and
(b) he has packaged the system or procedure pack and supplied relevant information to users incorporating relevant instructions from the manufacturers; and
(c) the whole activity is subjected to appropriate methods of internal control and inspection.
Where the conditions above are not met, as in cases where the system or procedure pack incorporate 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.
3. Any natural or legal person who sterilized, for the purpose of placing on the market, systems or procedure packs referred to in paragraph 2 or other CE-marked medical devices designed by their manufacturers to be sterilized before use, shall, at his choice, follow one of the procedures referred to in Annex IV, V or VI. The application of the abovementioned Annexes and the intervention of the notified body are limited to the aspects of the procedure relating to the obtaining of sterility. The person shall draw up a declaration stating that sterilization has been carried out in accordance with the manufacturer's instructions.
4. The products referred to in paragraphs 2 and 3 themselves shall not bear an additional CE marking. They shall be accompanied by the information referred to in point 13 of Annex I which includes, where appropriate, the information supplied by the manufacturers of the devices which have been put together. The declaration referred to in paragraphs 2 and 3 above shall be kept at the disposal of competent authorities for a period of five years.

Article 13

Decisions with regard to classification, derogation clause

1. Where a Member State considers that:
(a) application of the classification rules set out in Annex IX requires a decision with regard to the classification of a given device or category of devices;
or

(b) a given device or family of devices should be classified, by way of derogation from the provisions of Annex IX, in another class;
or
(c) the conformity of a device or family of devices should be established, by way of derogation from the provisions of Article 11, by applying solely one of the given procedures chosen from among those referred to in Article 11,
it shall submit a duly substantiated request to the Commission and ask it to take the necessary measures. These measures shall be adopted in accordance with the procedure referred to in Article 7 (2).
2. The Commission shall inform the Member States of the measures taken and, where appropriate, publish the relevant parts of these measures in the Official Journal of the European Communities.

Article 14

Registration of persons responsible for placing devices on the market

1. Any manufacturer who, under his own name, places devices on the market in accordance with the procedures referred to in Article 11 (5) and (6) and any other natural or legal person engaged in the activities referred to in Article 12 shall inform the competent authorities of the Member State in which he has his registered place of business of the address of the registered place of business and the description of the devices concerned.
2. Where a manufacturer who places devices referred to in paragraph 1 on the market under his own name does not have a registered place of business in a Member State, he shall designate the person(s) responsible for marketing them who is (are) established in the Community. These persons shall inform the competent authorities of the Member State in which they have their registered place of business of the address of the registered place of business and the category of devices concerned.
3. The Member States shall on request inform the other Member States and the Commission of the details referred to in paragraphs 1 and 2.

Article 15

Clinical investigation

1. In the case of devices intended for clinical investigations, the manufacturer, or his authorized representative established in the Community, shall follow the procedure referred to in Annex VIII and notify the competent authorities of the Member States in which the investigations are to be conducted.
2. In the case of devices falling within Class III and implantable and long-term invasive devices falling within Class IIa or IIb, the manufacturer may commence the relevant clinical investigation at the end of a period of 60 days after notification, unless the competent authorities have notified him within that period of a decision to the contrary based on considerations of public health or public policy.
Member States may however authorize manufacturers to commence the relevant clinical investigations before the expiry of the period of 60 days, in so far as the relevant ethics committee has issued a favourable opinion on the programme of investigation in question.
3. In the case of devices other than those referred to in the second paragraph, Member States may authorize manufacturers to commence clinical investigations, immediately after the date of notification, provided that the ethics committee concerned has delivered a favourable opinion with regard to the investigational plan.
4. The authorization referred to in paragraph 2 second subparagraph and paragraph 3, may be made subject to authorization from the competent authority.

5. The clinical investigations must be conducted in accordance with the provisions of Annex X. The provisions of Annex X may be adjusted in accordance with the procedure laid down in Article 7 (2).
6. The Member States shall, if necessary, take the appropriate steps to ensure public health and public policy.
7. The manufacturer or his authorized representative established in the Community shall keep the report referred to in point 2.3.7 of Annex X at the disposal of the competent authorities.
8. The provisions of paragraphs 1 and 2 do not apply where the clinical investigations are conducted using devices which are authorized in accordance with Article 11 to bear the CE marking unless the aim of these investigations is to use the devices for a purpose other than that referred to in the relevant conformity assessment procedure. The relevant provisions of Annex X remain applicable.

Article 16

Notified bodies

1. The Member States shall notify the Commission and other Member States of the bodies which they have designated for carrying out the tasks pertaining to the procedures referred to in Article 11 and the specific tasks for which the bodies have been designated. The Commission shall assign identification numbers to these bodies, hereinafter referred to as 'notified bodies'.

The Commission shall publish a list of the notified bodies, together with the identification numbers it has allocated to them and the tasks for which they have been notified, in the Official Journal of the European Communities. It shall ensure that the list is kept up to date.

2. Member States shall apply the criteria set out in Annex XI for the designation of bodies. Bodies that meet the criteria laid down in the national standards which transpose the relevant harmonized standards shall be presumed to meet the relevant criteria.
3. A Member State that has notified a body shall withdraw that notification if it finds that the body no longer meets the criteria referred to in paragraph 2. It shall immediately inform the other Member States and the Commission thereof.
4. The notified body and the manufacturer, or his authorized representative established in the Community, shall lay down, by common accord, the time limits for completion of the assessment and verification operations referred to in Annexes II to VI.

Article 17

CE marking

1. Devices, other than devices which are custom-made or intended for clinical investigations, considered to meet the essential requirements referred to in Article 3 must bear the CE marking of conformity when they are placed on the market.
2. The CE marking of conformity, as shown in Annex XII, must appear in a visible, legible and indelible form on the device or its sterile pack, where practicable and appropriate, and on the instructions for use. Where applicable, the CE marking must also appear on the sales packaging.

It shall be accompanied by the identification number of the notified body responsible for implementation of the procedures set out in Annexes II, IV, V and VI.

3. It is prohibited to affix marks or inscriptions which are likely to mislead third parties with regard to the meaning or the graphics of the CE marking. Any other mark may be affixed to the device, to the packaging or to the instruction leaflet

accompanying the device provided that the visibility and legibility of the CE marking is not thereby reduced.

Article 18

Wrongly affixed CE marking

Without prejudice to Article 8:

(a) where a Member State establishes that the CE marking has been affixed unduly, the manufacturer or his authorized representative established within the Community shall be obliged to end the infringement under conditions imposed by the Member State;

(b) where non-compliance continues, the Member State must take all appropriate measures to restrict or prohibit the placing on the market of the product in question or to ensure that it is withdrawn from the market, in accordance with the procedure in Article 8.

Article 19

Decision in respect of refusal or restriction

1. Any decision taken pursuant to this Directive:

(a) to refuse or restrict the placing on the market or the putting into service of a device or the carrying out of clinical investigations;

or

(b) to withdraw devices from the market,

shall state the exact grounds on which it is based. Such decisions shall be notified without delay to the party concerned, who shall at the same time be informed of the remedies available to him under the national law in force in the Member State in question and of the time limits to which such remedies are subject.

2. In the event of a decision as referred to in paragraph 1, the manufacturer, or his authorized representative established in the Community, shall have an opportunity to put forward his viewpoint in advance, unless such consultation is not possible because of the urgency of the measure to be taken.

Article 20

Confidentiality

Without prejudice to the existing national provisions and practices on medical secrets, Member States shall ensure that all the parties involved in the application of this Directive are bound to observe confidentiality with regard to all information obtained in carrying out their tasks. This does not affect the obligation of Member States and notified bodies with regard to mutual information and the dissemination of warnings, nor the obligations of the persons concerned to provide information under criminal law.

Article 21

Repeal and amendment of Directives

1. Directive 76/764/EEC is hereby repealed with effect from 1 January 1995.

2. In the title and Article 1 of Directive 84/539/EEC, 'human or' is deleted.

In Article 2 of Directive 84/539/EEC, the following subparagraph is added to paragraph 1:

'If the appliance is at the same time a medical device within the meaning of Directive 93/42/EEC (*) and if it satisfies the essential requirements laid down therein for that device, the device shall be deemed to be in conformity with the requirements of this Directive.

(*) OJ No L 169, 12. 7. 1993, p. 1.'

3. Directive 90/385/EEC is hereby amended as follows:

1. in Article 1 (2) the following two subparagraphs are added:

'(h) "placing on the market " means the first making available in return for payment or free of charge of a device other than a device intended for clinical investigation, with a view to distribution and/or use on the Community market, regardless of whether it is new or fully refurbished;
(i) "manufacturer " means the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party.
The obligations of this Directive to be met by manufacturers also apply to the natural or legal person who assembles, packages, processes, fully refurbishes and/or labels one or more ready-made products and/or assigns to them their intended purpose as a device with a view to their being placed on the market under his own name. This subparagraph does not apply to the person who, while not a manufacturer within the meaning of the first subparagraph, assembles or adapts devices already on the market to their intended purpose for an individual patient;'
2. in Article 9 the following paragraphs are added:
'5. During the conformity assessment procedure for a device, the manufacturer and/or the notified body shall take account of the results of any assessment and verification operations which, where appropriate, have been carried out in accordance with this Directive at an intermediate stage of manufacture.
6. Where the conformity assessment procedure involves the intervention of a notified body, the manufacturer, or his authorized representative established in the Community, may apply to a body of his choice within the framework of the tasks for which the body has been notified.
7. The notified body may require, where duly justified, any information or data which is necessary for establishing and maintaining the attestation of conformity in view of the chosen procedure.
8. Decisions taken by the notified bodies in accordance with Annexes II and III shall be valid for a maximum of five years and may be extended on application, made at a time agreed in the contract signed by both parties, for further periods of five years.
9. By derogation from paragraphs 1 and 2 the competent authorities may authorize, on duly justified request, the placing on the market and putting into service, within the territory of the Member State concerned, of individual devices for which the procedures referred to in paragraphs 1 and 2 have not been carried out and the use of which is in the interest of protection of health.';
3. the following Article 9a is inserted after Article 9:
'Article 9a
1. Where a Member State considers that the conformity of a device or family of devices should be established, by way of derogation from the provisions of Article 9, by applying solely one of the given procedures chosen from among those referred to in
Article 9, it shall submit a duly substantiated request to the Commission and ask it to take the necessary measures. These measures shall be adopted in accordance with the procedure referred to in Article 7 (2) of Directive 93/42/EEC (*).
2. The Commission shall inform the Member States of the measures taken and, where appropriate, publish the relevant parts of these measures in the Official Journal of the European Communities.
(*) OJ No L 169, 12. 7. 1993, p. 1.'
4. Article 10 shall be amended as follows:
- the following subparagraph shall be added to paragraph 2:

'Member States may however authorize manufacturers to start the clinical investigations in question before the expiry of the 60-day period, provided that the Ethical Committee concerned has delivered a favourable opinion with respect to the investigation programme in question.',
- the following paragraph shall be inserted:
'2a. The authorization referred to in the second subparagraph of paragraph 2 may be subject to approval by the competent authority.';
5. the following is added to Article 14:
'In the event of a decision as referred to in the previous paragraph the manufacturer, or his authorized representative established in the Community, shall have an opportunity to put forward his viewpoint in advance, unless such consultation is not possible because of the urgency of the measures to be taken.'

Article 22

Implementation, transitional provisions

1. Member States shall adopt and publish the laws, regulations and administrative provisions necessary to comply with this Directive not later than 1 July 1994. They shall immediately inform the Commission thereof.

The Standing Committee referred to in Article 7 may assume its tasks from the date of notification (19) of this Directive. The Member States may take the measures referred to in Article 16 on notification of this Directive.

When Member States adopt these provisions, these shall contain a reference to this Directive or shall be accompanied by such a reference at the time of their official publication. The procedure for such reference shall be adopted by Member States.

Member States shall apply these provisions with effect from 1 January 1995.

2. Member States shall communicate to the Commission the texts of the provisions of national law which they adopt in the field covered by this Directive.

3. Member States shall take the necessary action to ensure that the notified bodies which are responsible pursuant to Article 11 (1) to (5) for conformity assessment take account of any relevant information regarding the characteristics and performance of such devices, including in particular the results of any relevant tests and verification already carried out under pre-existing national law, regulations or administrative provisions in respect of such devices.

4. Member States shall accept the placing on the market and putting into service of devices which conform to the rules in force in their territory on 31 December 1994 during a period of five years following adoption of this Directive.

In the case of devices which have been subjected to EEC pattern approval in accordance with Directive 76/764/EEC, Member States shall accept their being placed on the market and put into service during the period up to 30 June 2004.

Article 23

This Directive is addressed to the Member States.

Done at Luxembourg, 14 June 1993.

For the Council

The President

J. TROEJBORG

(1) OJ No C 237, 12. 9. 1991 and OJ No C 251, 28. 9. 1992, p. 40.(2) OJ No C 150, 31. 5. 1993 and OJ No C 176, 28. 6. 1993.(3) OJ No C 79, 30. 3. 1992, p. 1.(4) OJ No 22, 9. 6. 1965, p. 369/65. Directive as last amended by Directive 92/27/EEC (OJ No L 113, 30. 4. 1992, p. 8).(5) OJ No L 147, 9. 6. 1975, p. 1. Directive as last amended by Directive 91/507/EEC (OJ No L 270, 26. 9. 1991, p. 32).(6) OJ No C 136, 4. 6. 1985, p. 1.(7) OJ No L 189, 20. 7. 1990, p. 17.(8) OJ No L 139, 23. 5. 1989, p. 19. Directive

as last amended by Directive 92/31/EEC (OJ No L 126, 12. 5. 1992, p. 11).(9) OJ No L 246, 17. 9. 1980, p. 1. Directive as last amended by Directive 84/467/Euratom (OJ No L 265, 5. 10. 1984, p. 4).(10) OJ No L 265, 5. 10. 1984, p. 1.(11) OJ No L 183, 29. 6. 1989, p. 1.(12) OJ No L 109, 26. 4. 1983, p. 8. Directive as last amended by Commission Decision 92/400/EEC (OJ No L 221, 6. 8. 1992, p. 55).(13) OJ No L 197, 18. 7. 1987, p. 33.(14) OJ No L 380, 31. 12. 1990, p. 13.(15) OJ No C 185, 22. 7. 1989, p. 8.(16) OJ No L 262, 27. 9. 1976, p. 139. Directive as last amended by Directive 84/414/EEC (OJ No L 228, 25. 8. 1984, p. 25).(17) OJ No L 300, 19. 11. 1984, p. 179. Directive as amended by the Act of Accession of Spain and Portugal.(18) OJ No L 262, 27. 9. 1976, p. 169. Directive as last amended by Commission Directive 92/86/EEC (OJ No L 325, 11. 11. 1992, p. 18).(19) This Directive was notified to the Member States on 29 June 1993.

ANNEX I

ESSENTIAL REQUIREMENTS I. GENERAL REQUIREMENTS 1. The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

2. The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.

In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order:

- eliminate or reduce risks as far as possible (inherently safe design and construction),
- where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated,
- inform users of the residual risks due to any shortcomings of the protection measures adopted.

3. The devices must achieve the performances intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in Article 1 (2) (a), as specified by the manufacturer.

4. The characteristics and performances referred to in Sections 1, 2 and 3 must not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use.

5. The devices must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information provided by the manufacturer.

6. Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended.

II. REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION 7. Chemical, physical and biological properties

7.1. The devices must be designed and manufactured in such a way as to guarantee the characteristics and performances referred to in Section I on the 'General requirements'. Particular attention must be paid to:

- the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,
- the compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device.

7.2. The devices must be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients, taking account of the intended purpose of the product. Particular attention must be paid to the tissues exposed and to the duration and frequency of exposure.

7.3. The devices must be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they must be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.

7.4. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and usefulness of the substance must be verified, taking account of the intended purpose of the device, by analogy with the appropriate methods specified in Directive 75/318/EEC.

7.5. The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device.

7.6. Devices must be designed and manufactured in such a way as to reduce, as much as possible, risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.

8. Infection and microbial contamination

8.1. The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use.

8.2. Tissues of animal origin must originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues.

Notified bodies shall retain information on the geographical origin of the animals.

Processing, preservation, testing and handling of tissues, cells and substances of animal origin must be carried out so as to provide optimal security. In particular safety with regard to viruses and other transferable agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process.

8.3. Devices delivered in a sterile state must be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions laid down, until the protective packaging is damaged or opened.

8.4. Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method.

8.5. Devices intended to be sterilized must be manufactured in appropriately controlled (e. g. environmental) conditions.

8.6. Packaging systems for non-sterile devices must keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization indicated by the manufacturer.
8.7. The packaging and/or label of the device must distinguish between identical or similar products sold in both sterile and non-sterile condition.
9. Construction and environmental properties
9.1. If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system must be safe and must not impair the specified performances of the devices. Any restrictions on use must be indicated on the label or in the instructions for use.
9.2. Devices must be designed and manufactured in such a way as to remove or minimize as far as is possible:
- the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features,
- risks connected with reasonably foreseeable environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration,
- the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given,
- risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.
9.3. Devices must be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention must be paid to devices whose intended use includes exposure to flammable substances or to substances which could cause combustion.
10. Devices with a measuring function
10.1. Devices with a measuring function must be designed and manufactured in such a way as to provide sufficient accuracy and stability within appropriate limits of accuracy and taking account of the intended purpose of the device. The limits of accuracy must be indicated by the manufacturer.
10.2. The measurement, monitoring and display scale must be designed in line with ergonomic principles, taking account of the intended purpose of the device.
10.3. The measurements made by devices with a measuring function must be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC (1).
11. Protection against radiation
11.1. General
11.1.1. Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to radiation shall be reduced as far as possible compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.
11.2. Intended radiation
11.2.1. Where devices are designed to emit hazardous levels of radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it must be possible for the user to control the emissions. Such devices shall be designed and manufactured to ensure reproducibility and tolerance of relevant variable parameters.

11.2.2. Where devices are intended to emit potentially hazardous, visible and/or invisible radiation, they must be fitted, where practicable, with visual displays and/or audible warnings of such emissions.
11.3. Unintended radiation
11.3.1. Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible.
11.4. Instructions
11.4.1. The operating instructions for devices emitting radiation must give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse and of eliminating the risks inherent in installation.
11.5. Ionizing radiation
11.5.1. Devices intended to emit ionizing radiation must be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and quality of radiation emitted can be varied and controlled taking into account the intended use.
11.5.2. Devices emitting ionizing radiation intended for diagnostic radiology shall be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimizing radiation exposure of the patient and user.
11.5.3. Devices emitting ionizing radiation, intended for therapeutic radiology shall be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the quality of radiation.
12. Requirements for medical devices connected to or equipped with an energy source
12.1. Devices incorporating electronic programmable systems must be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition (in the system) appropriate means should be adopted to eliminate or reduce as far as possible consequent risks.
12.2. Devices where the safety of the patients depends on an internal power supply must be equipped with a means of determining the state of the power supply.
12.3. Devices where the safety of the patients depends on an external power supply must include an alarm system to signal any power failure.
12.4. Devices intended to monitor one or more clinical parameters of a patient must be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.
12.5. Devices must be designed and manufactured in such a way as to minimize the risks of creating electromagnetic fields which could impair the operation of other devices or equipment in the usual environment.
12.6. Protection against electrical risks
Devices must be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed correctly.
12.7. Protection against mechanical and thermal risks
12.7.1. Devices must be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance, stability and moving parts.
12.7.2. Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking

account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.
12.7.3. Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.
12.7.4. Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle must be designed and constructed in such a way as to minimize all possible risks.
12.7.5. Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal use.
12.8. Protection against the risks posed to the patient by energy supplies or substances
12.8.1. Devices for supplying the patient with energy or substances must be designed and constructed in such a way that the flow-rate can be set and maintained accurately enough to guarantee the safety of the patient and of the user.
12.8.2. Devices must be fitted with the means of preventing and/or indicating any inadequacies in the flow-rate which could pose a danger.
Devices must incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source.
12.9. The function of the controls and indicators must be clearly specified on the devices.
Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user and, as appropriate, the patient.
13. Information supplied by the manufacturer
13.1. Each device must be accompanied by the information needed to use it safely and to identify the manufacturer, taking account of the training and knowledge of the potential users.
This information comprises the details on the label and the data in the instructions for use.
As far as practicable and appropriate, the information needed to use the device safely must be set out on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging. If individual packaging of each unit is not practicable, the information must be set out in the leaflet supplied with one or more devices.
Instructions for use must be included in the packaging for every device. By way of exception, no such instructions for use are needed for devices in Class I or IIa if they can be used safely without any such instructions.
13.2. Where appropriate, this information should take the form of symbols. Any symbol or identification colour used must conform to the harmonized standards. In areas for which no standards exist, the symbols and colours must be described in the documentation supplied with the device.
13.3. The label must bear the following particulars:
(a) the name or trade name and address of the manufacturer. For devices imported into the Community, in view of their distribution in the Community, the label, or the outer packaging, or instructions for use, shall contain in addition the name and address of either the person responsible referred to in Article 14 (2) or of the authorized representative of the manufacturer established within the Community or of the importer established within the Community, as appropriate;

(b) the details strictly necessary for the user to identify the device and the contents of the packaging;
(c) where appropriate, the word 'STERILE';
(d) where appropriate, the batch code, preceded by the word 'LOT', or the serial number;
(e) where appropriate, an indication of the date by which the device should be used, in safety, expressed as the year and month;
(f) where appropriate, an indication that the device is for single use;
(g) if the device is costum-made, the words 'custom-made device';
(h) if the device is intended for clinical investigations, the words 'exclusively for clinical investigations';
(i) any special storage and/or handling conditions;
(j) any special operating instructions;
(k) any warnings and/or precautions to take;
(l) year of manufacture for active devices other than those covered by (e). This indication may be included in the batch or serial number;
(m) where applicable, method of sterilization.
13.4. If the intended purpose of the device is not obvious to the user, the manufacturer must clearly state it on the label and in the instructions for use.
13.5. Wherever reasonable and practicable, the devices and detachable components must be identified, where appropriate in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components.
13.6. Where appropriate, the instructions for use must contain the following particulars:
(a) the details referred to in Section 13.3, with the exception of (d) and (e);
(b) the performances referred to in Section 3 and any undesirable side-effects;
(c) if the device must be installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe combination;
(d) all the information needed to verify whether the device is properly installed and can operate correctly and safely, plus details of the nature and frequency of the maintenance and calibration needed to ensure that the devices operate properly and safely at all times;
(e) where appropriate, information to avoid certain risks in connection with implantation of the device;
(f) information regarding the risks of reciprocal interference posed by the presence of the device during specific investigations or treatment;
(g) the necessary instructions in the event of damage to the sterile packaging and, where appropriate, details of appropriate methods of resterilization;
(h) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of sterilization of the device to be resterilized, and any restriction on the number of reuses.
Where devices are supplied with the intention that they be sterilized before use, the instructions for cleaning and sterilization must be such that, if correctly followed, the device will still comply with the requirements in Section I;
(i) details of any further treatment or handling needed before the device can be used (for example, sterilization, final assembly, etc.);

(j) in the case of devices emitting radiation for medical purposes, details of the nature, type, intensity and distribution of this radiation.
The instructions for use must also include details allowing the medical staff to brief the patient on any contra-indications and any precautions to be taken. These details should cover in particular:
(k) precautions to be taken in the event of changes in the performance of the device;
(l) precautions to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, acceleration, thermal ignition sources, etc.;
(m) adequate information regarding the medicinal product or products which the device in question is designed to administer, including any limitations in the choice of substances to be delivered;
(n) precautions to be taken against any special, unusual risks related to the disposal of the device;
(o) medicinal substances incorporated into the device as an integral part in accordance with Section 7.4;
(p) degree of accuracy claimed for devices with a measuring function.
14. Where conformity with the essential requirements must be based on clinical data, as in Section I (6), such data must be established in accordance with Annex X.
(1) OJ No L 39, 15. 2. 1980, p. 40. Directive as last amended by Directive 89/617/EEC (OJ No L 357, 7. 12. 1989, p. 28).
ANNEX II
EC DECLARATION OF CONFORMITY (Full quality assurance system) 1. The manufacturer must ensure application of the quality system approved for the design, manufacture and final inspection of the products concerned, as specified in Section 3 and is subject to audit as laid down in Sections 3.3 and 4 and to Community surveillance as specified in Section 5.
2. The declaration of conformity is the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned meet the provisions of this Directive which apply to them.
The manufacturer must affix the CE marking in accordance with Article 17 and draw up a written declaration of conformity. This declaration must cover a given number of the products manufactured and be kept by the manufacturer.
3. Quality system
3.1. The manufacturer must lodge an application for assessment of his quality system with a notified body.
The application must include:
- the name and address of the manufacturer and any additional manufacturing site covered by the quality system,
- all the relevant information on the product or product category covered by the procedure,
- a written declaration that no application has been lodged with any other notified body for the same product-related quality system,
- the documentation on the quality system,
- an undertaking by the manufacturer to fulfil the obligations imposed by the quality system approved,
- an undertaking by the manufacturer to keep the approved quality system adequate and efficacious,

- an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:
(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
(ii) any technical or medical reason connected with the characteristics or performance of a device leading for the reasons referred to in subparagraph (i) to systematic recall of devices of the same type by the manufacturer.
3.2. Application of the quality system must ensure that the products conform to the provisions of this Directive which apply to them at every stage, from design to final inspection. All the elements, requirements and provisions adopted by the manufacturer for his quality system must be documented in a systematic and orderly manner in the form of written policies and procedures such as quality programmes, quality plans, quality manuals and quality records.
It shall include in particular an adequate description of:
(a) the manufacturer's quality objectives;
(b) the organization of the business and in particular:
- the organizational structures, the responsibilities of the managerial staff and their organizational authority where quality of design and manufacture of the products is concerned,
- the methods of monitoring the efficient operation of the quality system and in particular its ability to achieve the desired quality of design and of product, including control of products which fail to conform;
(c) the procedures for monitoring and verifying the design of the products and in particular:
- a general description of the product, including any variants planned,
- the design specifications, including the standards which will be applied and the results of the risk analysis, and also a description of the solutions adopted to fulfil the essential requirements which apply to the products if the standards referred to in Article 5 are not applied in full,
- the techniques used to control and verify the design and the processes and systematic measures which will be used when the products are being designed,
- if the device is to be connected to other device(s) in order to operate as intended, proof must be provided that it conforms to the essential requirements when connected to any such device(s) having the characteristics specified by the manufacturer,
- a statement indicating whether or not the device incorporates, as an integral part, a substance as referred to in Section 7.4 of Annex I and data on the tests conducted in this connection,
- the clinical data referred to in Annex X,
- the draft label and, where appropriate, instructions for use;
(d) the inspection and quality assurance techniques at the manufacturing stage and in particular:
- the processes and procedures which will be used, particularly as regards sterilization, purchasing and the relevant documents,
- the product identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture;

(e) the appropriate tests and trials which will be carried out before, during and after manufacture, the frequency with which they will take place, and the test equipment used; it must be possible to trace back the calibration of the test equipment adequately.

3.3. The notified body must audit the quality system to determine whether it meets the requirements referred to in Section 3.2. It must presume that quality systems which implement the relevant harmonized standards conform to these requirements.

The assessment team must include at least one number with past experience of assessments of the technology concerned. The assessment procedure must include an inspection on the manufacturer's premises and, in duly substantiated cases, on the premises of the manufacturer's suppliers and/or subcontractors to inspect the manufacturing processes.

The decision is notified to the manufacturer. It must contain the conclusions of the inspection and a reasoned assessment.

3.4. The manufacturer must inform the notified body which approved the quality system of any plan for substantial changes to the quality system or the product-range covered. The notified body must assess the changes proposed and verify whether after these changes the quality system still meets the requirements referred to in Section 3.2. It must notify the manufacturer of its decision. This decision must contain the conclusions of the inspection and a reasoned assessment.

4. Examination of the design of the product

4.1. In addition to the obligations imposed by Section 3, the manufacturer must lodge with the notified body an application for examination of the design dossier relating to the product which he plans to manufacture and which falls into the category referred to in Section 3.1.

4.2. The application must describe the design, manufacture and performances of the product in question. It must include the documents needed to assess whether the product conforms to the requirements of this Directive, as referred to in Section 3.2 (c).

4.3. The notified body must examine the application and, if the product conforms to the relevant provisions of this Directive, issue the application with an EC design-examination certificate. The notified body may require the application to be completed by further tests or proof to allow assessment of conformity with the requirements of the Directive. The certificate must contain the conclusions of the examination, the conditions of validity, the data needed for identification of the approved design, where appropriate, a description of the intended purpose of the product.

In the case of devices referred to in Annex I, paragraph 7.4, the notified body shall, in view of the aspects addressed in that paragraph, consult one of the competent bodies established by the Member States in accordance with Directive 65/65/EEC before taking a decision.

The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.

4.4. Changes to the approved design must receive further approval from the notified body which issued the EC design-examination certificate wherever the changes could affect conformity with the essential requirements of the Directive or with the conditions prescribed for use of the product. The applicant shall inform the notified body which issued the EC design-examination certificate of any such changes made to

the approved design. This additional approval must take the form of a supplement to the EC design-examination certificate.
5. Surveillance
5.1. The aim of surveillance is to ensure that the manufacturer duly fulfils the obligations imposed by the approved quality system.
5.2. The manufacturer must authorize the notified body to carry out all the necessary inspections and supply it with all relevant information, in particular:
- the documentation on the quality system,
- the data stipulated in the part of the quality system relating to design, such as the results of analyses, calculation tests, etc.,
- the data stipulated in the part of the quality system relating to manufacture, such as inspection reports and test data, calibration data, qualification reports of the personnel concerned, etc.
5.3. The notified body must periodically carry out appropriate inspections and assessments to make sure that the manufacturer applies the approved quality system and must supply the manufacturer with an assessment report.
5.4. In addition, the notified body may pay unannounced visits to the manufacturer. At the time of such visits, the notified body may, where necessary, carry out or ask for tests in order to check that the quality system is working properly. It must provide the manufacturer with an inspection report and, if a test has been carried out, with a test report.
6. Administrative provisions
6.1. The manufacturer must, for a period ending at least five years after the last product has been manufactured, keep at the disposal of the national authorities:
- the declaration of conformity,
- the documentation referred to in the fourth indent of Section 3.1,
- the changes referred to in Section 3.4,
- the documentation referred to in Section 4.2, and
- the decisions and reports from the notified body as referred to in Sections 3.3, 4.3, 4.4, 5.3 and 5.4.
6.2. The notified body must make available to the other notified bodies and the competent authority, on request, all relevant information concerning quality system approvals issued, refused or withdrawn.
6.3. In respect of devices subject to the procedure in Section 4, when neither the manufacturer nor his authorized representative is established in the Community, the obligation to keep available the technical documentation shall fall to the person responsible for placing the device on the Community market or the importer referred to in Annex I, Section 13.3 (a).
7. Application to devices in Classes IIa and IIb
In line with Article 11 (2) and (3), this Annex may apply to products in Classes IIa and IIb. Section 4, however, does not apply.
ANNEX III
EC TYPE-EXAMINATION 1. EC type-examination is the procedure whereby a notified body ascertains and certifies that a representative sample of the production covered fulfils the relevant provisions of this Directive.
2. The application includes:
- the name and address of the manufacturer and the name and address of the authorized representative if the application is lodged by the representative,
- the documentation described in Section 3 needed to assess the conformity of the representative sample of the production in question, hereinafter referred to as the

'type', with the requirements of this Directive. The applicant must make a 'type' available to the notified body. The notified body may request other samples as necessary,
- a written declaration that no application has been lodged with any other notified body for the same type.
3. The documentation must allow an understanding of the design, the manufacture and the performances of the product and must contain the following items in particular:
- a general description of the type, including any variants planned,
- design drawings, methods of manufacture envisaged, in particular as regards sterilization, and diagrams of components, sub-assemblies, circuits, etc.,
- the descriptions and explanations necessary to understand the abovementioned drawings and diagrams and the operation of the product,
- a list of the standards referred to in Article 5, applied in full or in part, and descriptions of the solutions adopted to meet the essential requirements if the standards referred to in Article 5 have not been applied in full,
- the results of the design calculations, risk analysis, investigations, technical tests, etc. carried out,
- a statement indicating whether or not the device incorporates, as an integral part, a substance as referred to in Section 7.4 of Annex I and data on the tests conducted in this connection,
- the clinical data referred to in Annex X,
- the draft label and, where appropriate, instructions for use.
4. The notified body must:
4.1. examine and assess the documentation and verify that the type has been manufactured in conformity with that documentation; it must also record the items designed in conformity with the applicable provisions of the standards referred to in Article 5, as well as the items not designed on the basis of the relevant provisions of the abovementioned standards;
4.2. carry out or arrange for the appropriate inspections and the tests necessary to verify whether the solutions adopted by the manufacturer meet the essential requirements of this Directive if the standards referred to in Article 5 have not been applied; if the device is to be connected to other device(s) in order to operate as intended, proof must be provided that it conforms to the essential requirements when connected to any such device(s) having the characteristics specified by the manufacturer;
4.3. carry out or arrange for the appropriate inspections and the tests necessary to verify whether, if the manufacturer has chosen to apply the relevant standards, these have actually been applied;
4.4. agree with the applicant on the place where the necessary inspections and tests will be caried out.
5. If the type conforms to the provisions of this Directive, the notified body issues the applicant with an EC type-examination certificate. The certificate must contain the name and address of the manufacturer, the conclusions of the inspection, the conditions of validity and the data needed for identification of the type approved. The relevant parts of the documentation must be annexed to the certificate and a copy kept by the notified body.
In the case of devices referred to in Annex I, paragraph 7.4, the notified body shall, in view of the aspects addressed in that paragraph, consult one of the competent bodies established by the Member States in accordance with Directive 65/65/EEC before taking a decision.

The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.
6. The applicant must inform the notified body which issued the EC type-examination certificate of any significant change made to the approved product.
Changes to the approved product must receive further approval from the notified body which issued the EC type-examination certificate wherever the changes may affect conformity with the essential requirements or with the conditions prescribed for use of the product. This new approval must, where appropriate, take the form of a supplement to the initial EC type-examination certificate.
7. Administrative provisions
7.1. The notified body must make available to the other notified bodies on request, all relevant information on EC type-examination certificates and supplements issued, refused or withdrawn.
7.2. Other notified bodies may obtain a copy of the EC type-examination certificates and/or the supplements thereto. The Annexes to the certificates must be made available to other notified bodies on reasoned application, after the manufacturer has been informed.
7.3. The manufacturer or his authorized representative must keep with the technical documentation copies of EC type-examination certificates and their additions for a period ending at least five years after the last device has been manufactured.
7.4. When neither the manufacturer nor his authorized representative is established in the Community, the obligation to keep available the technical documentation shall fall to the person responsible for placing the device on the Community market or the importer referred to in Annex I, Section 13.3 (a).
ANNEX IV
EC VERIFICATION 1. EC verification is the procedure whereby the manufacturer or his authorized representative established in the Community ensures and declares that the products which have been subject to the procedure set out in Section 4 conform to the type described in the EC type-examination certificate and meet the requirements of this Directive which apply to them.
2. The manufacturer must take all the measures necessary to ensure that the manufacturing process produces products which conform to the type described in the EC type-examination certificate and to the requirements of the Directive which apply to them. Before the start of manufacture, the manufacturer must prepare documents defining the manufacturing process, in particular as regards sterilization where necessary, together with all the routine, pre-established provisions to be implemented to ensure homogeneous production and, where appropriate, conformity of the products with the type described in the EC type-examination certificate and with the requirements of this Directive which apply to them. The manufacturer must affix the CE marking in accordance with Article 17 and draw up a declaration of conformity.
In addition, for products placed on the market in sterile condition, and only for those aspects of the manufacturing process designed to secure and maintain sterility, the manufacturer must apply the provisions of Annex V, Sections 3 and 4.
3. The manufacturer must undertake to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:

(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
(ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in subparagraph (i) leading to systematic recall of devices of the same type by the manufacturer.
4. The notified body must carry out the appropriate examinations and tests in order to verify the conformity of the product with the requirements of the Directive either by examining and testing every product as specified in Section 5 or by examining and testing products on a statistical basis as specified in Section 6, as the manufacturer decides.
The aforementioned checks do not apply to those aspects of the manufacturing process designed to secure sterility.
5. Verification by examination and testing of every product
5.1. Every product is examined individually and the appropriate tests defined in the relevant standard(s) referred to in Article 5 or equivalent tests must be carried out in order to verify, where appropriate, the conformity of the products with the EC type described in the type-examination certificate and with the requirements of the Directive which apply to them.
5.2. The notified body must affix, or have affixed its identification number to each approved product and must draw up a written certificate of conformity relating to the tests carried out.
6. Statistical verification
6.1. The manufacturer must present the manufactured products in the form of homogeneous batches.
6.2. A random sample is taken from each batch. The products which make up the sample are examined individually and the appropriate tests defined in the relevant standard(s) referred to in Article 5 or equivalent tests must be carried out to verify, where appropriate, the conformity of the products with the type described in the EC type-examination certificate and with the requirements of the Directive which apply to them in order to determine whether to accept or reject the batch.
6.3. Statistical control of products will be based on attributes, entailing a sampling system ensuring a limit quality corresponding to a probability of acceptance of 5 %, with a non-conformity percentage of between 3 and 7 %. The sampling method will be established by the harmonized standards referred to in Article 5, taking account of the specific nature of the product categories in question.
6.4. If the batch is accepted, the notified body affixes or has affixed its identification number to each product and draws up a written certificate of conformity relating to the tests carried out. All products in the batch may be put on the market except any in the sample which failed to conform.
If a batch is rejected, the competent notified body must take appropriate measures to prevent the batch from being placed on the market. In the event of frequent rejection of batches, the notified body may suspend the statistical verification.
The manufacturer may, on the responsibility of the notified body, affix the notified body's identification number during the manufacturing process.
7. Administrative provisions
The manufacturer or his authorized representative must, for a period ending at least five years after the last product has been manufactured, make available to the national authorities:

- the declaration of conformity,
- the documentation referred to in Section 2,
- the certificates referred to in Sections 5.2 and 6.4,
- where appropriate, the type-examination certificate referred to in Annex III.

8. Application to devices in Class IIa

In line with Article 11 (2), this Annex may apply to products in Class IIa, subject to the following exemptions:

8.1. in derogation from Sections 1 and 2, by virtue of the declaration of conformity the manufacturer ensures and declares that the products in Class IIa are manufactured in conformity with the technical documentation referred to in Section 3 of Annex VII and meet the requirements of this Directive which apply to them;

8.2. in derogation from Sections 1, 2, 5 and 6, the verifications conducted by the notified body are intended to confirm the conformity of the products in Class IIa with the technical documentation referred to in Section 3 of Annex VII.

ANNEX V

EC DECLARATION OF CONFORMITY (Production quality assurance) 1. The manufacturer must ensure application of the quality system approved for the manufacture of the products concerned and carry out the final inspection, as specified in Section 3, and is subject to the Community surveillance referred to in Section 4.

2. The declaration of conformity is the part of the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned conform to the type described in the EC type-examination certificate and meets the provisions of this Directive which apply to them.

The manufacturer must affix the CE marking in accordance with Article 17 and draw up a written declaration of conformity. This declaration must cover a given number of identified specimens of the products manufactured and must be kept by the manufacturer.

3. Quality system

3.1. The manufacturer must lodge an application for assessment of his quality system with a notified body.

The application must include:

- the name and address of the manufacturer,
- all the relevant information on the product or product category covered by the procedure,
- a written declaration that no application has been lodged with any other notified body for the same products,
- the documentation on the quality system,
- an undertaking to fulfil the obligations imposed by the quality system is approved,
- an undertaking to maintain the practicability and effectiveness of the approved quality system,
- where appropriate, the technical documentation on the types approved and a copy of the EC type-examination certificates,
- an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:

(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which

might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
(ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in subparagraph (i) above leading to a systematic recall of devices of the same type by the manufacturer.
3.2. Application of the quality system must ensure that the products conform to the type described in the EC type-examination certificate.
All the elements, requirements and provisions adopted by the manufacturer for his quality system must be documented in a systematic and orderly manner in the form of written policy statements and procedures. This quality system documentation must permit uniform interpretation of the quality policy and procedures such as quality programmes, plans, manuals and records.
It must include in particular an adequate description of:
(a) the manufacturer's quality objectives;
(b) the organization of the business and in particular:
- the organizational structures, the responsibilities of the managerial staff and their organizational authority where manufacture of the products is concerned,
- the methods of monitoring the efficient operation of the quality system and in particular its ability to achieve the desired quality of product, including control of products which fail to conform;
(c) the inspection and quality assurance techniques at the manufacturing stage and in particular:
- the processes and procedures which will be used, particularly as regards sterilization, purchasing and the relevant documents,
- the product identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture;
(d) the appropriate tests and trials to be carried out before, during and after manufacture, the frequency with which they will take place, and the test equipment used; it must be possible adequately to trace back the calibration of the test equipment.
3.3. The notified body must audit the quality system to determine whether it meets the requirements referred to in Section 3.2. It must presume that quality systems which implement the relevant harmonized standards conform to these requirements.
The assessment team must include at least one member with past experience of assessments of the technology concerned. The assessment procedure must include an inspection on the manufacturer's premises and, in duly substantiated cases, on the premises of the manufacturer's suppliers to inspect the manufacturing processes.
The decision must be notified to the manufacturer after the final inspection and contain the conclusions of the inspection and a reasoned assessment.
3.4. The manufacturer must inform the notified body which approved the quality system of any plan for substantial changes to the quality system.
The notified body must assess the changes proposed and verify whether after these changes the quality system still meets the requirements referred to in Section 3.2.
After the abovementioned information has been received the decision is notified to the manufacturer. It must contain the conclusions of the inspection and a reasoned assessment.
4. Surveillance
4.1. The aim of surveillance is to ensure that the manufacturer duly fulfils the obligations imposed by the approved quality system.

4.2. The manufacturer authorizes the notified body to carry out all the necessary inspections and must supply it with all relevant information, in particular:
- the documentation on the quality system,
- the data stipulated in the part of the quality system relating to manufacture, such as inspection reports and test data, calibration data, qualification reports of the personnel concerned, etc.
4.3. The notified body must periodically carry out appropriate inspections and assessments to make sure that the manufacturer applies the approved quality system and supply the manufacturer with an assessment report.
4.4. In addition, the notified body may pay unannounced visits to the manufacturer. At the time of such visits, the notified body may, where necessary, carry out or ask for tests in order to check that the quality system is working properly. It must provide the manufacturer with an inspection report and, if a test has been carried out, with a test report.
5. Administrative provisions
5.1. The manufacturer must, for a period ending at least five years after the last product has been manufactured, make available to the national authorities:
- the declaration of conformity,
- the documentation referred to in the fourth indent of Section 3.1,
- the changes referred to in Section 3.4,
- the documentation referred to in the seventh indent of Section 3.1,
- the decisions and reports from the notified body as referred to in Sections 4.3 and 4.4,
- where appropriate, the type-examination certificate referred to in Annex III.
5.2. The notified body must make available to the other notified bodies, on request, all relevant information concerning the quality system approvals issued, refused or withdrawn.
6. Application to devices in Class IIa
In line with Article 11 (2), this Annex may apply to products in Class IIa, subject to the following exemption:
6.1. in derogation from Sections 2, 3.1 and 3.2, by virtue of the declaration of conformity the manufacturer ensures and declares that the products in Class IIa are manufactured in conformity with the technical documentation referred to in Section 3 of Annex VII and meet the requirements of this Directive which apply to them.
ANNEX VI
EC DECLARATION OF CONFORMITY (Product quality assurance) 1. The manufacturer must ensure application of the quality system approved for the final inspection and testing of the product, as specified in Section 3 and must be subject to the surveillance referred to in Section 4.
In addition, for products placed on the market in sterile condition, and only for those aspects of the manufacturing process designed to secure and maintain sterility, the manufacturer must apply the provisions of Annex V, Sections 3 and 4.
2. The declaration of conformity is the part of the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned conform to the type described in the EC type-examination certificate and meet the provisions of this Directive which apply to them.
The manufacturer affixes the CE marking in accordance with Article 17 and draws up a written declaration of conformity. This declaration must cover a given number of identified specimens of the products manufactured and be kept by the manufacturer.

The CE marking must be accompanied by the identification number of the notified body which performs the tasks referred to in this Annex.

3. Quality system

3.1. The manufacturer lodges an application for assessment of his quality system with a notified body.

The application must include:

- the name and address of the manufacturer,
- all the relevant information on the product or product category covered by the procedure,
- a written declaration specifying that no application has been lodged with any other notified body for the same products,
- the documentation on the quality system,
- an undertaking by the manufacturer to fulfil the obligations imposed by the quality system approved,
- an undertaking by the manufacturer to keep the approved quality system adequate and efficacious,
- where appropriate, the technical documentation on the types approved and a copy of the EC type-examination certificates,
- an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:

(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;

(ii) any technical or medical reason connected with the characteristics or the performance of a device for the reasons referred to in subparagraph (i) leading to a systematic recall of devices of the same type by the manufacturer.

3.2. Under the quality system, each product or a representative sample of each batch is examined and the appropriate tests defined in the relevant standard(s) referred to in Article 5 or equivalent tests are carried out to ensure that the products conform to the type described in the EC type-examination certificate and fulfil the provisions of this Directive which apply to them. All the elements, requirements and provisions adopted by the manufacturer must be documented in a systematic and orderly manner in the form of written measures, procedures and instructions. This quality system documentation must permit uniform interpretation of the quality programmes, quality plans, quality manuals and quality records.

It must include in particular an adequate description of:

- the quality objectives and the organizational structure, responsibilities and powers of the managerial staff with regard to product quality,
- the examinations and tests that will be carried out after manufacture; it must be possible to trace back the calibration of the test equipment adequately,
- the methods of monitoring the efficient operation of the quality system
- the quality records, such as reports concerning inspections, tests, calibration and the qualifications of the staff concerned, etc.

The aforementioned checks do not apply to those aspects of the manufacturing process designed to secure sterility.

3.3. The notified body audits the quality system to determine whether it meets the requirements referred to in section 3.2. It must presume that quality systems which implement the relevant harmonized standards conform to these requirements.
The assessment team must include at least one member with past experience of assessments of the technology concerned. The assessment procedure must include an inspection on the manufacturer's premises and, in duly substantiated cases, on the premises of the manufacturer's suppliers to inspect the manufacturing processes.
The decision must be notified to the manufacturer. It must contain the conclusions of the inspection and a reasoned assessment.
3.4. The manufacturer must inform the notified body which approved the quality system of any plan for substantial changes to the quality system.
The notified body must assess the changes proposed and verify whether after these changes the quality system will still meet the requirements referred to in Section 3.2.
After receiving the abovementioned information it must notify the manufacturer of its decision. This decision must contain the conclusions of the inspection and a reasoned assessment.
4. Surveillance
4.1. The aim of surveillance is to ensure that the manufacturer duly fulfils the obligations imposed by the approved quality system.
4.2. The manufacturer must allow the notified body access for inspection purposes to the inspection, testing and storage locations and supply it with all relevant information, in particular:
- the documentation on the quality system,
- the technical documentation,
- the quality records, such as inspection reports, test data, calibration data, qualification reports of the staff concerned, etc.
4.3. The notified body must periodically carry out appropriate inspections and assessments to make sure that the manufacturer applies the quality system and must supply the manufacturer with an assessment report.
4.4. In addition, the notified body may pay unannounced visits to the manufacturer. At the time of such visits, the notified body may, where necessary, carry out or ask for tests in order to check that the quality system is working properly and that the production conforms to the requirements of the Directive which apply to it. To this end, an adequate sample of the final products, taken on site by the notified body, must be examined and the appropriate tests defined in the relevant standard(s) referred to in Article 5 or equivalent tests must be carried out. Where one or more of the samples fails to conform, the notified body must take the appropriate measures.
It must provide the manufacturer with an inspection report and, if a test has been carried out, with a test report.
5. Administrative provisions
5.1. The manufacturer must, for a period ending at least five years after the last product has been manufactured, make available to the national authorities:
- the declaration of conformity,
- the documentation referred to in the seventh indent of Section 3.1,
- the changes referred to in Section 3.4,
- the decisions and reports from the notified body as referred to in the final indent of Section 3.4 and in Sections 4.3 and 4.4,
- where appropriate, the certificate of conformity referred to in Annex III.

5.2. The notified body must make available to the other notified bodies, on request, all relevant information concerning the quality system approvals issued, refused or withdrawn.
6. Application to devices in Class IIa
In line with Article 11 (2), this Annex may apply to products in Class IIa, subject to this derogation:
6.1. by derogation from Sections 2, 3.1 and 3.2 by virtue of the declaration of conformity the manufacturer ensures and declares that the products in Class IIa are manufactured in conformity with the technical documentation referred to in Section 3 of Annex VII and meet the requirements of this Directive which apply to them.
ANNEX VII
EC DECLARATION OF CONFORMITY 1. The EC declaration of conformity is the procedure whereby the manufacturer or his authorized representative established in the Community who fulfils the obligations imposed by Section 2 and, in the case of products placed on the market in a sterile condition and devices with a measuring function, the obligations imposed by Section 5 ensures and declares that the products concerned meet the provisions of this Directive which apply to them.
2. The manufacturer must prepare the technical documentation described in Section 3. The manufacturer or his authorized representative established in the Community must make this documentation, including the declaration of conformity, available to the national authorities for inspection purposes for a period ending at least five years after the last product has been manufactured.
Where neither the manufacturer nor his authorized representative are established in the Community, this obligation to keep the technical documentation available must fall to the person(s) who place(s) the product on the Community market.
3. The technical documentation must allow assessment of the conformity of the product with the requirements of the Directive. It must include in particular:
- a general description of the product, including any variants planned,
- design drawings, methods of manufacture envisaged and diagrams of components, sub-assemblies, circuits, etc.,
- the descriptions and explanations necessary to understand the abovementioned drawings and diagrams and the operations of the product,
- the results of the risk analysis and a list of the standards referred to in Article 5, applied in full or in part, and descriptions of the solutions adopted to meet the essential requirements of the Directive if the standards referred to in Article 5 have not been applied in full,
- in the case of products placed on the market in a sterile condition, description of the methods used,
- the results of the design calculations and of the inspections carried out, etc.; if the device is to be connected to other device(s) in order to operate as intended, proof must be provided that it conforms to the essential requirements when connected to any such device(s) having the characteristics specified by the manufacturer,
- the test reports and, where appropriate, clinical data in accordance with Annex X,
- the label and instructions for use.
4. The manufacturer shall institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective actions, taking account of the nature and risks in relation to the product. He shall notify the competent authorities of the following incidents immediately on learning of them:

(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
(ii) any technical or medical reason connected with the characteristics on the performance of a device for the reasons referred to in subparagraph (i) leading to systematic recall of devices of the same type by the manufacturer.
5. With products placed on the market in sterile condition and Class I devices with a measuring function, the manufacturer must observe not only the provisions laid down in this Annex but also one of the procedures referred to in Annex IV, V or VI. Application of the abovementioned Annexes and the intervention by the notified body is limited to:
- in the case of products placed on the market in sterile condition, only the aspects of manufacture concerned with securing and maintaining sterile conditions,
- in the case of devices with a measuring function, only the aspects of manufacture concerned with the conformity of the products with the metrological requirements.
Section 6.1. of this Annex is applicable.
6. Application to devices in Class IIa
In line with Article 11 (2), this Annex may apply to products in Class IIa, subject to the following derogation:
6.1. where this Annex is applied in conjunction with the procedure referred to in Annex IV, V or VI, the declaration of conformity referred to in the abovementioned Annexes forms a single declaration. As regards the declaration based on this Annex, the manufacturer must ensure and declare that the product design meets the provisions of this Directive which apply to it.
ANNEX VIII
STATEMENT CONCERNING DEVICES FOR SPECIAL PURPOSES 1. For custom-made devices or for devices intended for clinical investigations the manufacturer or his authorized representative established in the Community must draw up the statement containing the information stipulated in Section 2.
2. The statement must contain the following information:
2.1. for custom-made devices:
- data allowing identification of the device in question,
- a statement that the device is intended for exclusive use by a particular patient, together with the name of the patient,
- the name of the medical practitioner or other authorized person who made out the prescription and, where applicable, the name of the clinic concerned,
- the particular features of the device as specified in the relevant medical prescription,
- a statement that the device in question conforms to the essential requirements set out in Annex I and, where applicable, indicating which essential requirements have not been fully met, together with the grounds;
2.2. for devices intended for the clinical investigations covered by Annex X:
- data allowing identification of the device in question,
- an investigation plan stating in particular the purpose, scientific, technical or medical grounds, scope and number of devices concerned,
- the opinion of the ethics committee concerned and details of the aspects covered by its opinion,
- the name of the medical practitioner or other authorized person and of the institution responsible for the investigations,
- the place, starting date and scheduled duration for the investigations,

- a statement that the device in question conforms to the essential requirements apart from the aspects covered by the investigations and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the patient.

3. The manufacturer must also undertake to keep available for the competent national authorities:
3.1. for custom-made devices, documentation allowing an understanding of the design, manufacture and performances of the product, including the expected performances, so as to allow assessment of conformity with the requirements of this Directive.
The manufacturer must take all the measures necessary to ensure that the manufacturing process produces products which are manufactured in accordance with the documentation mentioned in the first paragraph;
3.2. for devices intended for clinical investigations, the documentation must contain:
- a general description of the product,
- design drawings, methods of manufacture envisaged, in particular as regards sterilization, and diagrams of components, sub-assemblies, circuits, etc.,
- the descriptions and explanations necessary to understand the abovementioned drawings and diagrams and the operation of the product,
- the results of the risk analysis and a list of the standards referred to in Article 5, applied in full or in part, and descriptions of the solutions adopted to meet the essential requirements of this Directive if the standards referred to in Article 5 have not been applied,
- the results of the design calculations, and of the inspections and technical tests carried out, etc.
The manufacturer must take all the measures necessary to ensure that the manufacturing process produces products which are manufactured in accordance with the documentation referred to in the first paragraph of this Section.
The manufacturer must authorize the assessment, or audit where necessary, of the effectiveness of these measures.
4. The information contained in the declarations concerned by this Annex should be kept for a period of time of at least five years.
ANNEX IX
CLASSIFICATION CRITERIA I. DEFINITIONS 1. Definitions for the classification rules
1.1. 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.
1.2. Invasive devices
Invasive device
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 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.
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.
1.3. 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.
1.4. Active medical device
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.
1.5. Active therapeutical device
Any active medical device, whether used alone or in combination with other medical devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or handicap.
1.6. Active device for diagnosis
Any active medical device, whether used alone or in combination with other medical devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities.
1.7. Central circulatory system
For the purposes of this Directive, 'central circulatory system' means the following vessels:
arteriae pulmonales, aorta ascendens, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachicephalicus, venae cordis, venae pulmonales, vena cava superior, vena cava inferior.
1.8. Central nervous system
For the purposes of this Directive, 'central nervous system' means brain, meninges and spinal cord.
II. IMPLEMENTING RULES 2. Implementing rules
2.1. Application of the classification rules shall be governed by the intended purpose of the devices.
2.2. If the device is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. Accessories are classified in their own right separately from the device with which they are used.

2.3. Software, which drives a device or influences the use of a device, falls automatically in the same class.
2.4. 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.
2.5. If several rules apply to the same device, based on the performance specified for the device by the manufacturer, the strictest rules resulting in the higher classification shall apply.
III. CLASSIFICATION 1. Non-invasive devices
1.1. Rule 1
All non-invasive devices are in Class I, unless one of the rules set out hereinafter applies.
1.2. Rule 2
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,
- 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,
in all other cases they are in Class I.
1.3. Rule 3
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, unless the treatment consists of filtration, centrifugation or exchanges of gas, heat, in which case they are in Class IIa.
1.4. Rule 4
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,
- 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 in Class IIa in all other cases, including devices principally intended to manage the micro-environment of a wound.
2. Invasive devices
2.1. Rule 5
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:
- are in Class I if they are intended for transient use,
- are in Class IIa if they are 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 cavity, in which case they are in Class I,
- are in Class IIb if they are 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.
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.
2.2. Rule 6

All surgically invasive devices intended for transient use are in Class IIa unless they are:
- intended specifically to diagnose, monitor or correct a defect 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,
- reusable surgical instruments, in which case they are in Class I,
- intended to supply energy in the form of ionizing radiation in which case they are in Class IIb,
- intended to have a biological effect or to be wholly or mainly absorbed 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 hazardous taking account of the mode of application, in which they are in Class IIb.

2.3. Rule 7

All surgically invasive devices intended for short-term use are in Class IIa unless they are intended:
- either specifically to diagnose, monitor or correct a defect 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,
- or specifically for use in direct contact with the central nervous system, in which case they are in Class III,
- or to supply energy in the form of ionizing radiation in which case they are in Class IIb,
- or to have a biological effect or to be wholly or mainly absorbed in which case they are in Class III,
- or to undergo chemical change in the body, except if the devices are placed in the teeth, or to administer medicines, in which case they are in Class IIb.

2.4. Rule 8

All implantable devices and long-term surgically invasive devices are in Class IIb unless they are intended:
- to be placed in the teeth, in which case they are in Class IIa,
- to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are in Class III,
- to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class III,
- or to undergo chemical change in the body, except if the devices are placed in the teeth, or to administer medicines, in which case they are in Class III.

3. Additional rules applicable to active devices

3.1. Rule 9

All active therapeutic devices intended to administer or exchange energy are in Class IIa unless their characteristics are such that they may administer or exchange energy to or from the human body in a potentially hazardous way, taking account of the nature, the density and site of application of the energy, in which case they are in Class IIb.

All active devices intended to control or monitor the performance of active therapeutic devices in Class IIb, or intended directly to influence the performance of such devices are in Class IIb.

3.2. Rule 10

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,
- if they are intended to image in vivo distribution of radiopharmaceuticals,
- if they are intended to allow direct diagnosis or monitoring of vital physiological processes, 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.

Active devices intended to emit ionizing radiation and intended for diagnostic and therapeutic interventional radiology including devices which control or monitor such devices, or which directly influence their performance, are in Class IIb.

Rule 11

All active devices intended to administer and/or remove medicines, body liquids or other substances to or from the body are in Class IIa, unless this is done in a manner:

- that is potentially hazardous, taking account of the 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.

3.3. Rule 12

All other active devices are in Class I.

4. Special Rules

4.1. Rule 13

All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in Article 1 of Directive 65/65/EEC, and which is liable to act on the human body with action ancillary to that of the devices, are in Class III.

4.2. Rule 14

All devices used for contraception or the prevention of the transmission of sexually transmitted diseases are in Class IIb, unless they are implantable or long term invasive devices, in which case they are in Class III.

4.3. Rule 15

All devices intended specifically to be used for disinfecting, cleaning, rinsing or, when appropriate, hydrating contact lenses are in Class IIb.

All devices intended specifically to be used for disinfecting medical devices are in Class IIa.

This rule does not apply to products that are intended to clean medical devices other than contact lenses by means of physical action.

4.4. Rule 16

Non-active devices specifically intended for recording of X-ray diagnostic images are in Class IIa.

4.5. Rule 17

All devices manufactured utilizing animal tissues or derivatives rendered non-viable are Class III except where such devices are intended to come into contact with intact skin only.

5. Rule 18

By derogation from other rules, blood bags are in Class IIb.

ANNEX X

CLINICAL EVALUATION 1. General provisions

1.1. As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I under the normal conditions of use of the device and the evaluation of the undesirable side-

effects must be based on clinical data in particular in the case of implantable devices and devices in Class III. Taking account of any relevant harmonized standards, where appropriate, the adequacy of the clinical data must be based on:
1.1.1. either a compilation of the relevant scientific literature currently available on the intended purpose of the device and the techniques employed as well as, if appropriate, a written report containing a critical evaluation of this compilation;
1.1.2. or the results of all the clinical investigations made, including those carried out in conformity with Section 2.
1.2. All the data must remain confidential, in accordance with the provisions of Article 20.
2. Clinical investigations
2.1. Objectives
The objectives of clinical investigation are:
- to verify that, under normal conditions of use, the performance of the devices conform to those referred to in Section 3 of Annex I, and
- to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device.
2.2. Ethical considerations
Clinical investigations must be carried out in accordance with the Helsinki Declaration adopted by the 18th World Medical Assembly in Helsinki, Finland, in 1964, as last amended by the 41st World Medical Assembly in Hong Kong in 1989. It is mandatory that all measures relating to the protection of human subjects are carried out in the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results.
2.3. Methods
2.3.1. Clinical investigations must be performed on the basis of an appropriate plan of investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims for the device; these investigations must include an adequate number of observations to guarantee the scientific validity of the conclusions.
2.3.2. The procedures used to perform the investigations must be appropriate to the device under examination.
2.3.3. Clinical investigations must be performed in circumstances similar to the normal conditions of use of the device.
2.3.4. All the appropriate features, including those involving the safety and performances of the device, and its effect on patients must be examined.
2.3.5. All adverse incidents such as those specified in Article 10 must be fully recorded and notified to the competent authority.
2.3.6. The investigations must be performed under the responsibility of a medical practitioner or another authorized qualified person in an appropriate environment.
The medical practitioner or other authorized person must have access to the technical and clinical data regarding the device.
2.3.7. The written report, signed by the medical practitioner or other authorized person responsible, must contain a critical evaluation of all the data collected during the clinical investigation.
ANNEX XI
CRITERIA TO BE MET FOR THE DESIGNATION OF NOTIFIED BODIES 1. The notified body, its Director and the assessment and verification staff shall not be the

designer, manufacturer, supplier, installer or user of the devices which they inspect, nor the authorized representative of any of these persons. They may not be directly involved in the design, construction, marketing or maintenance of the devices, nor represent the parties engaged in these activities. This in no way precludes the possibility of exchanges of technical information between the manufacturer and the body.

2. The notified body and its staff must carry out the assessment and verification operations with the highest degree of professional integrity and the requisite competence in the field of medical devices and must be free from all pressures and inducements, particularly financial, which might influence their judgment or the results of the inspection, especially from persons or groups of persons with an interest in the results of the verifications.

Should the notified body subcontract specific tasks connected with the establishment and verification of the facts, it must first ensure that the subcontractor meets the provisions of the Directive and, in particular, of this Annex. The notified body shall keep at the disposal of the national authorities the relevant documents assessing the subcontractor's qualifications and the work carried out by the subcontractor under this Directive.

3. The notified body must be able to carry out all the tasks assigned to such bodies by one of Annexes II to VI and for which it has been notified, whether these tasks are carried out by the body itself or on its responsibility. In particular, it must have the necessary staff and possess the facilities needed to perform properly the technical and administrative tasks entailed in assessment and verification. It must also have access to the equipment necessary for the verifications required.

4. The notified body must have:

- sound vocational training covering all the assessment and verification operations for which the body has been designated,
- satisfactory knowledge of the rules on the inspections which they carry out and adequate experience of such inspections,
- the ability required to draw up the certificates, records and reports to demonstrate that the inspections have been carried out.

5. The impartiality of the notified body must be guaranteed. Their remuneration must not depend on the number of inspections carried out, nor on the results of the inspections.

6. The body must take out civil liability insurance, unless liability is assumed by the State under domestic legislation or the Member State itself carries out the inspections directly.

7. The staff of the notified body are bound to observe professional secrecy with regard to all information gained in the course of their duties (except vis-à-vis the competent administrative authorities of the State in which their activities are carried out) pursuant to this Directive or any provision of national law putting it into effect.

ANNEX XII

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

- If the marking is reduced or enlarged the proportions given in the above graduated drawing must be respected.
- The various components of the CE marking must have substantially the same vertical dimension, which may not be less than 5 mm.

This minimum dimension may be waived for small-scale devices.

APPENDIX C

Field of application of directive "active implantable medical devices"

EUROPEAN COMMISSION

DG ENTERPRISE

Directorate G

Unit 4 - Pressure Equipment, Medical Devices, Metrology

MEDICAL DEVICES : Guidance document

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GUIDELINES RELATING TO THE APPLICATION OF :
THE COUNCIL DIRECTIVE 90/385/EEC ON ACTIVE IMPLANTABLE MEDICAL DEVICES
THE COUNCIL DIRECTIVE 93/42/EEC ON MEDICAL DEVICES

FIELD OF APPLICATION OF DIRECTIVE 90/385/EEC

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INTRODUCTION

These guidelines should be read in conjunction with the Directive 90/385/EEC relating to active implantable medical devices and the Directive 93/42/EEC relating to medical devices. They provide a practical support for the uniform application of these Directives. The guidelines deal with specific issues in the context of the aforementioned Directives. They are therefore of complementary nature to the general vade-mecum relating to the application of New Approach Directives.

LIST OF CONTENTS

(*) These parts of the guidelines will be circulated as separate working documents

I. FIELD OF APPLICATION

I. 2. DIRECTIVE 90/385/EEC ON ACTIVE IMPLANTABLE MEDICAL DEVICES

The Directive 90/385/EEC covers the placing on the market and putting into service of "active implantable medical devices".

2.1. Active implantable medical device

A product falls within the field of application of the Directive if it complies with the definition given in this Directive. That means, it must be a "medical device" as defined which is, at the same time, both "active" and "implantable".

2.1.1 The "device" definition within the meaning of Directive 90/385/EEC relates to a product intended by the manufacturer for a medical purpose "whether used alone or in combination, together with any accessories or software for its proper functioning". The medical purpose may be achieved either by a "stand alone device" or as a result of several devices acting each in combination with the other as part of a system. Where the medical purpose is achieved by a system, each element of the system may be regarded as a medical device. The device definition may consequently apply to the system as such or to interchangeable parts intended to form a system together with other devices, therefore for the purposes of the Directive on Active Implantable Medical Devices each part belonging to such system is covered by the Directive regardless of whether such part on its own is "active", "active implantable" or not.

Examples of AIMDs :

a)
- *implantable pulse generator for pacing including the electrode*
- *implantable pulse generator without electrode*
- *electrode*

b)
- *implantable drug administration device with or without catheter*
- *catheter for implantable drug administration device*

2.1.2. For the purpose of the Directive 90/385/EEC a medical device is active if it "relies for its functioning on a source of electrical energy or any source of power other than that directly generated by the human body or gravity. This includes, for instance, devices activated by means of pressure unless this effect is achieved by energy resulting from the body of the patient. The definition implies that the function of the device involves using the source of power to perform useful work. The mere transmission of heat, light, pressure or vibration does not mean that a device is active.

Examples :

- *a hydrocephalus pressure relief allowing release of cerebro-spinal fluid when a spring is overcome is not "active". Even where the setting of the spring can be adjusted by electro-magnetic means, it remains non-active as the medical function of the device is to relieve pressure, <u>not</u> to be adjusted,*

- *a drug delivery device in which the drug is driven from a reservoir by means of a stored energy source (spring, fluid, gas, etc...) is "active"*
- *an intravascular cathether containing a fibre-optic bundle connected to an external light source may be used to measure pressure or other characteristics of blood if some quality of the light can be changed by the blood characteristic and detected. Although the system as a whole depends on a power source to achieve its medical function (the measurement of a blood characteristic) the invasive element is not "active" as it does no more than transmit light*
- *a cochlear implant activated by an external power transmitter is regarded as "active" as the implanted component clearly depends on a power source for its function and its purpose is to convert the power it receives into electrical signals which trigger appropriate sensory channels in the brain, i.e. it performs useful work.*

2.1.3. An active medical device is defined as "implantable" if it is "totally or partly introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain after the procedure".

The Directive has been conceived for active devices for which a potential high risk may be inherent due to the fact that they are totally or partly implanted into the body. Such devices may present hazards in particular with regard to impossibility of maintenance, calibration or control and problems relating to the ageing of materials, as mentioned in several essential requirements of Annex 1 to the Directive. The attribute "implantable" has therefore to be interpreted bearing in mind those hazards typical for implantable devices.
For the aforementioned reasons, an external drug infusion pump, although for long-term or permanent use, which is connected to a catheter "partially introduced" into the body is not considered as an active implantable device.
One of the essential characteristics of an implantable device is its relatively long-term use. Distinction is to be made between an intended use of a device which is permanent or long-term in the order of several months compared to a temporary use during a given medical intervention. An external pacemaker, including its electrode, used for an interim process is thus not considered as "remaining after the procedure". The same applies to the use of an intra-aortic balloon pump. For the purpose of the Directive 90/385/EEC, the term "procedure" is to be interpreted as a process of diagnosis, monitoring or treatment which may last for some days, generally in hospital, and not necessarily exclusively relating to an operation carried out in the theatre in the course of which the device is placed in the body.

2.2. "Accessories" to an active implantable medical device are by definition "active implantable medical devices" and therefore covered by the Directive 90/385/EEC. This does not presuppose that the attributes "active" and "implantable" must be necessarily met by a product called "accessory". It is sufficient that a product in its intended purpose is ancillary to the purpose of an active implantable medical device in such a way that it enables the device to be used in accordance with the intended device purpose or that it enhances the purpose of a device as intended by the device manufacturer.
Following this a programmer or an external transmitter intended for activating or controlling the implantable part of the device is covered by the definition of "active implantable medical device".

2.3. exemplative list of active implantable medical devices. The subsequent list contains examples of types of devices which are normally covered by Directive 90/385/EEC :

1. implantable cardiac pacemakers
2. implantable defibrillators
3. leads, electrodes, adaptors for 1. and 2.
4. implantable nerve stimulators
5. bladder stimulators
6. sphincter stimulators
7. diaphragm stimulators
8. cochlear implants
9. implantable active drug administration device

10. catheters, sensors for 9.
11. implantable active monitoring devices
12. programmers, software, transmitters.

APPENDIX D

Treatment of computers used to program implantable pulse generators

EUROPEAN COMMISSION
DG ENTERPRISE
Directorate G
Unit 4 - Pressure Equipment, Medical Devices, Metrology

MEDICAL DEVICES : Guidance document

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GUIDELINES RELATING TO THE APPLICATION OF :

THE COUNCIL DIRECTIVE 90/385/EEC ON ACTIVE IMPLANTABLE MEDICAL DEVICES

THE COUNCIL DIRECTIVE 93/42/EEC ON MEDICAL DEVICES

TREATMENT OF COMPUTERS USED TO PROGRAM

IMPLANTABLE PULSE GENERATORS

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Purpose of the document

Identify the cases where commercially available computers should not be considered as medical devices.

Background

- Implantable pulse generators (IPG) and Defibrillators (ICD) fall into the scope of the AIMD Directive 90/385/EEC.

- Equipment specifically designed to program these implanted AIMD's are accessories of AIMD's. Therefore, they fall also into the scope of the above mentioned directive.

Commercially available computers are being used more and more as programmer for IPG's.

The Guidelines on medical classification specify that "multi-application equipment which may be used in combination with medical devices are not a medical device unless its manufacturer places it on the market with specific intended purpose of a medical device".

The definition of a medical device in the AIMD Directive is as follows:

"Medical device means any instrument, apparatus, appliance, material or other article, whether used alone or in combinations, together with any accessories or software for its proper functioning, intended by the manufacturer to be used for human being in the ..."

Definition of "intended use" (EC Directive 93/42/EEC):

"The intended use 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 promotional materials".

Definition of the system

The system allowing communication with the implantable parts of the AIMD is usually constituted as follows:

- a commercially available computer

- a wand (part of the system in contact with the patient from one side and connected to the computer on the other side. This part of the system may also include an interface module which, among other functions, provides electrical isolation between computer and wand).

- Software used to program the implantable parts of the AIMD.

Handling of the system

Manufacturers have the freedom

- either to consider the system as a whole and to affix the CE marking on the whole system

- or to consider each part of the system and to affix the CE marking on each part of the system.

Regulatory Status of the computer

A. The computer is a medical device in the following cases:

- the computer bears the trade name of the IPG manufacturer
- the original information provided with the computer has been replaced or modified
- modifications have been made to the software or hardware of the computer. These modifications have not been made according to the instructions provided by the manufacturer of the computer.

Note: For the purpose of this document it is understood that the insertion of a circuit board to an available PMCIA slot is not considered as a modification of the software as long as the insertion is performed in accordance with the computers manufacturer's instructions for use.

B. The computer is not a medical device in the following cases:

- The wand is connected to an existing port located usually on the back of the computer.

- The wand is connected to a dedicated circuit board to be inserted into an available PCMCIA slot accessible from the outside of the computer or located inside the computer.

The board is inserted into the computer according to the instructions given by the computer manufacturer and/or the board manufacturer.

Conformity assessment procedures when each part is considered separately.

- Wand, equipment which makes the link between the patient and the computer, dedicated programming software (program module, memory card or diskette) are AIMD's.

  Therefore they must satisfy all applicable essential requirements of the AIMD directive and bear the CE marking.

- The computer if not considered as a medical device should comply with applicable national regulations and as of January 1st, 1996 must bear the CE marking of conformity with the EMC directive.

The applicable standards are IEC 950 as well as the relevant EMC harmonized standards adopted by CENELEC and published in the Official Journal of the European Communities.

In this case the manual of the software of the wand dedicated for use with the computer must indicate either the characteristics of the computer required or some types of equipment (trade name and model) available on the market with which it can be used. The computer in this case shall not bear the CE marking of conformity with the AIMD.

- The computer if considered as a medical device, falls into the scope of the AIMD directive and therefore shall meet all the applicable essential requirements and be subject to the appropriate conformity assessment procedure. The computer shall bear the CE marking of conformity with the AIMD directive.

- Irrespective of the fact the computer is considered as a medical device or not, the manufacturer shall demonstrate that the system (wand + computer) is safe for the patient and the user.

- In order to avoid possible confusion between the AIMD and the EMC directive, the manual of the computer shall indicate the directive applied.

Conclusion

Unless the IPG/ICD manufacturer modifies its original intended purpose or affixes its trade name, commercially a available computers shall not be considered as medical device. Therefore the computer shall not be subject to the requirements of the AIMD directive.

APPENDIX E

Interface with other directives – Medical devices/medicinal products

EUROPEAN COMMISSION
DG ENTERPRISE
Directorate G
Unit 4 - Pressure Equipment, Medical Devices, Metrology

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GUIDELINES RELATING TO THE APPLICATION OF :
THE COUNCIL DIRECTIVE 90/385/EEC ON ACTIVE IMPLANTABLE MEDICAL DEVICES
THE COUNCIL DIRECTIVE 93/42/EEC ON MEDICAL DEVICES

DEMARCATION BETWEEN : - DIRECTIVE 90/385/EEC ON ACTIVE IMPLANTABLE MEDICAL DEVICES - DIRECTIVE 93/42/EEC ON MEDICAL DEVICES

AND - DIRECTIVE 65/65/EEC RELATING TO MEDICINAL PRODUCTS

AND -- RELATED DIRECTIVES

Foreword

The present Guidelines are part of a set of Guidelines relating to questions of application of EC-Directives on medical devices. They are legally not binding. The Guidelines have been carefully drafted through a process of intensive consultation of the various interested parties (Competent Authorities, Commission services, industries and other interested parties in both the medical devices and the medicinal products sectors) during which intermediate drafts were circulated and comments were taken up in the document. Therefore this document reflects positions taken in particular by the aforementioned interested parties.

Due to the participation of the aforementioned interested parties and of experts from Competent Authorities, it is anticipated that these guidelines will be followed within the Member States and, therefore, ensure uniform application of relevant Directive provisions.

Note: This document is a revision of an earlier document published in July 1995 as MEDDEV 14/93 Rev. 4

A. DEMARCATION BETWEEN MEDICAL DEVICES DIRECTIVES AND MEDICINAL PRODUCTS DIRECTIVES

A.1 Introduction

The determination of the borderline between the Medical Devices Directive 93/42/EEC (MDD) (OJ No.L 169, 12/7/93), the Active Implantable Medical Device Directive 90/385/EEC (AIMD) (OJ No. L189, 20/7/90) and the Medicinal Products Directive 65/65/EEC (MPD) including related directives, was one of the issues discussed at some length during the legislative procedure on the MDD. Therefore, in the MDD several provisions to establish the demarcation between both legal regimes have been laid down. It was recognised that the subject needs to be further explained and illustrated by practical guidance and examples. The present document has no legal force. It has nevertheless been elaborated by an expert group including experts from Member States' competent authorities for both medical devices and medicinal products, the European Commission, as well as industry trade associations. It is therefore intended that the document will provide useful guidance which should assist common positions to be taken throughout the European Union.

For the relevant definitions and legal requirements reference is made to:

Directive 93/42/EEC **MDD**	**Directive 65/65/EEC** **MPD**	**Medicinal Products** **Extension Directives**
Article 1 (2a): "medical device"	Article 1(3) : medicinal product	Directive 89/343/EEC relating to radiopharmaceuticals
Article 1 (3): "drug delivery devices"		Directive 89/342/EEC relating to immunological products
Article 1 (4): "devices incorporating medicinal substances with ancillary action"		Directive 89/381/EEC relating to blood products

A.2 General principles

As a general rule a relevant product is regulated either by the MDD or by the MPD. The authorization or conformity assessment procedure to be followed prior to placing a given product on the market will therefore be governed either by the MDD/AIMD or by the MPD. Normally the procedures of both directives do not apply cumulatively. For defined features, however, some cross-references are made within one regime to specific provisions of the other regime (see Article 1(4) in conjunction with Annex I, section 7.4 MDD; Article 1(3) MDD).

The definitions of medical device and medicinal product are reproduced here for reference.

Medical device (93/42/EEC)
"Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used on human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,

and which does 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;"

Medicinal product (65/65/EEC)
"Any substance or combination of substances presented for treating or preventing disease in human beings or animals.
Any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or in animals is likewise considered a medicinal product."

In order to decide which regime applies, the following criteria should be examined:

Step 1 The intended purpose of the product taking into account the way the product is presented (this is likely to establish if either the MDD or the MPD apply, rather than distinguish between the two regimes),
Step 2 The method by which the principal intended action is achieved.

The latter criterion, based on the "principal intended action" is crucial in the definition of a medical device. Typically the medical device function is fulfilled by physical means (including mechanical action, physical barrier, replacement of or support to organs or body functions, ...). The action of a medicinal product is generally achieved by pharmacological, immunological means or by metabolism.

The principal intended action of a product may be deduced from:

- the manufacturer's labelling and claims,
- scientific data regarding mechanism of action.

Although the manufacturer's claims are important, it is not possible to place the product in one or other category in contradiction with current scientific data. Manufacturers may be required to justify scientifically their rationale for classification of borderline products.

"Pharmacological means", in the context of the MDD and AIMD, is understood as an interaction between the molecules of the substance in question and a cellular constituent, usually referred to as a receptor, which either results in a direct response, or which blocks the response to another agent. Although not a completely reliable criterion, the presence of a dose-response correlation is indicative of a pharmacological effect.

"Immunological means", in the context of the MDD and AIMD, is understood as an action in or on the body by stimulation and/or mobilisation of cells and/or products involved in a specific immune reaction.

"Metabolic means", in the context of the MDD and AIMD, is understood as an action which involves an alteration, including stopping, starting or changing the speed of the normal chemical processes participating in, and available for, normal body function.

The fact that a product is itself metabolised does not imply that it achieves its principal intended action by metabolic means.

Medical devices may be assisted in their function by pharmacological, immunological or metabolic means, but as soon as these means are not any more ancillary with respect to the principal purpose of a product, the product becomes a medicinal product. The claims made for a product, in accordance with its method of action may, in this context, represent an important factor for its classification as medical device or medicinal product.

These principles are illustrated by bone cements and related products which appear in several of the following sections. Plain bone cement without antibiotics is a medical device since it achieves its primary intended purpose (the fixation of a prosthesis) by mechanical means. Bone cements containing antibiotics, where the principal intended purpose remains fixation of a prosthesis, are also medical devices. In this case the action of the antibiotic, which is to reduce the possibility of infection being introduced during surgery, is clearly ancillary. If however the principal intended purpose is to deliver the antibiotic, the product would be a medicinal product.

These principles are subject to certain exemptions as a consequence of which a number of products fall within the definition of "medicinal product", even if they fulfil their function by physical or chemical means, and not by pharmacological, immunological or metabolic means in the sense as described above. This applies, in particular, to antacids, in-vivo diagnostics, and to the products listed in A.4.2 which are "administered to human beings with a view to making a medical diagnosis" or to fulfil another purpose as indicated in the medicinal product definition. Unlike products which, in the absence of Community medical device legislation, had been assimilated to national medicinal product law and which are now regulated by MDD/AIMD (reclassification will take place in those Member States during the transitional period), the grouping as referred to in A.4.2 has been regarded throughout the EU as medicinal products within the meaning of Directive 65/65/EEC. The status of these products as medicinal products is retained as specified under A.4.2

A.3 Examples of medical devices

3.1 The following examples should, in view of their mode of action, generally be considered as medical devices subject to relevant criteria being met; the function of some of the devices indicated in these examples, e.g. bone cement, may be assisted by the presence of medicinal substances where such substances have an ancillary action to that of the device (see also A.5).

- bone cement (see A.5 and A.6),
- dental filling materials (see A.5 and A.6),
- materials for sealing, approximation, or adhesion of tissues (e.g. cyanocrylates, fibrin-based adhesives not of human origin),
- resorbable materials used in osteo-synthesis (e.g. pins or bone screws manufactured using polylactic acid),
- sutures, absorbable sutures,
- soft and hard tissue scaffolds and fillers (e.g. collagen, calcium phosphate, bioglass),
- bone void fillers intended for the repair of bone defects where the primary action of the device is a physical means or matrix, which provides a volume and a scaffold for osteoconduction (see A5 and A6),
- intrauterine devices (see A.5 and A.6),
- blood bags (see A.5),
- systems intended to preserve and treat blood (see A5),

Note : systems intended for the collection, storage and preservation of blood or blood components and as an ancillary function, the treatment of blood or blood components where this effect is achieved outside the human body, are classified as devices provided that any residual material is not intended to achieve its intended effect when the blood or cells are reintroduced into the body, e.g. systems incorporating chemicals activated by light to reduce the viral load where the quantity of chemical remaining has no intended effect when transfused.

This note does not cover substances introduced into an extracorporal circuit.

- viscoelastic materials with intended use for mechanical/physical purposes such as protection of tissues during and after surgery and separation of tissues. Such materials are also used as synovial fluid replacements where visco-supplementation provides support and lubrication.

Note : Additional pharmacological benefits claimed which are ancillary to the mechanical action do not alter the medical device status. However, certain of these materials such as some hyaluranon based products, where the predominant claims are of a pharmacological nature and not primarily related to any viscoelastic characteristics, are classed as medicinal products,

- gases and liquids for ocular endotamponades,
- cell separators, including those incorporating antibodies for cell marking,
- wound dressings, which may be in the form of liquids, gels and pastes, etc (e.g. hydrocolloid, hydrogel), (see A.4 and A.5),
- haemostatic products, for example patches, plugs and powders where the haemostatic effect results from the product's physical characteristics, or is due to the surface properties of the material. This includes products such as those containing collagen, or calcium alginate or oxidised cellulose where adhesion of platelets to the surface triggers platelet adhesion and aggregation (see A.4 and A.5).
- concentrates for haemodialysis,
- pressure reducing valves and regulators,
- irrigation solutions (including those used in the eye) intended for mechanical rinsing (see A5)

Note: If the solution contains a medicinal substance such as chlorhexidine where the principal intended purpose is to provide a local antimicrobial effect, it will be a medicinal product. Solutions incorporating substances for other purposes, e.g. antimicrobial agent for the preservation of the solution remain a medical device.

- devices such as catheters, guidewires and stents containing or incorporating radio isotopes where the radioactive isotope as such is not released into the body, used for example in cardiology for the prevention of restenosis.

3.2 The following products are covered by the MDD because they fall under the definition of "accessory". This is the case if they are intended specifically to be used together with a device to enable the device to be used in accordance with its intended purpose or to enhance the performance of the device.

- contact lens care products (disinfecting, cleaning, rinsing and hydrating solutions including those which aid the insertion and/or wearing of contact lenses without a therapeutic claim),
- disinfectants specifically intended for use with medical devices (e.g. endoscopes),

Note: Multipurpose disinfectants or sterilisation agents are not covered by MDD; they will be covered by the directive on biocides.

- lubricants specifically intended for use together with medical devices (e.g. for gloves, endoscopes, condoms),
- skin barrier powders and pastes or other skin care products specifically intended for use together with ostomy bags,
- challenge tests specifically intended to assess the tolerance to a given medical device, or its constituents (e.g. injectable collagen).
- gases used to drive cryoprobes and surgical tools (see A4)

A.4 Examples of medicinal products

The following examples should generally be considered as medicinal products subject to relevant criteria being met :

4.1. Products which fulfil their primary intended purpose by pharmacological, immunological or metabolic means,

- spermicidal preparations,
- gases intended to be used in anaesthesia and inhalation therapy, (e.g. Oxygen, medical air supplied in containers) including their primary containers,

Note: These gases are also used in minimal access surgery. However a product *intended* exclusively for minimal access surgery would be a medical device.

- topical disinfectants (antiseptics) for use on patients,
- haemostatic agents where primary mode of action is not mechanical such as certain collagens which have a molecular structure capable of a surface-independent demonstrated interaction with platelet receptors, and which achieves platelet adhesion through a pharmacological process.
- zinc paste for dermatological use

4.2. The following products are assimilated to medicinal products and therefore dealt with in accordance with 65/65/EC as medicinal products:

- water for injections, IV fluids and plasma volume expanders,
- haemofiltration substitution solutions,
- in vivo diagnostic agents, e.g. x-ray contrast media, NMR enhancing agents, fluorescent ophthalmic strips for diagnostic purposes, carrier solutions to stabilize micro-bubbles for ultrasound imaging,
- gases for in-vivo diagnostic purposes, including lung function, tests, e.g. carbon dioxide for vascular diagnostic purposes,
- solutions for peritoneal dialysis,
- antacids,
- artificial tears,
- fluoride dental preparations,

Note: Dental preparations with a typical device mode of action, such as cements or varnishes incorporating fluoride, are medical devices, where the fluorine is of ancillary action to that of the device. Certain products where the claims are primarily cosmetic in nature and where the fluorine level is less than 0.15% are cosmetic products (see 76/768/EEC and amending Directives).

- solutions administered in-vivo to the local circulation for the cooling of organs during surgery;

It should be noted that the Directive 89/343/EEC relating to radiopharmaceuticals applies also to generators, that means any system incorporating a fixed parent radionuclide the daughter radionuclide of which is to be removed by elusion or by any other method and used in a radiopharmaceutical (see article 1(2) of Directive 89/343/EEC).

4.3. Agents for transport, nutrition and storage of organs intended for transplantation,

Note: These products are not currently regulated in all Member States as medicinal products. However there was general consensus of public authorities that the medicinal products category is the most appropriate. Some of these products may have a metabolic effect, others however have no such effects.

A.5 Medical devices incorporating a medicinal substance with ancillary action

It follows from the definition of a medical device that devices may incorporate substances as an integral part which, if used separately, may be considered to be a medicinal product. This is specifically addressed in article 1(4) MDD which makes it clear that such products are devices, provided that the action of the medicinal substance is ancillary to that of the device, as reflected in the product claim and as supported by the scientific data provided by the manufacturer of the devices.

Examples of such devices are:

- catheters coated with heparin or an antibiotic agent,
- bone cements containing antibiotic (see A.3 and A.6),
- root canal fillers which incorporate medicinal substances with secondary action (see A.3 and A.6),
- blood bags containing anticoagulant or preservation agents (see A.3),

  Note : rule18 of Annex IX of the MDD applies to these products.

- soft tissue fillers incorporating local anaesthetics,

- bone void filler intended for the repair of bone defects where the primary action of the device is a physical means or matrix, which provides a volume and a scaffold for osteoconduction and where an additional medicinal substance is incorporated to assist and complement the action of the matrix by enhancing the growth of bone cells. In such cases, the ancillary nature would be determined by the performance of the matrix on its own and the extent of the enhancement of growth due to the presence of the substance. With reference to the overall purpose of the product, where the medicinal substance has such an effect that its ancillary nature cannot be clearly established, then the product should be considered in accordance with the concept of a drug delivery system (see section A6.2),
- haemostatic devices enhanced by the incorporation of collagen, where the primary action of the device is mechanical even though there may be ancillary action due to the presence of collagen having demonstrable action with platelet receptors resulting in platelet adhesion through a pharmacological process (see also A.3 and A.4),
- condoms coated with spermicides,
- electrodes with steroid-coated tip,
- wound dressings, surgical or barrier drapes (including tulle dressings) with antimicrobial agent (see A.6),
- intrauterine contraceptives containing copper or silver,
- ophthalmic irrigation solutions principally intended for irrigation which contain components which support the metabolism of the endothelial cells of the cornea (see A3).

It should be noted that the mere coating of a product with a chemical does not imply that the chemical is a medicinal substance. For example, hydroxyapatite, frequently used as coating for orthopaedic and dental implants, is not considered a medicinal substance. Other coatings which are in use and which are not medicinal substances are hydromers and phosphorylcholines.

Note : For the time being, products incorporating medicinal substances of human origin are excluded from the MDD.

A.6 Drug delivery system

6.1. The status of devices for drug delivery is addressed by article 1(3) MDD. A device which is intended to deliver a medicinal product is itself regulated as a medical device. The medicinal product which the device is intended to administer must, of course, be approved according to the normal procedures for medicinal products.

Examples :

- drug delivery pump,
- implantable infusion pump,
- iontophoresis device,
- nebulizer,
- syringe, jet injector.

Note: in a kit comprising an insulin pen and insulin cartridges, the pen is subjected to the MDD whereas the insulin cartridge is a medicinal product.

- spacer devices for use with metered dose inhalers,
- port systems.

6.2. However, if the device and the medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single product is regulated as a medicinal product (article 1(3), second subparagraph MDD). Examples of such products are :

- prefilled syringes,
- aerosols containing a medicinal product,
- nebulizers precharged with a specific medicinal product, and not for universal application,
- patches for transdermal drug delivery,
- implants containing medicinal products in a polymer matrix whose primary purpose is to release the medicinal product, for example plastic beads containing antibiotic for treating bone infections, or a matrix to release osteoinductive proteins into the surrounding bone (see also A5)
- intrauterine contraceptives whose primary purpose is to release progestogens,
- single-use disposable iontophoresis devices incorporating a medicinal product,
- wound treatment products comprising a matrix whose primary purpose is the administration of medicinal products, (see A.3 and A.5), for example wound dressings containing an antimicrobial agent where the primary action of the dressing is to administer the agent to the wound for the purpose of controlling infection,
- temporary root canal fillers incorporating medicinal products, whose primary purpose is to deliver the medicinal product (see A.3 and A.5).

In such cases the essential requirements of the MDD apply as far as the device related features of the product are concerned (for example as regards the mechanical safety features of a prefilled syringe). The labelling, however, should comply with the requirements of Directive 92/27/EEC applicable to medicinal products.

B. THE CONSULTATION PROCESS FOR DEVICES INCORPORATING A MEDICINAL SUBSTANCE HAVING ANCILLARY ACTION

B.1 Purpose of the consultation procedure

When referring to the appropriate essential requirement in the MDD - Annex 1, section 7.4 -, a Notified Body so concerned has a responsibility to address this requirement by "consulting one of the competent bodies established by the Member States in accordance with Directive 65/65/EEC before taking a decision" (MDD: Annex II section 4.3 and Annex III section 5).

The term "Competent Authority" is used in this document to represent such a competent body within the meaning of Directive 65/65/EEC, and indicates the authority responsible for the evaluation of application for medicinal products being placed on the market (see Annex for list of appropriate Competent Authorities).

In Essential Requirement 7.4 the expression "substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 65/65/EEC..." is used. This reflects the fact that in such cases, neither the device incorporating a medicinal substance nor the substance in itself is a medicinal product as defined in Directive 65/65/EEC. This requirement relates to substances which, otherwise, in the context of medicinal products may be an active constituent of a medicinal product and therefore be liable to act upon the body.

It is for this reason that the verification by the Competent Authority of the safety, quality and usefulness of the "medicinal substance" is to be carried out by analogy with the appropriate methods specified in Directive 75/318/EEC as amended by Directive 91/507/EEC.

The assessment of "usefulness" and "safety" has a particular implication when applied to a medicinal substance which is of ancillary purpose within a device/medicinal substance combination.

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.

By means of the consultation process the competent authority may make available relevant information concerning risks related to the use of the substance (e.g. resulting from pharmacovigilance).

The ultimate responsibility for the decision, as to whether the pertinent legal requirements are met, belongs to the Notified Body.

The consultation process is only applicable for devices incorporating a medicinal substance as specified in Annex 1, section 7.4 and only where the substance is liable to act upon the body with action ancillary to that of the device. Therefore, a contact lens solution containing an antiseptic agent where the purpose of the antiseptic is to preserve the solution does not fall under this procedure.

In line with Article 22(3) of the MDD, for a device which has already been granted a marketing authorisation as a medicinal product in at least one Member State the consultation procedure will be limited to a simple exchange of letters between the Notified Body and Competent Authority, provided the product is unchanged in all respects, including the information provided with the device.

B.2 Notified Body actions to initiate consultation process

a) The Notified Body should ensure that data supplied by the manufacturer in relation to the device and its intended use includes a specific segment regarding the medicinal substance being incorporated with ancillary purpose. Presentation of the data according to the format of the "Notice to Applicants" may facilitate the review by the Competent Authority Ref:("The Rules governing medicinal products", volume 2B)

b) This segment should include data concerning the safety, usefulness and quality of the medicinal substance, also appropriate details regarding information to be supplied with the device when placed on the market to permit the evaluation of the aforementioned features.

c) Before consulting a relevant Competent Authority the Notified Body should have come to a preliminary opinion regarding the suitability of the device with ancillary medicinal substance.

d) It is at the discretion of the Notified Body to choose the Competent Authority with whom he consults from the listed Competent Authorities as indicated in the annex. The European Medicines Evaluation Agency (EMEA) may be consulted, where the substance involved has been included in a medicinal product which has been evaluated by the EMEA.

e) The Notified Body may consider it of benefit to utilise, for the consultation, the appropriate Competent Authority previously responsible for a marketing authorisation for a medicinal product which incorporates the medicinal substance involved in the consultation process.

B.3 Documentation to be provided by the Notified Body to the competent authority for medicinal products

Because of the wide range of medical devices which incorporate medicinal substances, a flexible approach to the data requirements is necessary. Nevertheless the information should be based in principle, to the extent relevant, on the annex to Directive 91/507/EEC, which modifies Directive 75/318/EEC, as outlined in (a) to (q) below. It is envisaged that, where well-known medicinal substances for established purposes are involved, all aspects of safety and usefulness may not be required and many of the headings will be addressed by reference to the literature, including standard textbooks, experience and other information generally available. Nonetheless all headings should be addressed.

For new active substances and for known medicinal substances in a non-established purpose, comprehensive data is required to address items (a) to (q) below. The evaluation of such active substances would be performed in accordance with the principles of evaluation of new active substances. The principal headings of Directive 91/507/EEC are given below, together with comments on their applicability to medical devices. This represents a comprehensive checklist covering headings which may be appropriate depending on the circumstances relating to the case in question.

a) General information

A general description of the medical device including the manufacturer's claim regarding the purpose of the inclusion of the substance, together with a critical appraisal of the results of the risk analysis.

b) Qualitative and quantitative particulars of the constituents

A description of the substance and the amount (giving a range where appropriate) of the medicinal substance incorporated into each medical device. If the substance is modified during its incorporation into the device, relevant information shall be provided.

c) Description of method of manufacture

An overall description will already form part of the application to the Notified Body; the section dealing with incorporation of the medicinal substance in the device should be provided.

d) Controls of starting materials

The specification for the medicinal substance shall be provided. Where applicable, reference shall be to the European Pharmacopoeia or in the absence of an EP monograph to a national pharmacopoeia of one of the Member States. If no monograph is available from the Member States reference may be to other national monographs or to the manufacturer's specification and methods of analysis.

For new active substances and certain known substances additional information will be required which may be provided in the form of a Drug Master File. The guideline "Requirements in relation to active substances"[1] may be of assistance in providing circumstances where reference to a Pharmacopoeia monograph may need to be supplemented by further information.

e) Control tests carried out at intermediate stages of the manufacturing process of the medical device

This information is only necessary if it is directly relevant to the quality of the substance as incorporated in the medical device.

f) Control tests on finished product

Qualitative and quantitative tests carried out to control the medicinal substance in the device.

g) Stability

Information defined to show the medicinal substance maintains its desired function throughout the defined shelf-life of the device, taking account of the manufacturer's recommended storage conditions.

h) Toxicity

Reference to the known toxicological profile of the medicinal substance may be provided. In the case of new active substances, the results of toxicity tests, should be supplied. This may include information on toxicity and biocompatibility of the medical device which may be available from evaluation in accordance with the EN 30993 series of standards.

i) Reproductive function

Similar considerations to h) apply.

Sincerely yours, [1] *In "The Rules Governing Medicinal Products in the European Community, Volume III Addendum II".*

j) Embryo/foetal and perinatal toxicity
Similar considerations to (h) apply.

k) Mutagenic potential
Similar considerations to h) apply.

l) Carcinogenic potential
Similar considerations to h) apply. The need for data on carcinogenicity should be addressed taking account of available information on the medicinal substance, the results of genotoxicity testing, the chemical structure of the medicinal substance, and the duration of potential exposure to the substance.

m) Pharmacodynamics
This section should address the intended action of the medicinal substance in the context of its incorporation into a medical device.

n) Pharmacokinetics
It is anticipated that pharmacokinetic studies will not be required in the majority of cases. Some or all of the following areas may need to be addressed as appropriate:

- description of the pattern of local and systemic exposure to the medicinal substance,
- where the level of exposure fluctuates, the maximum level and duration of exposure should be considered,
- where it is considered possible that potential levels of systemic exposure may present a safety concern, maximum peak plasma concentration should be established, taking due consideration of individual variability,
- new active substances will require information on the release from the device, and, if relevant, its subsequent distribution and elimination.

o) Local tolerance
This is of particular relevance since the route of exposure to the medicinal substance may be different from its conventional application. The relevant results of device testing according to EN 30993 should be provided or, where appropriate, information from the scientific literature

p) Clinical documentation
Since the devices will normally be class III, clinical data will form part of the information provided to the Notified Body under annex II or III. This data will address the safety of the device in its entirety. The usefulness of the medicinal substance in the medical device should be addressed by clinical data or in other sections of the dossier.
An appropriate methodology for clinical investigations on medical devices is described in EN 540.

q) Labelling
Details supplied by the manufacturer of labelling or information to be provided with the device with regard to the medicinal substance, is to be supplied to the Competent Authority to assist in the understanding of the safety and usefulness of the substance together with the device.

B.4 The consultation process

a) The Notified Body, having requested a Competent Authority to provide an opinion concerning the medicinal substance and its application, should, together with the Competent Authority, agree such matters as: time-schedules, modalities to obtain further information, including clock stops, fees and practical arrangements for submission of data.

b) The Notified Body should make available to the Competent Authority relevant data as specified in B.3.

c) The Competent Authority should verify the data provided by the Notified Body. It should consider the use of the medicinal substance by analogy with existing information regarding the known applications and appropriate features of safety, quality and usefulness as they may be relevant to the specific intended purpose of the device incorporating the medicinal substance.

d) The Competent Authority should inform the Notified Body of its conclusions and advice as to the suitability of the medicinal substance in its proposed use.

e) The Notified Body should take into account the opinion of the Competent Authority and use its judgement to either approve the drug/device combination, after consideration of all aspects of risk/benefit in the intended or expected use of the product, or alternatively to reject the product. It may be that certain suggestions from the Competent Authority may be adopted by the manufacturer to render the product acceptable.

f) The Notified Body should inform the Competent Authority which was consulted of the decision reached by the Notified Body, and where this decision deviates from the opinion provided by the Competent Authority this will be shown. Where a Notified Body receives a negative opinion from the Medicinal Product Competent Authority, they should consult with the device Competent Authority before issuing a certificate.

g) During the consultation process the Notified Body concerned may withdraw the request and ask for the opinion of an alternative relevant Competent Authority. In this case, the previously consulted Competent Authority should be informed of the name of the new Competent Authority.

C. CONSULTATION BY COMPETENT AUTHORITIES FOR MEDICINAL PRODUCTS WITH REGARD TO MEDICINAL PRODUCTS WITH DEVICE RELATED FEATURES.

In accordance with Article 1(3) second subparagraph MDD, products placed on the market in such a way that a device and a medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single product shall be governed by Directive 65/65/EEC. In such cases the relevant essential requirements of Annex I MDD shall apply with regard to safety and performance related device features. Examples of such products are listed in A.6.2).

In such cases Competent Authorities responsible for the evaluation of the medicinal products in question would consult, if necessary, one of the Competent Authorities or Notified Bodies for medical devices. This consultation would cover the essential requirements of Annex I MDD for the relevant device features.

D. PROCEDURES FOR THE REPORTING OF ADVERSE INCIDENTS

The classification of the product, medicinal product or medical device, will determine which procedure should be followed for the reporting of an adverse incident; medicinal products to meet the requirements for pharmacovigilance and medical devices (including those referenced under section A5) to meet the requirements for medical device vigilance.

Note : guidelines are available on a medical device vigilance system (ref. MEDDEV. 2.12/1). Guidelines are available on a pharmacovigilance system.

A report should be made to a relevant authority and the authorities will liase as necessary.

LIST OF ADDRESSES OF COMPETENT AUTHORITIES FOR MEDICINAL PRODUCTS

COUNTRIES	ASSOCIATIONS	ADRESSES	PHONE	FAX
EUROPEAN UNION	European Medicines Evaluation Agency	7 West Ferry Circus, Canary Wharf; UK-London EO14 4HB	44/171/418.84.00	44/171/418.84.16
AUSTRIA	Bundesministerium für Arbeit, Gesundheit und Soziales, Gruppe VIII/C	Stubenring, 1 ; A-1010 Wien	43/1/71172-4673 (4674)	43/1/714.92.22
BELGIUM	Farmaceutische Inspectie	Rijksadministratief Centrum, Vesaliusgebouw; B-1010 Brussel	32/2/210.48.96	32/2/210.49.22
DENMARK	Danish Medicines Agency	Frederikssundsvej, 378; DK-2700 Brønshøj	45/44/889.111	45/44/917.373
GERMANY	* Bundesinstitut für Arzneimittel und Medizinprodukte * For blood products : Paul-Ehrlich-Institut, Bundesanstalt für Sera und Impfstoffe	Seestrasse 10-11, Postfach 33 00 13; D-14191 Berlin Postfach 1740; D-63207 Langen	49/30/4548-30 49/6103/770	49/30/4548-3207 49/6103/770123 oder 124
SPAIN	Direccion General Farmacia y Productos Sanitarios; Ministerio de Sanidad y Consumo	Paseo del Prado 18-20; E-28071 Madrid	34/1/596.40.15-16	34/1/596.40.69 (596.15.47) (596.15.48)
FINLAND	National Agency for Medicines, Pharmacological Department	Mannerheimintie 166; PO Box 55; FIN-00301 Helsinki	358/9/396.750	358/9/714.469
FRANCE	Agence du Médicament; Direction de l'Evaluation	143/145 Bd Anatole France; F-93200 Saint Denis	33/1/48.13.21.57	33/1/48.13.24.75 (48.13.20.98)
GREECE	E.O.F. (National Drug Organisation)	Mesogion 284; GR-155 62 Holargos	30/1/652.62.16	30/1/654.55.35
IRELAND	Irish Medicines Board	The Earlsfort Centre, Earlsfort Terrace IRL-Dublin 2	353/1/676.49.71(7)	353/1/676.84.90
ITALY	Direzione Generale del Servizio Farmaceutico - Ministero della Sanità	Viale della Civiltà Romana, 7 I-00144 Roma EUR	39/6/592.58.63	39/6/599.441.17
LUXEMBOURG	Direction de la Santé; Division de la Pharmacie et des Médicaments	10, rue C.M. Spoo L-2546 Luxembourg	352/478.55.93	352/224.458
NETHERLANDS	College ter beoordeling van geneesmiddelen, Ministerie van Welzijn, Volksgezondheid en Cultuur	Postbus 5811 NL-2280 HV Rijswijk (ZH)	31/70/340.72.10	31/70/340.51.55
PORTUGAL	INFARMED - Instituto Nacional da Farmacia e do Medicamento	Parque de Saùde de Lisboa; Av. do Brasil, 53 P- 1700 Lisboa	351/1/790.85.00 (795.78.36)	351/1/795.91.16
SWEDEN	Medical Products Agency	Husarg, 8; S-75103 Uppsala	46/18/174.691	46/1/548.566
UNITED KINGDOM	Medicines Control Agency; Department of Health	1 Nine Elms Lane; UK-London SW8 5NQ	44/171/273.02.00	44/171/273.04.93

APPENDIX F

Medical devices with a measuring function

EUROPEAN COMMISSION
DG ENTERPRISE
Directorate G
Unit 4 - Pressure Equipment, Medical Devices, Metrology

MEDICAL DEVICES : Guidance document

MEDDEV 2. 1/5

June 1998

GUIDELINES RELATING TO THE APPLICATION OF :

THE COUNCIL DIRECTIVE 90/385/EEC ON ACTIVE IMPLANTABLE MEDICAL DEVICES

THE COUNCIL DIRECTIVE 93/42/EEC ON MEDICAL DEVICES

MEDICAL DEVICES WITH A MEASURING FUNCTION

--- (())---

Background

Annex VII, paragraph 5 of MDD requires for class I devices with a measuring function that the manufacturer must also follow one of the procedures referred to in annex IV, V or VI, for the «aspects of manufacture concerned with the conformity of the products with the metrological requirements ».

It is therefore necessary to specify criteria for the existence of a « measuring function » in a medical device.

Criteria for devices with a measuring function

The following criteria, if fulfilled together, indicate that a device has a measuring function:

a) **<u>The device is intended by the manufacturer to measure</u>:**

- quantitatively a physiological or anatomical parameter, or
- a quantity or a qualifiable characteristic of energy or of substances delivered to or removed from the human body.

b) **<u>The result of the measurement</u>**

- is displayed in legal units or other acceptable units within the meaning of Directive 80/181/ECC[1] or
- is compared to at least one point of reference indicated in legal units or other acceptable units in compliance with the pre-mentioned directive.

c) The intended purpose implies accuracy, claimed explicitly or implicitly, where a non-compliance with the implied accuracy could result in a significant adverse effect on the patient's health and safety.

Note 1: The expression « claimed implicitly » covers cases where the user, on the basis of the designation of the device or of its accompanying documents, or on the basis of the common use is entitled to expect accuracy where the accuracy of the measurement has an impact on the diagnosis or therapy of the patient.

Note 2: Measuring activities during the manufacturing process including those for calibration purposes are not covered by this recommendation and do not imply a measuring function of the manufactured device.

Examples for devices with a measuring function

- device for measuring body temperature,

[1] OJ n° L39/40, 15.2.1980 as amended by Directive 89/617/EEC, OJ n° L357/28, 7.12.1989

- pacifier which includes a temperature display including those with only a change of colour where criteria b is met,

- device for indicating that a body temperature is above or below a specified value,

- non-active non-invasive device for measuring blood pressure ,

- non-active device for measuring intra-ocular pressure,

- device for measuring volume or pressure or flow of liquid or gases delivered to or removed from the human body (included any container with a graduation scale or with a single point graduation where criteria c is met).

Examples for devices without a measuring function

- patch for indicating trends of body temperature (where criteria b is not met),

- device for the delivery of liquid to the human body (e.g. medicine spoons, cups, droppers, without graduation or scale or display of measuring unit),

- device for displaying trends of physiological parameters (e.g. urine bags without graduation or scale, callipers for obesity),

- eye-test chart.

APPENDIX G

Notified bodies for AIMDD (90/385/EEC)

LIST OF BODIES NOTIFIED UNDER DIRECTIVE 90/385/EEC Active implantable medical devices

Name and address of the notified bodies	Identification number	Responsible for the following products	Responsible for the following procedures / modules	Annexes / articles of the directives
RWTÜV SYSTEMS GMBH Langemarkstrasse, 20 45141 ESSEN Germany	0044	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
NATIONAL STANDARDS AUTHORITY OF IRELAND (NSAI) Glasnevin 9 DUBLIN Ireland	0050	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 5
BSI PRODUCT SERVICES Maylands Avenue HP2 4SQ HEMEL HEMPSTEAD United Kingdom	0086	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 5
TÜV PRODUCT SERVICE GMBH Ridlerstraße 65 80339 MÜNCHEN Germany	0123	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
TÜV RHEINLAND PRODUCT SAFETY GMBH Am Grauen Stein 51105 Köln Germany	0197	All active implantable medical devices	EC declaration of conformity (complete quality assurance system)	Annex 2
DEUTSCHE GESELLSCHAFT ZUR ZERTIFIZIERUNG VON MANAGEMENTSYSTEMEN MBH August-Schanz Straße, 21 60433 FRANKFURT AM-MAIN Germany	0297	Active implantable medical devices (pacemakers, biostimulators, nerve stimulators, muscle stimulators, bladder stimulators, sphincter stimulators, diaphragm stimulator and ear stimulators)	EC declaration of conformity (complete quality assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 5
TÜV-ZERTIFIZIERUNGSGEMEINSCHAFT e.V. TÜV CERT Reuterstraße, 161 53113 BONN Germany	0298	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 5
BUREAU VERITAS QUALITY INTERNATIONAL (BVQI)	0301	All active implantable medical devices	EC declaration of conformity (complete quality	Annex 2

LIST OF BODIES NOTIFIED UNDER DIRECTIVE 90/385/EEC Active implantable medical devices

Name and address of the notified bodies	Identification number	Responsible for the following products	Responsible for the following procedures / modules	Annexes / articles of the directives
2nd Floor, Tower Bridge Road, 224-226 SE1 2TX LONDON United Kingdom			assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 5
AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS MINISTERIO DE SANIDAD Y CONSUMO Paseo del Prado, 18-20 28014 MADRID Spain	0318	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
KEMA QUALITY B.V. Utrechtseweg 310 (Postbus 9035) 6800 ET ARNHEM Netherlands	0344	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 5
CENTRUM VOOR MEDISCHE TECHNOLOGIE VAN HET INSTITUUT VOOR VEROUDERINGS- EN VAATZIEKTEN ONDERZOEK TNO Zernikedreef, 9 2333 CK LEIDEN Netherlands	0345	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
ISTITUTO SUPERIORE DI SANITA Viale Regina Elena, 299 00161 ROMA Italy	0373	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
TÜV- ÖSTERREICH Krugerstrasse 16 1010 WIEN Austria	0408	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
G-MED GROUPEMENT POUR L'ÉVALUATION DES DISPOSITIFS MÉDICAUX 33, avenue du Général Leclerc 92260 FONTENAY-AUX-ROSES France	0459	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5

LIST OF BODIES NOTIFIED UNDER DIRECTIVE 90/385/EEC Active implantable medical devices

Name and address of the notified bodies	Identification number	Responsible for the following products	Responsible for the following procedures / modules	Annexes / articles of the directives
MEDCERT ZERTIFIZIERUNGS- UND PRÜFUNGSGESELLSHAFT FÜR DIE MEDIZIN GMBH Vorsetzen 35 20459 HAMBURG Germany	0482	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 5
PRÜFANSTALT FÜR MEDIZINISCHE GERÄTETECHNISCHE UNIVERSITÄT GRAZ Inffeldgasse, 18 8010 GRAZ Austria	0636	Active implantable medicinal devices and their accessories	EC Type-examination EC verification	Annex 3 Annex 4
LABORATÓRIO DE ENSAIOS E METROLOGIA DA SAÚDE - LEMES Av. Padre Cruz, Complexo Inst. Ricardo J 1699 Lisboa Codex Portugal	0932	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
ORVOS- ÉS KÓRHÁZTECHNIKAI INTÉZET (ORKI) (INSTIT. FOR MEDICAL AND HOSPITAL ENGIN.) Diós Árok 3 1125 Budapest Hungary	1011	Implantable heart pacemakers	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
ELEKTROTECHNICKY ZKUSEBNI USTAV S.P. Pod Lisem 129 171 02 PRAHA 71 - Troja Czech Republic	1014	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
INSTITUT PRO TESTOVANI A CERTIFIKACI A.S. T. Bati 299 764 21 ZLIN Czech Republic	1023	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
SCHWEIZERISCHE VEREINIGUNG FÜR QUALITÄTS- UND MANAGEMENTSYSTEME (SQS) Bernstrasse, 103 3052 ZOLLIKOFEN	1250	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 5

LIST OF BODIES NOTIFIED UNDER DIRECTIVE 90/385/EEC Active implantable medical devices

Name and address of the notified bodies	Identification number	Responsible for the following products	Responsible for the following procedures / modules	Annexes / articles of the directives
Switzerland				
LGA INTERCERT ZERTIFIZIERUNGSGESELLSCHAFT MBH Tillystrasse, 2 90431 NÜRNBERG Germany	1275	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 5
EVPU, A. S. Trencianska 19 018 51 NOVA DUBNICA Slovakia	1293	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5
POLSKIE CENTRUM BADAN I CERTYFIKACJI S.A. (PCBC) ul. Klobucka 23A 02 699 Warsawa Poland	1434	All active implantable medical devices	EC declaration of conformity (complete quality assurance system) EC Type-examination EC verification EC declaration of conformity to type (assurance of production quality)	Annex 2 Annex 3 Annex 4 Annex 5

APPENDIX H

Electrical Safety Tests.
Standard EN 60601-1

6 Electrical Safety Tests

6.1 Normal condition and single fault conditions

A basic principle behind the philosophy of electrical safety is that in the event of a single abnormal external condition arising or of the failure of a single means of protection against a hazard, no safety hazard should arise. Such conditions are called "single fault conditions" (SFC's) and include such situations as the interruption of the protective earth conductor or of one supply conductor, the appearance of an external voltage on an applied part, the failure of basic insulation or of temperature limiting devices.

Where a single fault condition is not applied, the equipment is said to be in "normal condition" (NC). However, it is important to understand that in this condition, the performance of certain tests may compromise the means of protection against electric shock. For example, if earth leakage current is measured in normal condition, the impedance of the measuring device in series with the protective earth conductor means that there is no effective supplementary protection against electric shock.

Many electrical safety tests are carried out under single fault conditions since these represent the worst case and will give the most adverse results. Clearly the safety of the equipment under test may be compromised when such tests are performed. Personnel carrying out electrical safety tests should be aware that the normal means for protection against electric shock are not necessarily operative during testing and should therefore exercise due precautions for their own safety and that of others.

6.2 Protective Earth Continuity

The resistance of the protective earth conductor is measured between the earth pin on the mains plug and a protectively earthed point on the equipment enclosure (see figure 6). The reading should not normally exceed 0.2 O at any such point. The test is obviously only applicable to class I equipment.

In IEC60601, the test is conducted using a 50Hz current between 10A and 25A for a period of at least 5 seconds. Although this is a

type test, some medical equipment safety testers mimic this method. Damage to equipment can occur if high currents are passed to points that are not protectively earthed, for example, functional earths. Great care should be taken when high current testers are used to ensure that the probe is connected to a point that is intended to be protectively earthed.

HEI 95 and DB9801 Supplement 1 recommend that the test be carried out at a current of 1A or less for the reason described above. Where the instrument used does not do so automatically, the resistance of the test leads used should be deducted from the reading.

If protective earth continuity is satisfactory then insulation tests can be performed.

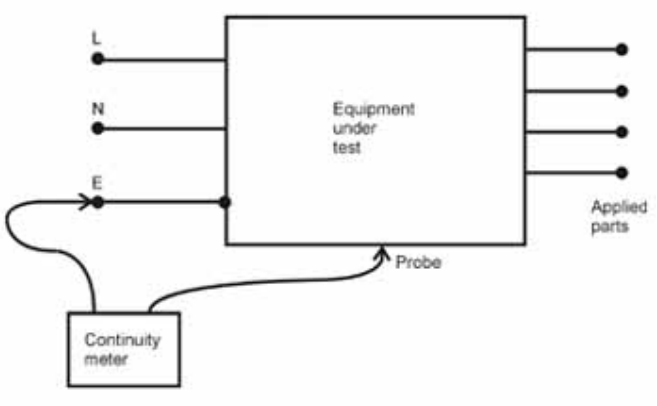

Figure 8. Measurement of protective earth continuity.

Applicable to	Class I, all types
Limit:	0.2
DB9801 recommended?:	Yes, at 1A or less.
HEI 95 recommended?:	Yes, at 1A or less.
Notes:	Ensure probe is on a protectively earthed point

6.3 Insulation Tests

IEC 60601-1, clause 17, lays down specifications for electrical separation of parts of medical electrical equipment compliance to which is essentially verified by inspection and measurement of leakage currents. Further tests on insulation are detailed under clause 20, "dielectric strength". These tests use AC sources to test equipment that has been pre-conditioned to specified levels of humidity. The tests described in the standard are type tests and are not suitable for use as routine tests.

HEI 95 and DB9801 recommend that for class I equipment the insulation resistance is measured at the mains plug between the live and neutral pins connected together and the earth pin. Whereas HEI 95 recommends using a 500V DC insulation tester, DB 9801 recommends the use of 350V DC as the test voltage. In practice this last requirement could prove difficult and it is acknowledged in a footnote that a 500 V DC test voltage is unlikely to cause any harm. The value obtained should normally be in excess of 50MΩ but may be less in exceptional circumstances. For example, equipment containing mineral insulated heaters may have an insulation resistance as low as 1MΩ with no fault present. The test should be conducted with all fuses intact and equipment switched on (see figure 9).

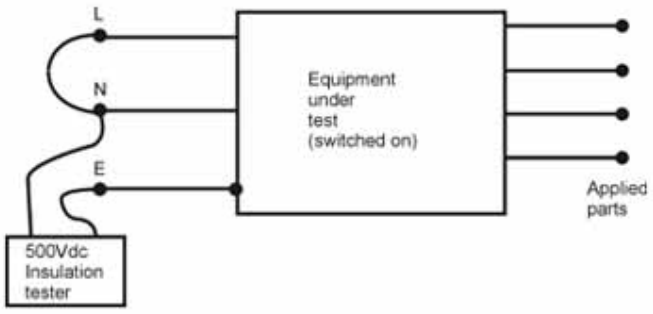

Figure 9. Measurement of insulation resistance for class I equipment

Applicable to	Class I, all types
Limits:	Not less than 50MΩ
DB9801 recommended?:	Yes
HEI 95 recommended?:	Yes
Notes:	Equipment containing mineral insulated heaters may give values down to 1MΩ. Check equipment is switched on.

HEI 95 further recommends for class II equipment that the insulation resistance be measured between all applied parts connected together and any accessible conductive parts of the equipment. The value should not normally be less than 50MΩ (see figure 10). DB9801 Supplement 1 does not recommend any form of insulation test be applied to class II equipment.

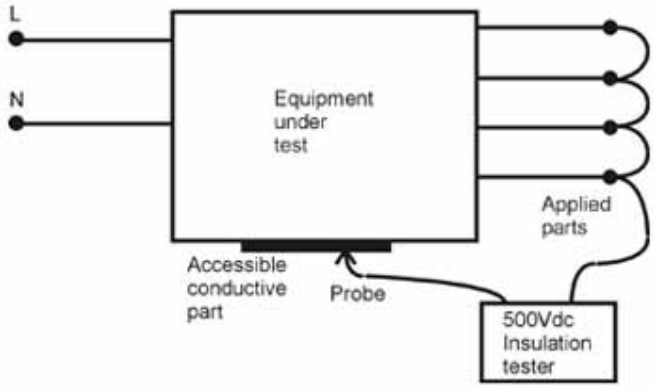

Figure 10. Measurement of insulation resistance for class II equipment.

Applicable to	Class II, all types having applied parts
Limits:	not less than 50MΩ.
DB9801 recommended?:	No
HEI 95 recommended?:	Yes
Notes:	Move probe to find worst case.

Satisfactory earth continuity and insulation test results indicate that it is safe to proceed to leakage current tests.

6.4 Leakage current measuring device

The leakage current measuring device recommended by IEC 60601-1 loads the leakage current source with a resistive impedance of about 1 kO and has a half power point at about 1kHz. The recommended measuring device was changed slightly in detail between the 1979 and 1989 version but remained functionally very similar. Figure 11 shows suitable arrangements for the measuring device. The millivolt meter used should be true RMS reading and should have an input impedance greater than 1 MΩ. In practice this is easily achievable with most good quality modern multimeters. The meter in the arrangements shown measures 1mV for each μA of leakage current.

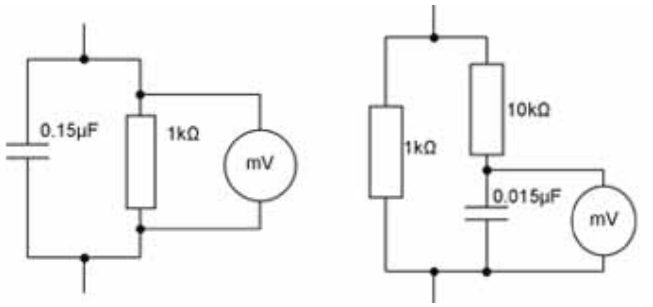

Figure 11. Suitable arrangements for measurement of leakage currents.

6.5 Earth Leakage Current

For class I equipment, earth leakage current is measured as shown in figure 12. The current should be measured with the mains polarity normal and reversed. HEI 95 and DB9801 Supplement 1 recommend that the earth leakage current be measured in normal condition (NC) only. Many safety testers offer the opportunity to perform the test under a single fault condition such as live or neutral conductor open circuit.

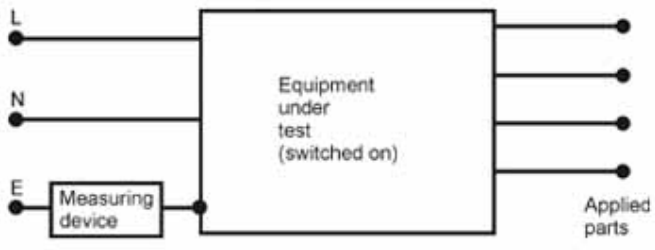

Figure 12. Measurement of Earth Leakage Current.

Applicable to	Class I equipment, all types
Limits:	0.5mA in NC, 1mA in SFC or 5mA and 10mA respectively for permanently installed equipment.
DB9801 recommended?:	Yes, in normal condition only.
HEI 95 recommended?:	Yes, in normal condition only.
Notes:	Measure with mains normal and reversed. Ensure equipment is switched on.

6.6 Enclosure leakage current

Enclosure leakage current is measured between an exposed part of the equipment which is not intended to be protectively earthed and true earth as shown in figure 13. The test is applicable to both class I and class II equipment and should be performed with mains polarity both normal and reversed. HEI 95 recommends that the test be performed under the SFC protective earth open circuit for class I equipment and under normal condition for class II equipment. DB9801 Supplement 1 recommends that the test be carried out under normal condition only for both class I and class II equipment. Many safety testers also allow the SFC's of interruption of live or neutral conductors to be selected. Points on class I equipment which are likely not to be protectively earthed may include front panel fascias, handle assemblies etc.

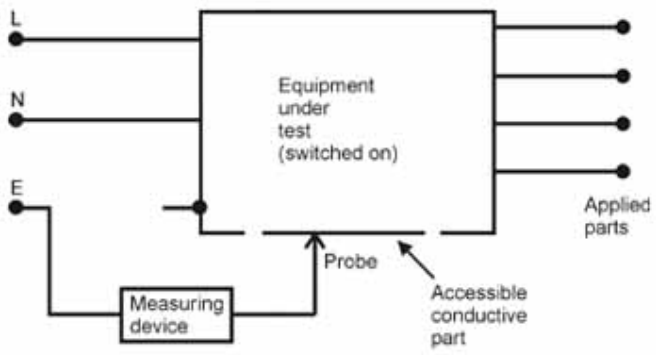

Figure 13. Measurement of Enclosure Leakage Current.

Applicable to	Class I and class II equipment, all types.
Limits:	0.1mA in NC, 0.5mA in SFC
DB9801 recommended?:	Yes, NC only
HEI 95 recommended?:	Yes, class I SFC earth open circuit, class II NC.
Notes:	Ensure equipment switched on. Normal and reverse mains. Move probe to find worst case.

6.7 Patient leakage current

Under IEC 60601-1 and HEI 95, for class I and class II type B and BF equipment, the patient leakage current is measured from all applied parts having the same function connected together and true earth (figure 14). For type CF equipment the current is measured from each applied part in turn and the leakage current leakage must not be exceeded at any one applied part (figure 15).

DB9801 Supplement 1 recommends that patient leakage current be measured from each applied part in turn for all types of equipment, although the recommended leakage current limits have not been revised to take into account the changed test method for B and BF equipment.

Great care must be taken when performing patient leakage current measurements that equipment outputs are inactive. In particular, outputs of diathermy equipment and stimulators can be fatal and can damage test equipment.

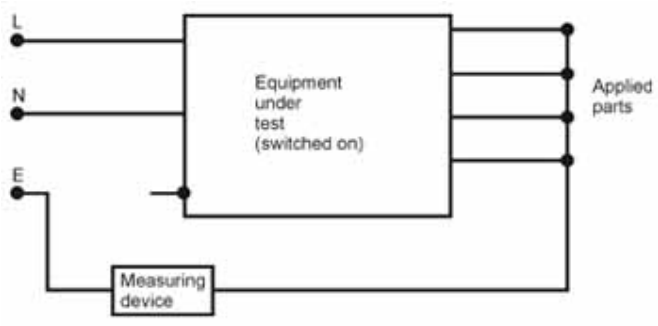

Figure 14. Measurement of Patient Leakage Current with applied parts connected together.

Applicable to	All classes, type B & BF equipment having

	applied parts.
Limits:	0.1mA in NC, 0.5mA in SFC.
DB9801 recommended?:	No
HEI 95 recommended?:	Yes, class I SFC earth open circuit, class II normal condition.
Notes:	Equipment on but outputs inactive. Normal and reverse mains.

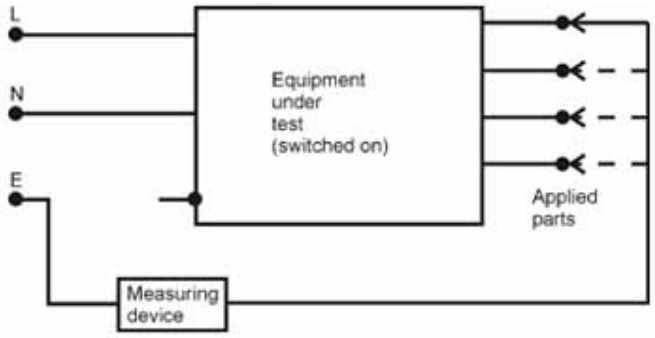

Figure 15. Measurement of patient leakage current for each applied part in turn

Applicable to	Class I and class II, type CF (B & BF for DB9801 only) equipment having applied parts.
Limits:	0.01mA in NC, 0.05mA in SFC.
DB9801 recommended?:	Yes, all types, normal condition only.
HEI 95 recommended?:	Yes, type CF only, class I SFC earth open circuit, class II normal condition.
Notes:	Equipment on but outputs inactive. Normal and reverse mains. Limits are per electrode.

6.8 Patient auxiliary current

Patient auxiliary current as defined in section 3.5 is measured between any single patient connection and all other patient connections of the same module connected together. It is not usual to test all possible combinations since together with all possible single fault conditions this would give an exceedingly large amount of data of questionable value.

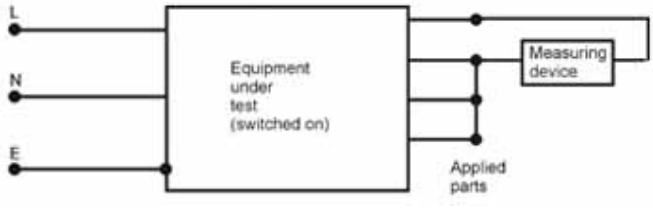

Figure 16. Measurement of patient auxiliary current.

Applicable to	All classes and types of equipment having applied parts.
Limits:	Type B & BF - 0.1mA in NC, 0.5mA in SFC. Type CF - 0.01mA in NC, 0.05mA in SFC.
DB9801 recommended?:	No.
HEI 95 recommended?:	No.
Notes:	Ensure outputs are inactive. Normal and reverse mains.

6.9 Mains on applied parts

By applying mains voltage to the applied parts, the leakage current that would flow from an external source into the patient circuits can be measured. The measuring arrangement is illustrated in figure 18.

Although the safety tester normally places a current limiting resistor in series with the measuring device for the performance of this test, a shock hazard still exists. Therefore, great care should be taken if the test is carried out in order to avoid the hazard presented by applying mains voltage to the applied parts.

Careful consideration should be given as to the necessity or usefulness of performing this test on a routine basis when weighed against the associated hazard and the possibility of causing problems with equipment. The purpose of the test under IEC 60601-1 is to ensure that there is no danger of electric shock to a

patient who for some unspecified reason is raised to a potential above earth due to the connection of the applied parts of the equipment under test. The standard requires that the leakage current limits specified are not exceeded. There is no guarantee that equipment performance will not be adversely affected by the performance of the test. In particular, caution should be exercised in the case of sensitive physiological measurement equipment. In short, the test is a "type test".

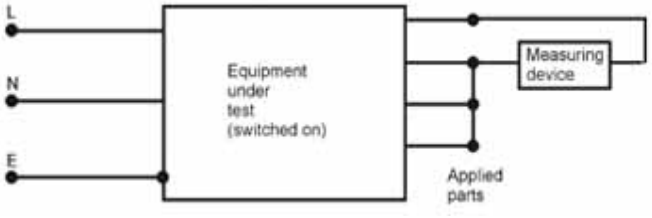

Figure 17. Mains on applied parts measurement arrangement.

Applicable to	Class I & class II, types BF & CF having applied parts.
Limit:	Type BF - 5mA; type CF - 0.05mA per electrode.
DB9801 recommended?:	No.
HEI 95 recommended?:	No
Notes:	Ensure outputs are inactive. Normal and reverse mains. Caution required, especially on physiological measurement equipment.

6.10 Leakage current summary

The following table summarises the leakage current limits (in mA) specified by IEC60601-1 for the tests most commonly performed as routine tests. Limits for DB9801 recommended tests are underlined. Limits for HEI 95 recommended tests are given in bold type.

Leakage current	Type B		Type BF		Type CF	
	NC	**SFC**	**NC**	**SFC**	**NC**	**SFC**
Earth	**0.5**	1	**0.5**	1	**0.5**	1
Earth for fixed equipment	5	10	5	10	5	10
Enclosure	**0.1**	**0.5**	**0.1**	**0.5**	**0.1**	**0.5**
Patient	**0.1**	**0.5**	**0.1**	**0.5**	**0.01**	**0.05**
Mains on applied part	-	-	-	5	-	0.05
Patient auxiliary	0.1	0.5	0.1	0.5	0.01	0.05

* For class II type CF equipment HEI95 recommends a limit for enclosure leakage current of 0.01mA as per the 1979 edition of BS 5724.

Table 2. Leakage current limits summary.

6.11 Comparison of HEI 95 and DB 9801 Supplement 1 recommendations

Test	**HEI 95**	**DB9801 Supplement 1**
Earth continuity	Use test current of 1A or less Limit 0.2ohm	Use test current of 1A or less Limit 0.2ohm
Insulation for Class 1 equipment	Measure between L and N connected together and E using 500v DC tester. Limit > 50MΩ. Investigate lower values	Measure between L and N connected together and E using 350v DC tester. Limit > 20MΩ. Investigate lower values
Insulation for Class II equipment	Measure between applied parts and accessible conductive parts of the equipment. Limit > 50MΩ. Investigate lower	No recommendation.

	values	
Earth leakage current	Measure in normal condition Limit < 0.5mA	Measure in normal condition Limit < 0.5mA
Enclosure leakage current	Measure in SFC, earth open circuit for Class-1, NC for Class-II Limit <0.5 mA for Class1 <0.1 mA for class II	Measure in NC only Limit < 0.1 mA
Patient leakage current	Measure from all applied parts connected together for B & BF equipment and from each applied part in turn for type CF. Measure under SFC, eart open circuit for Class 1, NC for classII. Limits : • Class I, B& BF < 0.5 mA • Class II, B& BF < 0.1 mA • Class I, CF < 0.05 mA per electrode • Class II, CF < 0.01 mA per electrode	Measure from each applied part in turn, for all types of equipment Measure under NC only Limits • Type B & BF <0.1 mA per electrode • Type CF < 0.01 per electrode

APPENDIX I

Biocompatibility Safety Tests.
Standard EN ISO 10993-1

Biocompatibility Safety Tests. Standard EN ISO 10993-1

The section that follows provides a brief description of the individual tests included in the ISO 10993/EN 30993 standard.

Cytotoxicity. The aim of in vitro cytotoxicity tests is to detect the potential ability of a device to induce sublethal or lethal effects as observed at the cellular level. According to ISO 10993-1, the in vitro cytotoxicity assay is one of two tests--the other is the sensitization test described below--that must be considered in the evaluation of all device categories. For additional information on biocompatibility testing please refer to page 32 of *Medical plastics and Biomaterials* May/June issue.

Three main types of cell-culture assays have been developed: the elution test, the direct-contact test, and the agar diffusion test. (The ISO 10993-5 standard gives a detailed description of all three methods.) In the elution test, an extract (eluate) of the material is prepared and added in varied concentrations to the cell cultures. Growth inhibition is a widely used parameter, but others may also be used. In the direct-contact test, pieces of test material are placed directly on top of the cell layer, which is covered only by a layer of liquid cell-culture medium. Toxic substances leaching from the test material may depress the growth rate of the cells or damage them in various ways. In the agar diffusion test, a piece of test material is placed on an agar layer covering a confluent monolayer of cells. Toxic substances leaching from the material diffuse through the thin agar layer and kill or disrupt adjacent cells in the monolayer. As always, the physical and chemical properties of the test material should be considered before the choice of the test system is made.

There is usually a good qualitative correlation between results from cell-culture tests and studies performed in vivo with respect to cytotoxicity versus primary tissue effects. It is important to recognize, however, that although cell-culture toxicity is in general a good and sensitive indicator of primary tissue compatibility, exceptions may arise in cases where leaching substances cause tissue damage in vivo through more complex mechanisms. At present, the in vitro cytotoxicity assays should be used as screening tests and considered primarily as supplements to the various in vivo tests.

Sensitization. The sensitization test recognizes a potential sensitization reaction induced by a device, and is required by the ISO 10993-1 standard for all device categories. The sensitization reaction is also known as allergic contact dermatitis, which is an immunologically mediated cutaneous reaction. This is in contrast to irritant contact dermatitis (skin irritation)--a skin reaction caused by the primary and direct effect of a substance on the skin. In animals, the sensitization reactions manifest themselves as redness (erythema) and swelling (edema).

The preferred animal species for sensitization testing is the albino guinea pig. (There is no reliable alternative in vitro test that can predict the sensitizing potential of a substance.) The various available guinea pig methods have certain features in common: an induction (sensitization) phase, when the potential allergen is presented to the organism, followed by a rest period and a subsequent challenge phase to determine whether or not sensitization has occurred.

One of the most recognized and validated assays is the guinea pig maximization test (GPMT). A test design very similar to the GPMT is widely used for assessing

the sensitizing potential of medical devices. After a challenge period, the skin reactions are graded on a ranking scale according to the degree of erythema and edema.

Predictive tests in guinea pigs are important tools in identifying the possible hazard to a population repeatedly exposed to a substance. Nevertheless, results from sensitization tests in guinea pigs have to be evaluated carefully. A positive test result in this assay may rate a substance as a stronger sensitizer than it appears to be during actual use. On the other hand, a negative result in such a sensitive assay ensures a considerable safety margin regarding the potential risk to humans.

Skin Irritation. The ISO 10993-10 standard describes skin-irritation tests for both single and cumulative exposure to a device. The preferred animal species is the albino rabbit, whose highly sensitive, light skin makes it possible to detect even very slight skin irritation caused by a substance. Skin-irritation tests of medical devices are performed either with two extracts obtained with polar and nonpolar solvents or with the device itself.

In the single-exposure test, rabbits are treated for several hours only, whereas for the cumulative test the same procedure is repeated for several days. All extracts and extractants are applied to intact skin sites. Skin reaction is seen as redness or swelling and is graded according to a specified classification system.

Dermal irritation is the production of reversible changes in the skin following the application of a substance, whereas dermal corrosion is the production of irreversible tissue damage (scar formation) in the skin. Materials that leak corrosive substances are not likely candidates for medical device production.

Intracutaneous Reactivity. The intracutaneous reactivity test is designed to assess the localized reaction of tissue to leachable substances. The test is required for consideration in nearly all the device categories in ISO 10993-1 (see Table III). Polar and nonpolar solvent extracts are administered as intracutaneous injections to rabbits. Undesirable intracutaneous reactivity includes redness or swelling.

Acute Systemic Toxicity. Acute systemic toxicity is the adverse effect occurring within a short time after administration of a single dose of a substance. ISO 10993-1 requires that the test for acute systemic toxicity be considered for all device categories that indicate blood contact. For this test, extracts of medical devices are usually administered intravenously or intraperitoneally in rabbits or mice.

Determining acute systemic toxicity is usually an initial step in the assessment and evaluation of the toxic characteristics of a substance. By providing information on health hazards likely to arise from short-term exposure, the acute systemic toxicity test can serve as a first step in the establishment of a dosage regimen in subchronic and other studies, and can also supply initial data on the mode of toxic action of a substance. The test is similar to the nonspecific toxicity test. Normally, only one of these two procedures is included in a test battery.

Genotoxicity. Genetic toxicology tests are used to investigate materials for possible mutagenic effects--that is, damage to the body's genes or chromosomes. The tests are performed both in vitro and in vivo. ISO 10993-1 requires the genotoxicity (mutagenicity) test to be considered for all device categories

indicating permanent (>30 days) body contact (except for surface devices with skin contact only).

A mutation is a change in the formation content of the genetic material (DNA code) that is propagated through subsequent generations of cells. Mutations can be classified into two general types: gene mutations and chromosomal mutations. Gene mutations are changes in nucleotide sequences at one or several coding segments within a gene; chromosomal mutations are morphological alterations or aberrations in the gross structure of the chromosomes.

The simplest and most sensitive assays for detecting induced gene mutations are those using bacteria. Gene mutations can also be detected in cultured mammalian cells. Current in vivo assays for gene mutations are cumbersome and not widely used. The simplest and most sensitive assays for investigating chromosomal aberrations are those that use cultured mammalian cells. However, two well-established in vivo procedures are also available: chromosomal aberrations can be studied in bone marrow or peripheral blood cells of rodents dosed with a suspect chemical or extract either by counting micronuclei in maturing erythrocytes (micronucleus test) or by analyzing chromosomes in metaphase cells.

In addition to these mutagenicity tests, various assays can measure the induction of an overall genotoxic response--an indirect indicator of potential damage to the genetic material.

Implantation. Implantation tests are designed to assess any localized effects of a device designed to be used inside the human body. Implantation testing methods essentially attempt to imitate the intended use conditions of an implanted material. Although different tests use various animal species, the rabbit has become the species of choice, with implantation performed in the paravertebral muscle. Implantation can be either surgical or nonsurgical: the surgical method involves the creation of a pouch in the muscle into which the implant is placed, while the nonsurgical method uses a cannula and stylet to insert a cylinder-shaped implant. Through a macroscopic examination (which may be supplemented with microscopic analysis), the degree of tissue reaction in the paravertebral muscle is evaluated as a measure of biocompatibility.

Hemocompatibility. The purpose of hemocompatibility testing is to look for possible undesirable changes in the blood caused directly by a medical device or by chemicals leaching from a device. Undesirable effects of device materials on the blood may include hemolysis, thrombus formation, alterations in coagulation parameters, and immunological changes. According to the ISO 10993-4 (EN 30993-4) standard, devices that only come into very brief contact with circulating blood--for example, lancets, hypodermic needles, or capillary tubes--generally do not require blood/device interaction testing.

ISO 10993-4 describes hemocompatibility tests in five different categories--thrombosis, coagulation, platelets, hematology, and immunology. Most of the individual tests are not discussed in detail, but they may be performed either in vivo or, preferably, in vitro. There is still some uncertainty with respect to what is actually required by the regulatory authorities for the hemocompatibility test.

Subchronic and Chronic Toxicity. Subchronic toxicity is the potentially adverse effect that can occur as a result of the repeated daily dosing of a substance to experimental animals over a portion of their life span. In the assessment and evaluation of the toxic characteristics of a chemical, the determination of

subchronic toxicity is carried out after initial information on toxicity has been obtained by acute testing, and provides data on possible health hazards likely to arise from repeated exposures over a limited time. Such testing can furnish information on target organs and the possibilities of toxin accumulation, and provide an estimate of a no-effect exposure level that can be used to select dose levels for chronic studies and establish safety criteria for human exposure.

In subchronic or chronic toxicity studies, one or two animal species are dosed daily, usually for a period of 3 to 6 months; the rat is the standard animal species of choice. The animals are given the test substance in increasing doses. The dose level of the low-dose group should be at the level of human exposure. When extracts of medical devices are employed, one dose level (the highest practically applicable volume) is often sufficient, since strong toxicity is generally not expected.

Carcinogenicity. The objective of long-term carcinogenicity studies is to observe test animals over a major portion of their life span to detect any development of neoplastic lesions (tumor induction) during or after exposure to various doses of a test substance.

Carcinogenicity testing is normally conducted with oral dosing. For implants and medical devices, however, only extracts can be tested and they must be administered intravenously, necessitating certain modifications of the standard procedure. There are only a very few products for which this comprehensive test can be justified.

In carcinogenicity studies, mice or rats are dosed every day for 18 to 24 months. For medical device extracts, one dose level (again the highest practically applicable volume) is usually sufficient. At the completion of the dosing period, all surviving animals are sacrificed and their organs and tissues examined microscopically for the presence of tumors. An increased incidence of one or more category of tumors in the dosed group would indicate that the product tested has the potential to induce tumors and could be considered a possible carcinogen in humans.

ALTERNATIVE TEST METHODS

As mentioned previously, a major goal in international toxicological testing is to reduce not only the use of in vivo studies but also the number of animals employed in these tests. A few of the in vivo procedures used today for testing medical devices may be of questionable worth for safety evaluation. However, the availability of accepted and validated in vitro assays is still limited. Substantial resources have been made available for validation of alternative in vitro assays in toxicology as replacements for animal tests, but it may take years before validated methods can be implemented, and any goal of replacing all in vivo studies with in vitro assays will probably never be met.

Recently, a working group under the auspices of the European Center for Validation of Alternative Methods (ECVAM) has recommended a few alternative methods that can be used for safer testing of medical devices.[5] These include two in vitro tests as potential substitutes for the in vivo assays for skin and eye irritation. However, the implementation of validated protocols and internationally accepted guidelines for these tests is likely to be delayed into the next century.

CONCLUSION

In recent years, the biological evaluation of medical devices has become more globally harmonized, concurrently with the publication of the ISO 10993 standard for medical device testing. Some countries still require their national guidelines to be met, but most accept ISO 10993 as a parallel alternative to their own regulations. European harmonization, represented by EN 30993, has made it easier to obtain the required CE marking for a product that will be accepted throughout the EU member countries. It must be emphasized that all guidelines, whether accepted or under preparation, should be regarded as more of a dynamic process than a rigid structure, since the various standards are subjected to continuous revision and evaluation. Impact on this work will come not only from authorities and notified bodies but also from national and international expert and working groups similar to ECVAM.

It is important that neither the ISO nor the EN guidelines be used as a prescriptive "cookbook" in the assessment of safety to humans. Recommended tests must be conducted with consideration for the information available from other sources, with knowledge of the type of material a device is made from, and with awareness of its planned end use.

Modern materials and process technology have opened up innumerable possibilities for the creation of new or improved medical devices. Current developments range from the formulation of novel polymers to innovative applications of metals, ceramics, composites, and tissue-engineered products. With a comprehensive, harmonized biological evaluation program rapidly gaining acceptance, the combined advances in materials technology, biotechnology, and medicine are likely to revolutionize the future of the industry.