"Development of a non-invasive baby sleep monitoring and intelligent control system for the prevention of unexpected death in previously healthy babies and early detection of risky situations."

D.1.1
Patterns of SIDS Risk, preventive actions, and Risk analysis for CE marking

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1 Introduction

1.1 Objective

This deliverable is addressed to present the results from the following tasks:

Task 1.1. SIDs risk patterns and preventive actions
Determine SIDs risk factors related to respiratory rate, mobility, temperature and gastroesophageal reflux, their ranges and frequencies and the special characteristics of newborns. Define actions in case of alarms. Two expert panels have been developed to obtain this information.

Task 1.2. Standards of medical care systems
Summarize the SoA and relevant standards related with medical equipment to fit the standards to achieve medical and CE mark in future commercialization. Preliminary risk analysis to detect potential risks.

1.2 Scope

The document covers the following points:

- **SIDS patterns and preventive action:** results of the expert panels regarding to SIDs risk factors and actions to be done in case of alarm.
- **Preliminary analysis for CE marking:** a revision of related directives has carried out. In addition, the consortium held a meeting on 16th December 2013 national body 0318 responsible for medical devices CE marking on Spain.
- **Conclusions:** Assessment of the results.
- **Annexes :**
  - Annex 1: CE marking. Essential requirements compliance.
  - Annex 2: CE marking. Checklist of general hazards applicable to the product.

1.3 Integration within the project objectives

This deliverable belongs to the "**WP1**. Users characterization and system requirements" which is part of the research section in the "Research, Technological development and innovation activities". This deliverable with D1.2 and D1.3 are the inputs to carry out the "**WP2**. Development of SIDS Preventive Actuations", "**WP3**. Development of the biosensing textiles" and "**WP4**. Intelligent communication and management system", corresponding to the technological development of the above mentioned activities, as shown in the Figure 1.

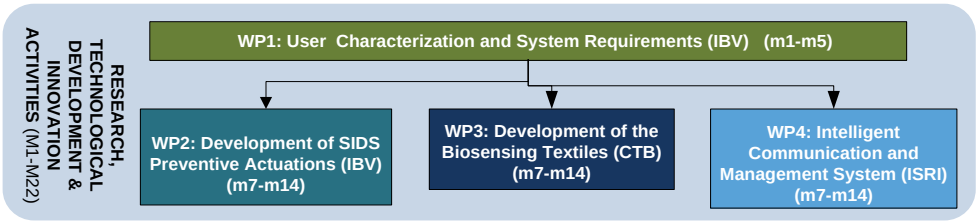


Figure 1. Block diagram.

2 SIDs risk factors and preventive actions

2.1 Introduction

The objective of this point is to outline the results of task 1.1. Thus, the main goal is to determine the following points, according to scientific bibliographic research and expertise of premature caregivers, paediatrics and neurophysiology doctors:

- SIDS risk factors, the ranges and frequencies associated to the biological signals related to those factors.
- Babies' characteristics taking into account babies age (in months) and outline differences between preterm and full-term babies if needed.
- Actuations foreseen in case of detection.

2.2 Methodology

The main goal of this point is to detail the methodology followed to carry out to answer the questions related to task 1.1.

A **first definition of ranges and frequencies** of the biological signals related to the main SIDS risk factor has been made through a comprehensive research.

Afterwards, **two expert panels with premature caregivers, paediatrics and neurophysiology doctors** have been carried out to confirm and complete the obtained data.

The aim of expert panels is to gather a group of people in a speech situation and a researcher who determines and moderates the conversation without participating in it, so that exhaustive information about the knowledge, the needs, interests and worries of a determinate expertise field can be obtained.

That technique is appropriated when the study aims to describe the perceptions of the experts about one situation, program, event, product or service. In this way, it is possible to obtain:

- Previous information about a determinate field, which we do not have any knowledge from.
- To determinate behaviours, attitudes, opinions, beliefs, motivations, habits, etc… of the people.
- To identify new concepts and uses of products and services.

This process has several advantages and some limitations, these are:

Advantages

- Exploratory and prospective technique which can give us information about strong and weak points of services, products, etc.
- Great flexibility: It can be used in a great number of different topics, people and environments.

Limitations

- It is a structural non statistic sample whose data cannot be extrapolated.
- Disadvantages of group interactions: problems in generalization, comparability, dislikes, etc.

The steps performed in order to complete the expert panels are:

1. Planning of the session.
2. Presentation of the session's goals and the participants. About 8 people and the moderator will take part in each expert panel.
3. Exploration. Opened questions where the participants give their opinion freely.
4. Investigation. Specific questions directed to concrete participants with the purpose of detailing some information. Do not raise more than 3 questions of this type.
5. Conclusions. The closing of the session can be a priority, the opinion about a promising situation or a revision of results with final contributions. Do not force the consensus.

2.3 SIDS risk factors

SIDS happens when babies are asleep [1] and newborn babies spend 15 hours per day sleeping. In fact, the term SIDS refer to infants who die in their sleep with no evidence of accidental asphysia, inflicted injury or organic disease [2]. SIDS is a multifactorial syndrome mainly related to overheating, prolonged apnea, gastroesophageal reflux or inadequate bedding system and posture. According to the Triple Risk Model [3], SIDS results when three factors simultaneously influence the infant: (a) an underlying vulnerability in the infant, (b) a critical developmental period, and (c) an exogenous stressor, e.g., hyperthermia [4]. In this model, such exogenous stressors are postulated to induce asphyxia, hypercapnia, and hypoxia.

Current evidence suggests that SIDS involves a convergence of stressors that probably results in the asphyxia of a vulnerable infant who has **defective cardiorespiratory or arousal defense systems during a critical developmental period** when immature defense mechanisms are not fully integrated. SIDS is due to multifactorial syndromes among the main factors are:

Heat stress: In human infants, high ambient temperatures and bundling in blankets or clothing increase the risk of SIDS [3]. The infant brain accounts for approximately 40% of an infant's total oxygen consumption and heat production, so overheating is a critical variable in cases of sudden infant death [5].

Defective Respiratory: Clinical observations in infants, analysis of heart-rate and respiration recordings in infants who subsequently died of SIDS, and physiological studies in animal models provide compelling evidence for a respiratory pathway in the majority of SIDS deaths [3].

Reflux: Gastro-esophageal reflux may happen when stomach contents are regurgitated into the esophagus. This is a common event in babies, but it may cause apnea if the material gets into the lung. Gastroesophageal reflux can cause sudden death in a vulnerable infant during a critical period of development through failure of "autoresuscitation" mechanisms. Gastric

contents are present in the lungs of 30% to 40% of infants whose deaths are attributed to sudden infant death syndrome (SIDS) [6] [7] [8].Thus, gastric aspiration may be a terminal event that some infants, representing a subset of SIDS cases, cannot overcome. [9]

Arousal: Arousal is an important survival mechanism when infants are confronted with hypoxia during sleep. The EEG changes that occur during arousal from sleep are traditionally thought to be produced by an ascending pathway resulting in activation of the cerebral cortex. Failure of arousal mechanisms likely plays an important role in the final pathway to death [10]. Serotonin receptor abnormalities have been found throughout the ventral medulla in victims of SIDS, possibly representing a network dysfunction that affects arousal and cardiorespiratory responses. The arousal response is a continuous process which reflects the activation of various structures, from subcortical to cortical areas. The arousal response to hypoxia stimulates breathing and ensures avoidance of life-threatening events, such as positional asphyxia [11]. The ability to initiate appropriate responses to hypoxia is considered a vital reflex in newborns [12]. Kato et al. found that the future SIDS victims spontaneously aroused from sleep less often than a group of age-matched control infants [13]. So, an inability to initiate the arousal response to hypoxia is considered a possible cause of SIDS, the main cause of infant mortality in industrialized countries [14] [15] [16]. This suggests that despite appearing well and physiologically normal, future SIDS victims may have subtle pre-existing abnormalities in their arousal pathways which prevent the progression to full cortical arousal [17].

So, a **failure to arouse is also one of the causes of SIDS,** if babies stop breathing during sleep; as a defence mechanism, they usually arouse and start breathing again. In effect, they revive themselves. However, if the baby does not arouse in time -fail to wake up and take a deep breath to end a prolonged apnea-, there is a second line of defense, gasping [1]. The infant's brain stimulates slow, deep, labored breaths that temporarily restore his oxygen supply. If this mechanism also fails, the infant will die from a lack of oxygen. The importance of arousal mechanisms related to SIDS is postulated by several reports ([18], [19], [20], [21], [22], [23], [24]). In fact two studies have provided evidence of decreased spontaneous arousals during sleep in SIDS compared with control infants ([25], [26]).

Measurements' ranges and frequencies

Respiratory rate

Normal physical findings in a newborn include a respiratory rate of 40 to 60 breaths per minute. During rapid eye movement (REM) sleep, infants often exhibit irregular respirations with pauses of 5 seconds or less. In contrast, during non-REM or quiet sleep, a newborn's respiratory rate is 5 to10 breaths per minute slower than in the awake or active (REM) sleep states.

Respiratory distress can be defined as tachypnea with respiratory rate greater than 60 breaths per minute, nasal flaring, chest retractions (intercostal, subcostal, and substernal), and

expiratory grunting. Irregular (see-saw) or slow respiratory rates of less than 30 breaths per minute, particularly if associated with gasping, are a worrisome sign. [27]

The respiratory rate of preterm infants is greater throughout the first half of the year becoming essentially equalized by 8 months of age. The peak difference between preterm and full-term occurs at age 10 weeks (Table 1), with the differences rapidly decreasing during the remainder of the first half-year. [28]

Age (wk)	Respiratory Rate (Breaths/min)		
	Preterm	Full-term	Difference
2	41±4	36±2	5.3
4	46±4	35±2	10.6[1]
6	43±4	37±2	6.6
8	48±8	36±2	12.2
10	44±5	31±1	13.7[2]
12	42±5	30±1	12.1[2]
14	39±4	30±1	9.5[2]
16	39±4	31±1	7.7[1]
18	34±3	29±1	4.7
22	30±2	28±1	1.7
26	32±2	28±1	3.5
30	32±3	28±1	4.0
34	29±2	27±1	1.7
38	30±2	29±2	0.7
42	27±1	27±3	-0.1
46	28±2	27±2	1.1
50	27±3	25±1	2.1

Table 1. Respiratory rate in preterm and full-term infants during quiet sleep [28]. Values are means ± SE. [1] P < .05. [2] P < .01.

Temperature

There are differences of temperature in newborns throughout the 4 EEGsleep-defined states. Preterm babies have higher rectal temperatures than fullterm babies. Nevertheless, no significant variations have been found in skin temperature between preterm and fullterm.

There exist average skin temperature differences among all states. Specifically, for average skin temperature between mixed frequency active and tracé alternant quiet sleep (Table 2) [29].

Variable	Mean		Standard deviation		Minimum		Maximum	
Preterm (n=34) / Full-term (n=25)	PT	FT	PT	FT	PT	FT	PT	FT
Mixed frequency active sleep								
Skin average	36.28	36.17	0.40	0.62	35.06	34.79	36.86	37.29
Skin variance	4.46	5.11	1.35	1.61	2.40	2.26	7.27	8.70
High voltage quiet sleep								
Skin average	36.27	36.10	0.44	0.73	34.97	34.29	36.95	37.28
Skin variance	4.36	4.92	1.53	1.42	1.94	2.56	7.53	9.00

Variable	Mean		Standard deviation		Minimum		Maximum	
Tracé alternant quiet sleep								
Skin average	36.19	36.05	0.41	0.69	35.06	34.37	36.84	37.35
Skin variance	4.24	4.91	1.38	1.52	1.81	2.10	7.14	8.85
Low voltage irregular active sleep								
Skin average	36.18	36.07	0.41	0.70	34.94	34.28	36.89	37.36
Skin variance	4.39	5.29	1.50	1.84	1.58	2.56	7.52	10.43

Table 2. Summary of temperature (ºC) data for preterm and full-term infants [29].

Gastroesophageal reflux

Gastro-oesophageal reflux (GOR) is defined as the passage of gastric contents into the oesophagus due to inappropriate relaxation of the lower oesophageal sphincter. It occurs in 50% of neonates less than 3 months of age and usually resolves by 12 to 18 months of age. Around 20% of neonates with GOR will require medical intervention.

Oesophageal pH monitoring is not routinely recommended in neonates as 75% of GOR may be due to non-acid or weakly acidic reflux.

A reflux episode was defined as a lower oesophageal pH of < 4 for 15 seconds or longer. [30]

Apnea

About 20-45% of preterm babies exhibit a periodic breathing pattern characterized by 3 or more respiratory pauses of greater than 3 seconds duration with less than 20 seconds respiration between pauses. This is called periodic breathing and is a normal event which usually does not merit any treatment.

Apnea is a pathological cessation of breathing that results in physiological changes (decrease in central drive, peripheral perfusion, cyanosis, bradycardia, hypotonia) and does merit treatment.

Apnea is defined as cessation of respiration for more than 20 sec or cessation of respiration of any duration accompanied by bradycardia (HR < 100/min) and/or cyanosis. [31]

2.4 Actions to be executed in case of alarm

When an alarm is fired, different actions have been established to be performed, depending on the alarm's level (Figure 2).

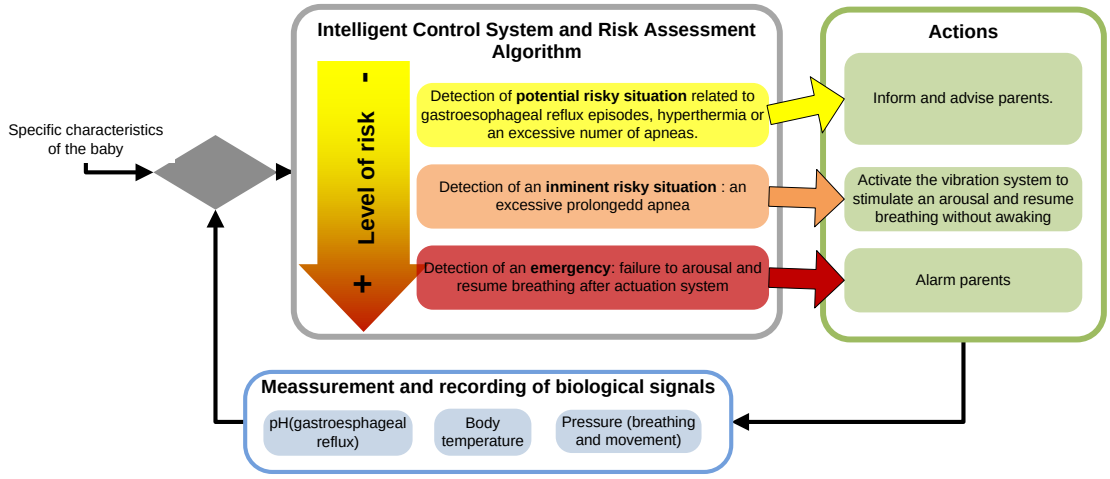


Figure 2. Decision algorithm

The algorithm which will decide the action to perform will be based on the level of risk. Therefore, there will be 3 different levels: yellow, orange and red, according to their risk level, where red is the maximum.

In the first level, the mattress will be able to detect a potential risk situation which alarm might be fired in that very moment or later, according to the risk for the baby and the parents' comfort.

The second level will be reached if the mattress detects a prolonged apnea, in which case the stimulus will be activated to stimulate an arousal without awaking the baby.

The third level is an emergency level, and will be reached only if the mattress' stimulus fails to arousal the baby. Then, the parents will be alarmed.

All of this will be done by measuring and recording the following biological signals:

- pH (in order to detect gastroesophageal reflux)

- body temperature (to detect any possible heat stress)

- pressure (to detect breathing and movement)

2.5 Expert panel's results

Risk factors identification

First of all paediatricians were asked to validate the preliminary risk factors related to SIDS:

- Hyperthermia
- Gastroesophageal reflux
- Breathing (Sleep apnea. respiratory rate)
- Movement
- Lack of arousals

Paediatricians confirm that **HYPERTHERMIA, SLEEP APNEA EPISODES, RESPIRATORY RATE AND LACK OF AROUSALS** are the more relevant factors strongly related to the SIDS.

In the case of **MOVEMENTS**, experts consider this factor is not critical to prevent SIDS. They prefer others factors, such as respiratory rate.

However, in the case of **GASTROESOPHAGEAL REFLUX,** unless it can cause a **sleep apnea reflection** when it occurs. Paediatricians are not sure if measurement of pH in the mattress could be enough considering that gastroesphageal reflux is usually measured at the interior of the oesophagus. The further use of the system could help gathering information in this sense.

Other factor that paediatricians consider would be interested to include in the system is **HEART RATE**. However, systems that measure heart rate are invasive but the main requisite of the system is **not to be invasive**. It is very difficult to measure the heart rate without a direct contact with the baby.

Measurement and recording of biological signals

Regarding to the identified risk factors, experts defined biological signals that must be measured and recorded by the system. The risk factors and the values of the associated biological signals that imply risks were determined. The risk factors in order of importance will be included in "D2.1. Report with the preventive actions in case of SIDS risk detected by BabyCareSleep").

Preventive actions

- **TO INFORM AND ADVICE PARENTS THE NEXT DAY**

Paediatricians consider that parents should be informed only in necessary cases. **The system should avoid false warnings to parents**.

Therefore, if everything regarding **PROLONGED SLEEP APNEA** is fine, the message to parents should be **NO EVENTS or NORMAL SITUATION**

However, experts consider useful inform parents if there is a risk situation regarding HYPERTHERMIA (detailed specifications will be included in "D2.1. Report with the preventive actions in case of SIDS risk detected by BabyCareSleep").

Moreover, some experts consider that if there is a risk situation regarding INCREASING RESPIRATORY RATE, the system should provide recommendations for parents to carry the baby to the paediatrician (detailed specifications will be included in "D2.1. Report with the preventive actions in case of SIDS risk detected by BabyCareSleep").

However, some experts consider the system should **not inform about situations not related to SIDS directly.**

- **STIMULATION SYSTEM**

If there is a **risk situation** regarding **PROLONGED APNEA**, the stimulation system should be activated. It is the **only situation when the stimulation system is activated**.

The stimulation system should stimulate an arousal and resume breathing**. Experts consider very important not to awake babies and not influence their sleeping quality.**

When the stimulation system is working, it is not possible to measure the breathing. Experts consider **very dangerous to measure at the same time because there might be false negative**. For this reason, the action of the stimulation system should not be continuous. Experts consider the best option that the stimulation system sends **"shocks", small stimuli**. After each shock, the system should measure breathing.

After a number of shocks without breathing (before emergency of PROLONGED APNEA) the parents' alarm should be activated and the **stimulus will be more intense**.

- **PARENTS' ALARM**

The main situation to send an alarm to parents immediately is if the **stimulation system does not work.**

- If after a number of "shocks", the baby is still not breathing. The alarm should notify parents **before the baby does not breathe 20 seconds (EMERGENCY OF PROLONGED APNEA)**.

Also regarding the body temperature, the alarm should be activated when there is an emergency (detailed specifications will be included in "D2.1. Report with the preventive actions in case of SIDS risk detected by BabyCareSleep").

Paediatricians consider the system should **not alert about situations not related to SIDS**. This would complicate the product and **the system should be simple**. For example, experts consider an emergency the polyapnea situation (high temperatures and decreasing of respiratory rate). However, this situation is not related to SIDS, so they consider not to alert. However, other experts consider interesting alarm to parents if babies arise a temperature under 35º during a while.

All experts consider the **alarm should be also auditory**.

- **TO INFORM PAEDIATRICIANS**

Parents could inform to the paediatricians with a report that register the most relevant events (high temperature, prolonged apnea and the time when the event occurs).

There were different opinions within groups regarding information to paediatricians:

- Some experts consider that it would be interesting the system send registered events to the paediatricians directly (via wifi) without parent's intervention. This information should not be visible for parents.
- Other experts prefer that the system does not inform to paediatricians regarding other aspects different to parents. (Although experts consider useful to know the sleeping habits of the baby)

Other aspects

The system should include a manual with an explanation for parents regarding how it works. Moreover, it should include advices to prevent SIDS. For example, advices regarding the room temperature, babies clothes and so on. Which action should be performed in each case will be included in "D2.1. Report with the preventive actions in case of SIDS risk detected by BabyCareSleep".

Below are presented **professionals that participate in the sessions**:

Pilar Codoñer	Chief of paediatric Service in Hospital Peset.
Julia Colomer	Paediatrician at Health Center Fuente San Luis. Professor in Paediatrics. Faculty of Medicine.
Amalia Lluch	Paediatrician at Health Center Ingeniero Joaquín Benlloch.
Javier Diez	Researcher in Public Health
Manuel Martinez	Paediatrician at Health center. República Argentina
Isabel Úbeda	Paediatrician at Health Center. L'Eliana
Trinidad Álvarez	Paediatrician at Health Center Barrio de la Luz
Isabel Izquierdo Macian	Chief of pediatric – Neonatology Service at La Fe Hospital. Coordinator at GT MSI of AEP Director of the 3rd "Libro Blanco de Muerte Súbita"
Gonzalo Pin Arboledas	Sleep Unit. Hospital Quirón
Mercedes García	Paediatrician at Consultorio Chile. Chief of pediatric – Neonatology Service at Hospital Universitari i Politècnic la Fe
Mercedes Peidro	Paediatrician at health Center Trafalgar
Mara Garcés Sánchez	Paediatrician at Health Center Nazareth
Eva Carbajal Roca	Paediatrician at Hospital Casa de la Salud

Figure 3. Expert panels developed on 18th December 2013.

3 CE Marking

3.1 Introduction

The objective of this point is to outline the results of task 1.2. Thus, the main goal is to describe the activities and conclusions obtained in order to **prepare a CE marking** from the beginning of the product development, being aware of all the requirements that BabyCareSleep product will have to fulfil before its market introduction.

It is important to highlight that **the consortium held a meeting on 16th December 2013 with national body 0318 responsible for medical devices CE marking on Spain** (Agencia Española de Medicamentos y Productos Sanitarios - AEMPS).

The following points provide an overview of the EU regulatory framework for medical devices, as well as an approach of the essential requirements to be fulfilled, and the steps to be followed by the manufacturer, in order to legally place a medical device on the EU markets.

Even with accreditation through the MDD, the BabyCareSleep will still need to comply with other relevant ISO standards relating to mattress design, sensors and electrical safety.

Should the product be destined for countries outside the EU (Russia, Mexico, Brazil, Australia, China, USA etc.), different requirements should be fulfilled and different procedures should be followed in order to obtain regulatory approval, depending on the regulatory framework set by each country's administration.

3.2 Introduction to CE marking

CE marking is a mandatory conformity mark for products placed on the market in the European Economic Area (EEA). With CE marking on a product, the manufacturer[1] declares that the product conforms to the essential requirements defined in the applicable EC New Approach Directives.

To mention only a few, examples of these EC New Approach Directives are:

- Directive 93/42 Medical Devices (MDD), and its modification 2007/47/CE,
- Directive 2006/95 Electrical Equipment (Low voltage),
- Directive 2004/108 Electromagnetic Compatibility (EMC),
- Directive 1999 Radio & Telecom, etc.

Essential requirements, which aim to ensure a high level of protection of human health and safety and the good functioning of the market are set out in the annexes to these EC directives.

[1] A manufacturer, in the meaning of New Approach, is the person who is responsible for designing and manufacturing a product with a view to placing i ton the Community market on his own behalf.

Essential requirements set up by New Approach directives may overlap or complement each other, depending on the hazards covered by these requirements that are related to the product in question. So compliance with Community legislation often requires simultaneous application of several EC New Approach directives and, possibly, other Community legislation[2]. Thus, depending both on the product features and its intended use, several directives could be applicable simultaneously to the BabyCareSleep product, and therefore all the essential requirements defined in these applicable directives should be fulfilled simultaneously.

Products may be placed on the market and put into service only if they are in compliance with the essential requirements. Before placing a product on the Community market, the manufacturer must subject the product to a conformity assessment procedure provided for in the applicable directive, with the view to affixing the CE marking.

In some cases a third party conformity assessment (carried out by the Notified Bodies[3] designated by the Member States) is required. This basically means a third party audit that the manufacturer must pass to get the conformity. The product features and its intended use, determine whether or not a third party conformity assessment procedure is required. Conformity assessments are generally required on products that are Class IIa, IIb or III.

As broadly speaking the essential requirements set in the different EC directives are mostly general requirements, often the specific requirements to be fulfilled by the manufacturer are defined in the Harmonized Standards. Each EC directive has an associated harmonized standards list which might help the manufacturer to meet the essential requirements.

Thus, harmonized standards are often the most suitable way for the manufacturer to fulfil the requirements, as compliance with harmonised standards provides a presumption[4] of conformity with the corresponding requirements of the EC Directives.

However the use of these standards remains voluntary and the manufacturer is free to choose any other technical solution that provides compliance with the mandatory essential requirements.

Once more, the product features and its intended use, determine which harmonized standards are needed to fulfil the requirements. In addition, as the interpretation of some essential requirements often becomes a rough task for the manufacturer, different European organisations regularly develop and publish several guidance documents (for example: MEDDEV (Medical Devices) and NBOG (Notified Body Operations Group) guidelines) to make this task easier. Although these guidance documents establish some consensus statements to

[2] For example: electronic devices may also fulfil with the environmental requirements defined in Directive 2002/96 Waste of electronic equipment (RAEE) and Directive 2011/65 Hazardous Substances (ROHS).

[3] If a Notified Body is involved in the approval, the number of the Notified Body must also appear adjacent to the CE marking,

[4] To create the capacity to confer this presumption of conformity, the references of harmonised standards must be published in the Official Journal of the European Union.

pursue the objective of ensuring uniform application of the directives within the EU, they are legally non-binding documents.

It must be noted that all these regulatory references (directives, harmonized standards, guidance documents, etc.) change relatively fast. Therefore, nowadays requirements might not be exactly equivalent to next year´s requirements[5].

So, considering all this wide and changeable regulatory framework, the point is to make a careful study of the BabyCareSleep project scope, considering the product desirable features and its intended use, in order to determine the different applicable directives, the essential requirements and the harmonized standards to be fulfilled, as well as verifying whether or not the conformity assessment procedure involves a Notified Body.

Although the essential requirements to fulfil depend on the applicable EC Directives, in order to get an idea of the main tasks to deal with, we could sum up the most common and important requirements:

- Perform the Safety Tests: In most cases the manufacturer needs to perform different safety tests (electric safety, electromagnetic compatibility, biocompatibility, etc.) to ensure that the product meets all the safety requirements demanded[6]. In most, if not all, of the countries in the EU there are specialist external testing services laboratories which can provide independent proof that the products conform with regulatory requirements.

- Prepare a Technical File: All CE marking directives require the manufacturer to prepare a technical file which should contain enough information to demonstrate that the product properly complies with the requirements set in the applicable directives. In most cases it comprises many different documents: general description of the apparatus and its parts, general arrangement drawing, block and circuit diagrams, datasheets, list of standards applied, test reports, records of the risk analysis, markings and labels, instructions (user, maintenance, installation, etc.), quality control procedures, etc. The information required in the Technical File will depend upon the Classification of the device. Class III products (the highest risk) require more documentation and proof in the Technical File than Class I products.

- Prepare a Declaration of Conformity: Basically it's a document in which the manufacturer states that the product meets all the requirements of the applicable directives.

[5] Actually, new versions of the most important harmonized standards of the MDD have been published during 2012 (ISO 13485, IEC 60601, ISO 14971). Furthermore the European Comission has recently gone through a new MDD draft, which might entail new and different requisites for the future.

[6] In most cases, the types of tests that must be performed to conform to safety requirements are defined in applicable harmonized standards.

- Implement a Quality Management System[7]: In some cases, the manufacturer must implement a Quality Management System, which will be audited by a Notified Body. The EC directives usually provide a specific harmonized standard that establishes helpful guidelines for a Quality Management System implementation.

- In some cases, depending both on the applicable directives and the manufacturer's country, other requirements may be demanded (licences, premarket notification, etc.).

3.3 EU regulatory framework for medical devices

The EU medical devices core legal framework[8] consists of 3 directives:

- Directive 90/385/EEC regarding active implantable medical devices,

- Directive 93/42/EEC regarding medical devices (MDD), and its modification 2007/47/CE,

- Directive 98/79/EC regarding in vitro diagnostic medical devices.

The **BabyCareSleep** product is most likely to fall under the Medical Devices Directive (MDD). The MDD is one of the EC New Approach Directives and consequently, in order for a manufacturer to legally place a medical device on the European market, the essential requirements of the MDD have to be met. Products conforming to the MDD must have a CE marking applied, and manufacturers' products meeting harmonised standards have a presumption of conformity to the Directive.

First of all, the manufacturer needs to verify whether or not the BabyCareSleep product is within the scope of the MDD. To do so, the manufacturer should determine if the BabyCareSleep product fits in the following definitions stated in the MDD:

*'**Medical device'** means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:*

- *diagnosis, prevention, monitoring, treatment or alleviation of disease,*

- *diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*

[7] As the implementation of a Quality Management System usually becomes itself a long and strategic Project, it should be a major consideration for the manufacturer.
[8] Understanding the abovementioned CE marking overview is a must to understand the medical devices regulatory framework.

- *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;*

The product features and its intended use are the key to determine if the product can really be considered as a medical device.

*'**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;*

*'**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;

It's worth mentioning that the MDD applies to medical devices and their accessories. Thus, for the purposes of the MDD, accessories shall be treated as medical devices in their own right.

*'**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;*

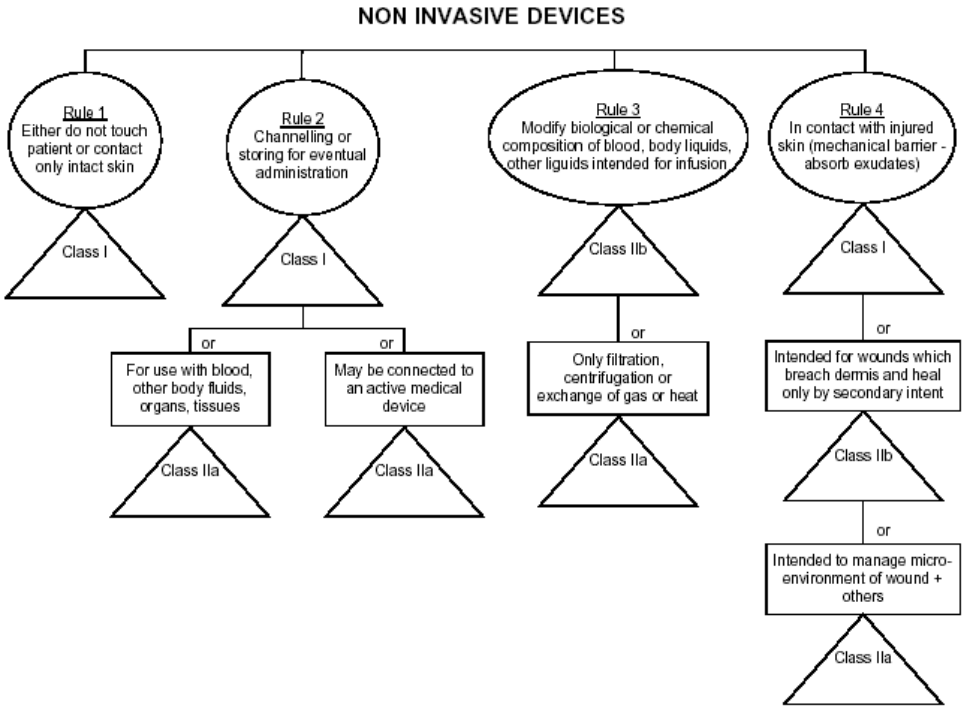
If the manufacturer can prove that, due to the product features and its intended use, the product can be considered as a medical device, this medical device must fulfil the essential requirements established in the MDD.

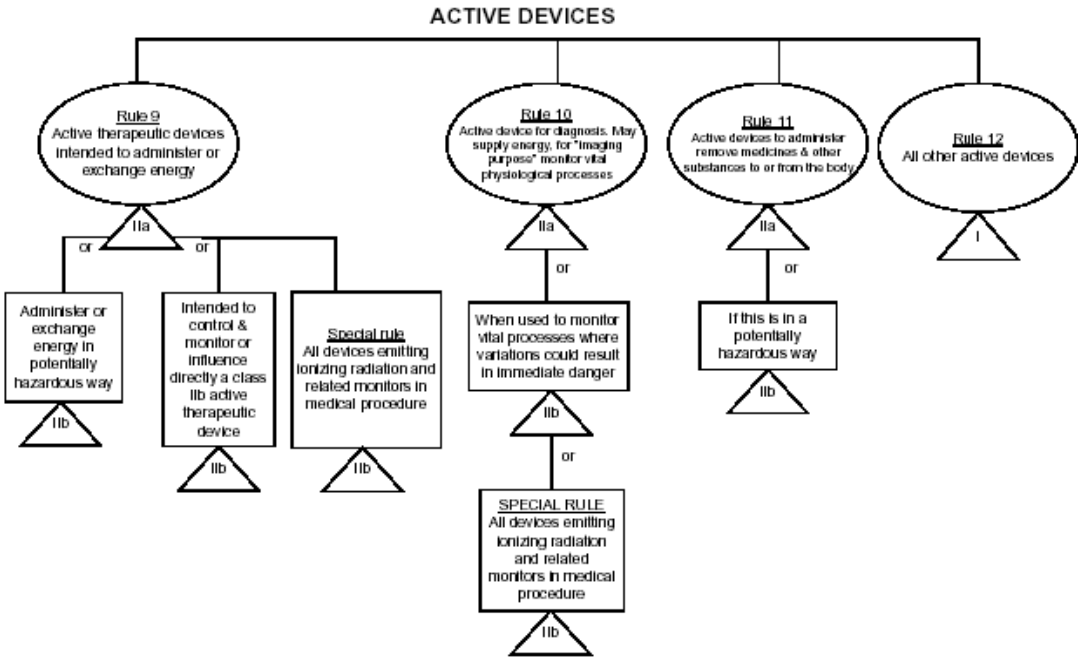
Strictly, it might be said that the manufacturer can't choose whether or not the product is a medical device. However in a few cases the consideration of the product as a medical device is not clear and the manufacturer has the chance of choosing whether or not the product is going to be considered as a medical device. Once more, everything depends on the product features and its intended use stated by the manufacturer on the labelling, in the instructions and/or in promotional materials. **It would be the decision of the appropriate notified body as to the classification required for the medical device**.

Next step is the **classification of the medical device**. As different requirements and different conformity assessment procedures are set for different classes of medical devices, the manufacturer must classify the medical device attending to the classification criteria established in the MDD (Annex IX). Thus, following a risk based classification, the devices can be considered as class I, class IIa, class IIb or class III, where:

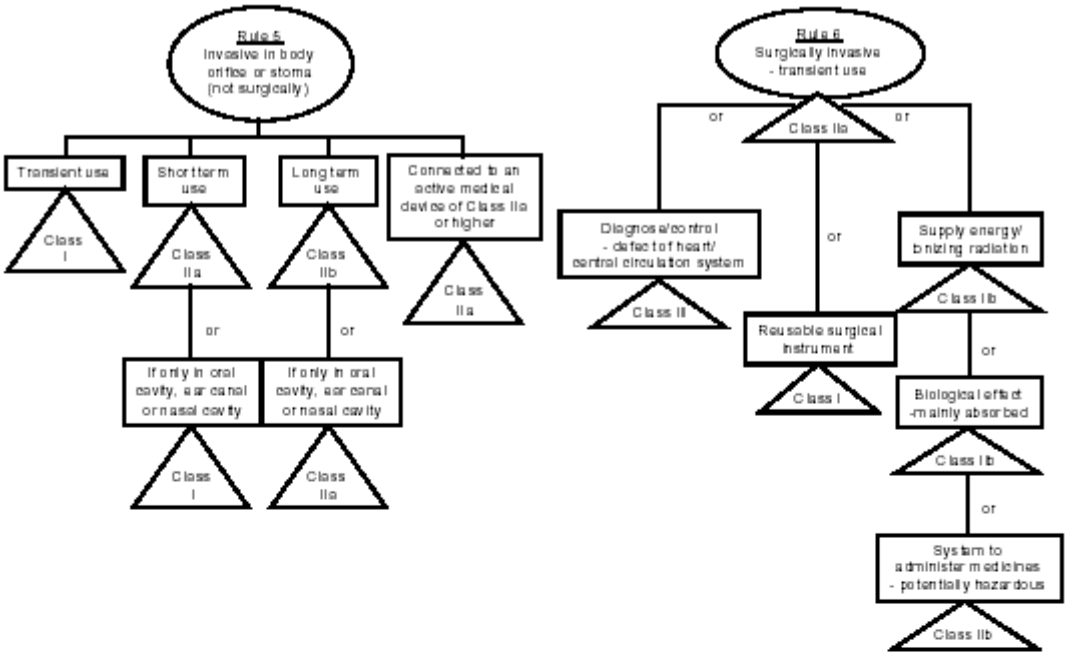
- Class I are low risk devices.
- Class IIa are low-medium risk devices.
- Class IIb are medium-high risk devices.
- Class III are high risk devices.

Risk is defined as the chance of harming the subject. Therefore a low risk device (Class I) is one that is external to the body whereas a Class III device may be one that is implantable, located near to the brain, heart or spinal column, or provides a biological or pharmaceutical effect. The following flow charts provide an overview of how to classify a new medical device according to the MDD Annex IX.

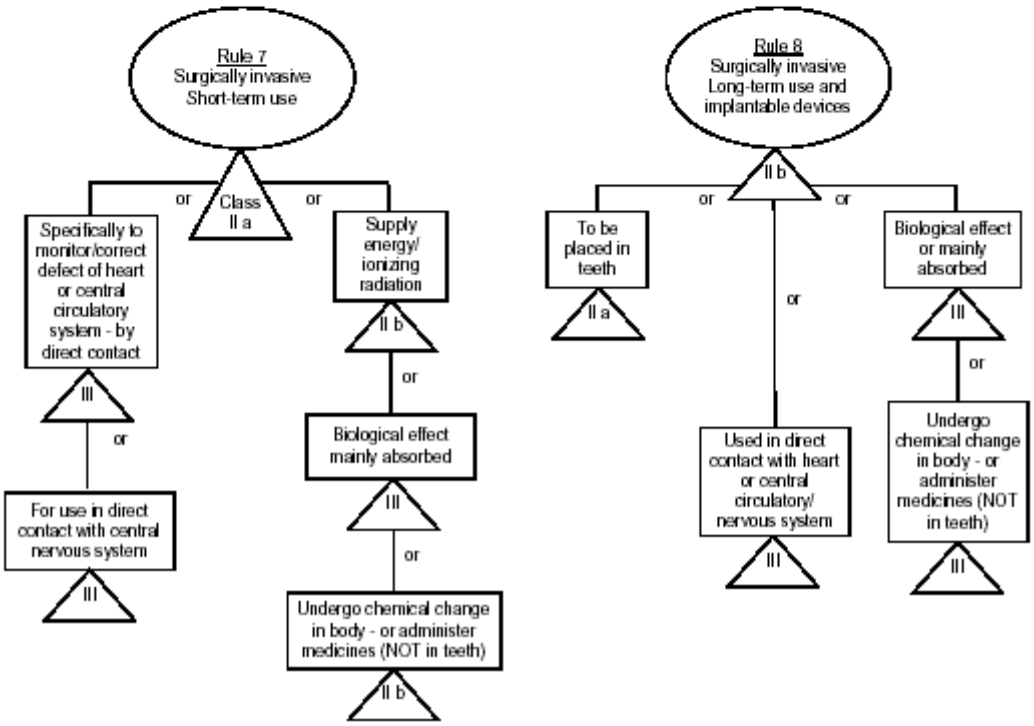


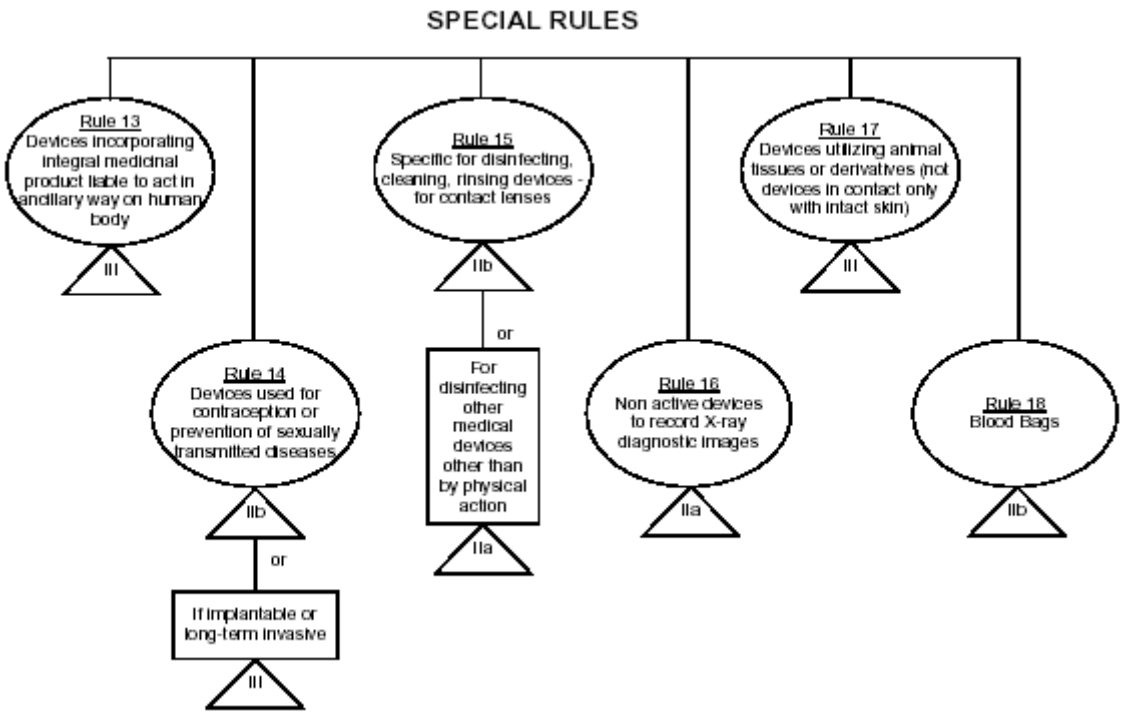

ACTIVE DEVICES
Rule 9
Active therapeutic devices intended to administer or exchange energy
IIa
or
or
Administer or exchange energy in potentially hazardous way
IIb
Intended to control & monitor or influence directly a class IIb active therapeutic device
IIb
Special rule
All devices emitting ionizing radiation and related monitors in medical procedure
IIb
Rule 10
Active device for diagnosis. May supply energy, for "imaging purpose" monitor vital physiological processes
IIa
or
When used to monitor vital processes where variations could result in immediate danger
IIb
or
SPECIAL RULE
All devices emitting ionizing radiation and related monitors in medical procedure
IIb
Rule 11
Active devices to administer remove medicines & other substances to or from the body
IIa
or
If this is in a potentially hazardous way
IIb
Rule 12
All other active devices
I

INVASIVE DEVICES



INVASIVE DEVICES





Following the guidelines of the MDD[9] and the guidance documents (MEDDEV, GHTF (Global Harmonisation Task Force) and NBOG guidelines) the manufacturer can determine the classification of the medical device. Obviously, more demanding requirements and stricter conformity assessment procedures are established for higher risk devices.

A major consideration is whether or not the conformity assessment procedure involves a Notified Body. In most cases, a Notified Body is required to carry out an audit. The scope of this audit is mainly the Technical File of the medical device and the manufacturer´s Quality Management System. For most Class I medical devices it is possible for the manufacture to self-certify the device. For some Class I devices and Class IIa and above, a notified body will have to audit the information provided by the manufacturer.

Furthermore, the medical devices' manufacturers usually need also to fulfil additional requirements (depending on the country) like obtaining a **manufacturing licence** and making a pre-market notification to the proper authorities.

So, considering the aforementioned, the point is to make a specific and careful study of the BabyCareSleep project scope, considering the product desirable features and its intended use, in order to verify whether or not the BabyCareSleep product is within the scope of the MDD. If that is the case, a classification of the medical device would determine the essential requirements and the harmonized standards to be fulfilled, as well as the applicable conformity assessment procedure.

[9] The MDD establishes in its annexes different conformity assessment procedures depending on the device class.

On the other hand it's worth mentioning that even if the BabyCareSleep product can't be considered as a medical device, it would probably fit in any of the other EC directives' scopes and therefore similar (though probably less demanding) requirements and conformity assessment procedures would be applicable.

From the flow charts provided above, it is likely that the BabyCareSleep device will be classified as either a Class I device or a Class IIa device. Under **Rule 1** (above) the device will be only contacting intact skin and would therefore be classified as Class 1 unless under **Rule 10** regarding active devices it is classed as an "active device for diagnosis – may supply energy for "Imaging purpose" to monitor vital physiological processes" in which case it could be classed as Class IIa. For example, a treadmill would normally be a Class 1 device if used in a medical environment however if it is used to assist in cardiac diagnosis it would be a Class IIa medical device. Nevertheless, considering that it is preventing a syndrome, if BabyCareSleep product is included under Class IIa or IIb should be agreed with the national body.

3.4 Preliminary risk analysis

A **preliminary conclusion** is that the BabyCareSleep project is likely to be either Class IIa or Class IIb according to the Medical Device Directive. Nevertheless the class should be agreed with the national body; which in this case should be AEMS from Spain because the SME integrating the final product is DELAX and they are located in Spain.

It is important to highlight that **the consortium (Delax and IBV) held a meeting on 16th December 2013 with national body 0318 responsible for medical devices CE marking on Spain** (Agencia Española de Medicamentos y Productos Sanitarios - AEMPS). The national body is aware of our product and they would be in touch with the consortium for further recommendation and confirmation about the class of device to be considered.

The preliminary risk analysis developed for the BabyCareSleep concept has identified:

- **The essential requirements**: A first identification of essential requirements is detailed in Annex 1.
- **Checklist of general hazards applicable to the product**: Annex 2 shows all the general hazards than can affect a product, grouped into five categories. It is mentioned if each hazard affects (Yes) or do not affect (No) the product.

4 Conclusions

4.1 SIDs risk factors and preventive actions

Scientific research regarding the **frequencies and ranges of the associated to SIDS** was carried out defining these parameters.

In addition, **two satisfactory expert panels** were developed obtaining very useful information that meets the goals of the task, and a great participation and acceptance from the professionals of paediatric field.

So, **the consortium has obtained the needed information** about:

- SIDS risk factors, the ranges and frequencies associated to the biological signals related to those factors.
- Babies' characteristics taking into account babies age (in months) and outline differences between preterm and full-term babies if needed.
- Actuations foreseen in case of detection.

4.2 CE marking conclusions

A **preliminary conclusion** is that the BabyCareSleep project is likely to be either Class IIa or Class IIb according to the Medical Device Directive. Nevertheless the class should be agreed with the national body; which in this case should be AEMS from Spain because the SME integrating the final product is DELAX and they are located in Spain. In this context, **the consortium (Delax and IBV) held a meeting on 16th December 2013 with national body 0318 responsible for medical devices CE marking on Spain** (Agencia Española de Medicamentos y Productos Sanitarios - AEMPS).

In addition, in this early stage of BabyCareSleep product, a first assessment of the **essential requirements** is detailed in Annex1 and the **checklist of general hazards applicable** to the product is shown in Annex 2.

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6 Annexes

Annex 1: Essential Requirements Compliance (CE marking)

Directive 93/42/CEE modified by Directive 2007/47/CE

Paragraph of Directive	Requirements	Yes	No
I. GENERAL REQUIREMENTS			
1	**Results of the Risk Analysis performed by the manufacturer** 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 intended 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. This shall include: — reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and — consideration of the technical knowledge, experience, education and training and where applicable the medical and physical conditions of intended users (design for lay, professional, disabled or other users).	X	
2	**Adopted solutions.** 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.	X	
3	**Demonstration of the performances attributed to the product.** 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.	X	
4	**Demonstration of the product's characteristics and performances maintenance, safely and within the valid established period.** The characteristics and performances referred to in Sections 1, 2 and 3 must	X	

	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	**Measures to assure the absence of alteration of the characteristics and performances during the transport and storage of the product.** 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.	X	
6	**a) Non-desired secondary effects** Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended.	X	
	b) **Conclusions about the benefit/risk balance of the product. Clinical assessment (Annex X).** Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X.	X	
II. REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION			
	7. Chemical, physical and biological properties		
7.1	**Materials selection (general data):** 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:	X	
	-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, - where appropriate, the results of biophysical or modelling research whose validity has been demonstrated beforehand.	X	
7.2	**Minimization of the contaminants and waste risk:** 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.	X	
7.3	**Use interactions:** 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	X	

	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	**Drugs incorporation.** 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 2001/83/EC and which is liable to act upon the body with action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC. For the substances referred to in the first paragraph, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking account of the intended purpose of the device, seek a scientific opinion from one of the competent authorities designated by the Member States or the European Medicines Agency (EMEA) acting particularly through its committee in accordance with Regulation (EC) No 726/2004 (1) on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device. When issuing its opinion, the competent authority or the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body. Where a device incorporates, as an integral part, a human blood derivative, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking into account the intended purpose of the device, seek a scientific opinion from the EMEA, acting particularly through its committee, on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the human blood derivative into the device. When issuing its opinion, the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body. Where changes are made to an ancillary substance incorporated in a device, in particular related to its manufacturing process, the notified body shall be informed of the changes and shall consult the relevant medicines competent authority (i.e. the one involved in the initial consultation), in order to confirm that the quality and safety of the ancillary substance are maintained. The competent authority shall take into account the data related to the usefulness of incorporation of the substance into the device as determined by the notified body, in order to ensure that the changes have no negative impact on the established benefit/risk profile of the addition of the substance in the medical device. When the relevant medicines competent authority (i.e. the one involved in the initial consultation) has obtained information on the ancillary substance, which could have an impact on the established benefit/risk profile of the addition of		X

	the substance in the medical device, it shall provide the notified body with advice, whether this information has an impact on the established benefit/risk profile of the addition of the substance in the medical device or not. The notified body shall take the updated scientific opinion into account in reconsidering its assessment of the conformity assessment procedure.		
7.5	**Leakage of substances.** 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. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction, in accordance with Annex I to Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. If parts of a device (or a device itself) intended to administer and/or remove medicines, body liquids or other substances to or from the body, or devices intended for transport and storage of such body fluids or substances, contain phthalates which are classified as carcinogenic, mutagenic or toxic to reproduction, of category 1 or 2, in accordance with Annex I to Directive 67/548/EEC, these devices must be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging as a device containing phthalates. If the intended use of such devices includes treatment of children or treatment of pregnant or nursing women, the manufacturer must provide a specific justification for the use of these substances with regard to compliance with the essential requirements, in particular of this paragraph, within the technical documentation and, within the instructions for use, information on residual risks for these patient groups and, if applicable, on appropriate precautionary measures.		X
7.6	**Non-intended incorporation of substances.** 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.		X
	8. Infection and microbial contamination		
8.1	**Adaptation to the design.** 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.	X	
8.2	**Animal fabrics.** 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.		X

	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 transmissible agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process.		
8.3	**Sterile products.** 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.		X
8.4	**Validated methods** Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method.		X
8.5	**Controlled conditions** Devices intended to be sterilized must be manufactured in appropriately controlled (e. g. environmental) conditions.		X
8.6	**Proper package for non-sterile products** 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.	X	
8.7	**Label to identify sterile or non-sterile products (in identic or similar products).** The packaging and/or label of the device must distinguish between identical or similar products sold in both sterile and non-sterile condition.		X
	9. Construction and environmental properties		
9.1	**Products destined to be used combined: combination restrictions.** 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.	X	
9.2	**Risk prevention associated to:**		
	Physical characteristics (vol/pressure, dimensional, ergonomics). the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features,	X	
	Environment (magnetic fields, pressure, temperature, etc.). risks connected with reasonably foreseeable environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration,	X	

	Reciprocal interferences with other products. the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given,	X	
	Materials' ageing and loss of precission. 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.	X	
9.3	**Explosion/Fire risk (in exposed to flammable substances products or able to favour the combustion)** 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.		X
	10. Devices with a measuring function		
10.1	**Precision and stability in the manufacturer indicated limits.** 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.	X	
10.2	**Ergonomical design principles.** The measurement, monitoring and display scale must be designed in line with ergonomic principles, taking account of the intended purpose of the device.	X	
10.3	**Measuring units (legals).** 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.	X	
	11. Protection against radiation		
11.1	**General**		
	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.		X
11.2	**Intended radiation**		
	a) Acceptable emission control. 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.		X
	b) Visual and loud alarms.		X

	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	**Non-intended radiation: risks minimization for patients, users and others.** 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.		X
11.4	**Use instructions: characteristics of the emitted radiation, protection means, use precautions, installation conditions, etc.** 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.		X
11.5	**Ionizing radiation:**		
	a) Emission regulation and control, and radiation quality. 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.		X
	b) Result/risk balance in radiodiagnosis. 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.		X
	c) Dosis control and emission type in radiotherapy. 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.		X
12. Requirements for medical devices connected to or equipped with an			
12.1	**Design adaptation.** 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. For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.	X	
12.2	**Source state control.** 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.	X	

12.3	**Alarms regarding failure in the electric supply.** Devices where the safety of the patients depends on an external power supply must include an alarm system to signal any power failure.	X	
12.4	**Alarms regarding risk situations.** 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.	X	
12.5	**Electromagnetic fields induction.** 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.	X	
12.6	**Electric risks protection.** 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.	X	
12.7	**Protection against mechanical and thermal risks:**		
	Mobile parts 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.	X	
	Vibration 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 meansavailable for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.	X	
	Noise 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.	X	
	Connexions. 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.	X	
	Accessible parts. 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.	X	
12.8	**Protection against the risks posed to the patient by energy supplies or substances:**		
	a) Of energy sources.	X	

	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.		
	b) Of substance administration. 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.		X
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.	X	
	13. Information supplied by the manufacturer		
13.1	**How information is provided: commercial package, use instructions. Information accompanies each individual product or several.** 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. Each device must be accompanied by the information needed to use it safely and properly, taking account of the training and knowledge of the potential users, and to identify the manufacturer.	X	
13.2	**Symbols and colours use: explanation.** 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.	X	
13.3	**Label.** *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 the authorised representative where the manufacturer does not have a registered place of business in the Community; (b) the details strictly necessary to identify the device and the contents of the packaging especially for the users;	X	

	(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. A manufacturer's indication of single use must be consistent across the Community; (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; (n) in the case of a device within the meaning of Article 1(4a), an indication that the device contains a human blood derivative.		
13.4	**Intended purpose of the product, if not obvious.** 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.	X	
13.5	**Identification of the products. Traceability.** 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.	X	
13.6	**Use instructions.** 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 sideeffects; (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	X	

	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. If the device bears an indication that the device is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used. If in accordance with Section 13.1 no instructions for use are needed, the information must be made available to the user upon request; (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, or human blood derivatives 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; (q) date of issue or the latest revision of the instructions for use.		

Annex 2: Checklist of general hazards applicable to the product (CE marking)

In the following table are shown all the general hazards than can affect a product, grouped into five categories. It is mentioned if each hazard affects (Yes) or do not affect (No) the product.

Generic hazards	Applicable
1. Hazards related to the energy and factors contributors.	
a) The electricity.	Yes
b) The heat.	Yes
c) The mechanic force.	No
d) The ionizing radiation.	No
e) The not ionizing radiation.	No
f) The moving parts.	Yes
g) The unexpected movement.	No
h) The suspended loads.	No
i) The failure of the patient supporting system.	No
j) The pressure (breaking of blood vessels).	No
k) The acoustic pressure.	No
l) The vibration.	Yes
m) The magnetic fields (ej. NMR)	Yes
2. Biologic hazards and factors contributors.	
a) The biocontamination.	No
b) The bioincompatibility.	Yes
c) The wrong chemical formulation (chemical composition).	No
d) The toxicity.	Yes
e) The alergenicity.	Yes
f) The mutagenicity.	No
g) The oncogenicity.	No
h) The teratogenicity.	No
i) The reinfection and/or crossed infection.	Yes
j) The difficulty to maintain the hygienic safety.	Yes
k) The degradation.	Yes
3. Environment hazards and factors contributors.	
a) The electromagnetic fields.	Yes
b) The susceptibility to the electromagnetic interference.	Yes

Generic hazards	Applicable
c) The emissions of electromagnetic interference.	No
d) The inadequate provision of power.	Yes
e) The inadequate provision of coolant.	No
f) The storage or operation outside the prescribed environmental conditions.	Yes
g) The mutual incompatibility with other products with which it is predicted uses.	Yes
h) The accidental mechanic damage.	Yes
i) The contamination due to the remainders and/or the remainder of the sanitary product.	Yes
j) The corrosion.	Yes
k) The flammability.	Yes
l) The inadequate interaction with the surroundings.	No
m) Vent restriction, perspiration	Yes
4. Resulting hazards of the incorrect exit of energy and substances.	
a) The electricity.	Yes
b) The radiation.	No
c) The volume.	No
d) The pressure.	No
e) The medicinal gas provision.	No
f) The provision of anaesthetic agents.	No
5. Hazards related to the use of the sanitary product and factors contributors.	
a) The inadequate labelling.	Yes
b) The inadequate instructions of use.	Yes
c) The inadequate specification of the accessories to use with the sanitary product.	Yes
d) The inadequate specification of the previous verifications to the use of the product.	Yes
e) The excessively complicated instructions of operation.	Yes
f) The inadequate specification of repair and maintenance.	Yes
g) The use of the product by nonqualified personnel without the due formation.	No
h) Reasonably foreseeable the incorrect use.	Yes
i) The insufficient warning on indirect effects.	No

Generic hazards		Applicable
j)	The inadequate warning of probable dangers derived from the sanitary product reusability for a single use.	No
k)	The incorrect measurement and other metrological aspects.	Yes
l)	The incompatibility with consumable/ accessory/ other products.	No
m)	The sharp edges and ends.	Yes
n)	The inadequate subjection or anchorage of components for the foreseeable use.	No
o)	The discomfort in the use and handling (ergonomic principles: position, effort, dimensions, mental stress, confused indication, etc.)	Yes
6.	**Interface with the unsuitable, inadequate or excessively complicated user (continuation man machine)**	
a)	The mistakes and errors of judgment.	Yes
b)	The lapses and the errors of cognitive memory.	Yes
c)	The slipping and errors by distraction (mental or physical).	Yes
d)	The violation or abbreviation of instructions, procedures, etc.	Yes
e)	A complex or confused system control.	Yes
f)	The ambiguous or non clear state of the product.	No
g)	The ambiguous or non clear presentation of adjustments, measurements or another information.	Yes
h)	The false representation of results.	Yes
i)	Visible, audible or insufficiently tactile signals.	Yes
j)	Confused disposition of the controls for an action, or confused representation of the visual reconnaissance to indicate a real state.	Yes
k)	Ways or controverter dispositions of the controls compared with those of the existing equipment.	Yes
7.	**Resulting hazards of a functional failure, the maintenance and the aging and factors contributors.**	
a)	The erroneous transference of data.	Yes
b)	The deficient or inadequate specification of the maintenance, including the inadequate specification of functional verifications after the maintenance.	Yes
c)	The inadequate maintenance.	Yes
d)	The inadequate determination of the end of the life utility of the sanitary product.	Yes
e)	The loss of electrical/mechanical integrity.	Yes
f)	The inadequate packaging (contamination and/or deterioration of the sanitary product).	Yes
g)	The reusability and/or incorrect reusability.	Yes
h)	The functional deterioration (for example, the gradual occlusion of the	Yes

Generic hazards		Applicable
	gas/fluid route or the change in the resistance to the fluid, electrical conductivity) like result of the repeated use.	
i)	Not to be suitable to the predicted functions (stability, subjection, halting, transport, etc.).	Yes
j)	The impossibility or difficulty of repair.	Yes