الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

# MDS – G008

## Guidance on Medical Devices Classification

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# Introduction

## Purpose

The purpose of this guidance is to help medical device manufacturers to correctly classify their devices in KSA.

## Scope

This guidance applies to the following products and parties:

- Medical devices and in-vitro medical devices (IVD)
- Medical devices manufacturers

## Background

SFDA has issued this document according to "Medical Devices Law" published by the Royal Decree No. (M/54) dated 6/7/1442H in reference to the following:

- Article Twenty-one, which stipulates that "The manufacturer shall classify medical devices and supplies in accordance with the Classification System."
- MDS-REQ1: Requirements for Medical Device Marketing Authorization.

# 1. Classification System

## General

The medical devices regulatory framework has a classification system for medical devices as per the classification rules specified in "MDS-REQ1: Requirements for Medical Device Marketing Authorization".

Table 1 - The classification levels for devices other than IVD Medical Devices

| Classification Level | Level of risk |
|---|---|
| Class A | Low |
| Class A – supplied sterile | Low-medium |
| Class A – incorporating a measuring function | Low-medium |
| Class A – reusable surgical instruments | Low-medium |
| Class B | Low-medium |
| Class C | Medium-high |
| Class D | High |

The manufacturer is responsible for determining the classification of a device using a set of classification rules based on the:

- manufacturer's intended use of the device
- level of risk to patients, users and other persons (the probability of occurrence of harm and the severity of that harm)
- degree of invasiveness in the human body
- duration of use

Identical devices may be classified differently if they are to be used in different parts of the body. Therefore, the manufacturer's intended use of the device is critical to determining the appropriate classification. The intended use can be obtained from the:

- Instructions for Use (IFU)
- Label
- Manufacturer's advertising materials
- Technical documentation

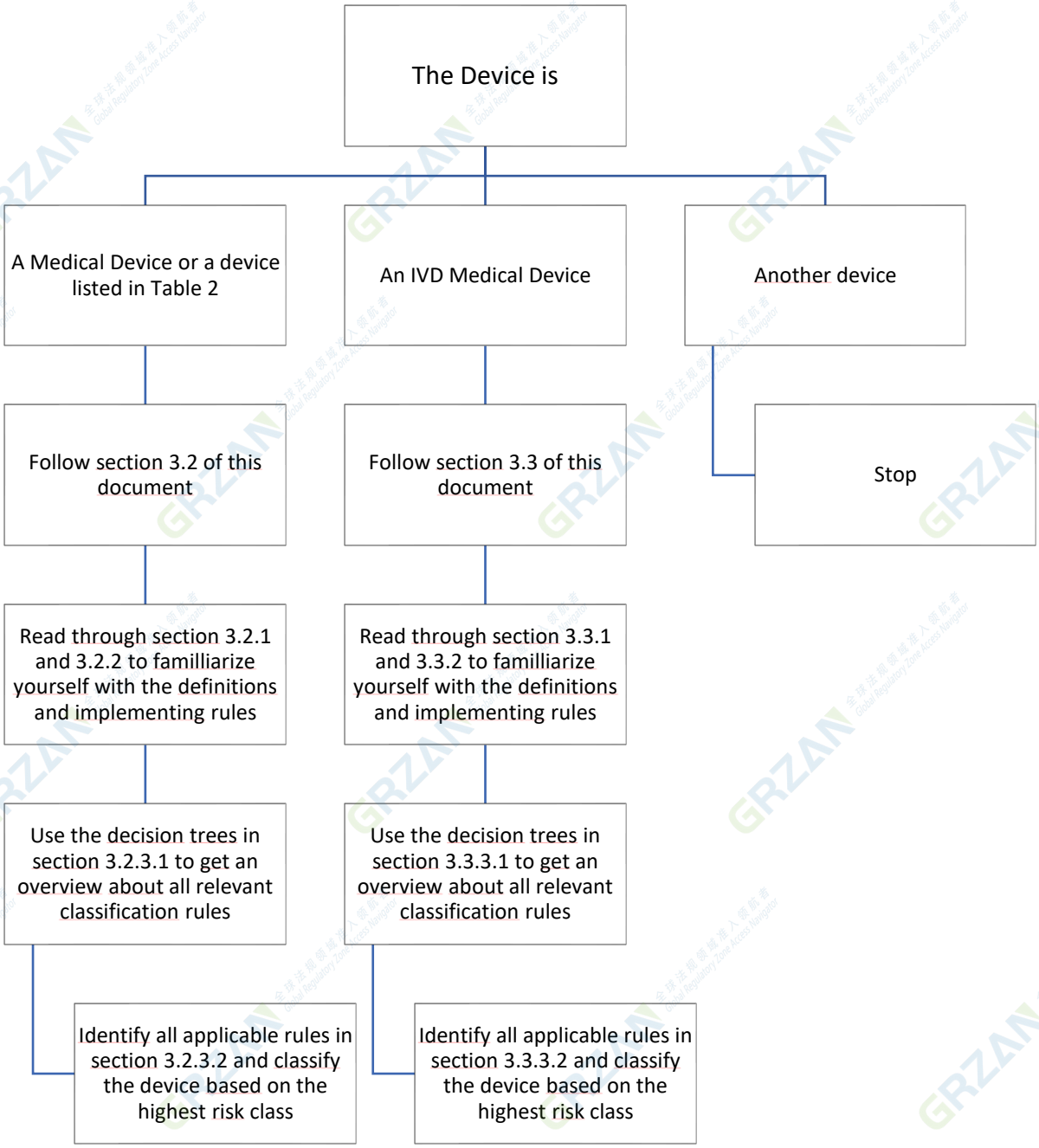
Table 2 - The classification levels IVD Medical Devices

| Classification | Level of risk |
|---|---|
| Class A | Low Individual Risk and Low Public Health Risk |
| Class B | Moderate Individual Risk and/or Low Public Health Risk |
| Class C | High Individual Risk and/or Moderate Public Health Risk |
| Class D | High Individual Risk and High Public Health Risk |

The manufacturer is responsible for determining the class of the IVD by:

- Using the classification rules for IVD medical devices, and
- Considering both the:
  - Intended use of the device,
  - Level of risk to the patient and public of an incorrect result.

Figure 1 - Classification process



## Medical devices without an intended medical purpose

The classification rules are based on different criteria such as the duration of contact with the patient, the degree of invasiveness and the part of the body affected by the use of the device. The implementing rules and related definitions are reproduced below, together with some additional guidance.

In addition to the devices meeting the definitions for medical devices and IVD medical devices per "Medical Devices Executive Regulation", the devices covered in Table 3 below shall also be classified using the classification rules for medical devices.

### Table 3 - Groups of products without an intended medical purpose

| # | Product description | Example |
|---|---|---|
| **1** | Contact lenses or other items intended to be introduced into or onto the eye. | Non-prescription colored contact lenses |
| **2** | Products intended to be totally or partially introduced into the human body through surgically invasive means for the purpose of modifying the anatomy or fixation of body parts with the exception of tattooing products and piercings. | Solid body contour modifying implant (e.g. horn implants) |
| **3** | Substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing. | Dermal fillers |
| **4** | Equipment intended to be used to reduce, remove or destroy adipose tissue, such as equipment for liposuction, lipolysis or lipoplasty. | Body sculpting equipment |
| **5** | High intensity electromagnetic radiation (e.g. infra-red, visible light and ultra-violet) emitting equipment intended for use on the human body, including coherent and non-coherent sources, monochromatic and broad spectrum, such as lasers and intense pulsed light equipment, for skin resurfacing, tattoo or hair removal or other skin treatment. | Intense pulsed light (IPL) machines for body hair removal |
| **6** | Equipment intended for brain stimulation that apply electrical currents or magnetic or electromagnetic fields that penetrate the cranium to modify neuronal activity in the brain. | Transcranial (nonsurgically invasive) stimulation |

# 2. Medical Devises Definition and Implementation Rules

## 2.1. Definition related to classification

### Duration of use

**'Transient'** means normally intended for continuous use for less than 60 minutes.
**'Short term'** means normally intended for continuous use for between 60 minutes and 30 days.
**'Long term'** means normally intended for continuous use for more than 30 days.

In certain instances, the duration of effect for a product needs to be considered as the duration of use. For instance, application of a topical cream to the skin may only take seconds to apply but the cream may remain in situ for many hours. The duration of use should therefore not be considered as the time taken to apply the product but rather the duration for which the product achieves its intended purpose. Refer to section 5.2.2.6 for guidance on continued use.

### Invasive

**'Body orifice'** means any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma.
Natural openings in the body can be considered as: Nostrils (nasal cavity), mouth (oral cavity), ear canal, anus, urinary meatus and vagina.

**'Injured skin or mucous membrane'** means an area of skin or a mucous membrane presenting a pathological change or change following disease, a wound.

**'Invasive device'** means any device which, in whole or in part, penetrates inside the body, either through a body orifice or through the surface of the body.

**'Surgically invasive device'** means:

- an invasive device which penetrates inside the body through the surface of the body, including through mucous membranes of body orifices with the aid or in the context of a surgical operation; and
- a device which produces penetration other than through a body orifice.

The term surgical operation used in this definition includes all clinical interventional procedures in which a device is placed into the body through the surface in the context of a surgical operation or other clinical procedure.

In this context it should be noted the following:

- A surgically created stoma used in urostomy, colostomy and ileostomy or permanent tracheostomy is considered to be a body orifice. Therefore, devices introduced into such a stoma are not surgically invasive. A surgically created opening to allow access to the circulatory system in contrast should not be considered to be such a "body orifice". Devices introduced into such an opening are surgically invasive.
- A device that administers energy to the body should not be considered as invasive if only energy penetrates the body and not the device itself. Energy as such is not a device and therefore it cannot be classified. Only the device generating the energy must be classified. However, if a device administers a substance, whether this substance is a medicine or a medical device, such a substance must be assessed in its own right (e.g. substances administered by a jet injector).

Any device which, in whole or in part, penetrates inside the body, either through a natural body orifice or through the surface of the body is an invasive device. A surgically invasive device always implies that it enters through an artificially created opening. This can be a large opening, such as a surgical incision, or it can be a pinprick opening created by a needle. Therefore, surgical gloves and needles used with syringes are surgically invasive.

The concept of surgically invasive should be understood as covering also liquids that are in invasive contact with organs, tissue or other parts of the body if the access for such liquids is through a surgically created opening.

Figure 2 - Difference between non-surgically and surgically invasive devices

Device, which, in whole or in part penetrates inside the body through:

| Non-Surgically Invasive Device (Rule 5) | Surgically Invasive Device (Rules 6, 7 and 8) |
|---|---|
| • **a body orifice e.g.:**<br>  • Natural opening in the body e.g.:<br>  • nostrils (nasal cavity)<br>  • mouth (oral cavity)<br>  • ear canals<br>  • anus<br>  • urinary meatus<br>  • vagina<br>• External surface of the eyeball<br>• Permanent artificial opening, e.g. stoma | • The surface of the body including through the mucous membrances of body orifice with the aid or in the contex of a surgical operation |

**'Implantable device'** means any device, including those that are partially or wholly absorbed, which is intended:

- to be totally introduced into the human body, or
- to replace an epithelial surface, or
- to replace the surface of the eye,

By clinical intervention and which is intended to remain in place after the procedure. any device intended to be partially introduced into the human body by clinical intervention and intended to remain in place after the procedure for at least 30 days shall also be deemed to be an implantable device.

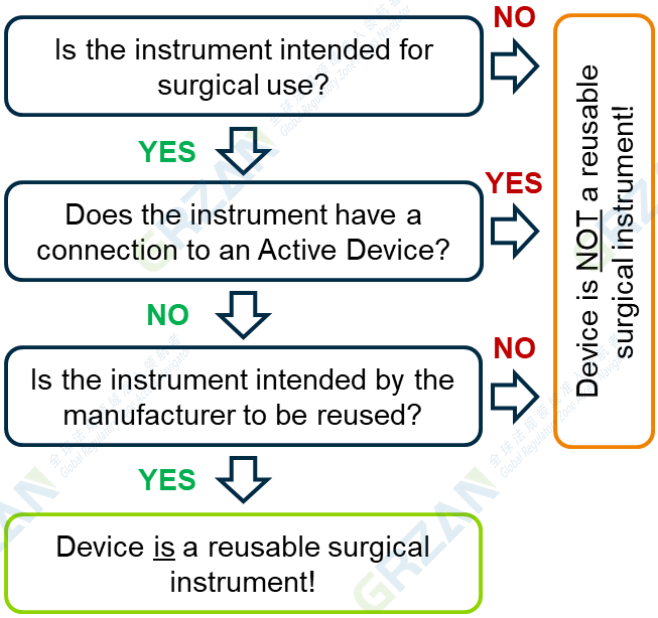
One of the key elements in defining an implantable device is the concept of "procedure". Thus, an implantable device must remain in the patient after the procedure. A "procedure" must be understood in this context to include the surgical procedure during which the implant is placed into the body and the immediate post-operative care that is associated with the procedure. The "procedure" does not extend to the conclusion of the therapeutic treatment, e.g. the removal of an implant must be considered to be another "procedure". Thus, a plate used to reduce a fracture

of the bone is an implant even if it is taken out after the fracture has healed. In this case the placing of the plate and its explanations are two different surgical procedures.

Some partially implanted devices are deemed to be implants. For instance, if an operation is carried out specifically to place an infusion port into the body, then such an infusion port would remain for at least 30 days after the procedure and consequently be an implant. However, a non-tunneled central venous catheter which is intended for use for temporary vascular access and intended to be removed after 7 – 10 days is not a long-term implantable device. Nor would a suture used for skin wound closure that is taken out prior to 30 days be considered an implant.

**'Reusable surgical instrument'** means an instrument intended for surgical use in cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilization have been carried out.

Figure 3 - Decision tree for reusable surgical instruments



**Critical anatomical locations:**

**'Central circulatory system'** means the following blood vessels: arteriae pulmonales, aorta ascendens, arcus aortae, aorta descendens to the bifurcatio aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachiocephalicus, venae cordis, venae pulmonales, vena cava superior and vena cava inferior, iliac arteries, femoral arteries and renal arteries.

**'Central nervous system'** means the brain, meninges, spinal cord, and cerebrospinal fluid.

## Active Medical Devices

Active device means any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose, or by gravity, and which acts by changing the density of or converting that energy.

Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be deemed to be active devices. Software shall also be deemed to be an active device

**'Software**, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right.

The following forms of energy can be considered: thermal, mechanical, electrical, radiant, nuclear, chemical, elastic, magnetic, light, sound, etc.

**Medical devices using prestored gases and/or vacuum as a power source** are regarded as active devices, as long as they fulfil both the criteria under the definition e.g. gas mixers with anaesthesia machines, aerosol pain relief sprays with a pre-stored propellant gas supply and gas-powered suction pumps.

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

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

**'Active therapeutic device'** means any active device used, whether alone or in combination with other devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or disability.

**'Active device intended for diagnosis and monitoring'** means any active device used, whether alone or in combination with other devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities.

Figure 4 - Overview active devices, active therapeutic devices and active devices intended for diagnosis & monitoring

| Active Therapeutic Device | Active Devices Intended for Diagnosis and Monitoring |
|---|---|
| • Active device used, whether alone or in combination with other devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or disability | • Active device used, whether alone or in combination with other devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities |

## Others

**'Non-viable'** means having no potential for metabolism or multiplication.

**'Derivative'** means a 'non-cellular substance' extracted from human or animal tissue or cells through a manufacturing process. The final substance used for manufacturing of the device in this case does not contain any cells or tissues.

**'Nanomaterial'** means a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm. Fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm shall also be deemed to be nanomaterials.

'**Particle'**, for the purposes of the definition of nanomaterial, means a minute piece of matter with defined physical boundaries.

**'Agglomerate'**, for the purposes of the definition of nanomaterial, means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components.

**'Aggregate'**, for the purposes of the definition of nanomaterial, means a particle comprising of strongly bound or fused particles.

**'Serious deterioration in state of health'** means any of the following:

- life-threatening illness or injury,
- permanent impairment of a body structure or a body function,
- hospitalisation or prolongation of patient hospitalisation,
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- chronic disease

## 2.2. Implementing rules

### 2.2.1. Intended purpose

Application of the classification rules shall be governed by the intended purpose of the devices. It is the intended purpose/use that determines the class of the device and not the particular technical characteristics of the device, unless these have a direct bearing on the intended purpose. e.g. incorporation of an ancillary substance, tissue of animal origin etc.

It is the intended and not the accidental use of the device that determines the class of the device. For instance, a suture organizer, that is intended to keep order of suture threads used in open heart surgery, should not be considered as an invasive device if in the normal use it can be kept outside the patient. Similarly, if a medical practitioner uses the device in a manner not intended by the manufacturer, this does not change the class of the device for the purpose of conformity assessment. However, if the normal clinical use of the device changes in time with evolving clinical practice such that the intended purpose and classification of the device changes this should be addressed by the manufacturer and the conformity of the device assessed for the new intended purpose.

It is the intended purpose assigned by the manufacturer to the device that determines the class of the device and not the class assigned to other similar products. For instance, two sutures that have the same composition may well have different intended purposes.

For a device to be "intended specifically" for the purpose referenced in a particular classification rule, the manufacturer must clearly indicate that the device is intended for such a specific purpose in the information accompanying the device. Otherwise it is deemed to have the intended use which is principally used and accepted in general medical practice. Only the following rules use the term “intended specifically”: Rules 6, 7, 10, 16 and 17.

### 2.2.2. Combination with another device and accessories

If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. Accessories for a medical device and for a product listed in Table 2 shall be classified in their own right separately from the device with which they are used.

Systems may be classified as a whole based on their intended use. As an alternative to classifying the system as a whole, the determination of the class of a particular device may be made with respect to the simplest configuration that can still be considered, in view of its proper functional features, as a device in its own right. A device that is part of a system, e.g. a tube in an extra corporeal circulation set, may be classed as a device in its own right rather than classifying the system as a whole. The device, however, must be cleared in its own right as a separate device in such instances.

Similarly, combined devices with parts that have different functional purposes may be analysed separately with respect to each of these parts. For instance, a drainage device will have an invasive tube and a non-invasive collection device. These components may be classified separately, provided that they are also cleared separately.

Figure 5 - Options for classifying a simple wound drainage device

A simple wound drainage device has three components that must be taken into consideration: the cannula, the tubing and the collector unit.

If the device is sold without a cannula, then the classification of the cannula does not need to be taken into account.

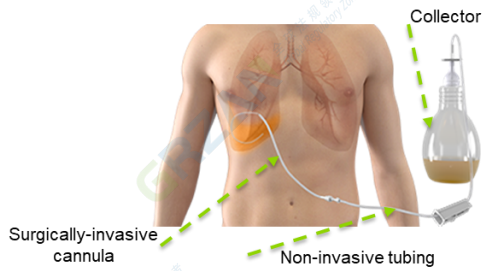
Assumptions:

- short term use (60 min > t < 30 days)
- collected liquids are not intended to be reinfused into the body nor reprocessed for eventual reinfusion

The clear conclusion here is that the manufacturer would have a choice of applying:

- Class B to the whole device or
- Carrying out separate conformity assessment procedures for the cannula on one hand and the tubing and collector on the other hand.

| Intended uses | Rule | Class |
|---|---|---|
| Surgically invasive cannula to reach a wound site in the pleural cavity to drain the cavity | 7 | B |
| Non-invasive tubing to evacuate body liquids towards the collector | 1 | A |
| Non-invasive collector to receive the body liquids | 1 | A |




### 2.2.3. Body parts

If the device is not intended to be used solely or principally in a specific part of the body, it shall be considered and classified on the basis of the most critical specified use.

Classification of the device will have to be determined on the basis of claims contained in the information provided with the device. The manufacturer must be sufficiently specific in that regard. If the manufacturer wants to avoid the particular higher classification, then it must clearly define on the labelling the intended purpose in such a way that the device falls into the lower class. The manufacturer must provide as a minimum requirement either appropriate positive or negative indications for use. For example, a catheter could be used within the

central circulatory system, however an explicit exclusion must be documented in the intended use to ensure it would not be classified in the higher class.

### 2.2.4. Devices falling into several (sub-) rules

If several rules, or if, within the same rule, several sub-rules, apply to the same device based on the device's intended purpose, the strictest rule and sub-rule resulting in the higher classification shall apply.

For instance, a wound dressing incorporating collagen is covered by rules 4 (Class A, Class B or Class C depending on intended use) and 18 (Class D), therefore the higher classification (Class D) would apply. All rules must be considered, for instance if an active device is also surgically invasive, the relevant rules for surgically invasive devices must also be considered.

### 2.2.5. Concept of continuous use

In calculating the duration referred to in Section 5.2.1.1, continuous use shall mean:

a) the entire duration of use of the same device without regard to temporary interruption of use during a procedure or temporary removal for purposes such as cleaning or disinfection of the device. Whether the interruption of use or the removal is temporary shall be established in relation to the duration of the use prior to and after the period when the use is interrupted or the device removed; and
b) the accumulated use of a device that is intended by the manufacturer to be replaced immediately with another of the same type.

For example, a scalpel may be used on the same patient throughout an operation that may last for several hours. The uninterrupted use for an intended purpose, i.e. cutting tissue, will normally not last for more than a few seconds at a time. Therefore, a scalpel is a transient use device.

However, where usage of a device is discontinued in order for the device to be replaced immediately by the same or an identical device (e.g. replacement of a ureteric catheter) this shall be considered an extension of the continuous use of the device.

If it cannot be demonstrated that components of the device are totally eliminated in the interval between uses, this is also considered as an immediate replacement.

#### 2.2.6. Devices allowing direct diagnosis

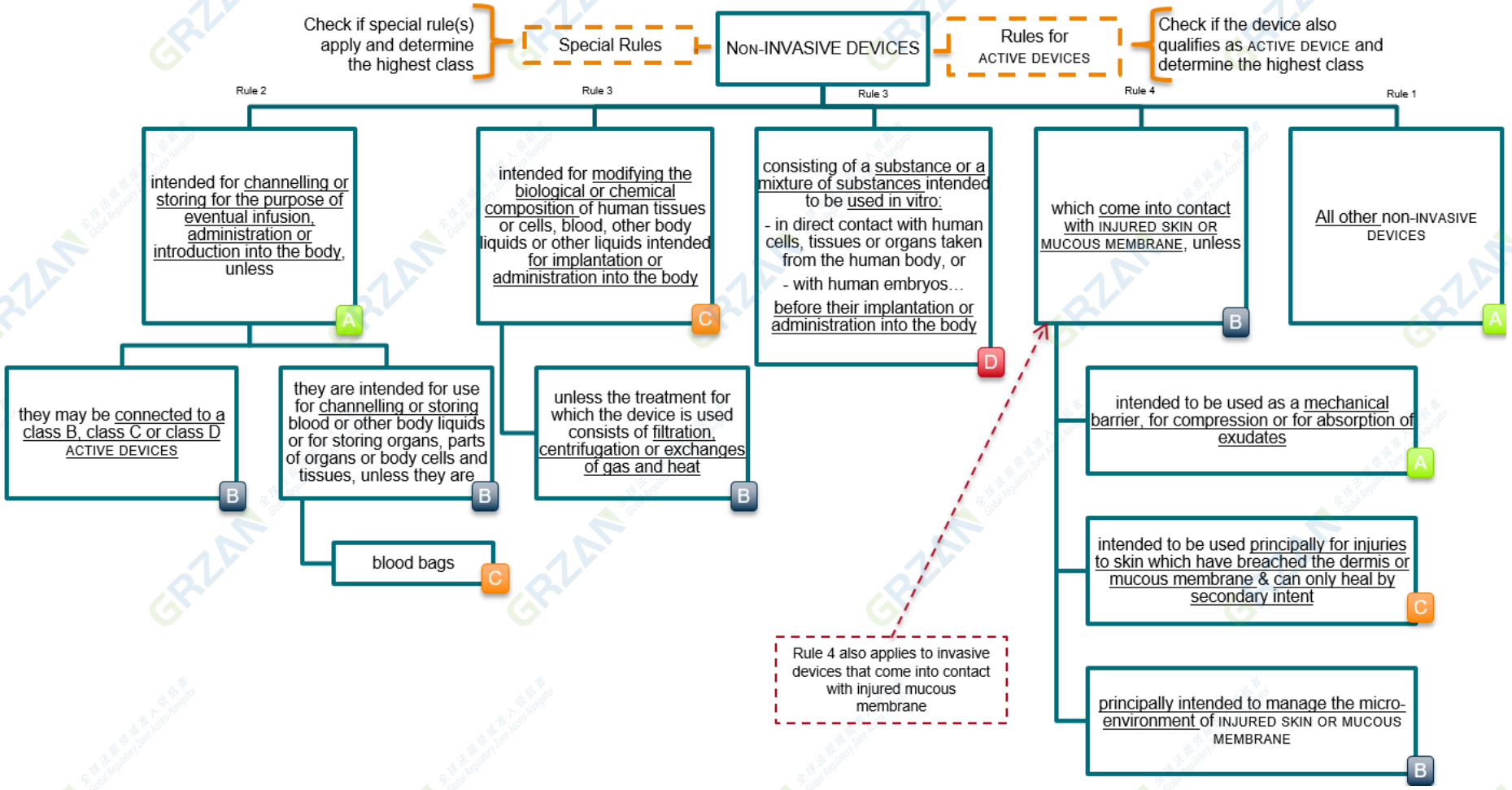
A device is considered to allow direct diagnosis when it provides the diagnosis of the disease or condition in question by itself or when it provides decisive information for the diagnosis.

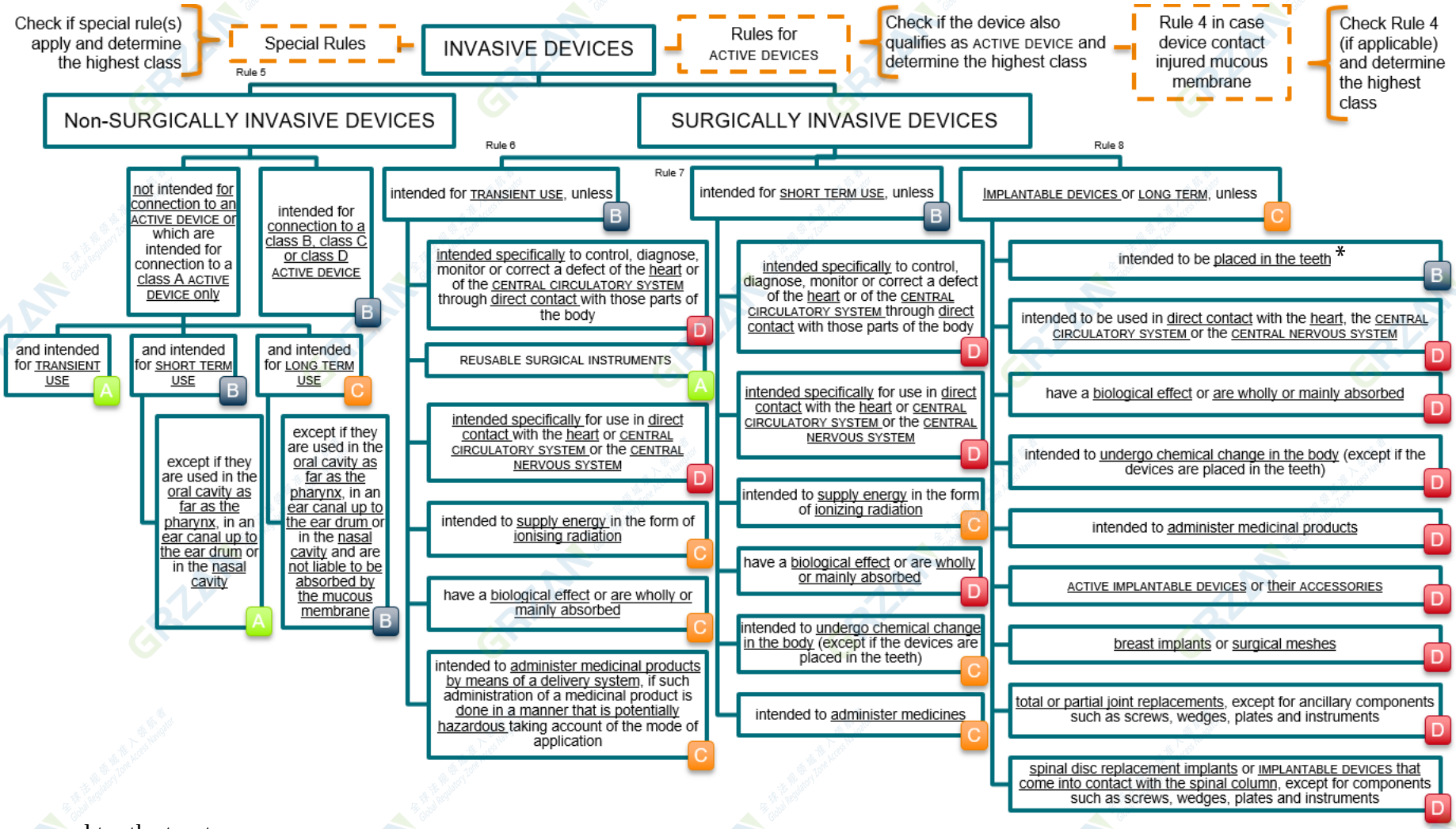
### 2.3. Explanation of the individual rules

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

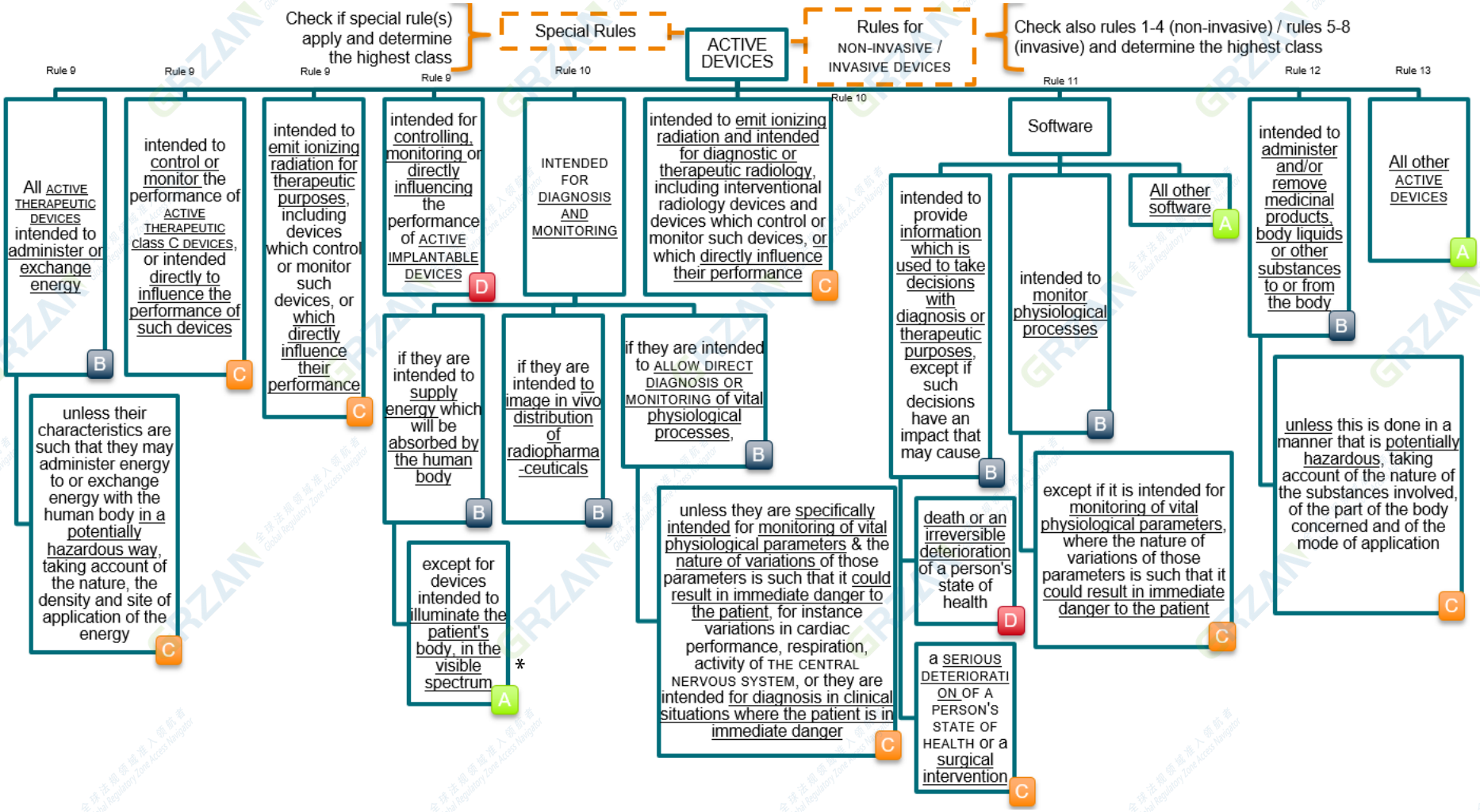
#### 2.3.1. Classification guidance chart for initial identification of probable device class

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

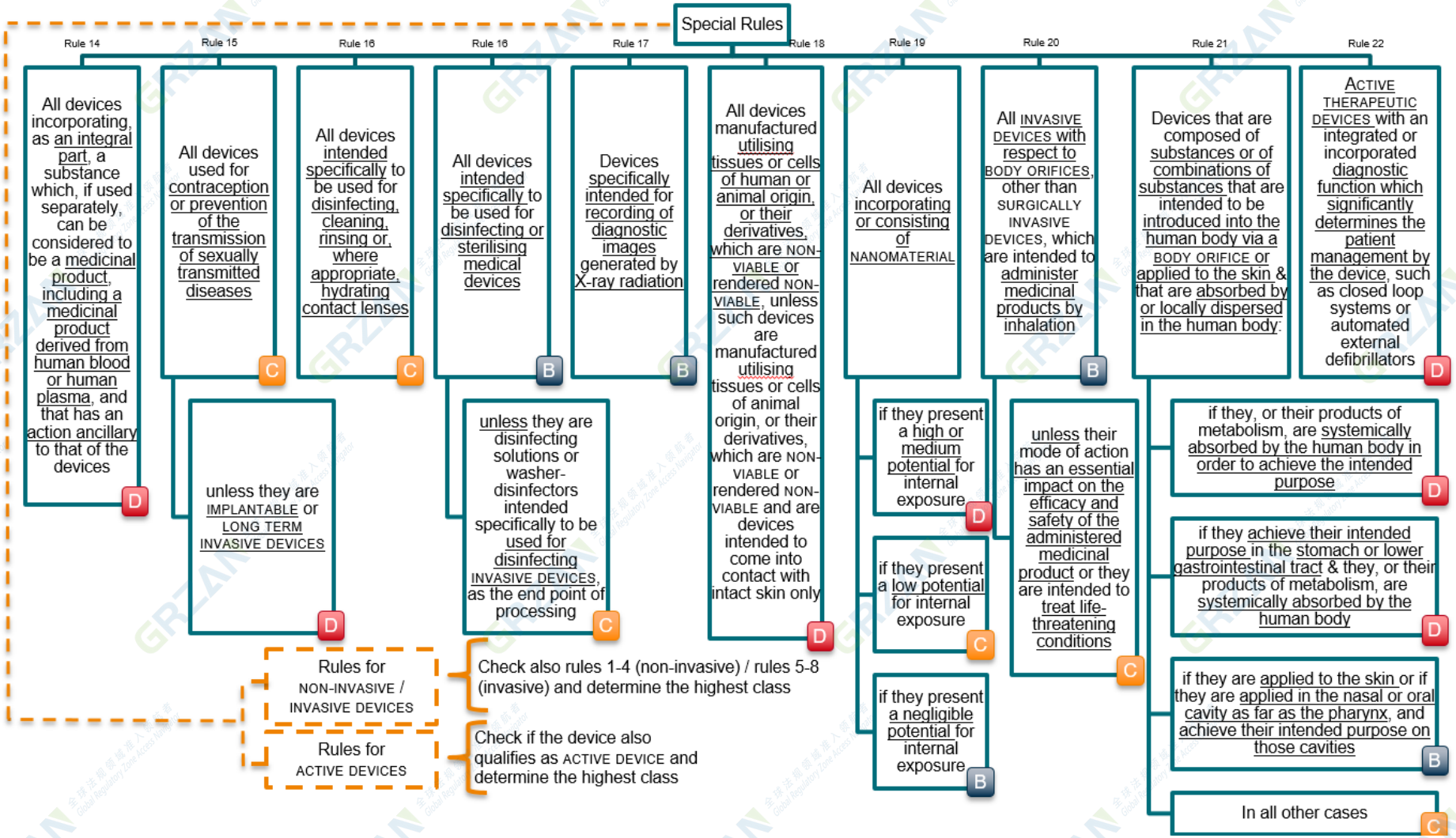

Check if special rule(s) apply and determine the highest class
Special Rules
NON-INVASIVE DEVICES
Rules for ACTIVE DEVICES
Check if the device also qualifies as ACTIVE DEVICE and determine the highest class
Rule 2
Rule 3
Rule 3
Rule 4
Rule 1
intended for channelling or storing for the purpose of eventual infusion, administration or introduction into the body, unless
A
they may be connected to a class B, class C or class D ACTIVE DEVICES
B
they are intended for use for channelling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, unless they are
B
blood bags
C
intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body
C
unless the treatment for which the device is used consists of filtration, centrifugation or exchanges of gas and heat
B
consisting of a substance or a mixture of substances intended to be used in vitro:
- in direct contact with human cells, tissues or organs taken from the human body, or
- with human embryos…
before their implantation or administration into the body
D
Rule 4 also applies to invasive devices that come into contact with injured mucous membrane
which come into contact with INJURED SKIN OR MUCOUS MEMBRANE, unless
B
intended to be used as a mechanical barrier, for compression or for absorption of exudates
A
intended to be used principally for injuries to skin which have breached the dermis or mucous membrane & can only heal by secondary intent
C
principally intended to manage the micro-environment of INJURED SKIN OR MUCOUS MEMBRANE
B
All other non-INVASIVE DEVICES
A




* or prepared tooth structure




* or near infra-red spectrum


Special Rules
Rule 14
All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, including a medicinal product derived from human blood or human plasma, and that has an action ancillary to that of the devices
D
Rule 15
All devices used for contraception or prevention of the transmission of sexually transmitted diseases
C
unless they are IMPLANTABLE or LONG TERM INVASIVE DEVICES
D
Rule 16
All devices intended specifically to be used for disinfecting, cleaning, rinsing or, where appropriate, hydrating contact lenses
C
Rule 16
All devices intended specifically to be used for disinfecting or sterilising medical devices
B
unless they are disinfecting solutions or washer-disinfectors intended specifically to be used for disinfecting INVASIVE DEVICES, as the end point of processing
C
Rule 17
Devices specifically intended for recording of diagnostic images generated by X-ray radiation
B
Rule 18
All devices manufactured utilising tissues or cells of human or animal origin, or their derivatives, which are NON-VIABLE or rendered NON-VIABLE, unless such devices are manufactured utilising tissues or cells of animal origin, or their derivatives, which are NON-VIABLE or rendered NON-VIABLE and are devices intended to come into contact with intact skin only
D
Rule 19
All devices incorporating or consisting of NANOMATERIAL
if they present a high or medium potential for internal exposure
D
if they present a low potential for internal exposure
C
if they present a negligible potential for internal exposure
B
Rule 20
All INVASIVE DEVICES with respect to BODY ORIFICES, other than SURGICALLY INVASIVE DEVICES, which are intended to administer medicinal products by inhalation
B
unless their mode of action has an essential impact on the efficacy and safety of the administered medicinal product or they are intended to treat life-threatening conditions
C
Rule 21
Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a BODY ORIFICE or applied to the skin & that are absorbed by or locally dispersed in the human body:
if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose
D
if they achieve their intended purpose in the stomach or lower gastrointestinal tract & they, or their products of metabolism, are systemically absorbed by the human body
D
if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities
B
In all other cases
C
Rule 22
ACTIVE THERAPEUTIC DEVICES with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators
D
Rules for NON-INVASIVE / INVASIVE DEVICES
Check also rules 1-4 (non-invasive) / rules 5-8 (invasive) and determine the highest class
Rules for ACTIVE DEVICES
Check if the device also qualifies as ACTIVE DEVICE and determine the highest class

### 2.3.2. General explanation of rules, practical issues and examples

#### Rule 1 - Devices that either do not come in direct contact with the patient or contact intact skin only General explanation of the rule.

This is a fallback rule applying to all devices that are not covered by a more specific rule. This is a rule that applies in general to devices that come into contact only with intact skin[1] or that do not touch the patient.

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

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

[1] Intact skin includes the skin around an established stoma unless the skin is breached. Signs of breached skin include, but not limited to, tears, erythema, oedema, weeping and infection. The definition of intact skin must apply for the continuous use of the device.

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| | | • Non-invasive conductive gels i.e. ultrasound gels[2]<br>• Non-invasive electrodes (electrodes for EEG or ECG)<br>• Image intensifying screens<br>• Permanent magnets for removal of ocular debris<br>• 3D printed surgical models used for treatment planning which are NOT placed in contact with the patient. |

### Rule 2 - Channeling or storing for eventual administration

These types of devices must be considered separately from the non-contact devices of rule 1 because they may be indirectly invasive. They channel or store substances that will eventually be administered to the body. Typically, these devices are used in transfusion, infusion, extracorporeal circulation and delivery of anesthetic gases and oxygen.
In some cases, devices covered under this rule are very simple gravity activated delivery devices.

This rule applies to non-invasive devices intended for channeling or storing blood, body liquids, cells or tissues, liquids or gases for specific purposes. Invasive devices, other than surgically invasive devices which are intended to administer medicinal products by inhalation, fall under the Rule 20.

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

| Class | RULE 2 | Description & examples |
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| **B** | All non-invasive devices intended for channeling or storing blood, body liquids, cells or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are classified as class B: | • Devices intended to be used as channels in active drug delivery systems, e.g. tubing intended for use with an infusion pump<br>• Devices used for channeling, e.g. antistatic tubing for anaesthesia, anaesthesia breathing circuits, oxygen tubing and masks |

[2] Ultrasound gels are not to be absorbed or locally dispersed within the body at the site of action in order to achieve their intended purpose.

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| | a) If they may be connected[3] to a class B, class C or class D active device; | • Syringes & tubing for infusion pumps |
| | b) If they are intended for use for channeling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, | • Devices intended to channel blood (e.g. in transfusion, extracorporeal circulation)<br>• Devices intended for temporary storage and transport of organs for transplantation (i.e. containers, bags and similar products)<br>• Devices intended for long term storage of biological substances and tissues such as corneas, sperm, human embryos, etc. (i.e. containers, bags and similar products)<br>• Fridges/freezers specifically intended for storing blood , tissues etc.<br>• Tubings/blood lines for extracorporeal treatment (dialysis and apheresis therapies) |
| **C** | Except for blood bags; blood bags are classified as class C. | Blood bags without a substance which, if used separately, can be considered to be a medicinal product |
| **A** | In all other cases, such devices are classified as class A. | • Non-invasive devices that provide a simple channeling function, with gravity providing the force to transport the liquid, e.g. administration sets for infusion<br>• Devices intended to be used for a temporary containment or storage function, e.g. cups and spoons specifically intended for administering medicines<br>• Empty syringes without needles |

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

## Rule 3 - Devices that modify biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body

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

These devices are normally used in conjunction with an active medical device covered under Rule 9 or Rule 12. Filtration and centrifugation should be understood in the context of this rule as exclusively mechanical methods.

| Class | RULE 3 | Description & examples |
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| **C** | All non-invasive devices intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body are classified as class C, | • Devices intended to remove undesirable substances out of the blood by exchange of solutes such as hemodialysers<br>• Devices intended to separate cells by physical means, e.g. gradient medium for sperm separation<br>• Haemodialysis concentrates<br>• Device removing specific blood cells (e.g. activated) by specific binding to a matrix |
| **B** | unless the treatment for which the device is used consists of filtration, centrifugation or exchanges of gas, heat, in which case they are classified as class B | • Particulate filtration of blood in an extracorporeal circulation system. These are used to remove particles and emboli from the blood<br>• Centrifugation of blood to prepare it for transfusion or autotransfusion excluding centrifuges for manufacturing a medicinal product<br>• Removal of carbon dioxide from the blood and/or adding oxygen<br>• Warming or cooling the blood in an extracorporeal circulation system |
| **D** | All non-invasive devices consisting of a substance or a mixture of substances intended to be used in vitro in direct contact with human | • Substances or mixture of substances for transport, perfusion, storage of organs intended for transplantation |

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| | cells, tissues or organs taken from the human body or used in vitro with human embryos before their implantation or administration into the body are classified as class D. | that do not achieve the principal intended action by pharmacological, immunological or metabolic means<br>• Devices for processing and preservation of human cells, tissues and organs<br>• Some agents for transport, nutrition and storage of organs intended for transplantation may be qualified and regulated as medical devices provided that they meet the definition of a medical device, taking into consideration the principal intended action and intended purpose of the product<br>• IVF or ART products without principal pharmacological/metabolic action (substances or mixture of substances)<br>• IVF cell media without human albumin |

### Rule 4 - Devices that come into contact with injured skin or mucous membrane General explanation of the rule

This rule is intended to primarily cover wound dressings independently of the depth of the wound. The traditional types of products, such as those used as a mechanical barrier, are well understood and do not result in any great hazard. There have also been rapid technological developments in this area, with the emergence of new types of wound dressings for which non-traditional claims are made, e.g. management of the micro-environment of a wound to enhance its natural healing mechanism.

More ambitious claims relate to the mechanism of healing by secondary intent, such as influencing the underlying mechanisms of granulation or epithelial formation or preventing contraction of the wound. Some devices used on breached dermis may even have a life-sustaining or lifesaving purpose, e.g. when there is full thickness destruction of the skin over a large area and/or systemic effect.

Dressings containing medicinal products which act ancillary to the dressing fall within Class D under Rule 14. Devices composed of other substances which are absorbed by or locally dispersed in the human body fall under Rule 21.

Products covered under this rule are extremely claim sensitive, e.g. a polymeric film dressing would be in Class B if the intended use is to manage the micro-environment of the wound or in Class A if its intended use is limited to retaining an invasive cannula at the wound site. Consequently, it is impossible to say a priori that a particular type of dressing is in a given class without knowing its intended use as defined by the manufacturer. However, a claim that the device is interactive or active with respect to the wound healing process usually implies that the device is in Class C.
Most dressings that are intended for a use that is in Class B or C, also perform functions that are in Class A, e.g. that of a mechanical barrier. Such devices are nevertheless classed according to the intended use in the higher class.

For such devices incorporating a medicinal product or a human blood derivative see Rule 14 or animal tissues or derivatives rendered non-viable see Rule 18.

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

| Class | RULE 4 | Description & examples |
|---|---|---|
| **A** | All non-invasive devices which come into contact with injured skin or mucous membrane & invasive devices that come into contact with injured mucous membrane are classified as:<br>a) Class A if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates; | • Wound dressings for skin or mucous, such as:<br>• Absorbent pads<br>• Island dressings<br>• Cotton wool<br>• Wound strips<br>• Adhesive bandages (sticking plasters, Band-Aid) |

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| | | • Gauze dressings which act as a barrier, maintain wound position or absorb exudates from the wound<br>• Ostomy bags |
| **C** | b) Class C if they are intended to be used principally for injuries to skin which have breached the dermis or mucous membrane and can only heal by secondary intent; | • Are principally intended to be used with severe wounds that have substantially and extensively breached the dermis, and where the healing process can only be by secondary intent such as:<br>• Dressings for chronic extensive ulcerated wounds<br>• Dressings for severe burns having breached the dermis and covering an extensive area<br>• Dressings for severe decubitis wounds<br>• Dressings incorporating means of augmenting tissue and providing a temporary skin substitute<br>• Dressings, pads or swabs intended for wound debridement |
| **B** | c) Class B if they are principally intended to manage the micro-environment of injured skin or mucous membrane; | • Have specific properties intended to assist the healing process by controlling the level of moisture at the wound during the healing process and to generally regulate the environment in terms of humidity and temperature, levels of oxygen and other gases and pH values or by influencing the process by other physical means<br>• Hydrogel dressings for wounds or injuries that have not breached the dermis or can only heal by secondary intent<br>• Non-medicated impregnated gauze dressings<br>• Polymer film dressings |
| **B** | d) Class B in all other cases. | These devices may specify particular additional healing properties whilst not being intended for extensive wounds requiring healing by secondary intent. |

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| | This rule applies also to the invasive devices that come into contact with injured mucous membrane. | • Dressings for nose bleeds (if purpose of the dressing is not to manage micro-environment) are in class A according to this rule<br>• Dental wound dressings not containing animal derived material |

### Rule 5 - Devices invasive with respect to body orifices

Invasiveness with respect to the body orifices (ear, mouth, nose, eye, anus, urethra and vagina) must be considered separately from invasiveness that penetrates through a cut in the body surfaces (surgical invasiveness). For short term use, a further distinction must be made between invasiveness with respect to the less vulnerable anterior parts of the ear, mouth and nose and the other anatomical sites that can be accessed through natural body orifices.

Surgically created stoma, which for example allows the evacuation of urine or faeces, should also be considered as a body orifice. Devices covered by this rule tend to be diagnostic and therapeutic instruments used in particular specialties (ENT, ophthalmology, dentistry, proctology, urology and gynaecology).

Regarding devices intended for connection to an active device: the strictest rule and sub-rule resulting in higher classification will apply. For instance, a trachea cannula for long-term use needs to be classified as class C. Devices composed of substances which are absorbed by or locally dispersed in the human body may also fall under Rule 21

| Class | RULE 5 | Description & examples |
|---|---|---|
| **A** | All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a class A active device are classified as:<br>a) Class A if they are intended for transient use; | • Handheld mirrors used in dentistry to aid in dental diagnosis and surgery<br>• Dental impression materials<br>• Tubes used for pumping the stomach<br>• Impression trays<br>• Enema devices<br>• Examination gloves<br>• Urinary catheters intended for transient use<br>• Prostatic balloon dilation catheters<br>• Embryo transfer catheter and insemination catheter |
| **B** | b) Class B if they are intended for short-term use, | • Short term corrective contact lenses<br>• Tracheal tubes<br>• Stents |

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| | | • Vaginal pessaries<br>• Indwelling urinary catheters intended for short term use<br>• Perineal reduction devices<br>• Gasses used for insufflation in the body<br>• Nasobilliary tubes |
| **A** | 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 the nasal cavity, in which case they are classified as class A; | • Materials for manufacturing dentures<br>• Materials for dental impressions<br>• Plastic syringe used to measure a quantity of medicinal product before oral administration to the patient<br>• Removable or fixed dental prostheses |
| **C** | c) Class C if they are intended for long-term use, | • Urethral stents<br>• Long term corrective contact lenses<br>• Tracheal cannulae for tracheostoma for long term use<br>• Urinary catheters intended for long term use<br>• Artificial eyes |
| **B** | 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 the nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class B. | • Orthodontic wires<br>• Fixed dental prostheses<br>• Fissures sealants |
| **B** | All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to a class B, class C or class D active device, are classified as class B. | • Tracheostomy or tracheal tubes connected to a ventilator<br>• Blood oxygen analysers placed under the eye-lid<br>• Powered nasal irrigators<br>• Nasopharyngeal airways<br>• Some enteral feeding tubes<br>• Fibre optics in endoscopes connected to surgical lasers<br>• Suction catheters or tubes for stomach drainage<br>• Dental aspirator tips<br>• Heat & moisture exchangers<br>• Endoscopes using a light source in the visible spectrum |

| Class | RULE 6 | Description & examples |
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| **B** | All surgically invasive[4] devices intended for transient use are classified as class B unless they: | • Suture needles, Hypodermic needles<br>• Needles of syringes<br>• Lancets<br>• Suckers<br>• Single use scalpels and single use scalpel blades<br>• Support devices in ophthalmic surgery<br>• Surgical swabs<br>• Drill bits connected to active devices<br>• Surgical gloves<br>• Etchants<br>• Tester of artificial heart valves<br>• Orthopaedic trials and jigs.<br>• Heart valve occluders, sizers and holders<br>• Swabs to sample exudates<br>• Single use aortic punches<br>• Guidewires or catheters used outside the central circulatory system |
| **D** | a) Are intended specifically to control, diagnose, monitor or correct a defect[5] of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class D; | • Cardiovascular catheters (e.g. angioplasty balloon catheters, stent delivery catheters/systems), including related guidewires, related introducers and dedicated[6] disposable cardiovascular surgical instruments e.g. electrophysiological catheters, electrodes for electrophysiological diagnosis and ablation<br>• Catheters containing or incorporating sealed radioisotopes, where the radioactive isotope is not intended to be released into the body, if used in the central circulatory system<br>• Distal protection devices<br>• Angioplasty balloon catheters<br>• Coronary artery probes |
| **A** | b) Are reusable surgical instruments, in which case they are classified as class A[7]; | • Scalpels and scalpel handles, reamers, drill bits, scissors<br>• Saws, that are not intended for connection to an active device<br>• Retractors forceps, excavators and chisels |

[4] "Surgically invasive device", "central circulatory system", “central nervous system” and "reusable surgical instruments" are defined terms. In particular, surgical instruments connected to an active device are not considered to be “reusable surgical instruments”.
[5] The expression "correct a defect" does not cover devices that are used accessorily in heart surgery procedures, e.g. clamps, aortic punch instruments. The first indent of this rule does not apply to aortic punches and similar cutting instruments which perform a similar function to a scalpel.
[6] Dedicated means that the intended purpose of the device or accessory is to specifically control, diagnose, monitor or correct a defect of the heart or of the central circulatory system.
[7] Surgical instruments which are not specifically intended for purposes described in the a), and irrespective of the site of application, are in class B, if they are intended for single use and in class A if they are reusable.

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| | | • Sternum retractors for transient use<br>• Staplers (outside the heart, central circulatory or central nervous system<br>• Dental Osteotomes |
| **D** | c) Are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as class D; | • Neuro-endoscopes<br>• Brain spatulas<br>• Direct stimulation canulae<br>• Spinal cord retractors<br>• Spinal needles<br>• Cranium guide for use in craniotomy<br>• Dura mater protection; Bone punch for use on the cranium (Intended use: The dura mater protection is intended to protect the dura mater during surgical procedures. It has direct contact to the CNS. The bone punch can be used at the cranium. A direct contact to the CNS is possible during application.)<br>• Peripherally inserted central catheter (PICC) line<br>• Heart valve occluders, sizers and holders<br>• Cardiovascular drainage cannula specifically intended to circulate blood whilst located in the heart or central vascular system<br>• Cryo-ablation of the heart or spine<br>• Appliers/Forceps for aneurysm clips |
| **C** | d) Are intended to supply energy in the form of ionising radiation in which case they are classified as class C; | Catheters containing or incorporating sealed radioisotopes, where the radioactive isotope as such is not intended to be released into the body, if used in the circulatory system, excluding the central circulatory system |
| **C** | e) Have a biological effect[8] or are wholly or mainly absorbed[9] in which case they are classified as class C; or | • Insufflation gases for the abdominal cavity<br>• Viscoelastic solution for ophthalmic surgery |
| **C** | f) Are intended to administer medicinal products by means of a delivery system, if such administration of a medicinal product is done in a manner that is potentially hazardous[10] taking account of the mode of application, in which case they are classified as class C. | Devices for repeated self-application where dosage levels and the nature of the medicinal product are critical, e.g., refillable insulin pens and analgesia pumps. |

[8] Biological effect: All materials and devices have the potential to affect tissues following use in a surgically invasive procedure. A material is considered to have a biological effect if it actively and intentionally induces, alters or prevents a response from the tissues that is mediated by specific reactions at a molecular level. Such a device may be described as bioactive.
[9] Wholly or mainly absorbed: The term absorption refers to the degradation of a material within the body and the metabolic elimination of the resulting degradation products from the body.
[10] The concept of "potentially hazardous manner" is related to the characteristics of the device and not the competence of the user.

### Rule 6 - Surgically invasive devices intended for transient use (<60 min)

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

### Rule 7 - Surgically invasive devices intended for short-term use (> 60 min <30 days)

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

| Class | RULE 7 | Description & examples |
|---|---|---|
| **B** | All surgically invasive devices intended for short-term use are classified as class B unless they: | • Clamps<br>• Skin closure devices<br>• Temporary filling materials<br>• Tissue stabilisers used in cardiac surgery<br>• Infusion cannulae<br>• Arthroscopy trocars<br>• Insufflation gases for surgically invasive endoscopic procedures |
| **D** | a) Are intended specifically to control, diagnose, monitor or correct a defect[11] of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class D; | • Cardiovascular catheters<br>• Cardiac output probes<br>• Temporary pacemaker leads<br>• Thoracic catheters intended to drain the heart, including the pericardium<br>• Carotid artery shunts<br>• Ablation catheter<br>• Heart bypass cannula (aortic perfusion cannula and venous drainage cannula)<br>• Peripherally inserted central catheter (PICC) line and central line |
| **D** | b) Are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as class D; | • Neurological catheters<br>• Cortical electrodes<br>• Central venous/vascular catheters |
| **C** | c) Are intended to supply energy in the form of ionizing radiation in which case they are classified as class C; | • Brachytherapy devices |

[11] The expression “correct a defect” does not cover devices that are used accessorily in heart surgery, e.g. tissue stabilizers.

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| **D** | d) Have a biological effect or are wholly or mainly absorbed in which case they are classified as class D; | • Absorbable sutures<br>• Biological/tissue adhesives<br>• Absorbable haemostatic sponge |
| **C** | e) Are intended to undergo chemical change in the body in which case they are classified as class C, except if the devices are placed in the teeth; or | • Surgical adhesive (other than biological)<br>• Vascular closure devices<br>• Haemostatic foams |
| **C** | f) Are intended to administer medicines[12], in which case they are classified as class C. | • Temporal dialysis catheter, CVVH catheter |

| Class | RULE 8 | Description & examples |
|---|---|---|
| **C** | All implantable devices and long-term surgically invasive devices are classified as class C unless they: | • Artificial ligaments for reinforcement<br>• Dental implants and abutments<br>• Shunts<br>• Stents and valves (e.g., pulmonary and peripheral)<br>• Nails and plates<br>• Intra-ocular lenses<br>• Internal closure devices (including vascular closure devices[13])<br>• Tissue augmentation implants (excluding breasts)<br>• Peripheral vascular catheters for long-term use<br>• Peripheral vascular grafts and stents<br>• Penile implants<br>• Non-absorbable sutures, non-biodegreable bone cements and maxillo-facial implants, viscoelastic surgical devices intended specifically for ophthalmic anterior segment surgery[14]<br>• Pedicle screws |
| **B** | a) Are intended to be placed in the teeth[15], or on a prepared tooth | • Bridges and crowns<br>• Dental filling materials and pins |

[12] Administration of medicines is more than just channelling, it implies also storage and/or influencing the volume and rate of the medicine delivered. Implanted capsules for the slow release of medicines are medicines and not medical devices.
[13] For closure of arteriotomies in the peripheral vascular system. (please refer to definition of central circulatory system)
[14] These products are implants because in normal conditions a significant amount of the substance remains at the surgical site after the procedure. If these devices contain animal tissues or derivatives of animal tissues, they are covered by Rule 18.
[15] Implants without bioactive coatings intended to secure teeth or prostheses to the maxillary or mandibular bones are in Class C following the general rule. Hydroxyapatite is considered as having biological effect only if so claimed and demonstrated by the manufacturer.

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| | structure, in which case they are classified as class B; | • Dental alloys, ceramics and polymers |
| **D** | b) Are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are classified as class D; | • Prosthetic heart valves<br>• Aneurysm clips<br>• Vascular prosthesis and stents<br>• Central vascular catheters<br>• Spinal stents<br>• CNS electrodes<br>• Cardiovascular sutures<br>• Permanent and retrievable vena cava filters<br>• Septal occlusion devices<br>• Intra-aortic balloon pumps<br>• External left ventricular assisting devices |
| **D** | c) Have a biological effect or are wholly or mainly absorbed, in which case they are classified as class D; | • Absorbable sutures<br>• Adhesives and implantable devices claimed to be bioactive through the attachment of surface coatings such as phosphorylcholine<br>• Biodegrable Bone Cements<br>• Elastoviscus fluids for joint movement (eg. hyaluronan of non-animal origin) |
| **D** | d) Are intended to undergo chemical change[16] in the body in which case they are classified as class D, except if the devices are placed in the teeth; | • Surgical adhesives for long term use |
| **D** | e) Are intended to administer medicinal products, in which case they are classified as class D; | • Rechargeable non-active drug delivery system<br>• Peritoneal dialysis |
| **D** | f) Are active implantable devices or their accessories, in which cases they are classified as class D; | • Cochlear implant system and accessories<br>• Implantable defibrillator (ICD)<br>• Implantable cardiac pacemakers<br>• Leads, electrodes, adaptors for pacemakers and<br>• implantable defibrillators<br>• Implantable nerve stimulators<br>• Implantable bladder stimulators<br>• Implantable sphincter stimulators<br>• Accessories to active implantable devices (with<br>• or without contact to the heart), be it implantable or non-implantable active or not: |

[16] The clause about chemical change under this rule does not apply to products such as bone cements where the chemical change takes place during the placement and does not continue in long term.

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| | | ○ torque wrench for implantable pulse generator / implantable cardioverter defibrillator<br>○ cables for programmer / pacing system analyser<br>○ magnet for Implantable Pulse Generator / Implantable Cardioverter Generator<br>○ programmer or an external transmitter intended for activating or controlling the implantable part of the device<br>○ implantable pacemaker leads |
| **D** | g) Are breast implants or surgical meshes, in which cases they are classified as class D; | • Breast implants<br>• Surgical meshes<br>• Tension free vaginal tape |
| **D** | h) Are total or partial joint replacements, in which case they are classified as class D, with the exception of ancillary components such as screws, wedges, plates and instruments; | • Total or partial joint replacements (hips, knees. Shoulders, elbows, fingers, wrists, ankles, toes) |
| **D** | i) Are spinal disc replacement implants or are implantable devices that come into contact with the spinal column, in which case they are classified as class D with the exception of components such as screws, wedges, plates and instruments. | • Spinal disc replacement implants<br>• Spinal fusion devices<br>• Spinal implants: hooks that fix the rod on the spinal column<br>• Stems that are implantable in contact with the spinal column<br>• Device placed in the disc space<br>• Interbody fusion devices |

### Rule 8 - Implantable devices and long-term surgically invasive devices (> 30 days)

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

## Rule 9 - Active therapeutic devices intended to administer or exchange energy, as well as active devices intended to control/monitor/directly influence certain devices

This rule covers many different groups of devices, such as:

- electrical equipment used in surgery such as lasers and surgical generators;
- stimulation devices;
- devices intended to emit ionizing radiation[17]
- for therapeutic purposes, including devices which control or monitor such devices, or which
- directly influence their performance;
- devices intended for controlling, monitoring or directly influencing the performance of active implantable devices.

| Class | RULE 9 | Description & examples |
|---|---|---|
| **B** | All active therapeutic devices intended to administer or exchange energy are classified as class B | • Electrical and/or magnetic and electromagnetic energy:<br>• Muscle stimulators<br>• External bone growth stimulators<br>• TENS devices<br>• Eye electromagnets<br>• Electrical acupuncture<br>• Cryosurgery equipment<br>• Thermal energy:<br>• Heat exchangers, except the types described below<br>• Mechanical energy:<br>• Powered dermatomes<br>• Powered drills<br>• Dental hand pieces<br>• Light:<br>• Phototherapy for skin treatment and for neonatal care<br>• Sound:<br>• Hearing aids<br>• Ultrasound:<br>• Equipment for physiotherapy<br>• Sleep apnoea ventilators without monitoring function |

[17] 'Ionising radiation' means energy transferred in the form of particles or electromagnetic waves of a wavelength of 100 nanometres or less (a frequency of 3 × 1015 hertz or more) capable of producing ions directly or indirectly.

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| **C** | Unless their characteristics are such that they may administer energy to or exchange energy with the human body in a potentially hazardous way[18], taking account of the nature, the density and site of application of the energy, in which case they are classified as class C. | • Kinetic energy:<br>• Lung ventilators<br>• Thermal energy:<br>• Incubators for babies<br>• Blood warmers<br>• Electrically powered heat exchangers (for example, those used with patients incapable of reacting, communicating and/or who are without a sense of feeling)<br>• Electrical energy:<br>• High-frequency electrosurgical generators, and electrocautery equipment, including their electrodes<br>• External pacemakers and defibrillators with no integrated or incorporated diagnostic function<br>• Electroconvulsive therapy equipment<br>• Coherent light:<br>• Surgical lasers<br>• Ultrasound:<br>• Lithotriptors, surgical ultrasound devices<br>• High-intensity focused ultrasound (HIFU) |
| **C** | All active devices intended to control or monitor the performance of active therapeutic class C devices, or intended directly to influence the performance of such devices are classified as class C. | • External feedback systems for active therapeutic devices<br>• Afterloading control devices |
| **C** | All active devices intended to emit ionizing radiation for therapeutic purposes, including devices which control or monitor such devices, or which directly influence their performance, are classified as class C. | • Ionizing radiation theray.<br>• Radioactive sources for afterloading therapy<br>• Brachytherapy therapy devices if the device also generates the radiation<br>• Therapeutic cyclotrons and linear accelerators<br>• Therapeutic X-ray sources |
| **D** | All active devices that are intended for controlling, monitoring or directly influencing the performance of active | • Programming units and pacing system analysers |

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

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|---|---|---|
| | implantable devices are classified as class D. | • Cardioscopes with pacing pulse indicators specifically intended to monitor active implantable devices<br>• Programmer for:<br>o Implantable pulse generator (IPG);<br>o Implantable cardioverter defibrillator (ICD);<br>o Implantable loop recorder<br>• Remote monitoring devices for active implantable devices |

### Rule 10 - Active devices for diagnosis and monitoring or intended for diagnostic or therapeutic radiology

This rule covers a whole range equipment in various fields for capture of physiological signals, as well as specifically therapeutic and diagnostic radiology. Note that devices for recording diagnostic X-ray images are covered by Rule 17. Devices specifically intended to monitor active implantable devices fall under Rule 8 or Rule 9.

| Class | RULE 10 | Description & examples |
|---|---|---|
| **B** | Active devices intended for diagnosis and monitoring are classified as class B:<br>a) If they are intended to supply energy which will be absorbed by the human body, | • Magnetic resonance equipment<br>• Pulp testers<br>• Evoked response stimulators<br>• Diagnostic ultrasound |
| **A** | Except for devices intended to illuminate the patient's body, in the visible spectrum, or near infra-red spectrum, in which case they are classified as class A; | • Examination lights<br>• Surgical microscopes intended to illuminate the patient's body in the visible spectrum.<br>• Dermatoscopes with integrated light sources |
| **B** | b) If they are intended to image in vivo distribution of radiopharmaceuticals; | • Gamma cameras<br>• Positron emission tomography and single photon emission computer tomography |
| **B** | c) If they are intended to allow direct diagnosis or monitoring of vital physiological processes[19], | • Electrocardiographs for screening/diagnosis with no monitoring purpose<br>• Electroencephalographs |

[19] Vital physiological processes and parameters include, for example respiration, heart rate, cerebral functions, blood gases, blood pressure and body temperature. Medical devices intended to be used for continuous surveillance of vital physiological processes in anaesthesia, intensive care or emergency care are in Class C, whilst medical devices intended to be used to obtain readings of vital physiological signals in routine check ups and in self-monitoring are in Class B. A thermal imaging device intended to monitor blood flow is not considered to be a temperature measuring device.

| | | |
|---|---|---|
| | | • Cardioscopes with or without pacing pulse indicators<br>• Electronic thermometers<br>• Electronic stethoscopes<br>• Electronic blood pressure measuring equipment |
| **C** | Unless they are specifically intended for monitoring of vital physiological parameters and the nature of variations of those parameters is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of the central nervous system, or they are intended for diagnosis in clinical situations where the patient is in immediate danger, in which cases they are classified as class C. | • Patient monitors (intended use: Monitor intended for multi-parameter patient monitoring. The device will produce visual and audible alarms if any of the physiological parameters monitored vary beyond pre-set limits and timed alarm recordings will be produced.), for example in intensive care monitoring, e.g. blood pressure, temperature, oxygen saturation<br>• Biological sensors<br>• Blood gas analysers used in open heart surgery<br>• Cardioscopes intended for monitoring of vital physiological parameters<br>• Apnoea monitors used in any setting including in home care |
| **C** | Active devices intended to emit ionizing radiation and intended for diagnostic or therapeutic radiology, including interventional radiology[20] devices and devices which control or monitor[21] such devices, or which directly influence their performance, are classified as class C. | • Diagnostic X-ray sources<br>• Computed Tomography Devices |

[20] Therapeutic interventional radiology refers to diagnosis being carried out during surgical procedures.
[21] This refers to active devices for the control, monitoring or influencing of the emission of ionizing and not to the subsequent processing, recording or viewing of the resulting image.

## Rule 11 - Software intended to provide information to inform decisions with diagnosis or therapeutic purposes or software intended to monitor physiological processes

This rule applies to stand-alone software:

Software or equipment attached to devices which do not specifically enable device(s) to be used in accordance with their intended purpose, or to specifically or directly assist the medical functionality of the device in terms of its/their intended purpose do not meet the definition of an accessory. Software used in conjunction with medical devices(s) which solely record, store or display information would generally not be considered devices. For example, software analogous to diaries for recording insulin doses would not be considered devices, unless an analysis is performed on the data or the device in some way alters the patients treatment, prescription, doses etc.

| Class | RULE 11 | Description & examples |
|---|---|---|
| **B** | Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class B, except if such decisions have an impact that may cause: | • Medical Device Software to diagnose sleep apnoea<br>• Medical Device Software intended to rank therapeutic suggestions for a health care professional based on patient history, imaging test results, and patient characteristics, for example, Medical Device Software that lists and ranks all available chemotherapy options for BRCA-positive individuals.<br>• Cognitive therapy Medical Device Software where a specialist determines the necessary cognitive therapy based on the outcome provided by the Medical Device Software. |
| **D** | a) Death or an irreversible deterioration of a person's state of health, in which case it is in class D; | • Medical Device Software to select dose of cytostatic drugs<br>• Medical Device Software intended to perform diagnosis by means of image analysis for making treatment decisions in patients with acute stroke. |
| **C** | b) A serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class C. | • Medical Device Software suggesting diagnoses based on test results |

| | | |
|---|---|---|
| | | • Medical Device Software which uses information from glucose monitoring to provide direction on administration of insulin for management of diabetes<br>• A mobile app intended to analyse a user's heartbeat, detect abnormalities and inform a physician accordingly.<br>• Medical Device Software intended for diagnosing depression based on a score resulting from inputted data on patient symptoms (e.g. anxiety, sleep patterns, stress etc.). |
| **B** | Software intended to monitor physiological processes is classified as class B, | • Medical Device Software monitoring of heart rate data intended as an aid<br>• Medical Device Software intended to monitor physiological processes that are not considered to be vital.<br>• Devices intended to be used to obtain readings of vital physiological signals in routine check-ups including monitoring at home. |
| **C** | Except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class C. | • Medical devices including Medical Device Software intended to be used for continuous surveillance of vital physiological processes in anaesthesia, intensive care or emergency care. |
| **A** | All other software is classified as class A. | • Medical Device Software used to make biomechanical measurements to aid rehabilitation<br>• Software intended to support conception by calculating the user's fertility status based on a validated statistical algorithm. The user inputs health data including basal body temperature (BBT) and menstruation days to track and predict ovulation. The fertility status of the current day is reflected by one of three indicator lights: red (fertile), green (infertile) or yellow (learning phase/cycle fluctuation). |

### Rule 12 - Active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body

This rule is intended to primarily cover drug delivery systems and anaesthesia equipment. If the device's intended route of drug delivery is pulmonary, Rule 20 applies.

| Class | RULE 12 | Description & examples |
|---|---|---|
| **B** | All active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body are classified as class B, | • Suction equipment<br>• Feeding pumps<br>• Jet injectors for vaccination<br>• Elastomeric pumps or balloon pumps for infusion |
| **C** | 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 classified as class C. | • Infusion pumps<br>• Ventilators<br>• Anaesthesia machines<br>• Anaesthetic vaporisers<br>• Dialysis equipment<br>• Blood pumps for heart-lung machines<br>• Hyperbaric chambers<br>• Pressure regulators for medical gases<br>• Medical gas mixers<br>• Moisture exchangers in breathing circuits if used on unconscious or non-spontaneously breathing patients<br>• Oxygen concentrator used to deliver oxygen enriched air directly to the patient |

### Rule 13 – All other active devices

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

| Class | RULE 13 | Description & examples |
|---|---|---|
| **A** | All other active devices are classified as class A. | • Devices intended in general for external patient support (e.g. electric hospital beds, patient hoists, electric wheelchairs, dental patient chairs)<br>• Dental curing lights |

### Rule 14 - Devices incorporating, as an integral part, an ancillary medicinal product, and medicinal products derived from human blood or blood plasma

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

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

| Class | RULE 14 | Description & examples |
|---|---|---|
| **D** | All devices incorporating, as an integral part[22], a substance which, if used separately, can be considered to be a medicinal product, as defined in "SFDA Products Classification Guidance", including a medicinal product derived from human blood or human plasma, as defined in "SFDA Products Classification Guidance", and that has an action ancillary to that of the devices, are classified as class D. | • Antibiotic bone cements<br>• Condoms with spermicide<br>• Endodontic materials with antibiotics<br>• Dressings incorporating an antimicrobial agent where the purpose of such an agent is to provide ancillary action on the wound including silver impregnated dressings<br>• Contraceptive intrauterine devices (IUDs) containing medicinal copper or silver<br>• Drug eluting stents, e.g. coronary, pulmonary<br>• Surgical sealants containing human serum albumin or thrombin<br>• Catheters coated with an anticoagulant or an antibiotic agent (e.g. heparin)<br>• Sponge impregnated with antibiotics<br>• Medicated root canal sealant<br>• Ophthalmic irrigation solutions principally intended for irrigation, which contain components supporting the metabolism of the endothelial cells of the cornea<br>• Implants coated with human fibrinogen<br>• Blood bags incorporating heparin or other substances as anticoagulant agents which, if used separately, can |

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

| | | |
|---|---|---|
| | | be considered to be a medicinal product<br>• IVF cell media with human albumin<br>• Catheter lubrication gels containing analgesia e.g. lidocaine |

### Rule 15 – Devices used for contraception or prevention of sexually transmitted diseases

This rule covers invasive, implantable and non-invasive medical devices for contraception or prevention of sexually transmitted diseases, i.e. this rule is not limited to devices based on physical barriers. The rule covers contraception devices and devices used in prevention of transmission of sexually transmitted diseases, where non-invasive, devices for transient or short-term use are of class C and long-term use or implantable devices are of class D.

Moreover, these intended uses relate to special cases of human vulnerability that cannot be covered by the normal criteria of time, invasiveness and organic function.

Although this rule covers two very different device applications, some devices may perform both functions, e.g. condoms.

Devices intended to prevent the sexual transmission of the HIV are also covered by this rule.

| Class | RULE 15 | Description & examples |
|---|---|---|
| **C** | All devices used for contraception or prevention of the transmission of sexually transmitted diseases are classified as class C, | • Condoms and femidoms (internal condoms)<br>• Contraceptive diaphragms<br>• Fertility monitors and medical device software intended to be used in contraception (e.g. by using the basal body temperature) |
| **D** | Unless they are implantable or long term invasive devices, in which case they are classified as class D. | • Contraceptive intrauterine devices (IUDs)<br>• Tubal ligation devices (e.g. clips or rings)<br>• Non-hormonal intrauterine |

| | | |
|---|---|---|
| | | contraceptive devices (IUD/IUCD or ICD)[23] |

### Rule 16 – Specifically disinfecting, cleaning, rinsing, hydrating or sterilizing devices

This rule covers substances and other equipment used principally in a medical environment to disinfect medical devices as well as fluids for cleaning, disinfection or hydration of contact lenses.

This rule is intended to cover various products used specifically with contact lenses such as solutions intended for storing contact lenses and solutions used to support contact lenses placed on the ocular surface.

| Class | RULE 16 | Description & examples |
|---|---|---|
| **C** | All devices intended specifically to be used for disinfecting, cleaning, rinsing or, where appropriate, hydrating contact lenses are classified as class C. | • Contact lens storing solutions<br>• Cleansers for contact lenses<br>• Ultraviolet, vibration, or ultrasonic devices for cleaning and disinfecting contact lenses |
| **B** | All devices intended specifically to be used for disinfecting or sterilising medical devices are classified as class B, | • Disinfectants specifically intended for non-invasive medical devices<br>• Sterilizers specifically intended to sterilize medical devices in a medical environment<br>• Washers-disinfectors intended specifically for disinfecting non-invasive medical devices |
| **C** | Unless they are disinfecting solutions or washer-disinfectors intended specifically to be used for disinfecting invasive devices, as the end point of processing, in which case they are classified as class C. | • Denture disinfecting products<br>• Washers-disinfectors for endoscopes or other invasive devices at the end point of processing (e.g. dental equipment)<br>• Disinfectants for the fluid pathways of haemodialysis equipment<br>• Solutions/disinfectors for trans oesophageal ultrasound probes) |

[23] Intrauterine contraceptives whose primary purpose is to release progestogens are not medical devices

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| | This rule does not apply to devices that are intended to clean devices other than contact lenses by means of physical action[24] only. | • Brushes specifically intended to clean medical devices by mechanical action<br>• Ultrasonic devices (for other devices than contact lenses) |

### Rule 17 – Devices to record X-ray diagnostic images

This rule covers stand-alone X-ray detectors and sensors as recording devices used in several types or modalities of medical imaging procedures, each of which uses different technologies and techniques. It covers non-active devices and active devices used to record X-ray diagnostic images of the human body. The intention of the rule is to cover primarily digital devices and analogous recording media, but not media (including digital media) used for subsequent image processing and storage.

| Class | RULE 17 | Description & examples |
|---|---|---|
| **B** | Devices specifically intended for recording of diagnostic images generated by X-ray radiation are classified as class B. | • X-ray films<br>• Photostimulable phosphor plates<br>• Digital x-ray detectors for recording images |

### Rule 18 – Devices manufactured utilizing tissue or cells of human or animal origin or their derivatives

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

The manufacture of some devices may use industrial raw materials which contain small amounts of tallow or tallow derivatives (e.g. stearates in polymers). Such substances are not considered as derivatives of animal tissues for the purpose of this rule which therefore does not apply.

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

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

| Class | RULE 18 | Description & examples |
|---|---|---|
| **D** | All devices manufactured utilizing tissues or cells of human or animal origin, or their derivatives[25], which are non-viable or rendered non-viable, are classified as class D, | • Animal derived biological heart valves<br>• Porcine xenograft dressings<br>• Implants and dressings made from collagen<br>• Devices made from animal sourced collagen/gelatin<br>• Devices utilizing hyaluronic acid of animal origin<br>• Substance-based devices containing collagen for use in body orifices<br>• Collagen dermal fillers<br>• Bone graft substitutes |
| **A** | Unless such devices are manufactured utilizing tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable and are devices intended to come into contact with intact skin[26] only. In which case they are class A. | • Leather components of orthopedic appliances |

### Rule 19 – Devices incorporating or consisting of nanomaterial

The use of nanomaterials in medical devices can vary considerably. Examples are the use of free nanomaterials as a medical device which is administered to the patient (e.g. iron oxide or gold nanomaterials for heat therapy against cancer), free nanomaterials in a paste-like formulation (e.g. dental filling composites), free nanomaterials added to a medical device (e.g. nanosilver as antibacterial agent in wound dressings), fixed nanomaterials forming a coating on implants to increase biocompatibility (e.g. nanohydroxyapatite) or to prevent infection (e.g. nanosilver), or embedded nanomaterials to strengthen biomaterials (e.g. carbon nanotubes in a catheter wall). In all these cases the potential exposure to the nanomaterials should be considered. It is additionally recognized that wear-and-tear of medical devices may generate nano-sized particles even when the medical device itself does not contain nanomaterials.

Humans may be exposed to nanomaterials from medical devices through various routes. Depending on the relevant exposure route based on the use of a specific medical device, the nanomaterials will encounter various barriers before they are taken up by the body. Patients

[25] Derivatives are products that are processed from animal tissues and exclude substances such as milk, silk, beeswax, hair, lanolin.
[26] Intact skin includes the skin around an established stoma unless the skin is breached.

and users (health care professionals) may be exposed, although the potential of exposure of patients and/or users will differ depending on the particular device and the way it is used. In general, the highest potential for exposure is associated with devices that consist of "free" nanomaterials or that are subject to the release/loosening of nanomaterials present as coatings on the surface of medical devices. In addition, exposure to nanomaterials from medical devices may also result from degradation or wear processes, when nanomaterials are fixed on the surface (e.g. as coating on implants) or are embedded within the material of the medical device.

**Examples of devices in current clinical practice:**

- **Non-invasive surface contacting medical devices**

These are medical devices, which come into contact only with the intact skin. Examples are antibacterial gowns and textiles to cover patients in the operating theatre, which contain silver nanoparticles.

- **Invasive surface contacting medical devices**

These are medical devices, which come into contact with breached or otherwise compromised skin. Examples are wound treatment products (wound dressings) containing nano-sized silver particles and metal oxide particles which are used for improved antibacterial and anti-fungal activity.

- **Invasive external communicating medical devices**

These are medical devices that come into contact with the blood path, either indirectly or with circulating blood, and devices in contact with tissue/bone/dentin. Examples include:

  - Catheters with a nanosilver coating for bladder drainage, hemodialysis and local administering of anaesthesia
  - Catheters with nanotopographical morphology imprinted onto the exposed surface
  - Polymer based dental composite filler materials and dental cements containing nanoparticles
  - Surgical and dental instruments with nanostructures used to enhance the cutting behavior and wear resistance of cutting instruments, e.g. scalpels, needles, catheters, burs for cutting bone or teeth
  - Instruments with nanostructures used to create non-sticky surfaces to facilitate handling and placement of materials

- **Invasive implantable medical devices**

These are medical devices which are 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 are intended to remain in place after the procedure. Examples include:

- Carbon nanotubes in bone cements for fixation of implanted prostheses
- Bone fillers with hydroxyapatite and tricalcium phosphate nanoparticles which facilitate rapid integration with the bone of the patient
- Surface coatings. The surface of implants can be modified with the aid of nanotechnologies to enable them to integrate better in the body (improved biocompatibility). In addition, coatings can be used for their antibacterial activity.
    - Joint prosthetics (hip, knee) with nanohydroxyapatite coating
    - Coronary stents with a diamond-like nano composite coating made of ultra-thin polymer

| Class | RULE 19 | Description & examples |
|---|---|---|
| **D** | Class D if they present a high or medium potential for internal exposure | • Bone fillers with nanomaterials in their formulation (not polymerized before blood/tissue contact, and degradable)<br>• Superparamagnetic iron oxide nanoparticles (Intended use: thermal ablation of tumors or thermal modulation of the tumor microenvironment by submission to alternating magnetic fields)<br>• Intravascular catheter made of non-degradable polymer, with nano-coating |
| **C** | Class C if they present a low potential for internal exposure | • Bone fixation screws/plates with a strongly bound nano-coating high potential<br>• Solution administration set made of non-degradable polymer, with a strongly bound nano-coating |
| **B** | Class B if they present a negligible potential for internal exposure | • Intravascular catheter for short term use made of nondegradable polymer, with nanomaterial embedded in the polymer matrix<br>• Solution administration set made of non-degradable polymer, with |

| | | |
|---|---|---|
| | | nanomaterial embedded in the polymer matrix<br>• Dental filling materials |

### Rule 20 – Invasive devices, intended to administer medicinal product by inhalation

Devices used to deliver therapeutic agents as aerosols are based on one of the three platforms: nebulizers, pressurized metered-dose inhaler (pMDI), and dry powder inhalers (DPIs).
The effectiveness of an aerosol therapy is largely dependent on how much of the medication will reach the intended site of deposition.

The major problems with the use of inhaler devices are the deposition of aerosolized particles in the oropharyngeal region and upper airways and the lack of coordination between the device activation and inhalation due to lack of patient training.

In contrast to other rules covering devices that administer medicinal products, Rule 20 is also specifically intended to cover medical devices where the impact of the medical device on the efficacy and safety of the administered medicinal product is critical. The rule also covers drug delivery products that are intended to treat life-threatening conditions.

| Class | RULE 20 | Description & examples |
|---|---|---|
| **B** | All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer medicinal products by inhalation are classified as class B, | • Spacer intended for metered dose inhalers (attached to the inhaler) unless treating life-threatening conditions<br>• Inhalers for nicotine replacement therapy (nicotine not included)<br>• Oxygen delivery system with a nasal cannula unless treating life-threatening conditions<br>• Inhalers and nebulizers in case their mode of action has probably no essential impact on the efficacy and safety of the administered medicinal product or which are not intended to treat life-threatening conditions |
| **C** | Unless their mode of action has an essential impact on the efficacy and safety of the administered medicinal product or they are intended to treat life-threatening conditions, in which case they are classified as class C. | • Nebulizers (not pre-charged with a specific medicinal product) where the failure to deliver the appropriate dosage characteristics could be hazardous<br>• Spacer metered dose inhalers for treatment of acute asthma |

## Rule 21 – Devices composed of substances that are introduced via a body orifice or applied to the skin

Self-care medical devices are composed of substances or combination of substances. They include, amongst others, products such as nasal solution primarily used for sufferers, often infants, with cold symptoms and blocked noses, substances to relieve throat discomfort, dentifrices for sensitive teeth, verruca and wart removers, gels for vaginal discomfort, other personal lubricants, cough syrups, products used for the reduction of bloating, denture cleansers and adhesives, creams to treat or prevent minor skin irritations or anti-flatulence products.

These are classified as devices in light of their mode of action which is not pharmacological, immunological or metabolic but relies on chemico-physical processes such as local pH changes, sequestering actions of molecules, and physical barrier formation.

Substances are treated as medicinal products in case the mode of active is pharmacological, immunological or metabolic.

The classification considers the site of application of the medical device as well as the site where the medical device performs its action in or on the human body. For the purpose of this rule nails are also considered as falling under 'skin'.

Manufacturers of substance-based devices should provide clear information supporting the mode of action through which the substance achieves the intended specific medical purpose as a basis for the application of this rule, including the site of application as well as the site where the action is achieved in or on the body.

| Class | RULE 21 | Description & examples |
|---|---|---|
| **D** | Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as:<br>a) Class D if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose; | Any device that is claimed to achieve its intended purpose through absorption or dispersion. |
| **D** | b) Class D if they achieve their intended purpose in the stomach or lower | • Gastrointestinal gas suppressant<br>• Na/Mg alginate, xyloglucan. |

| | | |
|---|---|---|
| | gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body; | • Fat absorbers that are systemically absorbed, themselves or their metabolites |
| **B** | • c) Class B if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities; | • Substance-based formulations for skin treatment<br>• Salt water used e.g. as nose or throat sprays<br>• Oral cough treatments achieving their intended purpose in the oral cavity as far as the pharynx |
| **C** | d) Class C in all other cases. | • Simethicone preparations for oral administration<br>• Active coal for oral administration<br>• Gel for vaginal moisturizing / vaginal lubricants<br>• Eye drops for hydration<br>• Ear drops<br>• Medical devices, for oral administration, for the treatment of diarrhea, e.g. kaolin, diosmectite<br>• Medical devices, for oral administration, for the treatment of obesity, e.g. fructooligosaccharides, glucomannan |

Rule 22 – Active therapeutic devices, with an incorporated diagnostic function

PHYSIOLOGIC CLOSED-LOOP CONTROLLERS in ME EQUIPMENT and ME SYSTEMS are expected to provide a successful strategy to improve PATIENT safety and reduce healthcare costs and also fall under this rule.

| Class | RULE 22 | Description & examples |
|---|---|---|
| **D** | Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, are classified as class D. | • Automated external defibrillators including their pads/electrodes<br>• Semiautomatic external defibrillators<br>• Automated closed loop insulin delivery system<br>• Automated external infusion pumps with integrated sensors to adapt the infusion therapy<br>• Devices in brain-computer interfaces (BCIs) – used for e.g. motor control in severely paralyzed patients |

| | | |
|---|---|---|
| | | • Closed-loop systems for deep brain stimulation (DBS) treatment of various neurological conditions<br>• Closed-loop dynamic neurochemical control of therapeutic interventions e.g. target-controlled anesthesia / infusion systems |

# 3. In Vitro Diagnostic Medical Devices Definition and Implementation Rules

## 3.1. Definition related to classification

**'Kit'**: means a set of components that are packaged together and intended to be used to perform a specific in vitro diagnostic examination

**'Specimen'** is a discrete portion of a body fluid or tissue taken from an individual for examination, study or analysis of one or more quantities or characteristics to determine the character of the whole. This also includes other materials, for example, hair, nails excretions, secretions, or a sample from the skin surface.

**'Specimen receptacle'** means a device, whether of a vacuum-type or not, specifically intended by its manufacturer for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination.

**'instrument'** means equipment or apparatus intended by a manufacturer to be used as an IVD medical device.

**'Device for self-testing'** means any device intended by the manufacturer to be used by lay persons, including devices used for testing services offered to lay persons by means of information society services.

**'Device for near-patient testing'** means any device that is not intended for self-testing but is intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient by a health professional.

**'First-line device'** is a device intended to be used to detect a marker or analyte, and which may be followed by a confirmatory assay. Devices intended to be used solely to monitor a previously determined marker or analyte are not considered first-line assays.

**'Confirmatory device'** is a device intended to be used for the confirmation of a reactive result from a first line assay.

**'Devices for monitoring'** are used for the measurement of the analyte (measurand) levels for the purpose of adjusting treatments/interventions as required.
Devices for monitoring include the following:
- Devices which are used to assess whether an analyte remains within physiological levels or within an established therapeutic drug range. These types of devices are designed to evaluate an individual's current state.
- Devices which are used for serial measurement, whereby multiple determinations are taken over time. These types of devices are typically used for the detection/assessment of disease progression/regression, disease recurrence, minimum residual disease, response/resistance to therapy, and/or adverse effects due to therapy. These types of devices are designed to evaluate changes in an individual's state.

**'Devices for screening'** are used to detect the presence of or the predisposition to a disease, disorder or other physiological state in a specimen from an individual, embryo or foetus not demonstrating clinically evident symptoms.
Depending on the nature of the condition and the targeted patient population, screening devices may be used routinely or may be restricted to "at risk" patients.
This also includes (for example) devices intended to assess the suitability of blood, blood components, cells, tissues or organs, or in any of their derivatives for transfusion, transplantation or cell administration, with respect to transmissible agents.

**'Companion diagnostic'** means a device which is essential for the safe and effective use of a corresponding medicinal product to:

- identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or
- identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product.

**'Calibrator'** means a measurement reference material used in the calibration of a device.

**'Control material'** means a substance, material or article intended by its manufacturer to be used to verify the performance characteristics of a device.

**'embryo' or 'foetus'** an unborn refers to stages in human development after zygote formation. A zygote is considered an embryo in particular from the period of conception to approximately the eighth week, and considered a foetus following this period until birth.
Samples from the embryo or foetus include samples from the embryonic/foetal membranes, fluids and excretions, the umbilical cord, and maternal samples (e.g. blood) containing embryonic/foetal material to be examined.

**'newborn'** a newborn, or neonate, refers to an infant in the first 28 days after birth.

**'Transmissible agent'** an agent capable of being transmitted to a person, as a communicable, infectious or contagious disease

**'Detecting the exposure to'** an agent means the indirect detection of an agent (present or past exposure).
- by detecting the presence of surrogate markers, such as antibodies against components of the agent.

**'Detecting the presence of'** an agent means the direct detection of the agent, by detecting
- the presence of the agent itself (e.g. bacterial, viral, fungal, parasitic, protozoal agents), or
- the presence of structural components derived from the agent, such as antigens or nucleic acids.

**'Offspring'** is the result of conception, at all stages of development, embryo and foetus, premature and full-term neonates, child and adult.

**'Infective/infectious agent'** is an agent capable of producing infection. This includes iatrogenic infections, i.e. those infections transmitted during medical treatment and care.

**'Life-threatening'** are diseases, conditions or situations that in general result in death. These are often untreatable; treatment options are limited or require major medical interventions.

**'Marker' 'analyte' or measurand** a substance or material; something that identifies or that is used to identify; a factor that establishes the nature of an entity or event; constituent of a sample with a measurable property.

## 3.2. Implementing rules

### 3.2.1. Intended purpose

Application of the classification rules shall be governed by the intended purpose of the devices. Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it shall be classified in the higher class.

### 3.2.2. Combination with another device

If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices.

### 3.2.3. Accessories

Accessories for an in vitro diagnostic medical device shall be classified in their own right separately from the device with which they are used.

### 3.2.4. Software

Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right.

### 3.2.5. Calibrators

Calibrators intended to be used with a device shall be classified in the same class as the device.

### 3.2.6. Control materials

Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes shall be classified in the same class as the device.

### 3.2.7. Multiple rules

The manufacturer shall take into consideration all classification and implementation rules in order to establish the proper classification for the device.

If several classification rules apply to the same device, the rule resulting in the higher classification shall apply.

### 3.2.8. First line, confirmatory and supplemental assays

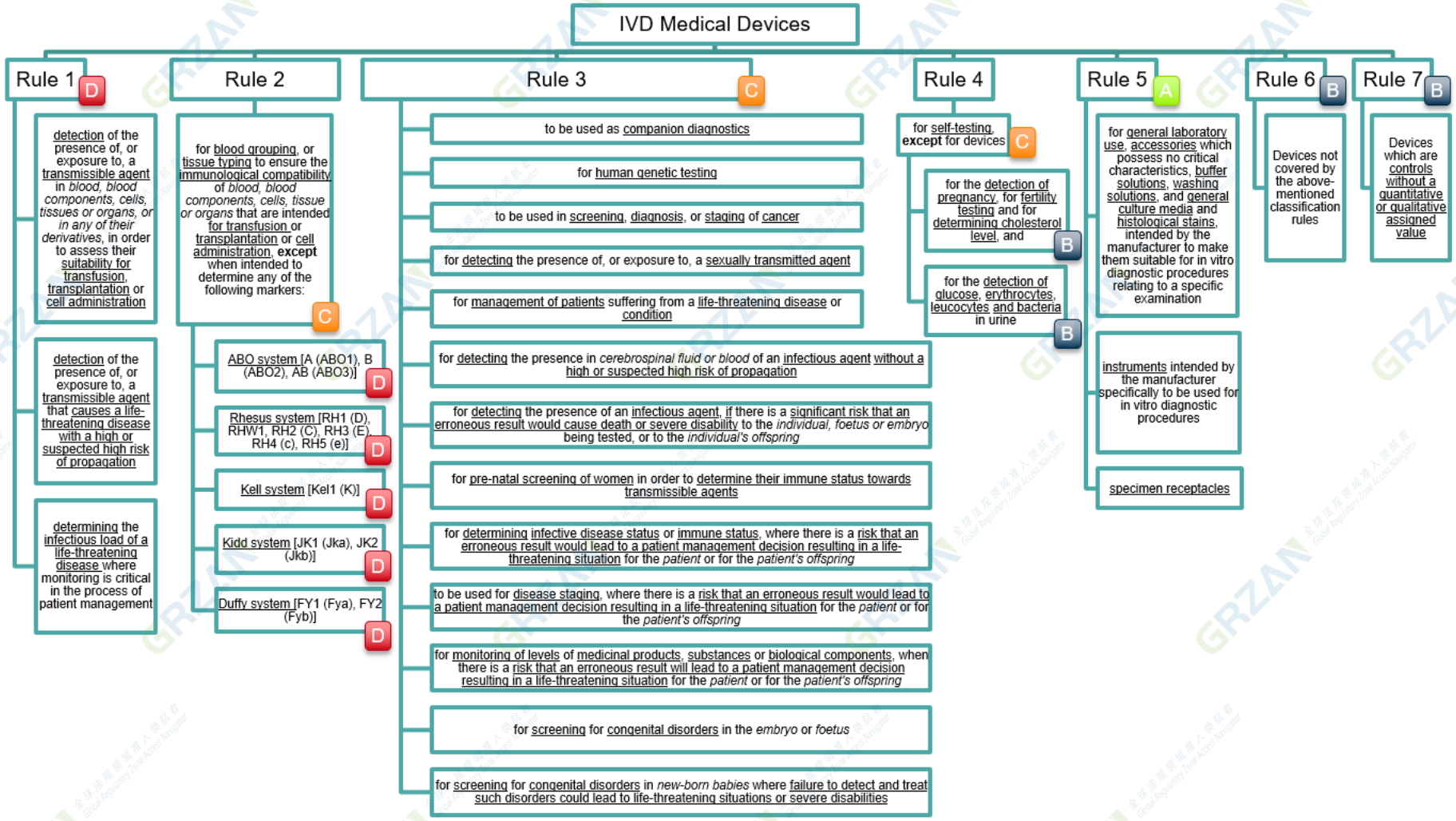
Each of the classification rules shall apply to first line assays, confirmatory assays and supplemental assays.

## 3.3. Explanation of the individual rules

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

### 3.3.1. Classification guidance chart for initial identification of probable device class

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


IVD Medical Devices
Rule 1
D
detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration
detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation
determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management
Rule 2
for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, except when intended to determine any of the following markers:
C
ABO system [A (ABO1), B (ABO2), AB (ABO3)]
D
Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)]
D
Kell system [Kel1 (K)]
D
Kidd system [JK1 (Jka), JK2 (Jkb)]
D
Duffy system [FY1 (Fya), FY2 (Fyb)]
D
Rule 3
C
to be used as companion diagnostics
for human genetic testing
to be used in screening, diagnosis, or staging of cancer
for detecting the presence of, or exposure to, a sexually transmitted agent
for management of patients suffering from a life-threatening disease or condition
for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation
for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual's offspring
for pre-natal screening of women in order to determine their immune status towards transmissible agents
for determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring
to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring
for monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring
for screening for congenital disorders in the embryo or foetus
for screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities
Rule 4
for self-testing, except for devices
C
for the detection of pregnancy, for fertility testing and for determining cholesterol level, and
B
for the detection of glucose, erythrocytes, leucocytes and bacteria in urine
B
Rule 5
A
for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination
instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures
specimen receptacles
Rule 6
B
Devices not covered by the above-mentioned classification rules
Rule 7
B
Devices which are controls without a quantitative or qualitative assigned value

### 3.3.2. General explanation of rules, practical issues and examples

Rule 1

Devices in this Class are intended to be used to ensure the safety of blood and blood components for transfusion and/or cells, tissues and organs for transplantation.
In most cases, the result of the test is the major determinant as to whether the donation/product will be used.

Serious diseases are those that result in death or long-term disability, that are often incurable or require major therapeutic interventions and where an accurate diagnosis is vital to mitigate the public health impact of the condition.

| Class | RULE 1 | Description & examples (non-exhaustive) |
|---|---|---|
| **D** | Devices intended to be used for the following purposes are classified as class D:<br>a) Detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration; | - Devices intended to be used for blood, organ and tissue donor screening, including screening and confirmatory assays for:<br>• Human immunodeficiency virus (HIV)<br>• Hepatitis C virus (HCV)<br>• Hepatitis B virus<br>• HTLV I/II<br>• Syphilis<br>-Any additional assays used to screen donors on a supplementary basis, such as those used to determine Cytomegalovirus status or to screen for Malaria; Trypanosoma cruzi; Epstein Barr virus and Toxoplasma gondii. |
| **D** | b) Detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation; | - Devices intended for the diagnosis of infection with, or exposure to:<br>• Severe acute respiratory syndrome-associated coronavirus (SARS CoV and SARS-CoV-2)<br>• MERS Coronavirus.<br>• Highly virulent pandemic influenza<br>• Variola virus (Smallpox virus)<br>• Haemorrhagic fever viruses (e. g. Ebola, Marburg, Lassa, Crimean-Congo Haemorrhagic fever<br>• HIV 1 & 2<br>• Hepatitis C virus<br>• Hepatitis B virus<br>• Hepatitis D Virus |

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| | | • HTLV I/II<br><br>Note: Applies to first-line assays, confirmatory assays and supplemental assays. |
| **D** | c) Determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management. | - Devices intended to be used for determining the infectious load in the context of life-threatening infectious diseases, after the disease status of the patient has been previously determined, and for which patient management options, including specific treatment, are based on monitoring the infectious load.<br>-Viral load is typically performed by nucleic acid amplification-based tests (NAT). e.g. Viral load assays for HIV, HBV, HCV |

### Rule 2

A high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation places the device into Class D.

The rule divides blood grouping devices into two subsets, Class C or D, depending on the nature of the blood group antigen the IVD medical device is designed to detect, and its importance in a transfusion setting.

| Class | RULE 2 | Description & examples (non-exhaustive) |
|---|---|---|
| **C** | Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C: | - Devices intended for testing for red blood cell antigens or antibodies for:<br>• Cw or V from the Rhesus system<br>• Cellano (k) from the Kell blood group system.<br>• Anti-Lea Monoclonal blood grouping reagent for transfusion purposes<br>• Any markers from MNS or Cartwright blood group systems<br><br>-All devices intended for use in tissue typing to detect antigens and antibodies for any human leukocyte antigens.<br><br>-All devices intended for HLA tissue typing are classified under this rule as class C devices when they are intended to be used for blood grouping, or tissue typing to ensure the immunological |

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| | | compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration.<br>- Devices intended for subtyping previously determined ABO system A group reactive patients (i.e. A1, A2, A3 etc.)<br>-Tests intended for the quantitative determination of antibodies to Rhesus system blood group antigens (i.e. anti-D) |
| **D** | a) ABO system [A (ABO1), B (ABO2), AB (ABO3)] in which case they are classified as class D. | - Devices intended for detecting the presence of: intended for detecting red blood cell antigens, antibodies or genetic markers specific to the high-risk blood group:<br>• ABO system [A (ABO1), B (ABO2), AB (ABO3)]<br>• Red blood cell kit with A1, A2, B and O cells used to detect naturally-occurring ABO blood group antibodies in patient and donor samples, in reverse grouping. |
| **D** | b) Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)] in which case they are classified as class D. | - Devices intended for detecting the presence of: intended for detecting red blood cell antigens, antibodies or genetic markers specific to the high-risk blood group:<br>• Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)]<br>• Foetal RhD typing kit. |
| **D** | c) Kell system [Kel1 (K)] in which case they are classified as class D. | - Devices intended for detecting the presence of: intended for detecting red blood cell antigens, antibodies or genetic markers specific to the high-risk blood group:<br>• Kell system [Kel1 (K)] |
| **D** | d) Kidd system [JK1 (Jka), JK2 (Jkb)] in which case they are classified as class D. | - Devices intended for detecting the presence of: intended for detecting red blood cell antigens, antibodies or genetic markers specific to the high-risk blood group:<br>• Kidd system [JK1 (Jka), JK2 (Jkb)] |
| **D** | e) Duffy system [FY1 (Fya), FY2 (Fyb)] in which case they are classified as class D. | - Devices intended for detecting the presence of: intended for detecting red blood cell antigens, antibodies or genetic markers specific to the high-risk blood group:<br>• Duffy system [FY1 (Fya), FY2 (Fyb)] |

## Rule 3

Devices in this Class present a moderate public health risk, or a high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation, or would have a major negative impact on outcome.

The devices provide the critical, or sole, determinant for the correct diagnosis. They may also present a high individual risk because of the stress and anxiety resulting from the information and the nature of the possible follow-up measures.

| Class | RULE 3 | Description & examples (non-exhaustive) |
|---|---|---|
| **C** | Devices are classified as class C if they are intended:<br>a) For detecting the presence of, or exposure to, a sexually transmitted agent; | - Devices intended to detect the presence or exposure to a sexually transmitted agent, such as:<br>• Chlamydia trachomatis<br>• Neisseria gonorrhoeae<br>• Syphilis (Treponema pallidum)<br>• Herpes simplex virus 1 & 2<br>• Lymphogranuloma venereum (C. trachomatis L-1, L-2, L-3)<br>• Human papillomavirus<br>• Trichomoniasis (Trichomonas vaginalis) |
| **C** | b) For detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation; | - Devices intended for detecting the presence of:<br>• Bacterial pathogens: Streptococcus pneumoniae, Group B Streptococcus, Neisseria meningitidis, Haemophilus influenza type B, Listeria spp., Borrelia burgdorferi, Mycobacterium tuberculosis.<br>• Fungal pathogens: Cryptococcus neoformans, Aspergillus spp.<br>• Viral pathogens: Varicella zoster virus, enterovirus, West Nile virus, chikungunya, Dengue, Zika, hepatitis A, hepatitis E. Hendra virus.<br>• Parasitic pathogen: Toxoplasma gondii.<br>• Detection of Prion diseases. |
| **C** | c) For detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or | - Devices intended for detecting the presence of:<br>• Bacterial pathogens: Treponema pallidum, Chlamydia trachomatis, Haemophilus influenzae type B meningitis, Neisseria meningitidis, Listeria meningitis (Listeria monocytogenes), Mycobacterium leprae, |

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| | embryo being tested, or to the individual's offspring; | Mycobacterium spp., Legionella spp., Streptococcus agalactiae, methicillin-resistant Staphylococcus aureus (MRSA) and multi-resistant Enterobacteriaceae (MRE).<br>• Parasitic pathogens: Toxoplasma gondii.<br>• Viral pathogens: Herpes simplex virus 1&2, cytomegalovirus, Rubella, Measles, Poliomyelitis, Parvovirus B19, Zika. |
| **C** | d) For pre-natal screening of women in order to determine their immune status towards transmissible agents; | - Devices covered by this rule are intended for the screening of pregnant women before birth in order to identify the presence of an acquired appropriately targeted immune response to transmissible agents. Devices intended to determine for prenatal screening the immune status of women towards:<br>• Cytomegalovirus.<br>• Rubella virus.<br>• Toxoplasma gondii.<br>• Varicella zoster virus.<br>• Zika.<br>• Parvovirus B19.<br>• Herpes simplex virus 1 & 2<br>• Measles virus<br>• Treponema pallidum<br>If tests to detect immune status for these infections are not specifically intended for prenatal screening, they are classified according to other rules. |
| **C** | e) For determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring; | - Devices intended to determine:<br>•Salmonella typhi in faeces, for the assessment of the carrier-status of patients.<br>•Antibodies from lymphocyte secretions immunoassay intended for the detection of active Mycobacterium tuberculosis infection.<br>•Quantitative virus-specific NAT tests (e.g. Cytomegalovirus, John Cunningham virus, Adenovirus, Enterovirus) to monitor an immunocompromised patient's (e.g. transplant patient) response to antiviral therapy.<br>•Methicillin-resistant Staphylococcus aureus and Staphylococcus aureus specific polymerase chain |

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| | | reaction assay for pre-surgical screening of patients to determine nasal carriage.<br>•Assays intended for the detection of IgM antibodies against rubella virus to identify an acute infection in pregnant women in order to determine whether specific treatment is necessary for protecting the foetus from virus-induced damage due to a lack of previously acquired immunity.<br>•Assays intended for the detection of IgM antibodies against HEV.<br>•Enzyme immunoassay intended for the quantitation of intrathecal antibodies against rubella virus in the diagnosis of rubella virus-induced encephalitis.<br>•Assays intended for the detection of antibodies in the recipient to potentially pathogenic viruses (e.g. anti-cytomegalovirus, anti-herpes simplex virus antibodies) to determine latent disease status of viral infection prior to organ or bone marrow transplantation.<br>•Screening assays comprising allergy panels, such as Multiple Allergen Simultaneous Tests (MAST), intended to detect IgE antibodies against several specific allergens that may lead to anaphylaxis, e.g. certain nutritional allergens or hymenoptera venom allergens. False-negative results with such MAST assays could increase the risk that the patient is not adequately managed for the occurrence of a life-threatening anaphylactic event.<br>•Assays intended for the detection of alloantibodies in the recipient associated with transplant rejection reactions, such as antibodies against -angiotensin II receptors type 1 (anti-AT1R) and against endothelin receptors type A (anti-ETAR).<br>•Interferon-Gamma Release Assays (IGRA)for Mycobacterium tuberculosis. |
| **C** | f) To be used as companion diagnostics; | - Applies to devices intended to be used as companion diagnostics.<br>• ‘Companion diagnostic’ (CDx) is defined as a device which is essential for the safe and effective use of a corresponding medicinal product to: |

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| | | • identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or<br>• identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product.<br><br>The identification of patients may comprise a quantitative or qualitative determination of specific markers. Such specific markers can be present in healthy subjects and/or in patients.<br><br>The emphasis 'before and/or during treatment' implies that CDxs may be intended to be applied before a treatment with a corresponding medicinal product is initiated, or during treatment, to identify if (still) the patient is (a) likely to benefit from the corresponding medicinal product or (b) likely to be at increased risk of serious adverse reactions.<br><br>Devices that are intended to be used for monitoring treatment with a medicinal product in order to ensure that the concentration of relevant substances in the human body is within the therapeutic window are not considered to be CDxs. e.g:<br><br>• CDx assay intended for the qualitative detection of the anaplastic lymphoma kinase protein in formalin-fixed, paraffin-embedded (FFPE) non-small cell lung carcinoma (NSCLC) tissue, and is indicated as an aid in identifying patients eligible for treatment with crizotinib or ceritinib.<br><br>• CDx assay intended for the quantitative detection of BCR-ABL1 transcripts and the ABL1 endogenous control mRNA in peripheral blood specimens from patients previously diagnosed with t(9:22) positive |

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| | | chronic myeloid leukemia, intended to measure BCR-ABL mRNA transcript levels during monitoring of treatment with nilotinib.<br><br>• CDx qualitative immunohistochemical assay using Monoclonal Mouse Anti-PD-L1, intended for use in the detection of PD-L1 protein in FFPE NSCLC and gastric or gastroesophageal junction (GEJ) adenocarcinoma tissues and is indicated as an aid in identifying patients for treatment with pembrolizumab. |
| **C** | g) To be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring; | • Devices intended for the quantitative measurement of Brain type natriuretic peptide (BNP) in whole blood or plasma samples, for the assessment of the severity of congestive heart failure.<br>• Devices intended for staging of enhanced liver fibrosis (ELF) for detecting the following markers: hyaluronic acid, procollagen III amino terminal peptide, tissue inhibitor or metalloproteinase.<br>• Medical device software intended to generate an estimated glomerular filtration rate (eGFR) or albumin creatinine ratio (ACR) for staging acute kidney injury (AKI).<br>• Medical device software intended to generate an enhanced liver fibrosis (ELF) score which correlates to the level of fibrosis.<br>• Medical device software intended to generate a model for end stage liver disease (MELD) score. |
| **C** | h) To be used in screening, diagnosis, or staging of cancer; | - Devices with the specific intended purpose to be used in screening, diagnosis or staging of cancer. Devices that are intended to be used in screening, diagnosis, or staging of cancer, may have the following functions: screening, patient management, monitoring, diagnosis or aid to diagnosis, prognosis and prediction.<br><br>• A faecal occult blood screening test (FOBT) or faecal immunochemical test (FIT) |

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| | | specifically intended to be used in colon cancer screening.<br>• A device intended for the quantitative/qualitative determination of IgG antibodies to Helicobacter pylori in human blood samples specifically intended to be used in gastric cancer screening.<br>• Papanicolaou (Pap) stain automated cervical cytology screening system, intended to process Pap cervical cytology slides and classify the cervical specimen as either normal or abnormal.<br>• A qualitative real-time PCR test intended for the detection of high-risk genotypes of Human Papillomaviruses for use in cervical cancer screening.<br>• Immunohistochemistry assay intended for the detection of c-KIT or CD117 tyrosine kinase receptor expression in normal and neoplastic formalin-fixed, paraffin-embedded tissues for histological evaluation, and gene mutation testing for KIT and platelet-derived growth factor receptor alpha in (familial) gastro-intestinale stromale tumor.<br>• Assay for the quantitative determination of the cancer associated antigen CA 125 (celomic epithelium-related glycoprotein associated with epithelial ovarian cancer) in serum.<br>• Immunohistochemistry assay intended to detect progesterone receptor in breast tumours to be used as an aid in the management, prognosis, and prediction of therapy outcome of breast carcinoma.<br>• Fluorescence in situ hybridisation (FISH) panels intended for the diagnosis of e.g. lymphoma, multiple myeloma and leukaemia.<br>• Targeted next generation sequencing test intended to be used in (haemato)-oncology, to detect acquired somatic mutations in DNA |

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| | | isolated from formalin-fixed paraffin embedded (FFPE) tumour tissue specimens.<br>• BRCA1 device intended for the detection of deletions or duplications in the human BRCA1 gene in order to confirm a potential cause and clinical diagnosis for hereditary breast and ovarian cancer and for molecular genetic testing of at-risk family members.<br>• Device applied in testing services intended for the analysis of 35 genes relevant to digestive tract tumours (various forms of colorectal cancer, stomach cancer and pancreatic cancer), breast cancer, ovarian cancer, skin cancer, thyroid tumours, and endocrine tumours (panel), intended to provide information on whether an individual carries genetic alteration that favour the onset of specific tumour diseases, identifying these genetic predispositions.<br>• Circulating Tumour Cell Kit (Epithelial) intended for the enumeration of circulating tumour cells (CTC) of epithelial origin in whole blood. The test is to be used as an aid in the monitoring of patients with metastatic breast, colorectal or prostate cancer. Serial testing for CTC should be used in conjunction with other clinical methods for monitoring metastatic breast, colorectal and prostate cancer, to allow assessment of patient prognosis and is predictive of progression free survival and overall survival.<br>• Breast carcinoma cell line (SK-BR-3) CTC Cell Control Kit intended as an assay control to ensure that the sample detection and identification systems are performing when using the CTC Kit. They express epithelial cell markers recognised by the antibodies in the Circulating Tumour Cell Kit and are used as a control for the performance of the assay. |
| **C** | i) For human genetic testing; | -Several methods can be used for genetic testing:<br>1) Molecular genetic tests.<br>2) Chromosomal genetic tests. |

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| | | Genetic testing may include devices intended to detect:<br>• Chromosomal conditions e.g. trisomy 21, trisomy 18, XXX syndrome.<br>• Abnormalities in genes associated with thrombophilia e.g. genes which code for factor V and prothrombin.<br>• Hereditary cancer syndromes e.g. hereditary breast/ovarian cancer (BRCA1/BRCA2 genes).<br>• Genetic risk Factors e.g. rheumatoid arthritis HLA DRB1, ankylosing spondylitis HLA B27, osteo-arthritis, pre-senilin mutation.<br>• Monogenetic disorders e.g. hemochromatosis, Huntington's disease, Tay Sacs, cystic fibrosis.<br>• Pharmacogenomic tests e.g. CYP liver enzymes CYP2C9 and CYP2C19.<br>• Preimplantation genetic diagnosis.<br>• XY disorders e.g. haemophilia, Duchenes muscular dystrophy, Fragile X. |
| **C** | j) For monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring; | - Devices intended to monitor an analyte with the purpose of adjusting patient management, such as treatments/interventions, as required.<br>Devices intended for monitoring:<br>• Cardiac marker for acute presenting patients: Troponin I, Troponin T, CKMB (when intended for monitoring cardiac muscle injury).<br>• Cortisol levels monitoring e.g. for patients with cortisol insufficiency.<br>• PT/APTT when used to assess major bleeds in acute presentations or patients with acute coagulopathy or for coumadin monitoring in patients without diagnosed coagulation disorder.<br>• Lithium for patients being treated for bipolar disorders. |

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| | | • Methotrexate when used for treating non-life-threatening conditions such as vasculitis, rheumatoid arthritis and psoriatic arthritis).<br>• Immunosuppressive (anti-rejection) medicinal products e.g. cyclosporine, sirolimus, tacrolimus.<br>• Antibiotic where under/over treatment can have a serious impact on individual or offspring e.g gentamicin.<br>• Anti-RhD antibody levels in pregnant women given additional Anti-D.<br>• Blood amylase e.g. acute pancreatitis, perforated peptic ulcer, acute biliary obstruction.<br>• Acute phase reactants e.g. C- reactive protein (CRP), procalcitonin when intended to be used to monitor infection response to therapy for life threatening conditions such as sepsis, necrotizing skin or tissue conditions, infective endocarditis, bacterial meningitis etc.<br>• Full blood count when used for monitoring for the development of a life threatening haematological disorder in patients being treated for other disorders/conditions, where this risk exists e.g. monitoring of patients with a diagnosis of schizophrenia for neutropenia/agranulocytosis.<br>• Bilirubin in response to treatment of neonatal jaundice. |
| **C** | k) For management of patients suffering from a life-threatening disease or condition; | Devices intended for:<br>• Enumeration of CD4 T lymphocytes in HIV infected patients to initiate treatment and ascertain the anti-viral therapy response.<br>• Measurement of D-Dimers in patients with thrombotic disorders.<br>• Laboratory risk score calculator indicator for necrotising fasciitis in necrotising soft tissue infections.<br>• HbA1c and blood glucose tests for the management of patients with diabetes.<br>• Monitoring anticoagulant therapy e.g. prothrombin Time/INR (warfarin), APTT |

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| | | (unfractionated heparin), anti-Xa chromogenic assays (low molecular weight heparin (LMWH), fondaparinux, rivaroxaban, and apixaban), anti-IIa chromogenic and clot-based assays (argatroban, bivalirudin, hirudin, and dabigatran).<br>• Digoxin monitoring.<br>• Anti-retroviral resistance testing in HIV infected patients. |
| **C** | l) For screening for congenital disorders in the embryo or foetus; | • Devices intended for screening of foetal aneuploidies (e.g. trisomy 13, trisomy 18 and trisomy 21), which include devices intended for the measurement of biochemical maternal serum markers.<br>• Reagents and medical device software evaluating the risk of foetal aneuploidies based on biochemical markers and other information, in particular non-invasive prenatal tests (NIPT).<br>• Devices intended to determine the foetal sex in cell-free foetal DNA in maternal blood, in the remit of sex-depending congenital disorders.<br>• Genetic test for cystic fibrosis.<br>• Genetic test for sickle cell disease.<br>• Huntington's chorea.<br>• Tay Sachs.<br>• Thalassaemia and other haemoglobin disorders. |
| **C** | m) For screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities. | -Examples of devices intended for screening in new-born babies for congenital disorders:<br>• Beta-thalassaemia.<br>• Biotinidase deficiency.<br>• Congenital adrenal hyperplasia – e.g 17-hydroxyprogesterone (17-OHP).<br>• Congenital hypothyroidism – e.g thyroxine.<br>• Cystic fibrosis – e.g. mutation and variant screening, immunoreactive trypsin.<br>• Galactosaemia – e.g. total galactose or galactose-1-phosphate uridyltransferase.<br>• Glutaric aciduria type 1. |

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| | | • Hyperphenylalaninaemia / phenylketonuria e.g phenylalanine (in blood); phenylpyruvic, phenyllactic, 2-OH phenylacetic (in urine).<br>• Homocystineuria (pyridoxine unresponsive) e.g. free homocystine, total homocysteine, and methionine (in blood and urine).<br>• Isovaleric acidaemia.<br>• Maple syrup disease (MSUD IA, IB, II) - e.g. branched-chain amino acids, allo isoleucine (in blood); branched-chain 2-ketoacids, branched-chain 2-hydroxy acids (in urine).<br>• Medium-chain acyl-CoA dehydrogenase deficiency – e.g. acylcarnitine measurement.<br>• Methylmalonic aciduria including cblA, cblB, cblC and cblD.<br>• Propionic aciduria.<br>• N-Acetylglutamate synthase deficiency – e.g. glutamine, alanine, citrulline, arginine (in blood).<br>• Sickle-cell disease.<br>• Tyrosinemia (I, II, III) – e.g. tyrosine (in blood); succinylacetone, 4-OH phenylpyruvic, 4-OH phenyllactic (in urine).<br>• Severe combined immunodeficiency (SCID) e.g. by TREC/KREC determination. |

Rule 4

In general, these devices are used by individuals with no technical expertise and thus the labelling and instructions for use are critical to the proper outcome of the test.

| Class | RULE 4 | Description & examples (non-exhaustive) |
|---|---|---|
| **C** | a) Devices intended for self-testing are classified as class C, | -All devices intended for self-testing are classified as class C:<br>• Tests for self-testing of blood sugar are in Class C.<br>• Self-testing devices for blood clotting, e.g. measurement of International Normalised Ratio (INR) are in Class C.<br><br>-Those classified in class D (e.g. HIV self-tests) will be classified as their own classification. |
| **B** | Except for devices for the detection of pregnancy, for fertility testing and | • Devices for detection of pregnancy (pregnancy self-test) |

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| | for determining cholesterol level, and devices for the detection of glucose, erythrocytes, leucocytes and bacteria in urine, which are classified as class B. | • Devices for fertility self-testing<br>• Devices for determining cholesterol level<br>• Devices for the detection of glucose, erythrocytes, leucocytes and bacteria in urine<br>• Urine self-test strips to detect glucose and other general urine chemistry analytes |
| | b) Devices intended for near-patient testing are classified in their own right. | -The classification of devices for near-patient testing follows the intended purpose of the device, as established by the manufacturer. This brings the classification of devices for near-patient testing in line with that of other devices intended for professional use. The manufacturer should check all the rules to determine the correct device classification.<br>• Class D (under Rule 1): Rapid test for detection of human immunodeficiency virus.<br>• Class D (under Rule 2): Pre-transfusion ABO compatibility test cards intended to be used at the recipients' bedside as precaution against ABO-incompatible transfusion.<br>• Class C (under Rule 3): Blood glucose reagents / strips for patient monitoring.<br>• Class C (under Rule 3): Mobile cardiac marker monitoring test for acute presenting patients: Troponin I, Troponin T, CKMB (when intended to be used for monitoring cardiac muscle injury).<br>• Class C (under Rule 3): Rapid test for the detection of methicillin-resistant Staphylococcus aureus.<br>• Class B (under Rule 6): Urine dipstick to determine urinary tract infection at point of care.<br>• Class B (under Rule 6): Quantitative test for haemoglobin as an aid in diagnosing iron deficiency.<br>• Class B (See Rule 6): Rapid tests for the detection of Group A Strep, Respiratory Syncytial Virus, and Influenza virus(es). |

## Rule 5

These devices present a low individual risk and no or minimal public health risk

| Class | RULE 5 | Description & examples (non-exhaustive) |
|---|---|---|
| **A** | The following devices are classified as class A:<br>a) Products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination; | • General microbiological culture media containing selecting agents, antimicrobial chromogenic agents, chemical indicators for colour differentiation.<br>• Solutions like cleaners, buffer solutions, lysing solutions, diluents specified for use with an IVD.<br>• Pipette with a specific fixed one volume specifically intended for a particular IVD test with specified human sample, e.g. blood coagulation pipettes with automatic timing (Accessory of coagulometer).<br>• General staining reagents like hematoxylin, eosin, pap and grams iodine.<br>• Kits for Isolation and purification of nucleic acids from human specimens.<br>• Library Prep reagents for preparation of DNA for downstream analysis by NGS sequencing.<br>• Nucleic acid quantitation kits.<br>• General reagents (not assay specific) used with a Class A instrument, e.g. general sequencing consumable reagents used with a sequencer. |
| **A** | b) Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures; | • Enzyme immunoassay analyser, PCR thermocycler, sequencer for NGS applications, clinical chemistry analyser.<br>• Instrument for automated purification of nucleic acids and PCR set-up. |
| **A** | c) Specimen receptacles. | • Specimen containers or evacuated or non-evacuated tubes, empty or prefilled with a fixative solution or other general reagent to preserve the condition, stimulation, transport, storage and collection of biological specimens |

## Rule 6

These devices present a moderate individual risk as they are not likely to lead to an erroneous result that would cause death or severe disability, have a major negative impact on patient outcome or put the individual in immediate danger.

The devices give results that are usually one of several determinants.

If the test result is the sole determinant however other information is available, such as presenting signs and symptoms or other clinical information which may guide a physician, such that classification into Class B may be justified.

Other appropriate controls may also be in place to validate the results.

This Class also includes those devices that present a low public health risk because they detect infectious agents that are not easily propagated in a population.

| Class | RULE 6 | Description & examples (non-exhaustive) |
|---|---|---|
| **B** | Devices not covered by the above-mentioned classification rules are classified as class B. | • Devices intended to detect and measure magnesium to assess electrolyte / magnesium homeostasis.<br>• Devices intended to detect and measure C-reactive protein or calprotectin to detect systemic inflammatory processes due to an active disease.<br>• Biochemical test for establishing the identification of microbiological culture isolates or for determining antimicrobial susceptibility of microbiological culture isolates except those permitting identification or determination of MIC associated with a life threatening condition.<br>• Devices to detect Helicobacter pylori, Clostridium difficile, adenovirus, rotavirus and Giardia lamblia.<br>• Non-typhoidal anti-salmonella antibodies to detect the exposure to an infectious agent.<br>• FSH device for fertility testing in blood.<br>• Devices intended for the detection of Candida albicans.<br>• Devices intended for the detection of or exposure to Entamoeba histolytica.<br>• Devices intended for the detection of Sarcoptes scabiei (genital scabies).<br>• Assay intended for the detection of autoantibodies (e.g. anti-sm/RNP and anti-SSA/Ro) associated with systemic lupus erythematosus (SLE), anti-neutrophil cytoplasmic antibodies [ANCAs] in systemic vasculitis), anti-aquaporin-4 antibodies (anti-AQP4) in |

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| | | neuromyelitis optica spectrum disorders (NMOSDs) or organ-specific autoimmune diseases (e.g. anti-Insulin antibodies in insulin-dependent diabetes).<br>• Antibody tests for HAV, dengue, chikungunya and West Nile virus.<br>• Assay intended for the detection of IgG antibodies against HEV.<br>• Devices intended for the detection of Influenza A/B virus (non-pandemic). |

Rule 7

For such controls, the qualitative or quantitative value is assigned by the user and not the manufacturer.

| Class | RULE 7 | Description & examples (non-exhaustive) |
|---|---|---|
| **B** | Devices which are controls without a quantitative or qualitative assigned value are classified as class B. | Applies to controls which are described as un-assayed where control values are assigned by the user and not the manufacturer. The manufacturer may indicate whether a specific analyte is present or absent in these controls without indicating expected assay results.<br>• Unassigned control sera.<br>• Control materials used to verify the migration of immunochromatographic assays.<br>• Unassigned QC Material as a heterozygous quality control to monitor analytical performance of the extraction, amplification and detection.<br>• Non-assay specific control plasmas for use in coagulation.<br>• Non-assay specific control serum containing multiple biochemical analytes.<br>• A DNA or RNA probe supplied for use as a non-assay specific normal control for in situ hybridisation (ISH). |

# Annexes

# Annex (A): List of Changes on the Previous Version

| Number & Date of the Previous Version | Changes Description |
|---|---|
| 1.0<br>10/04/2018 | • Update the following documents:<br>• Guidance on Medical Devices Classification (MDS-G42) to (MDS-G008).<br>• This document has been updated based on the new "Medical Devices Law" published by the Royal Decree, and its and Executive Regulation |