

Medical Device White Paper Series

# Explaining IVD classification issues

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## Introduction

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To comply with the Regulation on in vitro diagnostic medical devices (2017/746) (IVDR) manufacturers must classify their in vitro diagnostic (IVD) devices in accordance with the rules set out in Annex VIII of the Regulation. This white paper provides a historical perspective on the development of medical device and IVD device classification, explains the new rules and analyses the implications of the new system. Whilst it offers guidance, it should not be considered as a replacement for reading the full requirements of the Regulation.

Since the European Union started to regulate medical devices in the 1990s, a key element of the regulatory system has been the risk classification system based on human vulnerabilities. Its purpose was to ensure that devices would be regulated in a proportionate manner, whilst maintaining a high level of protection of health. The aim was also to minimize any unnecessary bureaucratic burden imposed on manufacturers. In particular, a rule-based system was devised to allow manufacturers themselves to identify the applicable risk class without having to formally apply for a classification decision from a competent authority or a notified body. It was also based on the realization that it would be prohibitively expensive to impose identical regulatory controls on all medical devices irrespective of the risk involved. The risk class would determine the appropriate conformity assessment route available to the manufacturer to achieve CE marking.

<sup>1</sup> Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on IVD medical devices and repealing Directive 98/79/EC and [Commission Decision 2010/227/EU](#).



This was initially implemented in the Directive concerning medical devices (93/42/EEC). The companion Directive on IVD medical devices (98/79/EC) did not contain a risk classification system as such. Instead, it established categories and lists of products allowing identification of the appropriate conformity assessment route. The new IVDR aligns the regulatory approach for IVD medical devices with that of the medical devices in general by establishing a set of risk-based classification rules.

The new rules are largely based on original work done by the Global Harmonization Task Force (GHTF). Much of the GHTF text is identical to the rules analysed in this guidance document, although there are some differences. The GHTF document is also helpful in improving the understanding of IVD classification because it provides a rationale for each of the rules.

There are some significant differences between the classification systems for medical devices and IVD medical devices under the new regulations. IVD medical devices cannot harm a patient directly in the same way that other medical devices can. The harm caused by IVD medical devices is indirect in the form of false positive and false negative results or incorrect quantitative results. Thus, the element of human vulnerability expressed often in anatomical terms is less evident in the IVDR classification. The emphasis is on criteria based on intended purpose. In addition, the use of medicinal substances is not a major factor in IVD classification as it is in classifying medical devices in general.

Another significant difference related to risk is that an IVD medical device can also endanger other persons than the patient if it fails to detect a highly contagious life-threatening agent.

Manufacturers of IVD medical devices will have to comply with the requirements of the new Regulation by 26 May 2022 in order to continue to place their devices on the European Union market. The main practical consequence of the new classification rules is that most IVD medical devices will need some form of certification by notified bodies. The timeline for compliance is more complex than suggested by the main compliance date of May 2022, but this does not affect classification decisions.

## Transition from the Directive to the Regulation

The Directive on IVD medical devices (98/79/EC) sets up specific categories of devices in order to determine the appropriate conformity assessment route. There is no clear indication of a hierarchy of risk although it is implied by the conformity assessment requirements to which each of these categories is subject to. This implied risk hierarchy is as follows, beginning with the highest risk category and ending with the lowest:

- Annex II List A related to determination of blood groups and the identification of markers for various blood borne pathogens — human immunodeficiency virus (HIV), human T-cell leukaemia-lymphoma virus (HTLV) and hepatitis as well as the detection of variant Creutzfeldt–Jakob Disease (vCJD)
- Annex II List B related to the detection of certain diseases
- Devices for self-testing (other than those listed in Annex II List A and B)
- All other IVD devices.

The risk classification system of the IVDR is rule based, although it retains a residue of the old system of the Directive by resorting to a certain degree of listing, in particular with respect to blood-borne markers (e.g. ABO blood typing).

The IVDR establishes four risk classes D, C, B, and A, with D being the highest risk class and A the lowest. There are altogether seven classification rules (Annex VIII). The Commission may issue implementing acts that would change the existing rules (Art. 47.3-4).

Broadly speaking the four classes cover IVD devices as follows:

Class D covers general life-threatening conditions and more specifically transmissible agents in blood and biological materials intended to be transplanted or re-administered into the body. Such transmissible agents may also present a high risk to the wider population. It also specifically covers blood grouping or tissue typing when this involves markers of the following systems: ABO, Rhesus, Kell, Kidd and Duffy.

Class C covers a diverse mix of high-risk IVD devices which present a lesser risk to the wider population. It tends to include situations where the failure of a diagnosis could be life-threatening, including testing for infectious diseases and cancer. It also covers fields such as companion diagnostics and genetic screening. In addition, Class C covers self-testing IVD devices in general (see exceptions below).

Class B is the default class that takes in all IVD devices that are not covered specifically in other classification rules. This is a departure from the system applied to other medical devices for which the default class is Class I, i.e. the lowest risk class. It tends to cover devices that present lower risks to the patient and the population at large than IVD devices in Classes D and C. Class B also covers self-testing IVD devices for pregnancy and fertility testing as well as detection of cholesterol levels and detection of glucose, erythrocytes, leucocytes and bacteria in urine. Controls without a quantitative or qualitative assigned value are also in Class B.

Class A covers broadly speaking laboratory devices (e.g. wash buffers), instruments and specimen receptacles.



The major consequence of the new classification system is that in contrast with the current system most IVD devices will be subject to verification and certification by notified bodies. Only Class A devices are allowed on the market based on self-certification.

Regulatory requirements will be more demanding under the IVDR for all IVD devices in any case, but the need to prove compliance to a notified body prior to CE marking will increase the burden on the manufacturers and result in a higher cost of regulatory compliance. In some cases, it may not be possible to generate adequate proof of compliance with the new requirements. These factors may result in some devices no longer being commercially viable.

## Classification and compliance requirements

### Requirements applying to devices in all risk classes

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Many requirements of the Regulation apply regardless of risk class, for instance:

- General Safety and Performance Requirements of Annex I (Art. 5.2)
- The risk class and the justification for the classification rule(s) must appear in the technical documentation (Annex II, Section 1.1f)
- The risk class must appear on the declaration of conformity (Annex IV, Section 5)
- Registration in Eudamed<sup>3</sup> with an indication of the risk class (Annex VI, Part A, Section 2.8)
- Quality management system procedures must cover classification (Annex IX, Chapter I, Section 2.2c)
- Certificates issued by the notified body shall identify the risk classification of the devices concerned (Annex XII, Chapter I, Section 4)
- Various documents related to performance studies must identify the risk class of the device (Annex XIV, Chapter I, Sections 1.10, 1.12 and 2.1).

Some requirements applicable to all devices should nevertheless be complied with in a manner that is proportionate to the risk class:

- Quality management system (Art. 10.8)
- Post-market surveillance system (Art. 78.1)
- Performance evaluation (Annex XIII, Part A, Section 1).

<sup>3</sup> European database on medical devices.



## Requirements depending on the risk class

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Some requirements apply to specific risk classes:

### Class D

- Special scrutiny of conformity assessment (Art. 50)
- The periodic safety update report (PSUR) (see below) must be submitted electronically to the notified body via Eudamed where the notified body must file its evaluation of the PSUR (Art. 81.2)
- The involvement of designated EU reference laboratories is a major change. They will verify the performance claimed by the manufacturer (Art. 48.5) and test samples (Art. 100.2).

### Classes C and D

- Drawing up a summary of safety and performance (Art. 29.1)
- Performance evaluation reports must be updated at least annually (Art. 56.6)
- Coordinated assessment of performance studies carried out in more than one Member State may be further prolonged by 50 days (Art. 74.6)
- A PSUR must be prepared for each device (and where relevant for each category or group of devices). It must summarize the results and conclusions of the analyses of the post-market surveillance data and be updated at least annually (Art. 81.1)
- The summary of safety and performance must be uploaded to the Eudamed database (Annex VI, Part A, Section 2.11).

## Class C

- The PSUR must be made available to the notified body and the competent authorities upon request (Art. 81.3)
- Member States may request designation of reference laboratories for the verification of the performance claimed by the manufacturer and the compliance with the applicable Common Specifications (Art. 100.3).

## Classes B, C and D

- The economic operators must indicate to the Member States where the device is or is to be made available when registering in Eudamed (Annex VI, Part A, Section 2.4).

## Classes A and B

- The post-market surveillance report must be updated when necessary and made available to the notified body and the competent authority upon request (Art. 80)
- For single-use devices, the Unique Device Identification (UDI) carrier can be on a multi-unit packaging instead of individual unit packaging (Annex VI, Part C, Section 4.3).

The implementation of the UDI carrier labelling will be introduced gradually depending on the risk class (Art. 24.4 and 113.3e) as follows:

- Class D: 26 May 2023
- Classes B and C: 26 May 2025
- Class A: 26 May 2027.

## **Conformity assessment**

The main differences in compliance requirements based on risk class relates to the conformity assessment route as specified in Art. 48:

- Class D: the manufacturer has a choice between two options
  - Annex IX, Chapters I, II (except for Section 5) and III or
  - Annex X together with Annex XI
- Class C: the manufacturer has a choice between two options
  - Annex X together with Annex XI Annex IX, Chapters I and III (including an assessment of the technical documentation of at least one representative device per generic device group) or

- Annex X together with Annex XI except its Section 5
- Class B: Annex IX, Chapters I and III (including an assessment of the technical documentation of at least one representative device per category of devices)
- Class A: self-declaration unless the devices are placed on the market in sterile condition in which case the manufacturer will apply Annex IX or XI.

The notified body has specific responsibilities with respect to risk classification:

- Verify the risk classification before issuing any quotation to the manufacturer relating to a specific conformity assessment (Annex VII, Section 4.2d)
- Draw up and keep up to date, for Class B and class C devices, a sampling plan for the assessment of technical documentation (Annex VII, Section 4.5a)
- The decision regarding the period of certification must take into account the risk class of the device (Annex VII, Section 4.8).

## Requirements applying to specific categories of devices

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It should be noted that particular requirements apply to certain categories of devices used in specific contexts such as:

- Companion diagnostics
- Performance studies
- Self-testing
- Near-patient testing
- In-house devices manufactured by and used in EU health institutions.

Devices intended for research use only without any medical objective are not subject to the requirements of the Regulation (Art. 1.3a).

There are significant specific conformity assessment requirements for devices intended for self-testing, near-patient testing and companion diagnostics in addition to and/or at variance with the above requirements. For instance whereas Class D devices are not normally subject to Section 5 in Chapter II of Annex IX, devices for self-testing and near-patient testing are subject to Section 5.1 and companion diagnostics to Section 5.2.



## Implementation of risk classification by the manufacturer

The manufacturer is responsible for identifying the risk class applicable to its IVD device. The notified body will verify the correctness of this classification for Classes B, C and D devices. A competent authority may also verify the classification, including for Class A devices. It is therefore important for manufacturers to have an adequate rationale documented on file for its classification decisions.

The manufacturer should proceed as follows:

- Determine the intended purpose of the device
- Ensure that the performance of the device and related scientific validity can be demonstrated
- Review all the classification rules and determine which is the highest risk class applicable to the device. It is possible that several rules apply or that the device has multiple intended uses; in that case the rule resulting in the highest risk class must be applied.



Devices are generally classified in their own right. This applies to situation when two or more devices are used together, standalone software and accessories. However, there are exceptions to this basic principle:

- Software which drives or influences the use of a device falls in the same class as that device
- Calibrators intended to be used with a device fall in the same class as that device
- 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.

## Interpretation of classification rules

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A new institutional structure has been created to support the implementation of the new regulations. The Medical Device Coordination Group (MDCG) plays a key role in this. Classification issues are among the tasks that the MDCG will have responsibility (Art. 99). Several working groups have been created under it, one of which will deal with issues of classification. Although the MDCG working groups are mainly composed of representatives of the Member States, access has also been provided for experts of stakeholders (industry trade associations, etc.).

Guidance was issued by the Commission on classification of medical devices under the old system. This is in process of being updated so it is likely that interpretation of the classification rules for IVD devices will emerge in due time from the MDCG.

The Commission may also adopt implementing acts to resolve issues of interpretation (Art. 47.5).

If the manufacturer and notified body disagree on the classification of an IVD device, the dispute can be referred to the competent authority of the Member State of the manufacturer or of the authorized representative. If the notified body is in a different Member State, the competent authority of that Member State will be consulted (Art. 47.2).

## Practical advice to manufacturers

### Challenges

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The challenges that both manufacturers and notified bodies must meet can be summarized as follows:

- The impact of a completely new risk-based classification system for IVD devices will increase dramatically the number of IVD devices subject to notified body scrutiny. This will imply substantially greater resource needs for both the manufacturers and the notified bodies as well as an increased cost burden for the manufacturers
- The increased emphasis on quality systems, performance evaluation and post-market surveillance will affect IVD devices in all classes, although the Regulation includes an element of proportionality that is likely to be understood as being a function of the risk class. It is also likely that the practical application of the principle of proportionality will raise many issues of interpretation
- The potential for adoption of implementing acts by the Commission that could bring about further changes in the classification system.

### Immediate actions to be taken

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You should carry out the following actions as soon as possible with respect to each of your IVD devices:

- Consider mapping out the basis for your claims (see Article 7) made because each product is likely to be subject to greater scrutiny than before. This would involve reviewing and critically assessing:
  - the intended purpose of your products
  - the performances for achieving the intended purpose

- available scientific and clinical evidence for supporting the claimed performances
  - if you find any gaps in the evidence, take action to fill them.
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- Identify the applicable risk class each of your products
  - Identify the new compliance requirements resulting from the new classification system
  - Carry out a gap analysis between your current compliance and the new requirements
  - Develop an action plan to deal with the new compliance requirements.

At the latest when your notified body is designated under the IVDR:

- Ensure that you have a common understanding between you and your notified body on any issues of interpretation regarding classification and the relevant compliance requirements. Please note that your notified body may require you to have a contract with them before they will comment on your compliance solutions or assess them
- Come to an agreement with your notified body on an implementation timeline.

You should understand that there may be fewer notified bodies under the IVDR than there are currently under the directives. There are presently 21 notified bodies able to certify IVD devices (58 for medical devices). There could be as few as seven notified bodies designated under the IVDR. It may take until late 2019 until the first notified bodies have been designated under the IVDR. Because of the possibility that timely access to the assessment and certification by notified bodies will become a scarcer resource, it is important to prepare already now for compliance. It is also important to establish early relations with the notified body with which you intend to form a relationship and resolve any potential disagreements about classification as early as possible. This process may involve approaching the relevant national competent authority for an opinion.

Class A IVD devices that do not require certification by a notified body need to achieve compliance and be self-certified by May 2022.

## Issues of interpretation

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New requirements always raise issues of interpretation. Over time many of these issues are resolved by authorities' decisions and guidance as well as decisions by courts both at the national and the European level. Meanwhile, when unresolved issues of interpretation arise, the process of coping with such a problem can be very difficult for both the manufacturer and the notified body.

### Section 1.10 of Annex VIII

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This states:

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

This is essentially a repeat of the principle stated in Section 1.7. 'The manufacturer shall take into consideration all classification and implementation rules in order to establish the proper classification for the device'. It also reinforces the idea that all types of assays (first line, confirmatory and supplemental) must be classified in their own right. No definitions of these types of assays are given in the IVDR, but the message is clear in that they are all covered without distinction. If more than one rule applies, then the manufacturer must comply with the rule that results in the highest class (Section 1.8).

## Rule 7

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The meaning of 'controls without a quantitative or qualitative assigned value' in Rule 7 has been the subject of some discussion. This might be construed to include controls containing a specific analyte, such as a pathogen, but does not claim an assigned quantity or specific quality parameters. However, the presence of a specific analyte in the control material can itself be considered as a 'qualitative' assigned value. This latter interpretation would limit the definition materials giving a specific signal without containing the actual analyte.

## Class A

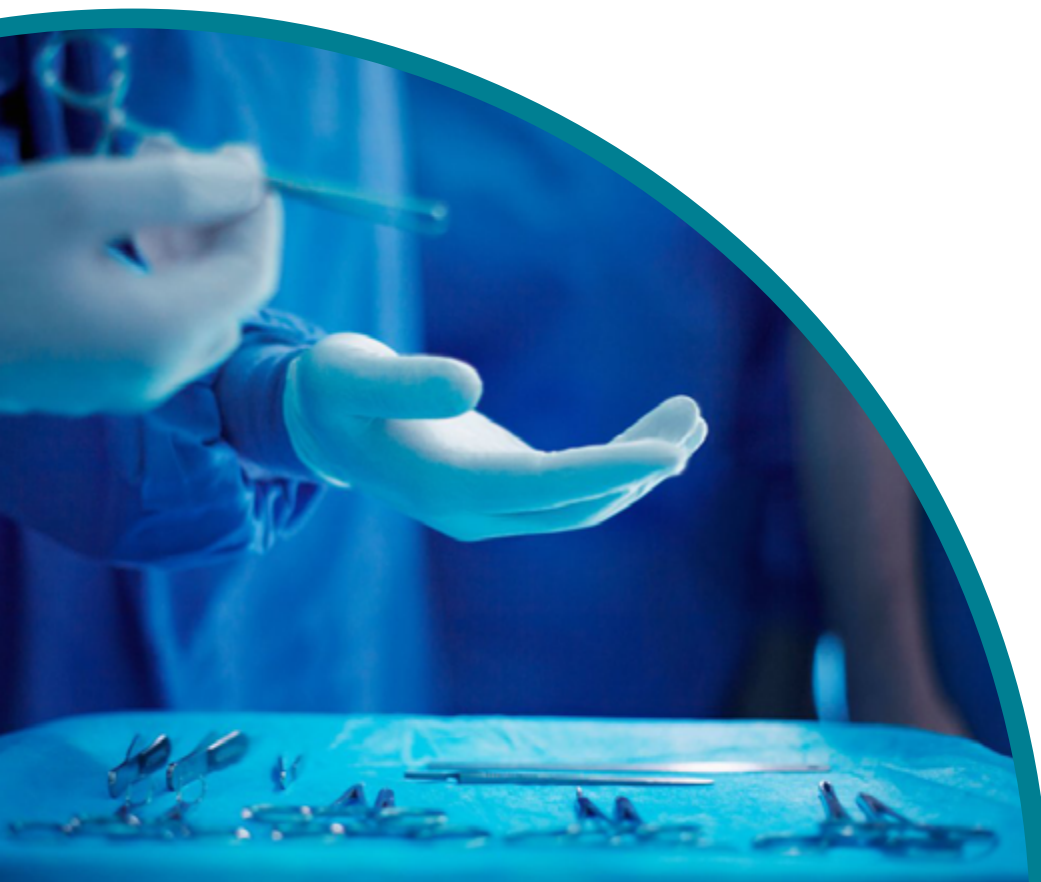
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Class A, as defined by classification Rule 5, is likely to be subject to debate, mainly because it is the only class that does not require the intervention of a notified body. Specific issues also arise from this rule.

## Instruments

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In placing instruments into Class A, the regulators probably had in mind the typical IVD analyser which, in order to produce results, has to work with reagent cartridges which are analyte/test specific. However, IVD instruments are being developed which can provide diagnostic information on biological markers without the use of any reagent at all.



For instance, refractometry on dried plasma spots provides diagnostic information. Such instruments are unlikely to remain in Class A. This type of instrumentation may emerge in a variety of diagnostic areas such as genetics and markers for cancer, Alzheimer's disease, etc.

A good example of these analysers is the common haematology analyser used daily in thousands of laboratories to provide information on blood. They do not use any analyte-specific reagents. They use a saline-water-based solution which is used to dilute the blood sample taken from the patient. This sample diluent is not really a 'reagent' in itself. Is it sustainable to leave haematology analysers in Class A? Or will they migrate to Class B? A solution could be to consider the sample diluent as the 'reagent' (Class B) which could leave the instrument in class A. But this solution would only work for the haematology analysers and not for the spectroscopy instruments above which do not use any liquid.

## General culture media

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'General culture media' are covered under Rule 5 as Class A devices. However, they are not defined in the IVDR which may create confusion as to what is meant by this term. There is no commonly accepted definition of this term either. Instead there are several types of culture media (CM): preservation CM, enrichment CM, selective CM, differential CM, resuscitation CM, isolation CM, fermentation CM, etc.

'General CM' or 'General Purpose CM' can be defined as media that have multiple effects, i.e.: can be used as selective, differential or resuscitation media. Because of the variety of CM and their intended purposes, it may not be appropriate to have them all in Class A. For instance, CM for methicillin-resistant *Staphylococcus aureus* — an infectious agent — could be regarded as inherently presenting a higher risk than Class A because of the extremely high-risk micro-organism with which it is associated.

The concept in Rule 5 of general purpose products becoming IVD devices (including CM) if the manufacturer expresses an intent that they are made 'suitable for in vitro diagnostic procedures relating to a specific examination' is likely to create much discussion on aspects such as how the intent would be expressed to cross the threshold into the IVD world? What is the meaning of 'specific examination?' etc.

## Conclusion

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The new system of risk classification of IVD medical devices is one of the few radical changes brought about by the new medical device regulations. It is an improvement on the current directive<sup>4</sup>. It aligns the classification of IVD medical devices with other medical devices and international practice as advocated by the GHTE. It is also a more comprehensive approach than the one in the current directive thus enabling an easier application to new IVD medical devices.

However, it also subjects most IVD medical devices to certification by notified bodies. This will improve patient safety. Nevertheless, the complex requirements and scrutiny by notified bodies will have a serious impact on the manufacturers of these products. Many may disappear from the European market as a result. The classification is essentially based on the intended purpose so the emphasis on proving a classification claim is likely to be on being able to prove performance. Some of the rules also introduce the concept of the severity of harm (e.g. likelihood of death in Rule 3(c)). Therefore, determining the applicable rule may require consideration of the clinical impact on the patient. Such an assessment is likely to require the opinion of clinical experts.

Problems of interpretation are less likely to arise for classification criteria that are very specific, e.g. determination of ABO system markers. More general terms such as 'life-threatening' may result in more issues of interpretation arising. Because many IVD medical devices have not been subject to notified body scrutiny before, it is possible that issues of interpretation of classification rules may arise very quickly. Manufacturers need to be vigilant and monitor how such problems of interpretation will be resolved through guidance and specific decisions.

<sup>4</sup> Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on IVD medical devices.



## Annex — Analysis of the rules<sup>5</sup>

Rules	Comments
<p><b>Rule 1</b> Devices intended to be used for the following purposes are classified as class D:</p>	
<p>— 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;</p>	<p>There is a long history of blood contamination and epidemics vectored by blood borne agents that explains the perception of high risk.</p> <p>If the assay is not meant to assess suitability for transfusion/transplantation/cell administration then appropriate disclaimers should be given.</p>
<p>— 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;</p>	<p>The concepts of 'life-threatening' and 'high risk of propagation' are key concepts in establishing the borderline between Class D and Class C. If an IVD fails to detect the presence of a transmissible agent that ultimately is likely to kill the patient, such a risk makes classifying it in Class D. This is even more so if the transmissible agent is highly contagious and failure to detect it could result in a pandemic.</p> <p>This is likely to cover the agents of diseases that were specifically identified in Annex II of the IVD Directive, i.e. HIV infection (HIV 1 and 2), HTLV I and II, and hepatitis B, C and D, as well as vCJD. These are not specifically listed in the Regulation as the aim is to avoid detailed lists that would be restrictive.</p> <p>It is nevertheless clear that this rule has a wide scope and is intended to also cover emerging pathogens with a high pandemic potential and high mortality, such as Ebola, regardless of whether they the devices are intended for diagnosis or blood screening.</p>
<p>— determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.</p>	

<sup>5</sup> Some of the comments are taken from the GHTF document on 'Principles of In Vitro Diagnostic (IVD) Medical Device Classification' or are inspired by it.

<p><b>Rule 2</b>  <b>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, except when intended to determine any of the following markers:</b></p> <ul style="list-style-type: none"> <li>— ABO system [A (ABO1), B (ABO2), AB (ABO3)];</li> <li>— Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)];</li> <li>— Kell system [Kel1 (K)];</li> <li>— Kidd system [JK1 (Jka), JK2 (Jkb)];</li> <li>— Duffy system [FY1 (Fya), FY2 (Fyb)];</li> </ul> <p>in which case they are classified as class D.</p>	<p>The markers listed as exceptions and classified as class D may result in a life-threatening risk in the event of an erroneous result.</p>
<p><b>Rule 3</b>  <b>Devices are classified as class C if they are intended:</b></p>	<p>Devices in Class C 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.</p>
<p>(a) for detecting the presence of, or exposure to, a sexually transmitted agent;</p>	
<p>(b) for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation;</p>	<p>For an infectious agent not to present a high risk of propagation, it should not be easily transmissible in humans.</p>
<p>(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 embryo being tested, or to the individual's offspring;</p>	



(d) for prenatal screening of women in order to determine their immune status towards transmissible agents;	
(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;	It is not clear whether 'immune status' is only linked to infections or if for example anti-erythrocytic antibodies would fit into this definition. The reference to immune status could also have implication in the area of cancer treatment.
(f) to be used as companion diagnostics;	'companion diagnostic' means a device which is essential for the safe and effective use of a corresponding medicinal product to:  (a) identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or  (b) 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; Art. 2 (7).
(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;	The concept of 'disease staging' is open to some interpretation. One possible definition is: <i>Disease staging is a clinically based measure of severity that uses objective medical criteria to assess the stage of disease progression. Its availability in automated form increases its ease of implementation in hospital reimbursement and management.</i> <sup>6</sup> IVD assays can be used to stage a disease in relationship with the increase/decrease of certain parameters that they are measuring.
(h) to be used in screening, diagnosis or staging of cancer;	
(i) for human genetic testing;	Not all genetic testing is covered here as there would also need to be a medical purpose for the IVDR to apply. For instance testing a persons' DNA for genealogical purposes would not be covered here.
(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;	This is distinct from companion diagnostics as explained in recital 12 'Devices that are used with a view to 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 companion diagnostics'.

<sup>6</sup> Conklin, J. E., Lieberman, J. V., Barnes, C. A. & Louis, D. Z. Disease staging: Implications for hospital reimbursement and management. Health Care Financing Review, 1984 (Suppl), 13–22.

<p>(k) for management of patients suffering from a life-threatening disease or condition;</p>	<p>Management of a life-threatening condition is different from detecting a life-threatening agent or condition since a management context implies that the presence of the disease or condition is already known. However, if the condition is covered under Rule 1 (sub-bullet for 'infectious load of a life-threatening disease where monitoring is critical in the process of patient management'), these devices will still be Class D as the highest rule would apply. Rule 3(k) will therefore apply to those diseases or conditions that are not posing a high or suspected high risk of propagation covered under Rule 1.</p> <p>The risk is therefore lesser and Class C is justified. This also provides additional clarification on the borderline between Classes D and C.</p> <p>The concepts of 'life-threatening' and 'high risk of propagation' are key in establishing the borderline between Classes D and C. If an IVD fails to detect the presence of a transmissible agent that ultimately is likely to kill the patient, such a risk makes classifying it in Class D. This is even more so if the transmissible agent is highly contagious and failure to detect it could result in a pandemic.</p>
<p>(l) for screening for congenital disorders in the embryo or foetus;</p>	
<p>(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.</p>	
<p><b>Rule 4</b></p> <p>(a) Devices intended for self-testing are classified as class C, except for devices for the detection of pregnancy, fertility testing and determining cholesterol level, and devices for the detection of glucose, <i>erythrocytes</i>, <i>leucocytes</i> and bacteria in urine, which are classified as Class B.</p>	<p>These devices are generally used by lay persons, i.e. individuals who do 'not have formal education in a relevant field of healthcare or medical discipline'<sup>7</sup></p>
<p>(b) Devices intended for near-patient testing are classified in their own right.</p>	<p>These are devices that are not intended for self-testing but are intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient by a health professional; Art.2 (6).</p>

<sup>7</sup> Art. 2(31) of the IVDR.

<p><b>Rule 5</b></p> <p>The following devices are classified as class A:</p> <p>(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;</p> <p>(b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures;</p> <p>(c) specimen receptacles.</p>	<p>See above comments on Class A in the Section Issues of interpretation.</p>
<p><b>Rule 6</b></p> <p>Devices not covered by the above-mentioned classification rules are classified as Class B.</p>	<p>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.</p>
<p><b>Rule 7</b></p> <p>Devices which are controls without a quantitative or qualitative assigned value are classified as Class B.</p>	<p>The purpose of this rule is not very clear as these devices would have been captured by Rule 6, unless it is to avoid a possible misinterpretation.</p> <p>The qualitative or quantitative value is assigned by the user and not the manufacturer.</p>

## References

- Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices (<https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R0746>)
- Principles of In Vitro Diagnostic (IVD) Medical device Classification, Global Harmonization Task Force, 19 February 2008 (<http://www.imdrf.org/docs/ghtf/final/sg1/procedural-docs/ghtf-sg1-n045-2008-principles-ivd-medical-devices-classification-080219.pdf#search=%22ivd%22>)

## Additional resources

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The European Commission's portal on the new regulations can be found at:

[http://ec.europa.eu/growth/sectors/medical-devices/new-regulations\\_en](http://ec.europa.eu/growth/sectors/medical-devices/new-regulations_en)

Guidance from UK's Competent Authority Medicines and Healthcare products Regulatory Agency (MHRA) can be found at:

<https://www.gov.uk/guidance/medical-devices-eu-regulations-for-mdr-and-ivdr>

## Contributors

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BSI is grateful for the help of the following people in the development of the white paper series.

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**Maurizio Suppo. Co-owner and Principle Consultant, Quarad**, obtained his Ph.D. in molecular biology from the University of Turin (Italy) in 1985. He has more than 33 years of experience in the field of regulatory affairs and quality systems. He held executive positions at Sorin Biomedica (now DiaSorin), Becton Dickinson, Dade Behring and Siemens Healthcare. He has been the Director of the European Diagnostic Manufacturers Association (EDMA) and had a significant role in the development of the European IVD Directive 98/79/EC. His knowledge and experience in RA&QS go beyond the European borders. He is a trained ISO-9001 & 13485:2016 auditor. He is also an expert MDSAP auditor with more than 500 MDSAP audit hours as a lead auditor. Maurizio joined Quarad in July 2012 and became partner and co-owner in January 2016. He is a regular speaker and chairman at international conferences and published more than 20 articles in the specialized press. He is fluent in Italian, English, French with a good knowledge of Spanish.

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Pete is the Director of the Surgical Materials Testing Laboratory (SMTL), based in Bridgend in South Wales, which is funded by the Welsh Government to test medical devices for the Welsh NHS and to provide technical advice on medical devices. He has worked in the medical devices field for 30+ years, and sits on a number of BSI, CEN and ISO medical device committees and groups. He chairs the Welsh Non-Luer Connectors Reference Group (WNCRG) for Welsh Government, which is coordinating the implementation of new ISO compliant non-Luer connectors across the Welsh NHS, and represents Welsh Government on medical devices on various other groups.

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Eamonn is a technical author, trainer and consultant in a range of life science areas including regulatory compliance, quality management, sterility assurance and standards development. He worked for Johnson & Johnson (J&J) for 17 years in positions of increasing responsibility for Quality and Regulatory Compliance for medical devices, pharmaceuticals and consumer products including Vice-President of Compliance, Vice-President of Market Quality and leading quality implementation for the EU medical devices regulation for J&J's Medical Devices companies. Prior to joining J&J, Eamonn spent 16 years with the UK Medical Devices Agency, including six years as Head of Device Technology and Safety. Eamonn is currently chair of ISO TC 198, Sterilization of Healthcare products, chair of CEN TC 204 'Sterilization of medical devices' and past chair of ISO TC 210 'Quality management and related general aspects for medical devices'. He received the BSI Wolfe-Barry medal in 2016 for his contribution to standards development.

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Paul has worked in the healthcare industry for over 35 years, joined BSI in 2010 to lead the organization in Saudi Arabia where it had been designated as a Conformity Assessment Body. Later, he managed BSI's Unannounced Audits programme. Since October 2015, he has been working with both the Notified Body and Standards organizations looking at how best to use the knowledge, competencies and expertise in both. Previously he held senior RA/QA leadership positions at Spacelabs Healthcare, Teleflex Medical, Smiths Medical and Ohmeda (formerly BOC Group healthcare business). Paul is a member of the Association of British Healthcare Industries (ABHI) Technical Policy Group and Convenor of the ABHI ISO TC 210 Mirror Group. He is Convenor of the BSI Committee that monitors all of the work undertaken by ISO TC 210, and Convenor of the BSI Subcommittee dealing with quality systems. As UK Delegation Leader to ISO TC 210, he is also actively involved in the work of national, European and international standards' committees.

## Published white papers



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- *The Proposed EU Regulations for Medical and In Vitro Diagnostic Devices: An Overview of the Likely Outcomes and Consequences for the Market*, Gert Bos and Erik Vollebregt
- *Generating Clinical Evaluation Reports – A Guide to Effectively Analysing Medical Device Safety and Performance*, Hassan Achakri, Peter Fennema and Ito Udofia
- *Effective Post-Market Surveillance – Understanding and Conducting Vigilance and Post-Market Clinical Follow-up*, Ibim Tariah and Rebecca Pine
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- *General Safety and Performance Requirements (Annex 1) in the New Medical Device Regulation – Comparison With the Essential Requirements of the Medical Device Directive and Active Implantable Device Directive*, Laurel Macomber and Alexandra Schroeder.
- *Do You Know the Requirements and Your Responsibilities for Medical Device Vigilance Reporting? – A Detailed Review on the Requirements of MDSAP Participating Countries in Comparison With the European Medical Device Regulation 2017/745*, Cait Gatt and Suzanne Halliday
- *Technical Documentation and Medical Device Regulation - A Guide for Manufacturers to Ensure Technical Documentation Complies With EU Medical Device Regulation 2017/745*, Dr Julianne Bobela, Dr Benjamin Frisch, Kim Roach and Michael Maier
- *Nanotechnology – What Does the Future Look Like for the Medical Devices Industry?* Prof Peter J Dobson, with Dr Matthew O'Donnell

- *Developing and Maintaining a Quality Management System for IVDs*, Melissa Finocchio
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- *The Impact and Potential for 3D Printing and Bioprinting in the Medical Devices Industry*, Kenny Dalgarno

## Forthcoming white papers

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-  *Recognising and Reducing Digital Risk in Healthcare: We Need to Up Our Game to Make Digital Innovation Safe and Effective*, Prof Harold Thimbleby
-  *The Convergence of Pharma and Medical Devices*, Barbara Nasto (working title)

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BSI (British Standards Institution) is the business standards company that equips businesses with the necessary solutions to turn standards of best practice into habits of excellence. Formed in 1901, BSI was the world's first National Standards Body and a founding member of the International Organization for Standardization (ISO). Over a century later it continues to facilitate business improvement across the globe by helping its clients drive performance, manage risk and grow sustainably through the adoption of international management systems standards, many of which BSI originated. Renowned for its marks of excellence including the consumer recognized BSI Kitemark™, BSI's influence spans multiple sectors including aerospace, construction, energy, engineering, finance, healthcare, IT and retail. With over 70,000 clients in 150 countries, BSI is an organization whose standards inspire excellence across the globe.

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