

Document number: SG1/N045R9 & Title: Principles of IVD Medical Devices Classification

Collation of Comments received

| Comment Number | Page / Section / Line | Editorial or Technical | Comment and rationale | Proposed revised text | SG 1 (IVD Subgroup Decision) |
|----------------|-----------------------|------------------------|--|---|--|
| 1. | Scope | Ed | Add reference to SG1/N029 | Add a footnote at end of second sentence: See SG1/N029:2005 Information Document Concerning the Definition of the Term 'Medical Device'. | Rejected There is a reference to the document in the section 3.0 references |
| 2. | All | Ed | - There are various expressions for In Vitro Diagnostic Medical Devices. - "IVD" is used without any explanation (e.g.) in vitro diagnostic medical device IVD Medical Devices IVD reagent IVD medical device IVDs IVD Device (Title of 6.2) | Unify them to one appropriate expression and/or Explain the abbreviation when it first appears in the document. | IVD Medical Device(s) |
| 3. | | | Every IVD which is intended to be used as high risk device, but not | | To be considered in conformity |

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| | | | yet listed up in Class A and B (e.g. new tests for detecting pathogens in a pandemic situation) should be defined transitionally as Class D or excluded (with special decision) from IVD-subject in order to make it available asap | | assessment. The test can be classified following the rules. Already covered in purpose third bullet point |
| 4. | | | <p>-the classification rules seem to be straight forward and are easier to follow than other similar schemes (Canadian scheme, for example). It may be wise to offer more examples of typical IVD analytes and their respective classification.</p> <p>-It is still not entirely clear how best to handle accessories as this document follows the EU definition of an accessory as an IVD, rather than the US definition. This needs greater clarification, I believe.</p> | | <p>Rejected given the wide variety of IVD Medical Devices we cannot provide an exhaustive list of examples</p> <p>Rejected no change to definition, definition defines accessory as an IVD and 6.2 states that they need to be classified separately</p> |
| 5. | | | <p>Why is the "Global Harmonization" group creating a 3rd classification scheme? We already have 2 (EU & FDA). They are not planning to change, so now we'll have 3.</p> <p>I have two comments the A-D classifications should be harmonized to 1 - 4. I would think that specimen containers with</p> | | <p>Rejected</p> <p>Rejected but note added to clarify that A,B,C,D is</p> |

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| | | | <p>preservatives in them could fall in their class B.</p> <p>Why is the classification scheme A --> B --> C --> D? FDA, Health Canada, Australian TGA, EU Medical Device Directive 93/42/EEC, etc., are based on a numerical system. It seems to me that, as a goal of harmonization, the classification scheme should have some consistency with the majority of device classification regulations already in place.</p> | | not binding as class identifiers in 6.3. |
| 6. | p. 2 | Ed | To be consistent with section 2.2 | Delete (including In Vitro Diagnostic Devices) following Essential Principles of Safety and Performance for Medical Devices. | Accepted |
| 7. | Pp4 Parasd 1 to 4 | Ed | Align with SG1/N015 | <p>The primary way in which the Global Harmonization Task Force (GHTF) achieves its goals is through the production of harmonized guidance documents suitable for implementation or adoption by member Regulatory Authorities, as appropriate taking into account their existing legal framework, or by nations with developing regulatory programmes.</p> <p>This guidance document is one of a series that together describe a global regulatory model for medical devices. Its purpose is to assist a manufacturer to allocate its medical device to an appropriate risk class using a set of harmonized principles. Regulatory Authorities have the responsibility of ruling</p> | Accepted |

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| | | | | <p>upon matters of interpretation for a particular medical device. Once assigned, such classification will prescribe how the manufacturer will demonstrate that its device complies with other documents in the series and, in particular, with those entitled Essential Principles of Safety and Performance of Medical Devices and Labelling for Medical Devices should it be required or requested so to do by a Regulatory Authority, Conformity Assessment Body, user or third party.</p> <p>This document should be read in conjunction with the GHTF document on Principles of Conformity Assessment for Medical Devices that recommends conformity assessment requirements appropriate to each of the four risk classes proposed herein. The linked development of documents on classification and conformity assessment are important to ensure a consistent approach across all countries/regions adopting the global regulatory model recommended by the GHTF, so that premarket approval for a particular device may become acceptable globally. Regulatory Authorities who may have different classification procedures are encouraged to adopt this GHTF guidance as the opportunity permits.</p> <p>This document has been developed to encourage and support global convergence of regulatory systems. It is intended for use by Regulatory Authorities, Conformity Assessment Bodies and industry, and will provide benefits in establishing, in a</p> | |
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| | | | | <p>consistent way, an economic and effective approach to the control of medical devices in the interest of public health.</p> <p>Regulatory Authorities that are developing classification schemes or amending existing ones are encouraged to consider the adoption of the system described in this document, as this will help to reduce the diversity of schemes worldwide and facilitate the process of harmonization.</p> | |
| 8. | Page 5 Section 2.3 Scope | Te | <p>An in vitro diagnostic medical device is defined as a device [...]. This includes reagents, control materials, calibrators, specimen receptacles [...]</p> <p>Comment: see proposed sentence.</p> | <p>“Internationally reference materials (e.g WHO) and materials used for externally quality assessment schemes are excluded.”</p> | Accepted with modification |
| 9. | Page 5 Section 2.1 Second paragraph, line 6 | Ed | <p>For consistency please omit (including In Vitro Diagnostic Devices.) since this was omitted from the second paragraph in section 2.2</p> | | Accepted |
| 10. | P.5 2.1 Rationale | Ed | <p>Delete “(including In Vitro diagnostic Devices)” so that the correct title of the final document is referred.</p> | <p>Essential Principles of Safety and Performance for Medical Devices. <i>(including In Vitro diagnostic Devices)</i></p> | Accepted |
| 11. | P5/S2.2/L21 | Tech | <p>There should be a coherence in the terms used throughout the</p> | <p>In line 21 replace</p> | Accepted |

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| | | | document, intended use and intended purpose are defined as synonyms in P7 Section 4.0 – a single term should be used throughout the document. | “intended purpose” by “intended use” | |
| 12. | p. 5, P1 | Ge | This document is specific for IVD medical devices | Insert “in vitro diagnostic (IVD)” in front of medical device. | Accepted |
| 13. | P5/S2.2/L25-29 | Te | 1) This GHTF document is not addressed only to manufacturers, Competent Authorities and Third party assessment bodies may benefit from it as well 2) The classification does not prescribe how to comply with the essential principles – the conformity assessment route does, therefore it is appropriate to make reference to that document. | Substitute L25-29 in section 2.2 by the following: Subsequently, such classification will determine the conformity assessment route as described in GHTF document on Principles of Conformity Assessment for In Vitro Diagnostic Medical Devices. | Accepted |
| 14. | P5/S2.3/L35-36 | Te | Calibrators are generally cited before control materials in ISO texts which refer to them, therefore it is appropriate to maintain the same listing in this document as well | In line 35-36, substitute “control materials, calibrators” by “calibrators, control materials” | Accepted |
| 15. | p.5, section 2.2 | Ge/Ed | Purpose should be specific for IVDs Grammatical correction | Add IVD in front of the term medical device in bullets 2 and 3 Last sentence should be “...or requested to | Accepted |

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| | | | | do so by a Regulatory.” | Text modified wording taken out |
| 16. | P5/S2.3/L36 | Ed | | Add comma after “software” | Accepted |
| 17. | p. 5, 1 st para | | - it would seem more consistent if, after the first appearance of the term “in vitro diagnostic (IVD) medical device” on Page 5 first paragraph of Rationale, that the term be consistently used wherever IVD medical device is mentioned or intended throughout the document. As it is now, some sentences just say “medial device”, some sentences say “in vitro diagnostic medical device”, and some sentences say “IVDs”. It would be helpful to pick one nomenclature and stick with it throughout. | | Accepted |
| 18. | p.6, para 4 | Ge | Today this area is unclear and the current GHTF document does little to help clarify it further. This document can offer a good unified source to put specificity around the subject. | Either the definition of Accessory or a new definition should clarify software used with IVD’s. Basically 2 forms of software: <ul style="list-style-type: none"> • Software whose only purpose is to manage patient data post-analysis and actual treatment. This software should not be considered either an IVD or medical device. The functionality of the software of course does need to be verified as a part of any V&V activity relating to the regulated instrument/system. | Rejected, it encompasses more than IVD |

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| | | | | <ul style="list-style-type: none"> Software whose function could affect either the outcome of results or their reporting through either the instrument or some other GUI (graphic user interface), should be considered to be a part of the IVD instrument / system they are used on and carry the same Risk as the IVD it is intended to be used with. | |
| 19. | Page 6, Section 4.0 Definitions: Device for Self-testing | Te | It is not relevant where the test is performed therefore we propose to cut out: “in a home or similar environment”. | “Device for Self-testing: Any device intended by the manufacturer for use by lay persons.” | Accepted |
| 20. | P6/S4.0/L26 | Te | There should be a coherence in the terms used throughout the document, intended use and intended purpose are defined as synonyms in P7 Section 4.0 – a single term should be used throughout the document. | In line 26 replace “intended purpose” by “intended use” | Accepted |
| 21. | P6/S4.0/L27-28 | Te | There should be a coherence in the terms used throughout the document, intended use and intended purpose are defined as synonyms in P7 Section 4.0 – a single term should be used throughout the document. | In lines 27-28 replace “intended purpose” by “intended use” | Accepted |

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| 22. | p.7, Note 2: | | Biosafety and bioterrorism testing and monitoring devices shall be defined as IVD's when be used with human samples only (in order to decide adequate treatment | Devices for biosafety and bioterrorism testing and monitoring of human samples are considered IVD's | Accepted note 2 in the definition has been removed as environmental samples not covered by FDA |
| 23. | Section 3.0 | Ed | Update references. | SG1/N029:2005 Information Document Concerning the Definition of the Term 'Medical Device'. SG1/N043:2005 Labelling for Medical Devices SG1/N041:2005 Essential Principles of Safety and Performance of Medical Devices SG1/N012:2000 Role of Standards in the Assessment of Medical Devices. | Rejected |
| 24. | Page 7 Section 4.0 Definitions: In vitro Diagnostic Medical Device | Te | According to the definition:[...] intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally [...] Solely or principally are vague expressions and they are not defined. These expressions make the definition indistinct. We propose to cut out "solely or principally." | "In Vitro Diagnostic Medical Device: A device, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body to provide information for diagnostic, monitoring or compatibility purposes. This includes reagents, control materials, calibrators, specimen receptacles, software and related instruments or apparatus or other articles." | Rejected to avoid confusion with borderline products |
| 25. | Page 7 Section 4.0 | Te | According to the definition:[...] This includes reagents, control | | Rejected serves as a safeguard |

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| | Definitions: In vitro Diagnostic Medical Device | | materials, calibrators, specimen receptacles, software and related instruments or apparatus or other articles. We propose either to cut out “other articles” or to define what this means in order to make the definition more distinct. | | for any other product that would meet the definition of an IVD medical Device |
| 26. | Page 7 Paragraph 12 | Te | See comment above for rationale. Please omit the words “...and preservation ..” and “...including transport devices...” from the definition below Specimen receptacle : a device, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment and preservation of specimens derived from the human body including transport devices for the purpose of in vitro diagnostic examination. | Specimen receptacle : a device, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment of specimens derived from the human body for the purpose of in vitro diagnostic examination. | Accepted with modification definition of specimen receptacle changed to eliminate preservation refer to 78 |
| 27. | P7/S4.0/L13 | Te | Calibrators are generally cited before control materials in ISO texts which refer to them, therefore it is appropriate to maintain the same listing in this document as well. | In P7 L13 substitute: “control materials, calibrators,” for “calibrators, control materials. | Accepted |
| 28. | P7/S4.0/L14 | Ed | | Add comma after “software” | Accepted |

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| 29. | P7/S4.0/L28 | Te | It is preferable to use references to published documents rather than to draft documents, therefore the reference to ISO 18113 should be substituted for one to ISO 15197. | In P7 L28 substitute: “ISO 18113-1” For “ISO 15197:2003” | Accepted |
| 30. | P7/S4.0/L30 | Te | Add “decentralized testing” as a synonym for near patient testing. | Change “Near patient (testing) To “Near patient (testing)/Decentralized testing”. | Rejected but modified definition |
| 31. | P7/S4.0/L30 | Te | It is preferable to refer to published definitions where these are available. In the case of Near patient testing a definition has been published in ISO TS 22870 “Point of care testing – requirements for quality and competence” | Substitute lines 30-31 with the following: “Near patient testing: Testing that is performed near or at the site of a patient with the result leading to possible change in the care of the patient (Ref ISO TS 22870:2004) | Withdrawn based on changes to 30. |
| 32. | Section 4.0 | Ed | Improved clarity | Accessory [to an IVD] | Rejected as an accessory is an IVD |
| 33. | Section 4.0 | Ed | Improved clarity | Devices for Self-testing: Any IVD device. | Accepted with modification |
| 34. | Section 4.0 | Ed | Delete definition of In Vitro Diagnostic Instrument since it does not appear in the text (the word “instrument” does. | In some cases the words “IVD medical device may be substituted otherwise leave it undefines an a self-evident term. | Accepted but dropped the word IVD in front of Instrument – applied same to the reagent |

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| 35. | Section 4.0 | | Improve the definition of “self-testing”. | Self-testing: Testing performed by a lay person on a specimen derived from his/her own body. | Rejected |
| 36. | Section 4.0 | Ed | Improved clarity | Specimen receptacle: a device specifically intended by its manufacturer for the primary purpose of containing and preservation of Etc. | Rejected because a vacuum tube collects the sample and does not only preserve it |
| 37. | Page 8 5.0 General Principles 2nd paragraph | Ed | Two periods: Delete one | The risk presented by a particular device depends substantially on its intended purpose. | Accepted |
| 38. | p.8, 2nd bullet | Ed | Self testing and near patient are two different categories | Replace the / between self-testing and near patient with the word “or” | Accepted refer to comment 42 |
| 39. | P8/S5.0/L6 | Te | There should be a coherence in the terms used throughout the document, intended use and intended purpose are defined as synonyms in P7 Section 4.0 – a single term should be used throughout the document. | In line 6 replace “intended purpose” by “intended use” | Accepted |
| 40. | P8/S5.0/L17 | Te | The text following line 17 is not a consequence of what precedes it. Thus the use of the term “therefore” is not appropriate. | Substitute line 17 “Therefore there is a need to classify an IVD medical device based on” | Accepted |

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| | | | | By “The classification of an IVD medical device is based on” | |
| 41. | P8/S5.0/L20 | Te | It is appropriate that the general principle of using the highest classification for a device whenever several classifications are possible should be added in this section. | At the end of the first bullet (L20) after “test is intended).” Add the following: “If the manufacturer specifies multiple intended uses, then the highest relevant risk class will apply.” | Rejected it is not a criteria it is a further factor building on the criteria in general principles |
| 42. | P8/S5.0/L21 | Te | It is the technical expertise of the user which is being referred to, not the kind of test. | At the end of line 21 change the phrase: “(laboratory testing versus self-testing/near patient)” to “(lay user or professional)” | Accepted but changed to lay person |
| 43. | P8/S5.0/L30 | Ed | This is a run on sentence for ease of comprehension a comma is required. | Insert after “reference materials” A comma “,” | Accepted but modified phrase |
| 44. | P8/S5.0/L31 | Ed | This is a run on sentence for ease of comprehension a comma is required. | Insert after “regulatory authority” A comma “,” | Accepted but modified phrase |
| 45. | p.9, 6.2, Note: | | Performance evaluation of IVD instruments and tests E.g.: a blood grouping analyzer and a blood grouping reagent should be evaluated together, but the reagent according to the assessment procedure for the highest risk class, the instrument according to the lowest risk class. | The interdependence of the instrument and the test methodology indicates the simultaneous performance evaluation of both, but each according to the assessment procedure required for the adequate risk class | Rejected comment does not add clarity |
| 46. | p.9, Sec. 6.2, 3 rd para | Te | Add definition for assigned value. Is simply stating + or – control an assigned value? | | Accepted Yes added qualitative and quantitative |

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| 47. | p.9, section 6.2, last para, the Note Line 1 | Te | For consistency please replace the word “equipment” with “instrument” | | Accepted |
| 48. | Page 9 6.2 Factors... 3rd paragraph | Te | The IVDSG should discuss further “except for controls with no assigned values which are Class B.” because this statement is not “factors influencing IVD medical device classification. “ It is the classification. We also have a question that all controls with no assigned values should be classified as Class B. (e.g.) Positive Control for HIV test. | Calibrator and control materials intended to be used with an IVD reagent should be treated in the same class as the IVD reagent except for controls with no assigned values which are Class B [Delete the latter half, or move to appropriate part of Section 8.] | Accepted with modification |
| 49. | Page 9 6.2 Factors... 4th Paragraph 1st bullet point | Ed | Extra space: Delete one space between “controls” and “or” | Where it controls or influences the | Accepted |
| 50. | p.9 3 rd bullet | Ge | Purpose should be specific for IVDs | Add IVD in front of the term medical device. | Accepted |
| 51. | Page 9 6.2 Factors... Note | Te | Delete this note to avoid the repetition: The same note appears in 8.0 Rule 5 as Note 2. | Note: Performance of software or equipment that is specifically required to perform a particular test will be assessed at | Rejected there is a lot of confusion around this matter and |

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| | | | | the same time as the test kit. The interdependence of the instrument and test methodology prevents the instrument from being assessed separately, even though the instrument itself is still classified as Class A. | reemphasis is therefore appropriate |
| 52. | p. 9, 6 th bullet | Ge | Not aligned with medical device classification document | Remove this bullet | Accepted |
| 53. | Page 9 or 10 6.3 Proposed General..... Last sentence above Fig.2 | Ed | No space: Add one space between “for” and ”in” | The concept is expanded in the GHTF guidance document entitled Premarket Conformity Assessment for in Vitro Diagnostic Medical Devices. | Accepted |
| 54. | p.9, 7 th bullet | Ge | Not aligned with medical device classification document. | Decisions on final classifications which deviate from the initial rules-based Classification should be weighed against the disadvantages of disharmonised International classification. | Accepted |
| 55. | Section 6.2 | Te | Add a penultimate paragraph to improve understanding. | The purpose of risk classification is to ensure that the regulatory controls applied to a medical device are proportionate to risk. At this time, conformity assessment requirements and other regulatory controls assigned to each class of device by different Regulatory Authorities have yet to be | First part is already covered Rejected Second part is not |

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| | | | | harmonized and may vary. | needed |
| 56. | Section 6.3 Fig 1. | Ed | Clarify the use of the word “individual”. | Use the phrase: “ the person providing the specimen for in-vitro examination”. | Rejected |
| 57. | P9/S6.1/L3 | Te | It is understood that this bullet is meant to convey the principle of a conformity assessment system whose requirements increase in a step-wise fashion. The terms “graduated system” does not convey this meaning. Furthermore the conformity assessment system does not act as a mechanism of control – that is the role of the legislation and the competent authorities. | Replace the end of the sentence: “efficient and graduated system of conformity assessment controls.” By “efficient and defined conformity assessment system.” | Accepted |
| 58. | P9/S6.1/L4-5 | Te | It should be made clear that the classification applies to the medical device. | Replace the bullet point “The determination of class should be based on a set of rules derived from those features of devices that create risk” by “The determination of classification for a device should be based on a set of rules derived from those features that create risk” | Accepted |
| 59. | P9/S6.1/L6-8 | Te | The intent of the rules should be unambiguous. – Regulatory Authorities may always evaluate the classification of a device, there is no need to introduce the concept of appropriate confirmation by Regulatory Authorities. | Replace the bullet point: “The set of rules should be sufficiently clear that manufacturers may readily identify the class of their medical devices, subject, when appropriate, to confirmation by the Regulatory Authority. | Accepted with addition of referring back to rules |

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| | | | | By The set of rules should allow manufacturers to readily identify the class of their medical devices. | |
| 60. | P9/S6.2/L19 | Te | The title of this section is misleading – Are not the recommendations made in section 6.1 also factors determining the classification of devices? | Replace the title of section 6.2 “Factors Influencing IVD Device Classification” By “Further Recommendations” | Accepted change title of 6.0 and introduced 7.0 |
| 61. | P9/S6.2/L20-21 | Te | The principle of having the highest applicable risk class determine the classification of a device should be enshrined as one of the general principles in the classification of devices, not as a further consideration (see also comment 14 on P8/S5.0/L20) | Delete the phrase “Where more than one of the classification rules applies to the IVD medical device, it should be allocated to the highest class indicated”. | Rejected see 41 but added following criteria to the general principles section |
| 62. | P9/S6.2/L27 | Te | For the sake of clarity the precise terms for the different control materials should be used when referring to them. | Replace the text in line 27 “Calibrators and control materials intended...” With “Calibrators and trueness control materials (with assigned values) intended...” | Accepted with modification with quantitative or qualitative assigned values added to the word controls |
| 63. | P9/S6.2/L28 | Te | For the sake of clarity the precise terms for the different control materials should be used when referring to them | Add in line 28 after “no assigned values” The phrase: “(e.g. precision controls)” | Accepted because the assigned values statement has been added to the first phrase |

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| | | | | | and the second phrase is dropped |
| 64. | P9/S6.2/L38 | Te | <p>The case of decentralized testing needs to be explained.</p> <p>Decentralized testing (near-patient testing) is carried out by medical professionals near or at the site of the patient with the result leading to a possible change in the care of the patient (ISO TS 22870) These assays can be performed on any parameter analyte which would range from the highest to the lowest risk class. Therefore devices intended for point of care should be classified on the basis of their intended analytical use ie: in the same fashion as laboratory tests</p> | <p>Add a bullet point which reads</p> <p>“As Near patient testing assays can be performed for devices which span all risk categories, these assays shall be classified according to the rules laid out in section 8.”</p> <p>Or (alternative)</p> <p>“Near patient testing assays shall be classified according to the rules laid out in section 8.”</p> | Remains a discussion point |
| 65. | P9/S6.2/L39-42 | Te | <p>This note presents two different concepts, that of performance software or equipment, and the interdependence of instruments and reagents. For the sake of clarity these two concepts should be separated into two separate notes.</p> | <p>On line 39 Add “1” after Note</p> <p>On line 40 Add</p> <p>“<carriage return> Note 2”</p> <p>after “test kit.”</p> | Accepted |
| 66. | p.10, 6.3, figure 1 | | <p>To prevent confusion of market actors, competent authorities and notified bodies who worked for years with the 98/79/EC directive we would propose to change the direction in the table: Class A for the highest risk (corresponding to List “A”), Class “B” for the next</p> | | Rejected |

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| | | | risk class (List “B”), Class C for selftesting devices (perhaps also for POCT devices), Class D for all others (“other IVD’s”). | | |
| 67. | p. 10, explanations to Figure 2 | | In-house testing shall be used for establishing intended performance data, but not for clinical performance evaluation We would add: batch verification due to CTS for high-risk devices. | Performance evaluation studies in laboratories for medical analyses or in other appropriate environments outside the manufacturer’s premises (98/79/EC, Art.1, (e) Batch verification due to common technical specifications for high risk devices (Class A and B). | Rejected |
| 68. | p.10, Last sentence | Ed | Grammar | Add a space between “for” and “in” | Accepted |
| 69. | P10/S6.3/L10 | Te | There should be a coherence in the terms used throughout the document, intended use and intended purpose are defined as synonyms in P7 Section 4.0 – a single term should be used throughout the document. | In line 10 replace “intended purpose” by “intended use” | Accepted |
| 70. | P10/S6.3/Figure 1 | Te | All IVD instruments will fall under the same category as the HPLC – which itself is an instrument. There should also be a distinction made between IVD instruments and instruments which are not intended for IVD purposes. | Replace within the table of figure 1 “HPLC,” With “IVD” | Accepted modified |
| 71. | P10/S6.3/L18 | Te | The characteristics enumerated are those of the conformity assessment | In line 18 replace “These regulatory controls” | Accepted modified taken |

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| | | | system, not those of regulatory control. | with “The conformity assessment system” | out the words regulatory controls |
| 72. | P10/S6.3/L21 | Te | Nowhere is the concept of manufacturer’s claims defined – it is in the interest of clarity to use a term which has already been defined. | In line 21 replace “claims” with “specified intended use” | Accepted |
| 73. | P10/S6.3/L23 | Te | Qualifying resources as “independent” is seen as potentially problematic. How is an independent resource defined? | In line 23 replace “independent” with “third party” | Rejected third party excludes certain groups in certain areas of the world, independent is more general |
| 74. | P11/S6.3/L1-2 | Te | Use the correct title of the document | In lines 1-2 replace “Premarket Conformity Assessment ...” With “Principles of Conformity Assessment...” | Accepted |
| 75. | P11/S7.0/L15-18 | Te | The first phrase of this bullet point is needlessly complex, it needs to be broken down into two sentences for the sake of simplicity and to refer to the correct section of the text rather than to the text which follows. Furthermore it should be made clear that it is the intended use of the device, not its features, which places it into a higher or lower risk class. | Replace in lines 15-18 the text “Take into considerations all the rules that follow in order to establish the proper classification for the device, noting that where an IVD medical device has features which are included in the manufacturer’s stated intended use that place it into more than one class, it will be classified in the highest class” With “Take into consideration all the rules as listed in section 8 in order to establish the | Accepted |

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| | | | | proper classification for the device. Where an IVD medical device has multiple intended uses as specified by the manufacturer, which places the device into more than one class, it will be classified in the higher class. | |
| 76. | P11/S7.0/L18 | Te | The determination of whether a device is subject or not to national rules should be a separate point. | After "... higher class", add a carriage return and add : "3. Determine that the device is not subject to special national rules that apply within a particular jurisdiction." | Accepted |
| 77. | p.11, Last sentences | Ed | Grammar | "...rules indicated below, and, as a consequence, a less vigorous conformity assessment procedure is carried out, this may be unacceptable to other jurisdictions." | Accepted |
| 78. | Section 8.0 Rule 5 Bullet 3 on page 14 | Te | FDA is concerned about receptacles containing transport media that is vital to the result of the test. E.g. Chlamydia transport media for culturing the organism using cell cultures to stain for microscopy. i.e. the recovery of the organism is dependent of the performance of the transport media. Please omit "eg., those containing transport media or preservatives." As an extension to this comment please change the Specimen receptacle definition. See comment below. | Specimen receptacles as defined in section 4.0 | Accepted with modification definition of specimen receptacle changed to eliminate preservation |

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| 79. | p.12, 8.0, Rule 1 | | <p>Change Class D to Class A</p> <p>Examples: pyrogenicity tests could be accepted (after specific discussion), but tests for bioterrorism agents in human samples should be Class D (now Class A), since these tests will be carried out in special labs only, not as routine test.</p> | Examples: Tests to detect infection by HIV, HCV, BBV, HTLV. This Rule applies... | Rejected |
| 80. | Page 12 Section 8.0 Classification Rules Rule 1, first bullet point | Te | <p>We propose to add tissue engineered products to this rule. The same risks/problems apply to these products as for the other products mentioned.</p> | “Devices intended to be used to detect the presence of, or exposure to, transmissible agents in blood, blood components, blood derivatives, cells, tissues or organs in order to assess their suitability for transfusion or transplantation, or for manufacturing of human engineered products, or” | Rejected a test would not be specifically created for these purposes, the human tissue engineering regulation should address that only approved tests should be used in the manufacturing of such products. |
| 81. | p.12, 8.0, Rule 2 | | <p>Change Class C to Class B</p> <p>We would add all devices listed in list “B” of the 98/79/EC directive, perhaps extended, e.g. with infectious diseases of high epidemiological importance, as well as other tumor markers than PSA.</p> | | Rejected |

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| 82. | p.12, Rule 3 | | We would accept a list of all reagents extending the former list “B” of Annex II (Class B), but we believe it will be too complicated for the manufacturer to classify due to specific risk criteria (see rationale), since these have different epidemiological importance in each region and could be affected by subjective decisions. | | Rejected |
| 83. | Page 12 8.0 Classification Rules Rule 1 | Ed | Mixture of singular and plural for the word “agent” transmissible agents in 1st bullet point a transmissible agent in 2nd bullet point. | Choose an appropriate form. | Accepted |
| 84. | Page 12 8.0 Classification Rules Rule 1 | Te | Delete the 3rd bullet point Delete “Tests for bioterrorism agents.” from Examples. During the discussion among SG1 members (larger group) in Gaithersburg, it was decided to delete “ Devices for biosafety and bioterrorism testing and monitoring are considered to be in vitro diagnostic medical devices. ” from 2.3 Scope and 4.0 Definitions of In Vitro Diagnostic Medical | Delete the 3rd bullet point Devices intended to be used to detect the presence of, or exposure, to an agent dispersed from a common source outside its normal conditions and which causes a serious disease and which may have a high potential for propagation. Delete “Tests for bioterrorism agents.” from Examples. | Accepted |

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| | | | Devices. The 3 rd bullet point and this example should be deleted accordingly. | | |
| 85. | P12/S8.0/L12-14 | Te | The third bullet point of Rule 1 refers to a situation which does not fit the definition of an IVD as stated in section 4.0 (see note 2 of the definition of an IVD – these devices are IVDs only in some jurisdictions) The classification rules should refer only to those devices which are defined as IVDs. – it should be up to the national classification rules to decide how to classify devices which come under their national definition of IVD. | Delete lines 12-14 (third bullet point of rule 1) | Accepted |
| 86. | P12/S8.0/L23-24 | Tech | <p>Pyrogenicity test (also called pyrogentest) is a common test to be made on all solutions intended for injection to a patient. (Including everything from physiological saline solution to blood units or any injectable drug solution) It is a normal quality control test, like sterility, made in order to ensure the patient safety after the injection of a solution.</p> <p>This in vitro (known as the “limulus test”) test has never been conceived or intended for use on samples derived from the human body in order to make a diagnosis of a physiological or pathological</p> | Delete the phrase from the examples: “Pyrogenicity tests marketed for detection of bacterial contamination of blood components.” | Accepted modified added Endotoxin activity assay to exclude the other tests |

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| | | | <p>state of the patient (see the definition of an IVD MD).</p> <p>Therefore it is not an IVD and it cannot be classified among IVDs, as it has never been intended for diagnostic purposes.</p> | | |
| 87. | P12/S8.0/L24-25 | Te | Examples should be from devices which are accepted as IVDs in all legislations (see also note on P12/S8.0/L14-16) | Delete the phrase from the examples: “Tests for bioterrorism agents” | Accepted |
| 88. | P12/S8.0/L31 | Te | A distinction should be made between the tests which determine the blood group (on samples where the blood group is not known, and therefore where an erroneous result could put a patient in an immediate life threatening situation) vs those which characterize the blood group into its subtypes A1-A5 (in these cases the blood group is already known, and there an erroneous result would not have as a consequence an imminent life threatening situation) | In line 31 after “anti-Kell” Add “determination” | Accepted |
| 89. | P12/S8.0/L42 | Te | It is the agent which is serious, not the sex. The phrase should be reworded to avoid confusion. | In line 42 replace “serious sexually transmitted agent” with “sexually transmitted serious agent” | Reject it is gramatically correct as it is |
| 90. | P13/S8.0/L22 | Te | Prothrombin time testing is an IVD test usually performed during a normal patient check-up (like eg glycaemia or cholesterolaemia) to assess the time of blood | Delete from the examples “Prothrombin time testing” | Rejected |

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| | | <p>coagulation expressed in seconds (normal range...) or other ways such as INR (Index Normalized Ratio normal range ...)</p> <p>It is one of the tests most frequently carried out in a medical laboratory. In a very low percentage of the population that is submitted to oral anticoagulant therapy (e.g. patients with implanted cardiac valves or with atrial fibrillation or deep venous thrombosis) this test has a more important role, by monitoring the efficacy of the anticoagulant drug on blood coagulability.</p> <p>The physician follows the trend of the INR values, adjusting the drug dosage which may vary from patient to patient.</p> <p>A range of values of INR is recommended for any of those patients (usually from 2 -3) in order to avoid too low values (<1) which may lead to a risk of coagulation and formation of thrombi, or too high values (>5-6) which may lead to a risk of haemorrhage.</p> <p>Both kinds of risk can be easily overcome by medical intervention or by awareness of the patient history.</p> <p>In case of a sudden recovery in a</p> | | |
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| | | | <p>hospital of a patient incapable of reporting his history, many different measures can be taken inside the hospital to avoid the risk of a life threatening situation, in case of a wrong result of the blood test for INR. What is important for any patient under anticoagulant therapy is the examination of a trend, rather than a single value especially if it is unexpected.</p> <p>As a conclusion the prothrombin time testing cannot be included in the same classification of IVDs whose erroneous results may lead to immediate life threatening situation, even in the small percentage of patients submitted to anticoagulant therapy.</p> | | |
| 91. | P13/S8.0/L22 | Te | <p>Digoxin tests is performed on blood of patients suffering from tachycardia or cardiac arrhythmia treated with a drug called “lanoxin” containing digoxin.</p> <p>The level of digoxin in the blood should stay in the range 0.8 to 1.30. Higher values of digoxin indicate the need of decreasing the drug dosage.</p> <p>In the case of an excess level of digoxin in the blood (the exact level is subject to interpatient variability) nausea can appear as a first symptom. No serious collateral effect will occur</p> | Delete the term “Digoxin” from the examples. | Accepted |

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| | | | affecting the health of the patient. The level of this substance in the blood will not result in an immediate life-threatening situation for the patient. | | |
| 92. | P13/S8.0/L32 | Te | Decentralized testing (near patient testing) is performed by a professional, and the risk should be determined by the analyte being measured as for other laboratory tests (ie decentralized testing for HIV should be in class D) | Delete the following in line 32 “near-patient testing and” | Remains a point of discussion |
| 93. | P13/S8.0/L37 | Te | Self testing is presumed to be carried out by a lay user with no technical expertise | Delete the following in line 37 “little, or” | Accepted |
| 94. | P13/S8.0/L41 | Te | Rule 4 should apply only to self testing devices | Delete the following in line 41 “near-patient devices for blood gases” | Remains a point of discussion |
| 95. | p.13, Rule 4 | | Change Class B to Class C We would define – in general – all self-testing devices as Class C, except these are intended for detecting diseases or other health parameters as defined in Class B or Class A. For the latter we should emphasize that most countries decided to regulate the use of selftesting devices belonging to Class A and B (former Annex II List “A” and “B”) when prohibiting sales of IVD’s for notifiable diseases for selftesting via drugstores and pharmacies, referring to epidemiological legislation. | IVD medical devices intended for self-testing and for near-patient testing under home conditions are classified generally as Class C, except those devices which are – by their nature – Class A or B devices. | Rejected |

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| 96. | p.13, Rule 5 | | Change Class A to Class D | | Rejected |
| 97. | Page 13 8.0 Classification Rules Rule 4 | Ed | Change the term “rapid” to “self” or “near-patient” in “Examples for class C” because both of them are listed in 4.0 Definition but “rapid” is not. | Examples for class C: Blood glucose monitoring, rapid self test for <i>Streptococcus B</i> , self test for Drugs of Abuse, occult blood test, near-patient devices for blood gases. | Accepted with modification |
| 98. | Rule 5, p. 14 | | I think certain specimen receptacles could be classed at a higher level only if generally recognized as being commonly used as an accessory to a higher risk classification device. I don't think receptacles that contain preservatives, (i.e. antimicrobials) should automatically be considered as being higher risk. | | Accepted definition of specimen receptacle changed refer to 78 and 26. |
| 99. | Page 14 Section 8.0 Classification Rules Rule 5: The following IVD medical devices are classified as class A Second bullet point | Te | According to rule 5: Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures are classified as class A. According to the factors that are influencing IVD Device Classification (Page 9 Section 6.2) - accessories should be classified separately. Following this, instruments that are defined as an accessory should be | | Rejected |

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| | | | classified in their own right. We believe that there might be a contradiction here. | | |
| 100. | Page 14 Paragraph 4 Line 1 | Te | Please omit “identification kits for cultured microorganisms” and the word “instrument” from the example and add the word “plain” to the “urine cup” | Examples: Selective/differential microbiological media, wash solutions, and plain urine cup. | Accepted plain and rejected other two |
| 101. | Page 14 Section 8.0 Classification Rules Rule 5: The following IVD medical devices are classified as class A Third bullet point. | Te | Comments as to whether certain specimen receptacles should be in a higher class. Comment: see proposed sentence. | Specimen receptacles for the transportation of clinical specimen intended for certain microorganisms which are sensitive for transportation (e.g. Neisseria gonorrhoeae, certain anaerobic bacterial strains etc) are classified as Class B/C. | Accepted definition of specimen receptacle changed |
| 102. | p.14, Rule 6 | | All devices, not listed in Class A and B and not intended for self-testing should be Class D | | Rejected |
| 103. | p. 149, Rule 6, middle of rationale | Ed | Grammar | “If it is the sole determinant, however other information is available such as presenting signs and symptoms or other clinical information which may guide a physician, | Accepted |

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| | | | | this risk classification may be justified.” | |
| 104. | P14/S8.0/L21 | Te | Note 2 refers to two different situations. For the sake of clarity break it down into two separate notes. | In line 21 after “test kit.” Add “<carriage return> Note 3:” | Accepted |
| 105. | P14/S8.0/L36 | Te | All hormones would be covered by this rule – reflect this in the example | Before “hormones” delete the word: “certain” | Accepted |
| 106. | p.14, Rule 5, Note 2 | | See Comment No. 2 | | Rejected |
| 107. | | | Often, with genetic testing, it is the application that changes the risk class. Is this dealt with adequately in the rules? " | | Yes, the rules were constructed based on the intended use and the risk associated with the individual and the public |