Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

FINAL DOCUMENT

Title: Comparison between the Common Submission Dossier Template (CSDT) format for In Vitro Diagnostic Medical Devices and the GHTF Summary Technical Documentation (STED) formats for In Vitro Diagnostic Medical Devices

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Preface

The document herein was produced by the Asian Harmonization Working Party. The document is intended to provide a basis and justification for the generation of a document to describe the content of a common submission file for In-vitro diagnostic medical devices, and has been subject to consultation throughout its development.

Introduction

The primary way in which the AHWP achieves its goals is through the production of a series of guidance documents that together describe an internationally harmonised regulatory model for medical devices, including In Vitro Diagnostic (IVD) medical devices. The purpose of such guidance is to harmonize the documentation and procedures that are used to assess whether a medical device, including an IVD medical device conforms to the regulations that apply in each jurisdiction. Eliminating differences between jurisdictions decreases the cost of gaining regulatory compliance and allows patients earlier access to new technologies and treatments.

The GHTF and AHWP have both identified as a priority the need to harmonize the documentation of evidence of conformity to the Essential Principles of safety and performance (hereafter referred to as Essential Principles). Each has prepared guidance on the content of summary technical documentation to be assembled and submitted to a Regulatory Authority or Conformity Assessment Body. The summary technical documentation should be prepared by the manufacturer in a format which provides different Regulatory Authorities or Conformity Assessment Bodies with the same body of documentary evidence that its IVD medical device conforms to the Essential Principles. The use of an agreed format should reduce costs for the manufacturer and reviewer, remove barriers to trade and facilitate timely international access to IVD medical devices.

The GHTF has prepared separate guidance documents on the STED for medical devices[1] and the STED for IVD medical devices[2].

The ASEAN has drafted the Common Submission Dossier Template (ASEAN CSDT), based on the GHTF STED for medical devices. Based on this document, ASEAN countries have developed a specific template for IVD medical devices[3]. A requirement for the CSDT for medical devices and IVD medical devices has been included into the draft of the ASEAN Medical Device Directive and will become the format of premarket submissions for ASEAN once the directive is implemented.

Based on the ASEAN CSDT and GHTF STED, AHWP will develop a guidance document for a template for a common submission file for IVD medical devices.

The AHWP WG2 has also considered the International Medical Device Regulators Forum (IMDRF)'s In-Vitro Diagnostics Market Authorization Table of Contents. This document is still in draft and may be further considered at a later time.

Recently, AHWP has done a comprehensive comparison between the ASEAN CSDT for IVD medical devices and the GHTF STED for IVD medical devices. The

1 GHTF/SG1/N011:2008: *Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED)*
2 GHTF/SG1/N063:2011: *Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices*
3 MDA/GD/IVD-4: *Common Submission Dossier Template (CSDT) of IVD Medical Device, July 2013, First Edition*

result of the comparison is given in the document. It is intended that the comparison will inform the development of an AHWP document on the common submission file for IVD medical devices.

Where other guidance documents within the series are referenced within this text, their titles are italicised for clarity.

Work Group 1a of the Asian Harmonisation Working Party (AHWP) has prepared this information document. Comments or questions about it should be directed to the Chair of AHWP Work Group 1a whose contact details may be found on the AHWP website[4].

Purpose

The availability of summary technical documentation in an agreed format should help eliminate differences in documentation requirements between jurisdictions, thus decreasing the cost of establishing and documenting regulatory compliance and allowing patients earlier access to new technologies and treatments.

This document is intended to provide information on the differences between the recommended content of the ASEAN CSDT for IVD medical devices and the GHTF STED for IVD medical devices to support building AHWP guidance for common submission file for IVD medical devices.

Comparison between ASEAN CSDT and GHTF STED

The document contains the comparison table between the two documents. The core content of each document is the required content of the technical documentation to be submitted to a regulatory authority. In this respect, the ASEAN CSDT for IVD medical devices contains detail which may enhance the GHTF STED for IVD medical devices; the combination of the two documents form the basis of the AHWP recommendation for a common submission file for IVD medical devices.

The CSDT incorporates the requirements for labeling and instructions for use, as well as for clinical evidence. The GHTF includes these requirements as headings only, with the detailed requirements included in separate guidance documents.

[4] www.ahwp.info

Table 1 – Key sections comparison between ASEAN IVD CSDT and GHTF IVD STED

ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011
1.0 Purpose	2.2 Purpose
2.0 Scope	2.3 Scope
3.0 Terms and Definitions	4.0 Definitions (only for Recognised Standard and Technical Documentation)
4.0 Preparation of a product Registration submission based on the ASEAN CSDT	5.0 Preparation and Use of the STED
5.0 Executive Summary	6.0 Device Description including Variants (Configuration) and Assessories
6.1 Relevant essential principles and method used to demonstrate conformity	7.0 Essential Principles Checklist
6.2 Device Description	8.0.Risk Analysis and Control Summary
6.3 Product verification and validation documents	9.2 Manufacturing Process 9.3 Manufacturing Sites
6.4 Device Labelling	10.0 Product Verification and Validation
6.5 Risk Analysis	11.0 Labelling
6.6 Manufacturer Information	12.0 Format of the STED
	13.0 Declaration of Conformity

Table 2 – Contents comparison between ASEAN IVD CSDT and GHTF IVD STED

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
Purpose	1 Purpose This document aims to provide guidance on the preparation of a product registration application for (IVD) medical devices using the ASEAN (CSDT). In particular, this document serves to clarify the information to be submitted in each section of the CSDT and the format that this information is to be submitted in.	2.2 Purpose This document is intended to provide guidance on the content of the STED for IVD medical devices to be assembled and submitted, where applicable, to a RA or CAB for premarket review, and for use post-market to assess continuing conformity to the Essential Principles.	
Scope	2 Scope This document applies to products that fall within the definition of an IVD medical device, as defined in MDA/GD-1: Definition of Medical Device, including those used for the in vitro examination of specimens derived from the human body.	2.3 Scope This document applies to all products that fall within the definition of an IVD medical device that appears within the GHTF document Principles of In Vitro Diagnostic Medical Devices Classification3.	
Terms and Definitions	3 Terms and definitions ● Calibrator ● Control material ● Instrument ● In vitro Diagnostic (IVD) medical device ● Lay person ● Manufacturer ● Near patient testing (POC) ● Performance evaluation	● Calibrator: None ● Control material: None ● Instrument: GHTF/SG1/N045:2008 Principles of IVD Medical Devices Classification - - 4.0 Definitions ● In Vitro Diagnostic (IVD) Medical Device: GHTF/SG1/N071:2012 Definition of the Terms Medical Device and In Vitro Diagnostic (IVD) Medical Device - 5.2 In Vitro	IVD STED reference other GHTF documents, rather than incorporating the details into the text (as the IVD CSDT has).

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	• Reagent • Registrant • Self- Testing • Specimen Receptacle	Diagnostic (IVD) Medical Device • Lay person: GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices - 4.0 Definitions • Manufacturer: GHTF/SG1/N055:2009 Definitions of the Terms Manufacturer, Authorised Representative, Distributor and Importer -5.1 Manufacturer • Near patient testing: GHTF/SG1/N045:2008 Principles of IVD Medical Devices Classification - 4.0 Definitions • Performance evaluation: GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices - 4.0 Definitions • Reagent: GHTF/SG1/N045:2008 Principles of IVD Medical Devices Classification - 4.0 Definitions • Registrant : None • Self- Testing: GHTF/SG1/N045:2008 Principles of IVD Medical Devices Classification - 4.0 Definitions • Specimen Receptacle: GHTF/SG1/N045:2008 Principles of IVD Medical Devices Classification - 4.0 Definitions	
Preparation of a product Registration submission	4.1 The registrant shall take note of the following pointers when preparing a CSDT dossier for submission to Medical Device	5.1 Preparation Manufacturers of all Classes of IVD medical	No explanation of the

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	Authority (MDA): a) the prepared CSDT dossier must contain all the section s, i.e. sections 5.0 to 6.6.1. Where there are sections not applicable to the medical device, the reason for the non-applicability should be provided under the section heading b) the CSDT dossier must be prepared in English; c) copies of labelling, certificates and reports that are referenced within the CSDT submission shall be submitted as annexes to the CSDT- d) all reports submitted as part of the CSDT shall be signed-off by the manufacturer; e) where supporting documents such as reports or certificates are provided, every documents must be submitted in full .All copies of labelling , certificated reports and other documents must be submitted f) all copies of labeling, certificates, reports and other documents submitted must be legible g) all certificates submitted must be legible;	devices are expected to demonstrate conformity of the IVD medical device to the Essential Principles of Safety and Performance of Medical Devices5 through the preparation and holding of technical documentation that shows how each IVD medical device was developed, designed and manufactured together with the descriptions and explanations necessary to understand the manufacturer's determination with respect to such conformity. This technical documentation is revised to reflect the current status of the IVD medical device through normal application of the manufacturer's QMS. For the purpose of conformity assessment, the manufacturer assembles the STED from existing technical documentation to provide evidence to the RA/CAB that the subject IVD medical device is in conformity with the Essential Principles. The STED reflects the status of the IVD medical device at a particular moment in time (e.g. at the moment of premarket submission or when requested by a RA for post-market purposes) and is prepared in order to meet regulatory requirements. The flow of information from the technical documentation to the STED is illustrated in Figures 1 and 2. It can be seen from these figures that the content of the STED is the same for both pre and post market use but the circumstances for the use of the STED are	relationship between the IVD CSDT and the manufacturer's technical information. No explanation in the IVD CSDT that it reflects the status of a device at a particular moment of time (unlike the technical documentation).

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	must be within its validity period is indicated 4.2 The level of detail of information to be provided under each CSDT section will depend on the IVD medical device class and the evaluation route, i.e. abridged or full evaluation. Registrants are advised to refer to the Guidance on Product Registration for details on the data requirements for each IVD medical device class and evaluation route.	different. Where the STED is submitted to a RA/CAB, it should be in a language acceptable to the reviewing organisation. The depth and detail of the information contained in the STED will primarily depend on the classification of the subject IVD medical device. Further considerations when developing the individual sections of the STED include, for instance: a) a high degree of complexity in the subject IVD medical device. b) the IVD medical device incorporates novel technology; For the purpose of STED, examples of novel technology include: 1) there has been no such IVD medical device available on any market for the relevant analyte (measurand); 2) the procedure involves analytical technology not used in connection with a given analyte (measurand) or other parameter on the market. c) the IVD medical device is an already marketed IVD medical device type that is now	IVD STED provides examples of what is 'novel'.

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
		being offered for an intended use different from the original one; d) the IVD medical device type has been associated with a significant number of adverse events known to the manufacturer, including use errors6; e) the IVD medical device incorporates novel or hazardous materials of concern; f) the IVD medical device raises specific public health concerns (e.g. virulent influenza pandemic). The STED should contain summary information on selected topics, and may contain detailed information on certain specific topics (as outlined in Part 2 of this guideline) and an Essential Principles checklist (EP checklist). The information provided may include, for example, abstracts, high level summaries, or existing controlled documents, as appropriate, sufficient to communicate key relevant information and allow a reviewer to understand the subject and assess the validity of that information. The EP checklist is created as part of the manufacturer's technical documentation and is controlled by the manufacturer's QMS. It provides a tabular overview of the Essential Principles and identifies those that are applicable to the IVD medical device, the	Information on EP Checklist first appears here. Section on EP Checklist is later in the IVD STED.

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
		chosen method of demonstrating that the device conforms to each relevant Essential Principle and the reference of the controlled document that is relevant to a specific Essential Principle. While many controlled documents are referenced in the EP checklist, only some may be contained within the STED. The cited references to the controlled documents also allow easy identification of additional relevant documents and data.	
		5.2 The Use of the STED in the Premarket Phase In the premarket phase, the STED will be prepared and submitted to the RA/CAB for Class C and D IVD medical devices. For Class A and B IVD medical devices, the STED will be prepared and submitted only at the request of a RA/CAB7 (see Figure 1). In this case, the manufacturer should be able to assemble and submit it in the timeframe indicated by the RA/CAB. The content of any submitted STED should be traceable by the manufacturer for future reference.	No explanation of the pre- market purposes of the IVD CSDT.
		5.3 The Use of the STED in the Post-market Phase In the post-market phase, the RA/CAB may	No explanation of the pre- market purposes of the IVD CSDT.

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
		request submission of a STED to investigate the continued conformity for any Class of IVD medical device (see Figure 2). The STED would not typically be used to aid the post-market investigation of adverse events, or the reporting of data from post-market registries or studies, where different types of information are likely to be called for. If requested, the manufacturer should be able to prepare and submit the STED in the timeframe indicated by the RA/CAB. The content of any submitted STED should be traceable by the manufacturer for future reference.	
		5.4 The Use of the STED to Notify Changes to the RA/CAB Where prior approval of a proposed change to an IVD medical device is required, the STED may be used in support of this process. Guidance on this case will be provided in the future.	No explanation of the purpose of resubmitting the CSDT.
Executive Summary	5 Executive summary An executive summary shall be provided with the CSDT, which shall include the following information- a) an overview, e.g., introductory descriptive		No requirement for an Executive Summary in IVD STED.

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	information on the medical device, the intended uses and indications for use of the medical device, any novel features and a synopsis of the content of the CSDT; b) commercial marketing history; c) intended uses and indications in labeling; d) list of regulatory approval or marketing clearance obtained; e) status of any pending request for market clearance from USFDA, EU, TGA, MHLW (Japan), Canada; f) important safety / performance related information. **Guidance**: (a) If the medical device contains any novel features, e.g. nanotechnology, a description of the novel feature is to be provided. (b) For commercial marketing history, the list of countries where the medical device is marketed and the year of introduction into each country is to be provided. i) Copies of certificates or approval letters from each reference agency for the IVD medical device are to be provided as an annex to the CSDT submission. For CE marked devices, the declaration of conformity by the manufacturer / AR must		

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	be submitted, in addition to the EC certificate issued by the notified bodies. ii) declaration on labeling, packaging and instructions for use (IFU): • if the labeling, packaging and IFU of the IVD medical device for sale in Malaysia is identical to that approved by the reference agency, a declaration that the labeling, packaging and IFU of the IVD medical device for sale in Malaysia is identical to that approved by each reference agency is to be provided. • if the labeling, packaging and IFU of the IVD medical device for sale in Malaysia is not identical to that approved by the reference agency, the differences between Malaysia's labeling, packaging and IFU and each reference agency's approved labeling, packaging and IFU is to be described. The reason for the differences must also be provided. (c) For important safety / performance related information, the following information is to be provided: i) summary of reportable adverse events and field safety corrective actions (FSCA) for the IVD medical device for the past 5 years. This is to be provided in a tabular format as given below. If there have not been adverse events		

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	or FSCAs to date, an attestation that this is the case is required.		
Relevant Essential Principles	6.1 Relevant essential principles and method used to demonstrate conformity The CSDT should identify the Essential Principles of Safety and Performance of Medical Devices that are applicable to the device. The CSDT should identify the general method used to demonstrate conformity to each applicable Essential Principle. The methods that may be used include compliance with recognized or other standards, state of the art or internal industry methods, comparisons to other similar marketed devices, etc. The CSDT should identify the specific documents related to the method used to demonstrate conformity to the Essential Principles. 6.1.1 Essential principles and evidence of conformity The evidence of conformity can be provided in tabular form with supporting documentation available for review as required. A sample of the essential principles conformity checklist is included in Appendix A. For example, a completed Essential	7.0 Essential Principles (EP) Checklist The STED should include an EP checklist that identifies: a) the Essential Principles; b) for each Essential Principle whether it applies to the IVD medical device and if not, why not; c) the method used to demonstrate conformity with each Essential Principle that applies; and d) the reference to the actual technical documentation that offers evidence of conformity with each method used. The method used to demonstrate conformity may include one or more of the following: a) conformity with recognized or other standards[5]; b) conformity with a commonly accepted industry test method; c) conformity with appropriate in-house test methods that have been validated	Both documents have their Sections arranged in a different order.

[5] GHTF/SG1/N044:2008 *Role of Standards in the Assessment of Medical Devices*

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	Principles conformity checklist can be used to demonstrate that a recognized test standard was used as part of the method to demonstrate conformity to one Essential Principle. As such, CSDT would then include a declaration of conformity to the standard, or other certification permitted by the Regulatory Authority, and a summary of the test data, if the standard does not include performance requirements. When the manufacturer uses international or other standards to demonstrate conformity with the Essential Principles, the CSDT should identify the full title of the standard, identifying numbers, date of the standard, and the organization that created the standard. When the manufacturer uses other means, such as internal standards, the CSDT should describe the means. Not all the essential principles will apply to all devices and it is for the manufacturer of the device to assess which are appropriate for his particular device product. In determining this, account must be taken of the intended purpose of the device. **Guidance:** The Essential Principles (EP) conformity checklist is to be prepared based on the list of EPs found in the Regulations. The IVD medical	and verified; d) Comparison to an IVD medical device already available on the market. The EP checklist should include a cross-reference to the location of such evidence both within the full technical documentation held by the manufacturer and within the STED (when such documentation is specifically required for inclusion in the Summary Technical Documentation as outlined in this guidance).	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	device to which the EP conformity checklist is applicable shall be identified on the checklist itself. Where applicable, the various configurations of the IVD medical device covered by the checklist are to be identified in the checklist. The columns in the recommended format for the checklist shall be completed as follows- (a) Applicable to the IVD medical device? (i) Either a 'Yes' or 'No' answer is required. If the answer is 'No' this shall be briefly explained. For example: For an IVD medical device that does not incorporate biological substances, the answer to MDA/GD/IVD-2 EPSP 5.2 would be 'No – The IVD medical device does not incorporate biological substances.' (b) Method of conformity (i) State the title and reference of the standard(s), industry or in-house test method(s), comparison study(ies) or other method used to demonstrate compliance. For standards, this shall include the date of the standard and where appropriate, the clause(s) that demonstrates conformity with the relevant EP. Where a standard is referred to more than once in the checklist, the reference number and date can be repeated.		

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	(c) Identity of specific documents (i) This column shall contain the reference to the actual technical documentation that demonstrates compliance to the EP, i.e. the certificates, test reports, study reports or other documents that resulted from the method used to demonstrate compliance, and its location within the technical documentation.		
Device Description	6.2.1 Device description and features Besides a general description of the device, a more detailed description of the device attributes is necessary to explain how the device functions, the basic scientific concepts that form the fundamentals for the device, the component materials and accessories used in its principles of operation as well as packaging. A complete description of each functional component, material or ingredient of the device should be provided, with labeled pictorial representation of the device in the form of diagrams, photographs or drawings, as appropriate. **Guidance:** The following information shall be submitted to meet the requirements of this section:	6.1 Device Description The STED should include the following device descriptive information: a) The intended use of the IVD medical device. This may include: 1) what is detected 2) its function (e.g. screening, monitoring, diagnosis or aid to diagnosis); 3) the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate; 4) whether it is automated or not; 5) whether it is qualitative or quantitative; 6) the type of specimen(s) required (e.g. serum, plasma, whole blood, tissue biopsy, urine);	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	(a) A general description of the principle of assay method or instrument principles of operation. (b) A description of all components of the IVD medical device, including but not limited to- (i) antibodies, antigens, nucleic acid primers; (ii) buffers, assay controls and calibrators; (iii) substrates used to detect antigen-antibody complexes; and (iv) reagents provided with the IVD medical device or recommended for use. (c) A description of the specimen collection and transport materials provided with the IVD medical device or recommended for use. (d) For automated assays, a description of the appropriate instrumentation characteristics or dedicated instrumentation. (e) A description or complete list of various configurations of the IVD medical device to be registered as a family or group, if applicable. For example, a family of pregnancy rapid test can consist of device available in different configurations, such as a test strip or in a cassette. Refer to Appendix B. (f) A description of the accessories, other IVD medical devices and other products that are not IVD medical devices, which are intended to be	7) testing population; b) the intended user (lay person or professional); c) a general description of the principle of the assay method or instrument principles of operation; d) the Class of the device and the applicable classification rule according to Principles of In Vitro Diagnostic Medical Devices Classification ; e) A description of the components (e.g. reagents, assay controls and calibrators) and where appropriate, a description of the reactive ingredients of relevant components (such as antibodies, antigens, nucleic acid primers). and where applicable: f) a description of the specimen collection and transport materials provided with the IVD medical device or descriptions of specifications recommended for use; g) for instruments of automated assays: a description of the appropriate assay characteristics or dedicated assays; h) for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation; i) a description of any software to be used with	

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	used in combination with the IVD medical device. For example, a lancet, which is a medical device and not an IVD medical device that is provided in the package to the user to perform a test. Note: Supporting documents, in CSDT format, must be provided for the medical device accompanying the IVD medical device. (g) Risk class and the applicable classification rule for the IVD medical device according to the Regulations.	the IVD medical device; j) a description or complete list of the various configurations/variants of the IVD medical device that will be made available; k) a description of the accessories, other IVD medical devices and other products that are not IVD medical devices, which are intended to be used in combination with the IVD medical device.	
	6.2.2 Intended Use This means the use for which the medical device is intended, for which it is suited according to the data supplied by the manufacturer in the instructions as well as the functional capability of the device. **Guidance**: The intended use of an IVD medical device shall include information on the following- (a) Type of analyte or measurand of the assay. (b) Whether the test is quantitative or qualitative. (c) Role of the test in the clinical use e.g.	6.1 Device Description The STED should include the following device descriptive information: a) The intended use of the IVD medical device. This may include: 1) what is detected 2) its function (e.g. screening, monitoring, diagnosis or aid to diagnosis); 3) the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate; 4) whether it is automated or not; 5) whether it is qualitative or quantitative;	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	screening, diagnostic or detection, aid to diagnostic, monitoring. (d) Disease or condition that the test is intended for. (e) Type of specimen to be used e.g. serum, plasma etc. (f) The intended users (e.g. self-testing by lay person, near-patient by trained personnel or professionals). (g) Assay type e.g. immunoassay, chemistry, cytochemistry, image analysis, immunohistochemistry. (h) The specific name of the instrument required for the assay, if any. For instruments, the intended use shall also include the modes of operation for instruments e.g., random access, batch, stat, open tube, closed tube, automatic, manual.	6) the type of specimen(s) required (e.g. serum, plasma, whole blood, tissue biopsy, urine); 7) testing population; b) the intended user (lay person or professional);	IVD STED does not call for information on assay type and specific name of the instrument required for the assay of 'Intended Use'.
	6.2.3 Instructions of use These are all necessary information from the manufacturer including the procedures, methods, frequency, duration, quantity and preparation to be followed for safe use of the medical device. Instructions needed to use the device in a safe manner should, to the extent possible, be included on the device itself and/or	11.0 Labelling The STED should typically contain a complete set of labelling associated with the device as described in GHTF guideline Labelling for Medical Devices. Information on labelling should include the following: ● labels on the device and its packaging;	IVD STED references another GHTF document, specific to labels and instructions for use, rather than incorporating the details into the text (as the IVD CSDT has). IVD CSDT has separate

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	on its packaging by other formats / forms.	● instructions for use; and Where the STED is submitted to a RA/CAB, the labelling set should be in a language required by the reviewing jurisdiction. For inclusion in a STED, the labelling should contain the final content as determined by the manufacturer but does not have to be in the final (printed) format.	sections on 'Instructions for Use' (6.2.3) and 'Device Labelling' (6.4).
	6.2.4 Limitations This is a general description of the disease or condition and the patient population for which the device should not be used for the purpose of diagnosing, treating, curing or mitigating. **Guidance:** For example, a limitation of an assay using specimens from patients who have received preparations of mouse monoclonal antibodies for therapy when tested with assay kits which employed mouse monoclonal antibodies. It may show either falsely elevated or depressed values.		IVD STED has no specific requirement regarding 'Limitations'.
	6.2.5 Warnings This is the specific hazard alert information that a user needs to know before using the		IVD STED has no specific requirement regarding 'Warnings'.

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	device. **Guidance:** For products containing biological material, radioactive material, explosive material and any other hazardous material, safety warnings must be included.		
	6.2.6 Precautions This alerts the user to exercise special care necessary for the safe and effective use of the device. They may include actions to be taken to avoid effects on patients / users that may not be potentially life-threatening or result in serious injury, but about which the user should be aware. Precautions may also alert the user to adverse effects on the device of use or misuse and the care necessary to avoid such effects.		IVD STED has no specific requirement regarding 'Precautions'.
	6.2.7 Materials This section must include complete details of material specifications, including raw materials. a) All components of the IVD medical device shall be listed and chemically and biologically characterised, including antibodies, antigens, assay controls, substrates used to detect antigen-antibody complexes, and test reagents. Appropriate references shall be cited.	6.1 Device Description e) A description of the components (e.g. reagents, assay controls and calibrators) and where appropriate, a description of the reactive ingredients of relevant components (such as antibodies, antigens, nucleic acid primers).	

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	b) If synthetic peptides are used, the peptide sequence shall be provided. c) If components are of biological origin or recombinant, the source must be indicated and details on production must be provided. These details would include the strain of the virus, the cell line for cultivation of the virus, sequences of relevant nucleic acids and amino acids, etc., used in the manufacturing process of viral lysate, purified proteins, recombinant and synthetic proteins. d) If applicable, process validation results to be provided to substantiate that manufacturing procedures are in place to minimise biological risks, in particular, with regard to viruses and other transmissible agents. This also includes inactivation of infectious organisms in reagents and the production of reagents. e) if applicable, information to be provided on irradiating components, nonionising or ionising (e.g. Iodide-131 in the Radioimmunoassay kit, radio-labelled Phosphorus-32 DNA probes in Southern blots) f) if applicable, information to be provided on the poison or controlled substance (e.g. Buprenorphine in drug assay kit).		IVD STED has no specific requirement on biological origin components and irradiating components
	6.2.8 Other relevant specifications The functional characteristics and technical		IVD STED has no specific requirement

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	performance specifications for the device including, as relevant, accuracy, sensitivity, specificity of measuring and diagnostic medical devices, reliability and other factors; and other specifications including chemical, physical, electrical, mechanical, biological, software, sterility, stability, storage and transport, and packaging to the extent necessary to demonstrate conformity with the relevant Essential Principles. **Guidance:** A list of the features, dimensions and performance characteristics of the IVD medical device that would typically appear in the package insert and instruction manual, will satisfy the requirements of this section.		regarding 'Other relevant specifications'.
	6.2.9 Other descriptive information Other important descriptive characteristics not detailed above, to the extent necessary to demonstrate conformity with the relevant Essential Principles.		
Product Verification and Validation documents	6.3 Product verification and validation documents This section includes data from pre-clinical and clinical studies. The data required is to the extent appropriate to the complexity and risk	10.0 Product Verification and Validation The information provided in the product verification and validation section of the STED will vary in the level of detail as determined by	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	class of the device. **Guidance:** For all aspects of verification and validation described in this section, where no testing was undertaken for the IVD medical device, a rationale for that decision must be provided. Evidence to support the rationale shall be provided. The suitability of the IVD medical device for each of the intended specimen type, such as serum, plasma, whole blood etc, shall be verified and validated through both preclinical and clinical evidence. If specimens containing anti-coagulants are recommended for use, study shall be included.	the classification of the device. Also other characteristics as outlined in section 5.1 will influence the level of detail of the STED. As a general rule, the STED should summarise the results of verification and validation studies undertaken to demonstrate conformity of the IVD medical device with the Essential Principles that apply to it. Where appropriate, such information might come from the literature. For the purpose of the STED document, 'summary' and 'detailed information' are defined as: 1. Summary Information A summary should provide enough information to allow the RA/CAB to assess the validity of that information. This summary should contain a brief description of: a) the study protocol, b) the study results, c) the study conclusion. This summary may include: a) Where a recognized standard exists, a declaration/certificate of conformity to a recognized standard can be provided with a	No explanation of level of detail of the information provided in IVD CSDT.

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		summary of the data if no acceptance criteria are specified in the standard; b) In the absence of a recognized standard, a declaration/certificate of conformity to a published standard that has not been recognized might be provided if it is supported by a rationale for its use, and summary of the data, and a conclusion, if no acceptance criteria are specified in the standard; c) In the absence of a recognized standard and non-recognized published standards, a professional guideline, industry method, or in-house standard may be referred to in the summarized information. However, it should be supported by a rationale for its use, a description of the method used, a summary of the data in sufficient detail and a conclusion to allow assessment of its adequacy; d) A review of relevant published literature regarding the device/analyte (measurand) or substantially similar IVD medical devices. 2. Detailed Information Detailed information should include: a) the complete study protocol, b) the method of data analysis,	

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		c) the complete study report, d) the study conclusion. For detailed information, when a recognized standard exists that contains the protocol and the method of data analysis, this information can be substituted by a declaration/certificate of conformity to the recognized standard. However, a summary of the data and conclusions should be provided. For clinical performance (which is part of the clinical evidence), the detailed information will typically include individual data points (formatted raw data) for a Class D IVD medical device. Where appropriate, actual test result summaries with their acceptance criteria should be provided and not just pass/fail statements.	
Pre- clinical studies	6.3.1 Pre-clinical studies The Information on preclinical studies to establish the safety and performance of the IVD medical device for its intended use must be provided. The pre-clinical studies provided should include information on study design, complete test or study protocols, methods of data analysis, data summaries and study conclusions. The most common characteristics that must be validated should include but are	10.1 Analytical Performance The statements and descriptions in the following sections refer to all IVD medical devices. It must be noted however that there are applicability differences between instrumentation and reagent-based assays, and that the assays themselves may be quantitative, semi-quantitative or qualitative in nature. There may be limited applicability of some of the following subsections for qualitative or semi-quantitative assays. Where possible, comments	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	not limited to- ● Analytical Sensitivity ● Analytical Specificity and Interference ● Precision (Repeatability / Reproducibility) ● Linearity / Assay's Measuring (Reportable) Range ● Traceability and Expected Values ● Cut-off Value ● Trueness ● Stability of reagent ● Specimen stability ● Performance Characteristics for Instrument (if applicable): ■ Accuracy ■ Precision / Reproducibility ■ Linearity ■ Carryover ■ Interfering Substances ■ Projected useful life ■ Software Verification and Validation Studies	regarding instrumentation or qualitative assays appear in the subsections.	
	Guidance: (a) Analytical Sensitivity Data on analytical sensitivity shall include	10.1.2.2 Analytical sensitivity This section should include information about the study design and results. It should provide a description of specimen type and	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	information on the following- (i) the specimen type and preparation including matrix, analyte levels, and how levels were established; (ii) the number of replicates (runs, days, instruments, and operators, as appropriate) included at each concentration tested; (iii) the statistical method used; (iv) the results of the analytical limits at low levels (e.g., limit of detection, functional sensitivity); (v) the definition / calculation used to determine assay sensitivity. For example- • Number of standard deviations above the mean value of the sample without analyte. Include mean and standard deviation; and • Lowest concentration at which %CV and accuracy are within specified criteria and describe the evaluations to determine they were met; (vi) For qualitative assay, include the percent of replicates that test positive at each concentration and evaluate the 95% interval for cut-off and limit of detection.	preparation including matrix, analyte (measurand) levels, and how levels were established. The number of replicates tested at each concentration should also be provided as well as a description of the calculation used to determine assay sensitivity. For example: a) Number of standard deviations above the mean value of the sample without analyte (measurand), commonly referred to as 'limit of blank' (LoB). b) Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand), commonly referred to as 'limit of detection' (LoD). c) Lowest concentration at which precision and/or trueness are within specified criteria, commonly referred to as 'limit of quantitation' (LoQ). Typically for a Class C and D IVD medical devices, detailed information would be provided.	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	(b) Analytical Specificity and Interference Data on analytical specificity shall include information on the following- (i) a description of study design and statistical methods; (ii) the specimen description and preparation including matrix, analyte levels present in the sample, how these levels were established; and (iii) a list of the potentially cross-reactive and interfering substances tested including those where a similar syndrome can be associated with more than one analyte / agent / organism. Also include the concentrations at which these substances were present in the samples (indicate highest concentration tested and / or lowest concentration at which an effect was observed). Finally, include the number of replicates tested for each substance.	10.1.2.3 Analytical specificity This section should describe interference and cross reactivity studies to determine the analytical specificity, defined as the ability of a measurement procedure to detect or measure only the analyte (measurand) to be detected, in the presence of other substances/agents in the sample. Provide information on the evaluation of potentially interfering and cross reacting substances/agents on the assay. Information should be provided on the substance/agent type and concentration tested, sample type, analyte (measurand) test concentration, and results. Interferents and cross reacting substances/ agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources such as: a) Substances used for patient treatment (e.g. therapeutic drugs, anticoagulants, etc.); b) substances ingested by the patient (e.g. over the counter medications, alcohol, vitamins, foods, etc.); c) substances added during sample preparation (e.g. preservatives, stabilizers); d) substances encountered in specific specimens types (e.g. haemoglobin, lipids,	IVD STED incorporates the details into the text.

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		bilirubin, proteins); e) analytes of similar structure (e.g. precursors, metabolites) or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that may mimic the test condition (e.g. for a hepatitis A assay: test specimens negative for hepatitis A virus, but positive for hepatitis B virus). Typically, interference studies involve adding the potential interferent to the sample and determining any bias of the test parameter relative to the control sample to which no interferent has been added. Typically for Class C and D IVD medical devices, detailed information would be provided	
	(c) Precision (Repeatability / Reproducibility) Data on precision shall include information on the following- (i) description of studies and results to evaluate estimates of total variability for each specimen type. Include, as appropriate, repeatability (within-run) and reproducibility such as between-day, between-run, within-day, between-sites, between-lots, between instrument, and between operator(s), etc;	10.1.2.1.2. Precision of measurement This section should describe repeatability and reproducibility studies. 10.1.2.1.2.1. Repeatability This section should include repeatability estimates and information about the studies used to estimate, as appropriate, within-run variability. Repeatability data is obtained for instrumentation in conjunction with an appropriate assay.	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	(ii) description of specimens (samples) used to study variability including matrix, sample type (e.g., patient samples, spiked samples, control material), and preparation, including analyte levels and how they were established. The relationship between the analyte levels to measuring (reportable) range and medical decision points must also be described; (iii) description of sources of variability examined (e.g., runs, instruments, operators, days; sites at which variability studies were performed; reagent lots and instruments studies with identifying information); (iv) description of statistical methods used to analyse data; include any model assumptions; (v) for quantitative or qualitative assays with numerical values, the number of measurements, mean, standard deviation, and %CV for each parameter tested and for each level tested; and (vi) For qualitative assays, the number of replicates, the concentration of the sample, the number of positive and negative results, and the number of invalid or equivocal results, if applicable. For reproducibility studies on qualitative tests, an estimation of the precision of the method at analyte	Typically for Class C and D IVD medical devices, detailed information would be provided. Note 1: Such studies should include the use of samples that represent the full range of expected analyte (measurand) concentrations that can be measured by the test as claimed by the manufacturer. Note 2: If a recognized standard is used, a declaration/certificate of conformity to the recognized standard along with a summary of the data and conclusions should be provided. 10.1.2.1.2.1. Reproducibility This section should include reproducibility estimates and information about the studies used to estimate, as appropriate, variability between days, runs, sites, lots, operators and instruments. Such variability is also known as "Intermediate Precision". Reproducibility data is obtained for instrumentation in conjunction with an appropriate assay. Typically for Class C and D IVD medical devices, detailed information would be provided. Note 1: Such studies should include the use of samples that represent the full range of	

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	concentrations near the cut-off.	expected analyte (measurand) that can be measured by the test as claimed by the manufacturer. Note 2: If a recognized standard is used, a declaration/certificate of conformity to the recognized standard along with a summary of the data and conclusions should be provided	
	(d) Linearity / Assay's Measuring (Reportable) Range Data on linearity / assay's measuring shall include information on the following- (i) the linear range, measuring (reportable) range and information on how these were established. For quantitative and semi-quantitative assays, the analytical data to support linearity and the description on the recovery of the assay in graphic and tabular form; (ii) the linear range and measuring (reportable) range. Include the measure of deviation from linearity, if applicable; (iii) description of how reportable range is determined including acceptable criteria or results for accuracy, precision, or other characteristics within this range; (iv) description of specimen type and	10.1.2.5 Measuring range of the assay This section should include a summary of studies which define the measuring range (linear and non-linear measuring systems) including the limit of detection and describe information on how these were established. This summary should include a description of specimen type, number of samples, number of replicates, and preparation including information on matrix, analyte (measurand) levels and how levels were established. If applicable, add a description of high dose hook effect and the data supporting the mitigation (e.g. dilution) steps. Typically for Class C and D IVD medical devices, detailed information would be provided.	IVD CSDT incorporates the details into the text.

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	preparation including information on matrix, analyte levels, and the methods used to determine the target levels; (v) the number of samples, the number of replicates, and the statistical methods used; (vi) the results such as estimates of slope, intercept with confidence intervals, and R2 value of regression; (vii) provide the range of percent recovery at each concentration (observed value / target value); (viii) description on how results outside the measuring (reportable) range are reported to the user; (ix) description on the validation of instructions for out-of-range specimens, if applicable; and (x) discussion of possible high-dose hook effect, if applicable.		
	(e) Traceability & Expected Values (Controls, Calibrators, Methods) Data on traceability and expected values shall include information on the following- (i) where applicable, summary information about traceability of calibrators and trueness control material. Include for examples,	10.1.2.4 Metrological traceability of calibrator and control material values Where applicable, summarize the information about metrological traceability of values assigned to calibrators and trueness control materials. Include, for example, methods and acceptance criteria for the metrological traceability to reference materials	

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	methods and acceptable criteria for traceability to reference material and description of value assignment and validation; and (ii) a description on how the recommended calibration and control testing frequency were established, validation of the standard curve by replicate analysis of calibrators, and validation of quality control, as appropriate (e.g., novel, internalised quality control). Note: Precision control material used for establishing reproducibility does not require traceability to reference material.	and/or reference measurement procedures and a description of value assignment and validation. Precision control materials, used when establishing the reproducibility of a measurement procedure do not require the assessment of metrological traceability to a reference material or a reference method. Typically for a Class D IVD medical device, detailed information would be provided.	
	(f) Cut-off Value Data on cut-off value shall include information on the following- (i) the rationale for the units, cut-off and/or categories of the results; (ii) a description of specimen preparation including analyte levels, matrix, and how the level was established; (iii) the statistical method used (e.g., Receiver Operator Characteristic Analysis); and (iv) a definition of equivocal zone, if	10.1.2.6 Definition of assay cut-off This section should provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, including: a) the population(s) studied (demographics / selection / inclusion and exclusion criteria / number of individuals included); b) method or mode of characterization of specimens; and c) statistical methods e.g. Receiver Operator Characteristic (ROC) to generate results and if applicable, define gray-zone/equivocal	

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	applicable.	zone. Typically for Class C and D IVD medical devices, detailed information would be provided.	
	(g) Trueness Data on trueness shall include information on the following- (i) the measure of trueness in the closeness of agreement between the average value obtained from a large series of test results and an accepted reference value; and (ii) bias of the measurement procedure shall be determined by a suitable recovery or comparison of procedures experiments, and provides the methodology and the rational of its use.	10.1.2.1 Analytical performance characteristics While measurement trueness, affected by systematic error, is normally expressed in terms of bias, measurement precision, affected by random error, is naturally expressed in terms of standard deviation 10.1.2.1.1.Trueness of measurement This section should provide information on the trueness of the measurement procedure and summarize the data in sufficient detail to allow assessment of the adequacy of the means selected to establish the trueness. Trueness measures apply to both quantitative and qualitative assays only when a reference standard or method is available. Typically for Class C and D IVD medical devices, detailed information would be provided.	
	(h) Stability of reagent Data on stability of reagent shall include information on the recommended shelf life or storage conditions for in use or opened and	10.3 Stability (excluding specimen stability) This section should describe claimed shelf life, in use stability and shipping studies.	IVD STED incorporates the details into the text.

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	unopened IVD medical device, and also taking into consideration of variable conditions including temperature, freeze / thaw cycle and its duration during usage (including for on-board use), and for transportation. The studies shall be provided from at least 3 lots or batches. If real-time stability is not available, an accelerated study is acceptable for initial shelf life claim while continuing real time studies to be performed. Statistical method used also to be provided. The final real time study report must be submitted when completed.	10.3.1 Claimed shelf life This section should provide information on stability testing studies to support the claimed shelf life. Testing should be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these lots do not need to be consecutive lots). Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies. Typically for Class C and D IVD medical devices, detailed information would be provided. Such detailed information should describe: a) the study report (including the protocol, number of lots, acceptance criteria and testing intervals); b) when accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies; c) conclusions and claimed shelf life. Note: Shelf life can be derived from the lot with the longest real time stability data as	

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		long as accelerated or extrapolated data from all three lots are comparable. 10.3.2 In use stability This section should provide information on in use stability studies for one lot reflecting actual routine use of the device (real or simulated). This may include open vial stability and/or, for automated instruments, on board stability. In the case of automated instrumentation if calibration stability is claimed, supporting data should be included. Such detailed information should describe: a) the study report (including the protocol, acceptance criteria and testing intervals); b) conclusions and claimed in use stability. Typically for Class C and D IVD medical devices, detailed information would be provided. 10.3.3 Shipping stability This section should provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated	

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		shipping conditions. Shipping studies can be done under real and/or simulated conditions and should include variable shipping conditions such as extreme heat and/or cold. Such information should describe: a) the study report (including the protocol, acceptance criteria); b) method used for simulated conditions; c) conclusion and recommended shipping conditions. Typically for a Class C and D IVD medical device, detailed information would be provided.	
	(i) Specimen stability Data on specimen stability shall include information on the following- (i) description of the recommended method for the specimen's collection, storage and transportation; and (ii) the specimen stability validation studies for the collection, storage and transportation methods. Elements to be validated would include but not limited to storage duration, temperature limits, and freeze / thaw cycle.	10.1.1 Specimen type This section should describe the different specimen types that can be used. This should include their stability and storage conditions and is typically applicable to all systems and assay types. Stability includes storage and where applicable transport conditions. Storage includes elements such as duration, temperature limits and freeze/thaw cycles. This section should include summary information for each matrix and anticoagulant when applicable, including a description of the	IVD CSDT has no specific requirement

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		measurement procedure for comparison or determination of measurement accuracy. This includes information such as specimen type tested, number of samples, sample range (using spiked samples as appropriate) or target concentrations tested, calculations and statistical methods, results and conclusions. Typically for a Class D IVD medical device, detailed information would be provided.	regarding 'matrix comparison'.
	(j) Performance Characteristics for Instrument (if applicable): Data to support the performance characteristics for instruments shall include information on the following: (i) Accuracy Comparison information on each test parameter to either a reference method or an IVD medical device with the same intended use. The testing pool shall contain samples representative of the appropriate population, including an equal number of males and females for which samples span the reportable range. Specimens that are close to the clinically critical decision point(s) must be included. Data to be presented using linear regression, including 95% confidence intervals for the slope and y-intercept and scatter plots.		No requirement in IVD STED.

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	(ii) Precision / Reproducibility Estimation of intra, inter, lot-to-lot, operator-to-operator, and total imprecision for each measurand parameter of the IVD medical device using samples that span the testing range. (iii) Linearity Information on how linearity was established and indication on whether this conformed to any available reference or methodology. (iv) Carryover Studies to demonstrate lack of over estimation of results due to the carryover effect. The testing pool shall consist of samples at clinically meaningful levels. For investigation of potential carry-over, at least five runs with alternating high-positive and negative specimens shall be performed during robustness studies. The high positive samples shall comprise of samples with naturally occurring high virus titres. (v) Interfering Substances Studies to show possible interference of substances such as lipids, haemoglobin, bilirubin, etc. (vi) Projected useful life		

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	For IVD medical device that does not have expiry dates, the projected useful life of the IVD medical device must be provided. Manufacturer may refer to TS/ISO 14969 (Medical devices – Quality management systems – Guidance on the application of ISO 13485:2003) for information on how to determine the projected useful life.		
	(vii) Software Verification and Validation The correctness of a software product is a critical product characteristic that cannot be fully verified in a finished product. The manufacturer must provide evidence that validates the software design and development process. This information shall include the results of all verification, validation and testing performed in-house and in a user's environment prior to final release, for all of the different hardware configurations identified in the labeling, as well as representative data generated from both testing environments.	10.4 Software Verification and Validation The STED should contain evidence of the validation of the software, as used in the finished device. This information should typically include the summary results of all verification, validation and testing performed in-house and as applicable in an actual user environment prior to final release. It should also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling. Typically for a Class D IVD medical device, detailed information would be provided.	
Clinical Evidence	6.3.2 Clinical evidence This section should indicate how any applicable requirements of the EPs for clinical evaluation of the device have been met. Where applicable, this evaluation may take the form of a systematic review of existing bibliography,	10.2 Clinical Performance Where relevant, the STED should contain data on the clinical performance of the IVD medical device. This clinical performance data is one of the elements of clinical evidence that demonstrates	IVD STED references other GHTF guidance documents

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	clinical experience with the same or similar medical devices, or by clinical investigation. Clinical investigation is most likely to be needed for higher risk class medical device, or for medical device where there is little or no clinical experience. **Guidance:** The clinical evidence to be provided shall include the information mentioned in this section. For any IVD medical device, if discrepant test results are identified as part of an evaluation, these results shall be resolved as far as possible, using one or more of the following approaches- • by evaluation of the discrepant sample in further test systems; • by use of an alternative method or marker; • by a review of the clinical status and diagnosis of the patient; and • by the testing of follow-up-samples.	the conformity of the IVD medical device to the Essential Principles that apply to it. Note: Analytical performance and clinical performance are elements of clinical evidence. More detailed recommendations regarding these elements of the STED will be provided in guidance developed in cooperation with SG5. Reference: ● GHTF/SG5/N6:2012 Clinical Evidence for IVD medical devices – Key Definitions and Concepts ● GHTF/SG5/N7:2012 Clinical Evidence for IVD medical devices – Scientific Validity and Performance Evaluation ● GHTF/SG5/N8:2012 Clinical Evidence for IVD Medical Devices - Clinical Performance Studies for In Vitro Diagnostic Medical Devices	
	(a) Clinical (Diagnostic) Sensitivity Data on clinical (diagnostic) sensitivity shall		Information on what is to be incorporated into the IVD STED provided

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	include information on the following- (i) the methodology including its statistical method, results, discussion and conclusion for the study; (ii) the total individual positive specimens and the sero-conversion panels used in the study. For positive specimens, where different virus subtypes and genotypes are available, studies of these subtypes specimens must be included. For Class D IVD medical device, when testing the sero-conversion specimens, the diagnostic sensitivity during the early infection phase (sero-conversion) has to represent the state of the art; (iii) the probability that the IVD medical device gives a positive result in the presence of the target marker; and (iv) Negative predictive values to be included in the calculation.		in GHTF SG5 documents.
	(b) Clinical (Diagnostic) Specificity Data on clinical (diagnostic) specificity shall include information on the following- (i) the methodology including its statistical method, results, discussion and conclusion for the study; (ii) the total individual negative specimens in		Information on what is to be incorporated into the IVD STED provided in GHTF SG5 documents.

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	the study. Negative specimens used in a performance evaluation shall be defined so as to reflect the target population for which the test is intended, for example blood donors, clinical samples or hospitalised patients including pregnant women, and potentially interfering samples; (iii) the probability that the IVD medical device gives a negative result in the absence of the target marker; and (iv) Positive predictive values to be included in the calculation.		
	(c) Comparison Studies Using Clinical Specimens Comparison studies using clinical specimens shall include information on the following- (i) Method comparison: All performance evaluations shall be carried out in direct comparison with an established state of the art IVD medical device. The established product for comparison must have obtained marketing clearance from the reference agencies, namely Australia TGA, Canada TPP, Europe, Japan MHLW, and US FDA. Study design shall include-		Information on what is to be incorporated into the IVD STED provided in GHTF SG5 documents.

Elements	ASEAN IVD CSDT MDA/GD/IVD-4 (First Edition, July 2013)	GHTF IVD STED GHTF/SG1/NO63: 2011	Comment
	• description on the test methods, • information on the comparator(s) (e.g., reference IVD medical device, reference method), • the sample type(s) (e.g., unaltered patient specimens, spiked or diluted patient specimens, spiked patient pools, and control material), matrix, number of samples, sample range, • when appropriate, number / types of sites, sample selection methods, inclusion / exclusion criteria, overall demographic description of patients represented by the samples (e.g., age, gender, race, how/whether samples represent the intended use population), number of individuals represented, and • statistical methods used to generate results (e.g., regression methods, data exclusion, number of observation represented by each data point). Results shall include- • Description on the overall results and / or results from specific sites and patient groups, as appropriate,		

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	• For quantitative tests, information such as slope and intercept (with confidence intervals), correlation coefficient, measure of scatter around the regression line, measure of bias at medical decision levels. • In some cases, a graph (x-y graph or bias plot) can be included, and • For qualitative or semi-quantitative tests, percent agreement with comparator for positive / negative samples, confidence intervals. (ii) Matrix comparison Study design shall include- • for each matrix in the intended use, the method for comparison or determination of accuracy, and • sample types tested, number of samples, sample range or target concentrations tested and calculations / statistical methods. Results / Acceptance criteria shall include- • the accuracy of the new matrix or results of the matrix comparison.		

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	(d) Clinical Cut-off This information shall include- (i) the established cut-off and its validation for the new IVD medical device; and (ii) if applicable, the "equivocal zone" is to be defined, and include a description of how results within this zone are reportable to the user.		Information on what is to be incorporated into the IVD STED provided in GHTF SG5 documents.
	(e) Reference Interval (Expected Values) This information shall include- (i) the reference interval for this measured and the method used to determine it; (ii) the literature references establishing the reference intervals and justification for applying this range to the new IVD medical device; (iii) a description of the methods for determining the reference intervals if they are not well established from the literature or if the range cannot be transferred to the new IVD medical device; (iv) the description of the population studies (demographics, inclusion / exclusion criteria, number of individuals); (v) any separate reference intervals for		Information on what is to be incorporated into the IVD STED provided in GHTF SG5 documents.

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	subclasses where clinically justified; (vi) the method of clinical diagnosis of the reference population(s); and (vii) the statistical method used to calculate the ranges.		
	(f) Additional requirements for IVD medical device for self-testing and near patient testing (if applicable) The field evaluation report shall be provided. Study results and data shall:- (i) show the handling suitability of the IVD medical device; and (ii) determine the IVD medical device's performance when used by the intended users following instructions provided in the labeling and without the assistance from the professionals. Also, there shall be a study to show that the correct result can be obtained by the intended users, when compared to the laboratory professionals.		Information on what is to be incorporated into the IVD STED provided in GHTF SG5 documents.
	6.3.2.1. Use of existing bibliography Copies are required of all literature studies, or existing bibliography, that the manufacturer is using to support safety and effectiveness. These will be a subset of the bibliography of		Information on what is to be incorporated into the IVD STED provided in GHTF SG5 documents.

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	references. General bibliographic references should be medical device-specific as supplied in chronological order. Care should be taken to ensure that the references are timely and relevant to the current application. Clinical evidence of effectiveness may comprise device-related investigations conducted domestically or other countries. It may be derived from relevant publications in a peer-reviewed scientific literature. The documented evidence submitted should include the objectives, methodology and results presented in context, clearly and meaningfully.		
Device Labelling	6.4 Device labeling The device labeling refers to any written, printed or graphic representation affixed to a medical device or any part of its packaging, or accompanying a medical device, when the medical device is being supplied. This section should summarize or reference or contain the following labeling data to the extent appropriate to the complexity and risk class of the device, which is generally considered as "labeling"- • Labels on the device and its packaging; • Instructions for use;	11.0 Labelling The STED should typically contain a complete set of labelling associated with the IVD medical device as described in GHTF guideline Labelling for Medical Devices . Information on labelling should include the following: a) Labels on the IVD medical device (immediate and outer container) b) Instructions for use Where the STED is submitted to a RA/CAB, the labelling set should be in a language required by the reviewing jurisdiction. For inclusion in a STED, the labelling should	IVD STED references another GHTF guidance document, rather than incorporating the details into the text (as the IVD CSDT has).

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	• Physician's manual. Any information and instructions given to the patient, including instructions for any procedure the patient is expected to perform (if applicable). 6.4.1 Samples of labels on the medical device and its packaging This is the printed, written or graphic product information provided on or attached to one or more levels of packaging, including the outer packaging or the outside container wrapper. Any pack labeling, which is not provided on the outer packaging must be easily legible through this outer packaging. If it is physically impossible to include samples of labels (e.g. large warning labels affixed onto an X-ray machine), alternative submission methods (e.g. photographs or technical drawings), to the extent appropriate, will suffice to meet the requirements of this section. 6.4.2 Instructions for use The instructions for use is commonly referred to as the physician's manual, user manual, operator's manual, prescriber's manual	contain the final content as determined by the manufacturer but does not have to be in the final (printed) format. Reference: GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices	

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	or reference manual. It contains directions under which the physician or end-user can use a device safely and for its intended purpose. This should include information on indications, contraindications, warnings, precautions, potential adverse effects, alternative therapy and the conditions that should be managed during normal use to maintain the safety and effectiveness of the medical device. **Guidance:** The submission dossier shall typically contain a complete set of labeling associated with the IVD medical device as prescribed in the Regulation. The following information is to be provided: (a) The labels (i) The labels on the IVD medical device and its packaging are to be provided for the primary and secondary levels of packaging and shall be provided in the original colour. The labels can be provided in the form of artwork. (ii) Labels provided must be in English. (iii) Labels must be provided for all the components of an IVD medical device system, members of a IVD medical device family and accessories submitted for		

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	registration. Alternatively, a representative label may be submitted for variants, provided the variable fields on the artwork are annotated, and the range of values for the variable fields are indicated. (b) The instructions for use shall contain information on the proper use of the IVD medical device, such as:- (i) the intended use, (ii) directions for use, (iii) limitations, (iv) warnings, (v) precautions, (vi) materials, (vii) storage requirements, (viii) expiration/stability dating, (ix) specimen handling and its storage requirements, (x) results (calculations, formulas, interpretation), (xi) performance characteristics (summarise analytical and diagnostic sensitivity, specificity, reproducibility, etc.), and (xii) study design (population studies, N, type of sample, matrix, dilution, target		

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	concentrations, etc.). (c) Apart from IVD medical device labeling, the promotional material and product brochures shall be provided in this section to aid in the evaluation of the IVD medical device. Note: Inclusion of promotional materials as part of the submission requirement for CSDT does not constitute approval by the Authority of the claims contained within the promotional materials.		
Risk analysis	6.5 Risk analysis This section should summarize or reference or contain the results of the risk analysis. This risk analysis should be based upon international or other recognized standards, and be appropriate to the complexity and risk class of the device. 6.5.1 Results of risk analysis A list of possible hazards for these devices must be prepared. Indirect risks from medical devices may result from device-associated hazards, such as moving parts, which lead to sustained injury, or from user-related hazards, such as ionizing radiation from an X-ray machine. The evaluation of these risks against the claimed benefits of the device and the	8.0 Risk Analysis and Control Summary The STED should contain a summary of the risks identified during the risk analysis process and a description of how these risks have been controlled to an acceptable level. Preferably, this risk analysis should be based on recognised standards and be part of the manufacturer's risk management plan. The summary should address possible hazards for the IVD medical device such as the risk from false positive or false negative results, indirect risks which may result from IVD medical device-associated hazards, such as instability, which could lead to erroneous results, or from user-related hazards, such as reagents containing infectious agents.	

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	method(s) used to reduce risk to acceptable levels must be described. The individual or organization that carries out the risk analysis must be clearly identified. The technique used to analyze risk must be specified, to ensure that it is appropriate for the medical device and the risk involved. **Guidance:** Information required in this section is to be provided in the form of a risk management report. It is recommended that the risk management activities be conducted according to ISO 14971. A risk management report will contain details of the risk analysis, risk evaluation, risk control conducted for the IVD medical device. The risks and benefits associated with the use of the IVD medical device shall be described.	The results of the risk analysis should provide a conclusion with evidence that remaining risks are acceptable when compared to the benefits. Typically for a Class D IVD medical device a detailed report would be provided.	
Manufacturer information	6.6 Manufacturer information This section should summarize or reference or contain documentation related to the manufacturing processes, including quality assurance measures, which is appropriate to the complexity and risk class of the medical device.	9.0 Design and Manufacturing Information 9.1 Device Design The STED should contain information to allow a reviewer to obtain a general understanding of the design applied to the IVD medical device. It should include a description of the critical ingredients of an assay such as antibodies,	IVD STED asks for information on the stages of design.

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		antigens, enzymes and nucleic acid primers provided or recommended for use with the IVD medical device. For instruments this would include a description of major subsystems, analytical technology (e.g. operating principles, control mechanisms), dedicated computer hardware and software. For instruments and software, an overview of the entire system would be required, including an Architecture Design Chart which is typically a flowchart of the relationships among the major functional units in the software, including relationships to hardware and to data flows such as networking. For standalone software, this would typically include a description of the data interpretation methodology (i.e. algorithms). For self-testing devices the design should include a description of the design aspects that make it suitable for lay person use. Typically for a Class D IVD medical device detailed information on material specifications would be provided. This section is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. If design takes place at multiple sites, a	

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		controlling site must be identified.	
	6.6.1 Manufacturing process Manufacturing process for the medical device should be provided in the form of a list of resources and activities that transform inputs into the desired output. EXAMPLE: The manufacturing process should include the appropriate manufacturing methods and procedures, manufacturing environment or condition, and the facilities and controls used for the manufacturing, processing, packaging, labeling, storage of the medical device. Sufficient detail must be provided to enable a person generally familiar with quality systems to judge the appropriateness of the controls in place. A brief summary of the sterilization method and processing should be included, if any. If multiple facilities are involved in the manufacture of medical device, the applicable information (e.g. quality assurance certificates issued by an accredited third party inspection body) for each facility must be submitted. Firms that manufacture or process the medical device under contract to the manufacturer may elect to submit all or a portion of the manufacturing information applicable to their facility directly to the Regulatory Authority in the form of a master file. The manufacturer	9.2 Manufacturing Processes Only for Class D, the STED should contain information to allow a reviewer to obtain a general understanding of the manufacturing processes. It is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. This information may take the form of a process flow chart showing, for example, an overview of production including the technologies used, assembly and packaging of the finished IVD medical device. This section should include details of any in-process and final product testing (e.g. the manufacturer's QC release program 9.3 Manufacturing Sites For the activities in 9.2, the STED should identify the sites where these activities are performed (this does not include the sites of all suppliers of raw materials but only the sites that are involved in critical manufacturing activities). If QMS certificates, or the equivalent, exist for these sites, they may be annexed to the STED.	No requirement for a 'process flow chart' in the IVD CSDT

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	should inform these contractors of the need to supply detailed information on the medical device. However, it is not the intent of this section to capture information relating to the supply of sub-components (i.e. unfinished medical device) that contributes towards the manufacture of the finished medical device itself. **Guidance:** (a) Information on the manufacturing process shall be provided in sufficient detail to allow a general understanding of the manufacturing processes. Detailed proprietary information on the manufacturing process is not required. The information may be presented in the form of a process flow chart showing an overview of production, controls, assembly, in-process and final product testing, and packaging of the finished IVD medical device. (b) If the manufacturing process is carried out at multiple sites, the manufacturing activities carried out at each site shall be clearly identified. For example: (i) If the manufacturing process of a product consists of a number of subassembly processes, the manufacturing sites where each of these subassembly processes are carried out must be identified, and the		

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	relationship between these processes must be shown; or (ii) If multiple sites manufacture the same product, each of these sites must be identified. The sites (including contract manufacturers) where design and manufacturing activities are performed shall be identified. (c) Quality Management System certificates are to be provided for the design and manufacturing sites (including contract manufacturers) as an annex to the CSDT submission. This requirement does not apply to raw material manufacturers (for example, contract manufacturers of sodium azide). (d) For Class D IVD medical device, the batch release plan shall be provided to demonstrate that each batch consistently identifies the relevant antigens, epitopes, and antibodies. The batch release plan shall be provided as an annex, with detailed information on the establishment of the batch release panel, including the number of positive and negative panel.		
		12.0 Format of the STED While this guidance document makes no specific recommendation for the format of the STED, it would be helpful to both	No requirement for the Format of IVD CSDT.

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		manufacturers and reviewers if the STED was organized such that it incorporates the same sections as described in this guidance document e.g. Device Description, Reference to Previous Device Generation(s) and/or Similar Devices or Device History, Essential Principles Checklist, etc.	
		13.0 Declaration of Conformity The Declaration of Conformity is not part of the STED. However, it may be annexed to the STED once the conformity assessment process has been completed. The content of the Declaration of Conformity is described in GHTF/SG1/N46:2007 Principles of Conformity Assessment for In Vitro Diagnostic Medical Devices.	No requirement for a Declaration of Conformity in IVD CSDT.