



PROPOSED DOCUMENT
Global Harmonization Task Force

Title: Summary Technical Documentation (STED) for Demonstrating
Conformity to the Essential Principles of Safety and Performance of In
Vitro Diagnostic Medical Devices

Authoring Group: Study Group 1 of the Global Harmonization Task Force

Date: March 26, 2009

Table of Contents

1.0	<i>Introduction</i>	5
2.0	<i>Rationale, Purpose and Scope</i>	6
2.1	Rationale	6
2.2	Purpose	6
2.3	Scope	6
3.0	<i>References</i>	6
4.0	<i>Definitions</i>	7
PART 1 - PURPOSE OF THE STED		
5.0	<i>Preparation and Use of the STED</i>	7
5.1	Preparation	7
5.2	The Use of the STED in the Premarket Phase	9
5.3	The Use of the STED in the Post-market Phase	10
5.4	The Use of the STED to Notify Changes to the RA/CAB	10
PART 2 - CONTENTS OF THE STED		
6.0	<i>Device Description including Variants (Configurations) and Accessories</i>	11
6.1	Device Description	11
6.2	Reference to Previous Device Generation(s) and/or Similar Devices or Device History	12
6.2.1	For an IVD medical device not yet available on any market	12
6.2.2	For an IVD medical device already on the market in any other jurisdiction	12
7.0	<i>Essential Principles (EP) Checklist</i>	12
8.0	<i>Risk Analysis and Control Summary</i>	13
9.0	<i>Design and Manufacturing Information</i>	13
9.1	Device Design	13
9.2	Manufacturing Processes	13
9.3	Design and Manufacturing Sites	14
10.0	<i>Product Validation and Verification</i>	14
10.1	Analytical Studies	15
10.1.1	Specimen type	15
10.1.2	Accuracy	15
10.1.3	Traceability of calibrators and control materials.....	17
10.1.4	Analytical Sensitivity	17
10.1.5	Analytical Specificity.....	18
10.1.6	Measuring range of the assay	18
10.1.7	Validation of Assay Cut-off.....	18
10.2	Stability (excluding specimen stability)	19
10.2.1	Claimed Shelf life	19

10.2.2	In use stability	19
10.2.3	Shipping stability	20
10.3	Software Verification and Validation	20
10.4	Clinical Evidence	20
11.0	Labelling	20
12.0	Format of the STED.....	21
13.0	Declaration of Conformity	21
Appendix A	22

Preface

The document herein was produced by the Global Harmonization Task Force, a voluntary group of representatives from medical device regulatory authorities and the regulated industry. The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

There are no restrictions on the reproduction, distribution, translation or use of this document. However, incorporation of this document, in part or in whole, into any other document does not convey or represent an endorsement of any kind by the Global Harmonization Task Force.

1.0 Introduction

The primary way in which the GHTF achieves its goals is through the production of a series of guidance documents that together describe a global regulatory model for IVD medical devices. The purpose of such guidance is to harmonize the documentation and procedures that are used to assess whether 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.

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 consistent way, an economic and effective approach to the control of medical devices in the interest of public health. It seeks to strike a balance between the responsibilities of Regulatory Authorities to safeguard the health of their citizens and their obligations to avoid placing unnecessary burdens upon the industry.

The GHTF has 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). This guideline provides recommendations on the content of summary technical documentation (STED) to be assembled and submitted to a Regulatory Authority or Conformity Assessment Body. It should enable a manufacturer to prepare a STED and provide 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 the STED should reduce costs for the manufacturer and reviewer, remove barriers to trade and facilitate timely international access to IVD medical devices.

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

The regulatory requirements of some countries do not, at this time, align fully with this guidance.

Study Group 1 of the Global Harmonization Task Force (GHTF) has prepared this guidance document. Comments or questions about it should be directed to either the Chairwoman or Secretary of GHTF Study Group 1 IVD Subgroup whose contact details may be found on the GHTF web page¹.

¹ www.ghrf.org

2.0 Rationale, Purpose and Scope

2.1 Rationale

Manufacturers are expected to prepare, and either hold or provide timely access to, technical documentation that shows how each IVD medical device was developed, designed and manufactured. This technical documentation, typically controlled in the manufacturer's quality management system (QMS), is often extensive and sections of it may be held in different locations. The documentation is updated to reflect any changes made during the lifecycle of the IVD medical device.

It is advantageous to both RAs/CABs and the regulated industry if a subset of this technical documentation is used for selected premarket and postmarket conformity assessment activities. This technical documentation subset is intended to be in a consistent, summarised or abridged form, with sufficient detail to allow the RA/CAB to fulfil its obligations. In the main, the documents contained within this subset are derived from the technical documentation held by the manufacturer and allow the manufacturer to demonstrate that the IVD medical device to which it applies conforms to the *Essential Principles of Safety and Performance of Medical Devices*.

The availability of such Summary Technical Documentation (STED) should help eliminate differences in documentation requirements between jurisdictions, thus decreasing the cost of gaining regulatory compliance and allowing patients earlier access to new technologies and treatments.

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 to a RA or CAB for premarket review, and for use post-market to assess continuing conformity to the Essential Principles of Safety and Performance.

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 Classification*"².

3.0 References

GHTF/SG1/N044:2008 *Role of Standards in the Assessment of Medical Devices*.

GHTF/SG1/N45:2007 *Principles of In Vitro Diagnostic Medical Devices Classification*.

² SG1/N045:2007 Principles of In Vitro Diagnostic Medical Devices Classification

GHTF/SG1/N29:2005 *Information Document Concerning the Definition of the Term 'Medical Device'*.

GHTF/SG1/N46:2007 *Principles of Conformity Assessment for In Vitro Diagnostic Medical Devices*.

GHTF/SG1/N41:2005 *Essential Principles of Safety and Performance of Medical Devices*.

GHTF/SG1/N43:2005 *Labelling for Medical Devices*.

4.0 Definitions

Calibrator: substance, material or article intended by its manufacturer to be used in the calibration of a measuring instrument or measuring system.

(Source : ISO 18113-1 **Error! Reference source not found.** – pending for FDIS vote)

Control material: substance, material or article intended by its manufacturer to verify the performance of an IVD medical device (Source : ISO 18113-1 **Error! Reference source not found.** – pending for FDIS vote)

Recognised Standard: Standard deemed to offer the presumption of conformity to specific Essential Principles of safety and performance.

Technical Documentation: the documented evidence, normally an output of the quality management system, which demonstrates conformity of a device to the Essential Principles of Safety and Performance of Medical Devices.³

PART 1 – PURPOSE OF THE STED

5.0 Preparation and Use of the STED

5.1 Preparation

Manufacturers of all classes of IVD medical devices are expected to demonstrate conformity of the IVD medical device to the *Essential Principles of Safety and Performance of Medical Devices* 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 updated to reflect the current status of the IVD medical device.

For the purpose of conformity assessment, the manufacturer creates 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

³ SG1/N041:2005 Essential Principles of Safety & Performance of Medical Devices

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.

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 depend on:

- a) the classification of the subject IVD medical device;
- b) the complexity of the subject IVD medical device.

It also depends upon whether the device has the following characteristics:

- a) it incorporates novel technology;
For the purpose of STED, examples of how novel technology can be demonstrated include:

(a) there has been no such IVD medical device continuously available on any market for the relevant analyte (measurand);

(b) the procedure involves analytical technology not continuously used in connection with a given analyte (measurand) or other parameter on the market.

- b) it is an already marketed IVD medical device type that is now being offered for an intended use different from the original one;
- c) the IVD medical device type has been associated with a significant number of adverse events, including use errors⁴;
- d) it incorporates novel or potentially hazardous materials;
- e) the IVD medical device type raises specific public health concerns.

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.

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 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 are contained within the STED. The cited references to the controlled documents facilitate requests from a RA/CAB to provide additional information.

⁴ See GHTF/SG2 guidance documents.

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/CAB⁵ (see Figure 1).

NOTES:

- a) For Class A and B IVD medical devices where the STED is prepared on request, the manufacturer should be able to assemble and submit it in the timeframe indicated by the RA/CAB. A copy of any submitted STED will be held by the manufacturer for future reference.

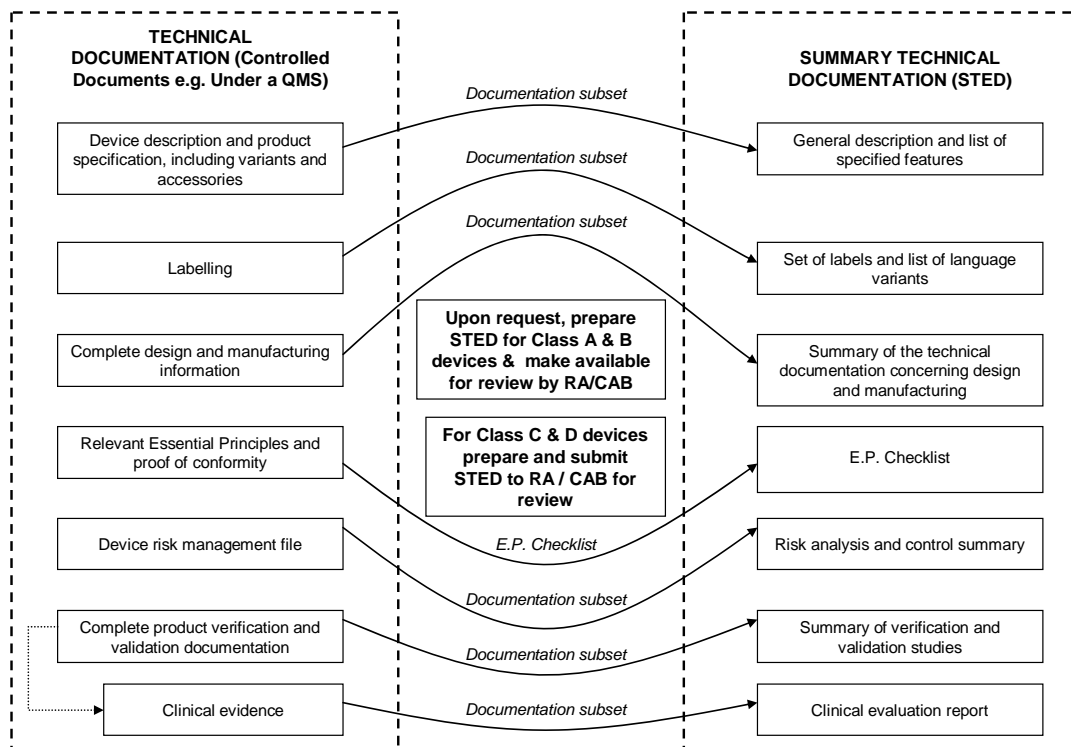


FIGURE 1: PREMARKET USE OF THE STED

⁵ See GHTF/SG1/N46:2008 Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices.

5.3 The Use of the STED in the Post-market Phase

In the post-market phase, the RA/CAB may request submission of a STED either to investigate conformity of a Class A or B IVD medical device or the continued conformity of a Class C or D IVD medical device (see Figure 2).

The STED would not typically be used to aid the postmarket investigation of adverse events, or the reporting of data from postmarket registries or studies, where different types of information are likely to be called for.

NOTES:

- a) The manufacturer should be able to prepare and submit the STED in the timeframe indicated by the RA/CAB.
- b) A copy of any submitted STED should be held by the manufacturer for future reference.

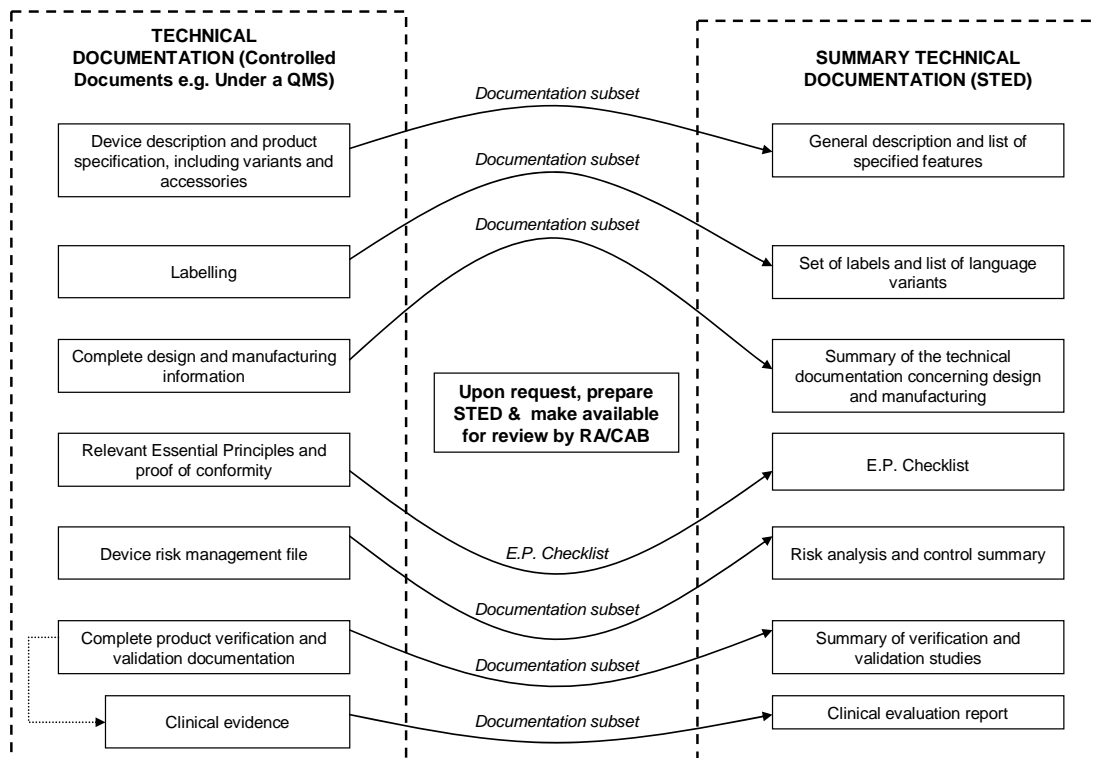


FIGURE 2: POST-MARKET USE OF THE STED

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.

PART 2 – CONTENTS OF THE STED

6.0 Device Description including Variants (Configurations) and Accessories

6.1 Device Description

The STED should include the following device descriptive information:

- a) the intended use. This may include what is detected by the assay; whether the assay is automated; what the instrument is intended for; whether the test is qualitative or quantitative, for a specific disorder, for a condition or risk factor of interest that the test is intended to detect, define or differentiate; the type of specimen(s) required (eg. serum, plasma, whole blood, tissue biopsy, urine); testing population;
- b) a clear statement of the function of the IVD medical device (screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease);
- c) a general description of the principle of the assay method or instrument principles of operation;
- d) the intended user (lay person or professional);
- e) the Class of the device and the applicable classification rule according to *Principles of In Vitro Diagnostic Medical Devices Classification*;
- f) a description of all components of the assay, including but not limited to antibodies, antigens, nucleic acid primers, buffers, assay controls and calibrators provided with the IVD medical device or recommended for use, substrates used to detect antigen-antibody complexes and reagents;
- g) a description of the specimen collection and transport materials provided with the IVD medical device or recommended for use;
- h) for instruments of automated assays : a description of the appropriate assay characteristics or dedicated assays;
- i) for automated assays : a description of the appropriate instrumentation characteristics or dedicated instrumentation;
- j) if applicable a description of any software to be used with the IVD medical device;
- k) if applicable, a description or complete list of the various configurations/variants of the IVD medical device that will be made available;
- l) if applicable, 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 Reference to Previous Device Generation(s) and/or Similar Devices or Device History

6.2.1 For an IVD medical device not yet available on any market

Where relevant to demonstrating conformity to the Essential Principles, and to provide general background information, the STED should provide a summary of:

- a) the manufacturer's previous generation(s) of the IVD medical device, if such exist; and/or
- b) the manufacturer's similar IVD medical devices available on the market.

6.2.2 For an IVD medical device already on the market in any other jurisdiction

This information may include a summary of the number of adverse event reports related to the safety and performance for this IVD medical device and the number of IVD medical devices placed on the other markets.

7.0 Essential Principles (EP) Checklist

The STED should include an EP checklist that identifies:

- a) the Essential Principles of Safety and Performance;
- b) whether each Essential Principle 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 precise identity of the controlled document/s 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 standards⁶;
- b) conformity with a commonly accepted industry test method;
- c) conformity with appropriate in-house test methods that have been validated and verified;
- d) equivalence to a manufacturer's similar 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).

A sample checklist is included in Appendix A.

⁶ See SG1/N012 *Role of Standards in the Assessment of Medical Devices*

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 contain a list of possible hazards for the IVD medical device which should include but not be limited to 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.

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 complete report would be provided.

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 components of the assay such as antibodies, antigens, enzymes, nucleic acid primers, assay controls and calibrators provided or recommended for use with the IVD medical device, substrates used to detect antigen-antibody complexes and reagents. 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 brief description of each site's activity should be provided. This information may take the form of a flow chart.

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. The information may take the form of a process flow chart showing, for example, an overview of production including the technologies used, assembly, any in-process and final product testing, and packaging of the finished IVD medical device.

9.3 Design and Manufacturing Sites

For the activities in 9.1 and 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 design and manufacturing activities). If QMS certificates, or the equivalent, exist for these sites, they may be annexed to the STED.

10.0 Product Validation and Verification

The information provided in the product validation and verification section of the STED will vary in the level of detail as determined by:

- a) the class of the device
- b) the complexity 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 validation and verification studies undertaken to demonstrate conformity of the IVD medical device with the Essential Principles that apply to it.

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 summary of the data if no acceptance criteria are specified in the standard (e.g. Electromagnetic Compatibility, Electrical safety);
- a) 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 (e.g. Clinical Laboratory Standards Institute (CLSI));
- b) 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;
- c) A review of relevant published literature regarding the device/analyte (measurand) or substantially similar IVD medical devices.

Detailed information should include:

- a) the complete study protocol,
- b) the method of data analysis,

- c) the complete study report,
- d) the study conclusion.

For clinical evidence, the detailed information will typically include raw data or line listing for a Class D IVD medical device.

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 along with a summary of the data and conclusions.

Note 1: where appropriate, actual test result summaries with their acceptance criteria should be provided and not just pass/fail statements.

10.1 Analytical Studies

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. Stability includes storage and where applicable transport conditions. Storage includes elements such as duration, temperature limits, freeze/thaw cycles.

This section should include summary information for each matrix, anticoagulant when applicable, including a description of the method for comparison or determination of 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.

10.1.2 Accuracy

This section should describe trueness and precision studies.

Note: The general term Accuracy is currently used to cover both Trueness and Precision, whereas this term was used in the past to cover only the one component now named Trueness.

While **trueness**, affected by systematic error, is normally expressed in terms of bias, and **precision**, affected by random error, is naturally expressed in terms of standard deviation, **accuracy** is affected by a combination of systematic and random effects that contribute as individual components of the total error of measurement.

10.1.2.1 Trueness

This section should provide information on the trueness of the result of the assay as determined by the following means:

- a) Comparison with a reference material of higher order, if available, including appropriate details of the reference material used and/or
- b) Use of a reference method including appropriate details of the reference method used or
- c) Conformity to a professional guideline, industry method, or in-house standard, supported by a rationale for its use and a description of the method used,

and summary of the data in sufficient detail to allow assessment of the adequacy of the selected means.

Typically for a Class C and D IVD medical device, detailed information would be provided.

10.1.2.2 Precision

This section should describe reproducibility and repeatability studies.

10.1.2.2.1 Reproducibility

This section should include reproducibility estimates and information about the studies used to estimate total variability and as appropriate between-day, between-run, between-sites, between-lots, between operators, between instrument variability.

Typically for a Class C and D IVD medical device, 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 in the target population.

Note 2: Summary information could be appropriate if a standard is used.

10.1.2.2.2 Repeatability

This section should include repeatability estimates and information about the studies used to estimate total variability and as appropriate within-run variability.

Typically for a Class C and D IVD medical device, 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 in the target population.

Note 2: Summary information could be appropriate if a standard is used.

10.1.3 Traceability of calibrators and control materials

Where applicable, summarize the information about traceability of calibrators and trueness control materials. Include, for example, methods and acceptance criteria for traceability to reference materials and a description of value assignment and validation.

Precision control materials used when establishing reproducibility do not require traceability to a reference material.

Typically for a class D IVD medical device, detailed information would be provided.

10.1.4 Analytical Sensitivity

This section should include information about the study design and results. It should provide a description of specimen type and 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), (Include mean and standard deviation),
- b) Lowest concentration at which %CV and accuracy are within specified criteria. (State these specified criteria and describe the evaluations to determine they were met).
- c) Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand). (Clarify statistical methods used and result).

Typically for a Class C and D IVD medical device, detailed information would be provided.

10.1.5 Analytical Specificity

This section should describe interference and cross reactivity studies to determine the analytical specificity.

Provide information on the evaluation of potentially interfering and cross reacting substances/agents on the assay. Information should be provided on the types and levels tested, sample type, analyte (measurand) test concentration, and results.

Typically for a Class C and D IVD medical device, detailed information would be provided.

Note: 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 substances used for patient treatment (e.g., therapeutic drugs, anticoagulants, etc.); substances ingested by the patient (e.g., over the counter medications, alcohol, vitamins, foods, etc.); substances added during sample preparation (e.g., preservatives, stabilizers); substances encountered in specific specimens types (e.g., haemoglobin, lipids, bilirubin, proteins) 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.

10.1.6 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 lower 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 a Class C and D IVD medical device, detailed information would be provided.

10.1.7 Validation of Assay Cut-off

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 clinical diagnosis to characterize specimens as being positive or negative; and

- c) statistical methods e.g. Receiver Operator Characteristic (ROC) to generate results and if applicable, define gray-zone/equivocal zone.

Typically for a Class C and D IVD medical device, detailed information would be provided.

10.2 Stability (excluding specimen stability)

This section should describe claimed shelf life, in use stability and shipping studies.

10.2.1 Claimed Shelf life

This section should provide information on stability testing studies for at least three different manufactured lots to support the claimed shelf life. Accelerated studies are acceptable for initial shelf life claim but need to be followed up with real time stability studies.

Typically for a Class C and D IVD medical device, detailed information would be provided.

Such information should describe:

- a) the study protocol used
- b) the method used for accelerated studies
- c) the study report
- d) conclusions and claimed shelf life

Note: Shelf life can be derived from the lot with the longest real time stability data as long as accelerated data from all three lots are comparable.

10.2.2 In use stability

This section should provide information on in use stability studies for one lot. 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 information should describe:

- a) the study protocol used
- b) the study report
- c) conclusions and claimed in use stability

Typically for a Class C and D IVD medical device, detailed information would be provided.

10.2.3 Shipping stability

This section should provide information on shipping stability studies for one lot.

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 protocol used
- b) method used for simulated conditions
- c) study report
- d) conclusion and recommended shipping conditions

Typically for a Class C and D IVD medical device, detailed information would be provided.

10.3 Software Verification and Validation

The STED should contain information on the software design and development process and 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.

10.4 Clinical Evidence

The STED should contain the clinical evidence that demonstrates conformity of the IVD medical device to the Essential Principles that apply to it. More detailed recommendations regarding this element of the STED will be provided in guidance developed in cooperation with SG5.

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 (revised)* and a list of language variants for the jurisdiction where the marketing authorization is being sought. 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 a pre-market STED, the labelling should contain the final content as determined by the manufacturer but does not have to be in the final (printed) format.

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 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*.

Appendix A

Essential Principles (EP) Checklist

The EP checklist can be used by Regulatory Authorities, CABs and even manufacturers themselves to readily understand how the manufacturer demonstrates compliance to the Essential Principles for a particular device. The EP checklist also allows easy identification of relevant documents and data for conformity assessment purposes.

The contents of the checklist will vary among IVD medical devices. Very simple IVD medical devices will have short EP checklists as many of the Essential Principles may not be applicable. In these cases, the supporting references to be included in the checklist will be minimal. More complex IVD medical devices are more likely to reference a larger number of standards, test reports and documents. The EP checklist in those cases might be many pages long.

The following is a recommended template for the EP checklist. Preparation of the EP checklist as outlined below will provide a useful overview of the manufacturer's conformity to the Essential Principles. The consistent use of this template will support harmonization across jurisdictions.

How to fill in the checklist

a) Identity of the IVD medical device

The manufacturer should identify the IVD medical device, and when applicable the various configurations/variants covered by the checklist.

b) Applicable to device?

Is the listed Essential Principle applicable to the IVD medical device? Here the answer is either 'Yes' or 'No'. If the answer is 'No' this should be briefly explained.

Example: For an IVD medical device that does not incorporate biological substances, the answer to Essential Principle 5.8.2 would be 'No – The IVD medical device does not incorporate biological substances'.

c) Method used to demonstrate conformity

In this column, the manufacturer should state the type(s) of method(s) that it has chosen to demonstrate conformity e.g. the recognised standard(s), industry or in-house test method(s), comparison study(ies) or other method used.

d) Method reference


After having stated the method in the previous column, here the manufacturer should name the title and reference the recognised standard(s), industry or in-house test method(s), comparison study(ies) or other method used to demonstrate conformity. For standards, this should include the date of the standard and where appropriate, the clause(s) that demonstrates conformity with the relevant EP.

e) Reference to Supporting controlled documents

This column should contain the reference to the actual technical documentation that demonstrates conformity to the Essential Principle, i.e. the certificates, test reports, study

reports or other documents that resulted from the method used to demonstrate conformity and its location within the STED.

Note: The table that follows is for illustrative purposes only. The Essential Principles listed in the first column should be extracted from the latest version of the GHTF's guidance document *Essential principles of Safety and Performance of Medical Devices*". Those incorporated into this document are extracted from GHTF/SG1/N41:2005.

Essential Principles Checklist	
Identity of IVD medical device:	

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
General Requirements				
5.1 Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.				

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>5.2 The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed:</p> <ul style="list-style-type: none"> ▪ identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse, ▪ eliminate risks as far as reasonably practicable through inherently safe design and manufacture, ▪ reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms, ▪ inform users of any residual risks. 				
<p>5.3 Devices should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions within the scope of the definition of a medical device applicable in each jurisdiction.</p>				
<p>5.4 The characteristics and performances referred to in Clauses 5.1, 5.2 and 5.3 should not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.</p>				
<p>5.5 The devices should be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.</p>				

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
5.6 The benefits must be determined to outweigh any undesirable side effects for the performances intended.				
Design and Manufacturing Requirements				
5.7 Chemical, physical and biological properties				
5.7.1 The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Clauses 5.1 to 5.6 of the 'General Requirements'. Particular attention should be paid to: <ul style="list-style-type: none"> ▪ the choice of materials used, particularly as regards toxicity and, where appropriate, flammability, ▪ the compatibility between the materials used and biological tissues, cells, body fluids, and specimens, taking account of the intended purpose of the device, ▪ the choice of materials used should reflect, where appropriate, matters such as hardness, wear and fatigue strength. 				
5.7.2 The devices should be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.				
5.7.3 ----- etc. -----				
5.7.4 ----- etc. -----				
5.7.5				
5.7.6				