



FINAL 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 17th, 2011

Table of Contents

1.0	Introduction	5
2.0	Rationale, Purpose and Scope	5
2.1	Rationale	5
2.2	Purpose	6
2.3	Scope	6
3.0	References	6
4.0	Definitions	7
5.0	Preparation and Use of the STED	8
5.1	Preparation	8
5.2	The Use of the STED in the Premarket Phase	9
5.3	The Use of the STED in the Post-market Phase	11
5.4	The Use of the STED to Notify Changes to the RA/CAB	11
6.0	Device Description including Variants (Configurations) and Accessories	12
6.1	Device Description	12
6.2	Reference to the Manufacturer's Previous Device Generation(s) and/or Similar Devices or Device History	13
6.2.1	For an IVD medical device not yet available on any market.....	13
6.2.2	For an IVD medical device already available on the market in any jurisdiction.....	13
7.0	Essential Principles (EP) Checklist	13
8.0	Risk Analysis and Control Summary	14
9.0	Design and Manufacturing Information	14
9.1	Device Design	14
9.2	Manufacturing Processes	15
9.3	Manufacturing Sites	15
10.0	Product Verification and Validation	15
10.1	Analytical Performance	17
10.1.1	Specimen type.....	17
10.1.2	Analytical performance characteristics.....	18
10.1.2.1	Accuracy of measurement.....	18
10.1.2.1.1	Trueness of measurement.....	18
10.1.2.1.2	Precision of measurement.....	18
10.1.2.2	Analytical sensitivity.....	19
10.1.2.3	Analytical specificity.....	19
10.1.2.4	Metrological traceability of calibrator and control material values.....	20

10.1.2.5	Measuring range of the assay.....	21
10.1.2.6	Definition of assay cut-off.....	21
10.2	Clinical Performance	21
10.3	Stability (excluding specimen stability)	21
10.3.1	Claimed shelf life.....	22
10.3.2	In use stability.....	22
10.3.3	Shipping stability.....	22
10.4	Software Verification and Validation	23
11.0	Labelling	23
12.0	Format of the STED	23
13.0	Declaration of Conformity	24
	Appendix A	25

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 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 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 (RAs), Conformity Assessment Bodies (CABs) 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.

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 Chair or Secretary of GHTF Study Group 1 IVD Subgroup whose contact details may be found on the GHTF website¹.

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

¹ www.ghtf.org

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 revised to reflect any changes made during the lifecycle of the IVD medical device through normal application of the manufacturer's QMS.

It is advantageous to both RAs/CABs and the regulated industry if a subset of this technical documentation is used for selected premarket and post-market 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*².

The availability of such Summary Technical Documentation (STED) 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.

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.

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*³.

3.0 References⁴

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*.

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

² SG1/N041:2005 *Essential Principles of Safety & Performance of Medical Devices*

³ SG1/N045:2007 *Principles of In Vitro Diagnostic Medical Devices Classification*

⁴ The listed documents are subject to periodic review and may be superseded by later documents. The reader is encouraged to refer to the GHTF website to confirm whether the referenced documents remain current.

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

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*⁵.

⁵ SG1/N041:2005 *Essential Principles of Safety & Performance of Medical Devices*

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*⁵ 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 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 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 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.

⁶ See SG2/N45R8:2006 *Medical Devices Post-market Surveillance: Global guidance for Adverse Reporting for Medical Devices*.

⁷ See GHTE/SG1/N46:2008 *Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices*.

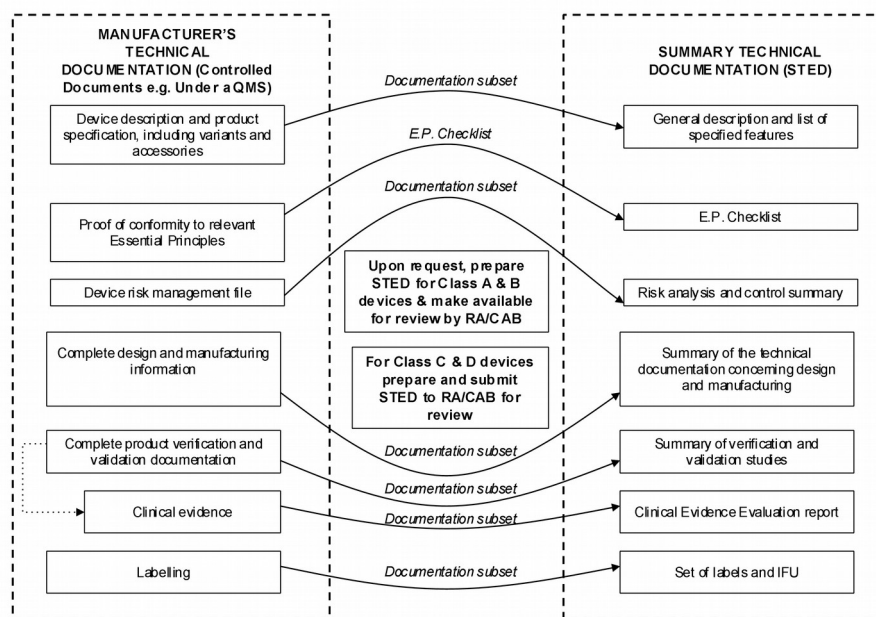


FIGURE 1: PREMARKET USE OF THE STED

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 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.

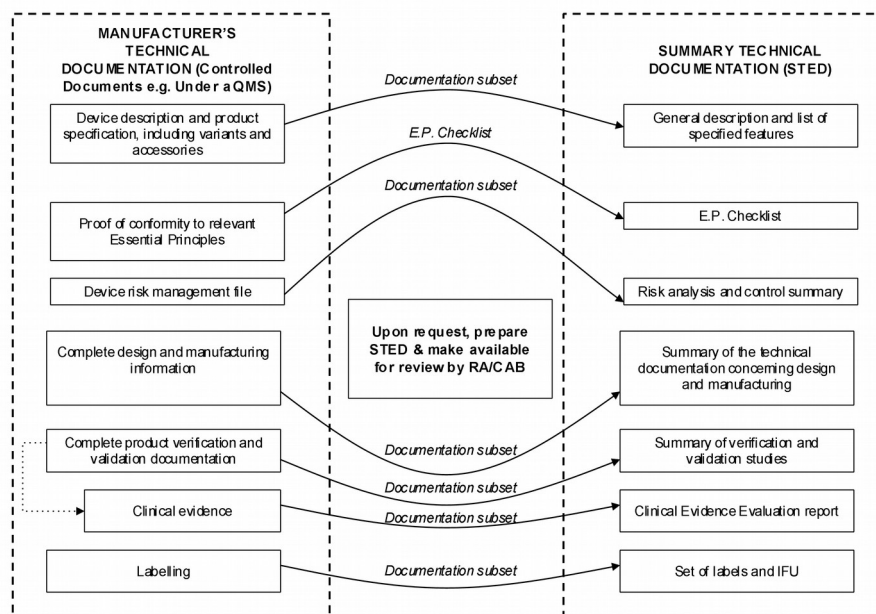


FIGURE 2: POST-MARKET USE OF THE STED

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 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);
 - 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*⁸;
- 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;

⁸ SG1/N045:2007 *Principles of In Vitro Diagnostic Medical Devices Classification*

- h) for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation;
- i) a description of any software to be used with 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 Reference to the Manufacturer's Previous Device Generation(s) and/or Similar Devices or Device History

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 may provide a summary of:

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

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

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

External certificates and documents which give written evidence of conformity with the Essential Principles may be annexed to the STED.

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 standards⁹;
- b) conformity with a commonly accepted industry test method;
- c) conformity with appropriate in-house test methods that have been validated 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).

A sample checklist is included in Appendix A.

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.

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.

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, antigens, enzymes and nucleic acid primers provided or recommended for use with the IVD medical device.

⁹ GHF/SG1/N044:2008 *Role of Standards in the Assessment of Medical Devices*

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 controlling site must be identified.

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.

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 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 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,

- 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.

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 regarding instrumentation or qualitative assays appear in the subsections.

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 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.

Analytical performance characteristics

10.1.2.1 Accuracy of measurement

This section should describe both trueness and precision studies.

Note: The general term measurement 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 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.

Accuracy is affected by a combination of systematic and random effects that contribute as individual components of the total error of measurement.

10.1.2.1.1. 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.

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.

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.

10.1.2.1.2.2. 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 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.

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 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.

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, 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.

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 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.

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.

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 zone.

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

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 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.

10.3 Stability (excluding specimen stability)

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

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 long as accelerated or extrapolated data from all three lots are comparable.

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.

Shipping stability

This section should provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated 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.

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.

11.0 Labelling

The STED should typically contain a complete set of labelling associated with the IVD medical device as described in GHF guideline *Labelling for Medical Devices*¹⁰. 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 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.

10 GHF/SG1/N43:2005 *Labelling for Medical Devices*

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.

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 should 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, if included in the STED, its location.

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. 				
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.				
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.				
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.				
5.6 The benefits must be determined to outweigh any undesirable side effects for the performances intended.				

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
Design and Manufacturing Requirements				
5.7 Chemical, physical and biological properties				
<p>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:</p> <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. 				
<p>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.</p>				
5.7.3 ----- etc. -----				
5.7.4 ----- etc. -----				
5.7.5				
5.7.6				