Asian Harmonization Working Party

WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

Draft Guidance

Common Submission Dossier Template

1.0 Introduction

The document is intended to provide guidance for submission of device information to the regulatory authorities; structured in the format of one common template acceptable by all AHWP member economies regulators. It is envisaged that a Common Submission Dossier Template (CSDT) will harmonize the differences in documentation formats that presently exist in different AHWP member economies jurisdictions. The adoption of this guidance document in AHWP member economies will eliminate the preparation of multiple dossiers, arranged in different formats but with essentially the same contents, for regulatory submission to different regulatory authorities.

2.0 Scope

This guidance document describes the format for an AHWP member economy harmonized common submission dossier template and provides general recommendation on the content of the formatted elements. This document does not recommend any new or additional technical documents above and beyond what should be created by the manufacturer[1] to comply with existing requirements to demonstrate conformity to the Essential Principles [GHTF SG1/N041], and to address any country-specific requirements.

This document applies to all products that fall within the definition of a medical device[2] (See Appendix A).

Essentially, the CSDT contains elements of the Summary Technical Documentation (STED) [GHTF SG1/N011R17][3] for demonstrating conformity to the Essential Principles of Safety and Performance of Medical Devices.

The format of the CSDT recommended herein is based upon the goal of both regulators and manufacturers to strive for the least burdensome means to demonstrate conformity to the Essential Principles for all classes of medical devices.

Requirements for post-market vigilance or adverse event reporting are outside the scope of this

1 "Manufacturer" must be understood as including the legal manufacturer, its authorized representative or any other person who is responsible for placing the device on the market.

2 GHTF/SG1/N29R16:2005, Information Document Concerning the Definition of the Term "Medical Device"

3 Text in italics in this document are similar to those in the GHTF STED Document

document.

3.0 Executive Summary

An executive summary shall be provided with the common submission dossier template, which shall include the following information:

- an overview, e.g., introductory descriptive 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;
- commercial marketing history;
- intended uses and indications in labelling;
- list of regulatory approval or marketing clearance obtained;
- status of any pending request for market clearance; and
- important safety/performance related information.

4.0 Elements of the Common Submission Dossier Template

4.1 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.*

4.1.1 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 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.

4.2 *Device Description* (According to GHTF Classification)

Description	**A**	**B**	**C**	**D**
Device Description				
Intended Use/Indications for Use				
Product Drawing/Product Brochure				
Material/Component List				
Statement on Shelf Life (Sterile Product only)				

(The aforementioned matrix is in its draft form; it describes the type and amount of information to be submitted for the various classes of devices. The draft matrix is to be discussed further, pending consensus on adoption of a 4-class risk based classification system.)

4.2.1 *Device description* & 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 *labelled pictorial representation of the device* in the form of *diagrams, photographs or drawings*, as appropriate.

4.2.2 *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.

4.2.3 *Indications*

This is a general description of the disease or condition that the device will diagnose, treat, prevent, cure or mitigate and includes a description of the target patient population for which the device is intended.

4.2.4 *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 shall, to the extent possible, be included on the device itself and/or on its packaging by other formats / forms.

4.2.5 *Contraindications*

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. Contraindications are conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit.

4.2.6 Warnings

This is the specific hazard alert information that a user needs to know before using the device.

4.2.7 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.

4.2.8 Potential adverse effects

These are potential undesirable and serious outcomes (death, injury, or serious adverse events) to the patient/user, or side effects from the use of the medical device, under normal conditions.

4.2.9 Alternative therapy

This is a description of any alternative practices or procedures for diagnosing, treating, curing or mitigating the disease or condition for which the device is intended.

4.2.10 *Materials*

A description of the materials of the device and their physical properties to the extent necessary to demonstrate conformity with the relevant Essential Principles. The information shall include complete chemical, biological and physical characterization of the materials of the device.

4.2.11 Other Relevant *Specifications*

The functional characteristics and technical performance specifications for the device including, as relevant, accuracy, sensitivity, specificity of measuring and diagnostic 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.

4.2.12 Other Descriptive Information

Other important descriptive characteristics not detailed above, to the extent necessary to demonstrate conformity with the relevant Essential Principles (for example, the biocompatibility category for the finished device).

NOTE: For simple, low risk devices, the above information will typically be contained in already existing sales brochures, instructions for use, etc.

4.3 Summary of Design Verification and Validation Documents

This section *should summarize or reference or contain design verification and design validation data to the extent appropriate to the complexity and risk class of the device*:

Such documentation should typically include:

- *declarations/certificates of conformity to the "recognized" standards listed as applied by the manufacturer; and/or*
- *summaries or reports of tests and evaluations based on other standards, manufacturer methods and tests, or alternative ways of demonstrating compliance.*

EXAMPLE: *The completed Table of Conformity to the Essential Principles that a recognized test standard was used as part of the method to demonstrate conformity to one Essential Principle*. Section 3.0 of the CSTD would then *include a declaration of conformity to the standard, or other certification permitted by the relevant Regulatory Authority, and a summary of the test data, if the standard does not include performance requirements.*

The data summaries or tests reports and evaluations would typically cover, as appropriate to the complexity and risk class of the device:

- *a listing of and conclusions drawn from published reports that concern the safety and performance of aspects of the device with reference to the Essential Principles;*
- *engineering tests;*
- *laboratory tests;*
- *biocompatibility tests;*
- *animal tests;*
- *simulated use;*
- *software validation.*

4.3.1 Pre-clinical Studies

Details must be provided on all biocompatibility tests conducted on materials used in a device. At a minimum, tests must be conducted on samples from the finished, sterilized device. All materials that are significantly different must be characterized. Information describing the tests, the results and the analyses of data must be presented.

Complete pre-clinical physical test data must be provided, as appropriate. The report must include the objectives, methodology, results and manufacturer's conclusions of all physical studies of the device and its components. Physical testing must be conducted to predict the adequacy of device response to physiological stresses, undesirable conditions and forces, long-term use and all known and possible failure modes.

Pre-clinical animal studies used to support the probability of effectiveness in humans must be reported. These studies must be undertaken using good laboratory practices. The objectives, methodology, results, analysis and manufacture's conclusions must be presented. The study conclusion should address the device's interactions with animal fluids and tissues and the functional effectiveness of the device in the experimental animal model(s). The rationale (and limitations) of selecting the particular animal model should be discussed.

4.3.1.1 Software Validation Studies (if applicable)

The correctness of a software product is another critical product characteristic that cannot be fully verified in a finished product. The manufacturer and/or device sponsor must provide evidence that validates the software design and development process. This information should 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 labelling, as well as

representative data generated from both testing environments.

4.3.1.2 Devices Containing Biological Material

Results of studies substantiating the adequacy of the measures taken with regards to the risks associated with transmissible agents must be provided. This will include viral clearance results for known hazards. Donor screening concerns must be fully addressed and methods of harvesting must also be fully described. Process validation results are required to substantiate that manufacturing procedures are in place to minimize biological risks.

4.3.2 *Clinical Evidence*

This section *should indicate how any applicable requirements of the Essential Principles for clinical evaluation of the device have been met. Where applicable, this evaluation may take the form of a systematic review of existing bibliography, clinical experience with the same or similar devices, or by clinical investigation. Clinical investigation is most likely to be needed for higher risk class devices, or for devices where there is little or no clinical experience.*

4.3.2.1 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 references. General bibliographic references should be 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. The conclusions on the outcome of the clinical studies should be preceded by a discussion in context with the published literature.

4.4 Device *Labelling*

This is the descriptive and informational product literature that accompanies the device any time while it is held for sale or shipped, such as any physician's manuals, pack labeling, promotional material and product brochures etc. This section *should summarize or reference or contain the following labelling data to the extent appropriate to the complexity and risk class of the device, which is generally considered as "labelling"*:

- Sample of labels on the device and its packaging

- Instructions for use
- Other literature or training materials
- Instructions for installation and maintenance (if applicable).
- Any information and instructions given to the patient, including instructions for any procedure the patient is expected to perform (if applicable).

4.4.1 Samples of Labels on the 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 labelling, 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.

4.4.2 Instructions for Use, Training Materials & Instructions for Installation and Maintenance

The instructions for use is commonly referred to as the physician's manual, user manual, operator's manual, prescriber's manual 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 device. Where applicable, this section should include instructions for training of the end-users for competent use of the device for its intended purpose, as well as installation and maintenance of the device.

4.5 *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.*

4.5.1 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 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 device and the risk involved.

4.6 *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 device.*

4.6.1 Manufacturing Process

Manufacturing process for the 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 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 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 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 should inform these contractors of the need to supply detailed information on the 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 device itself.

References

SG1/N009 *Labeling for Medical Devices*
SG1/N015 *Medical Devices Classification*
SG1/N029 *Information Document Concerning the Definition of the Term 'Medical Device'.*

SG1/N041	*Essential Principles of Safety and Performance of Medical Devices (including In Vitro Diagnostic Devices)*
SG1/N043	*Labeling for Medical Devices (including In Vitro Diagnostic Devices)*
SG1/N011R17	*Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED)*

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APPENDIX A – GHTF Definition of a Medical Device

GHTF/SG1/N29R16:2005, Information Document Concerning the Definition of the Term "Medical Device"

"Medical device" means any instrument, apparatus, implement, machine, appliance, implant, *in vitro reagent* or calibrator, software, material or other similar or related article:-

a) intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:
· diagnosis, prevention, monitoring, treatment or alleviation of disease,
· diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
· investigation, replacement, modification, or support of the anatomy or of a physiological process,
· supporting or sustaining life,
· control of conception,
· disinfection of medical devices,
· providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body;

and

b) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.

The definition of a device for *in-vitro* examination includes, for example, reagents, calibrators, sample collection and storage devices, control materials, and related instruments or apparatus. The information provided by such an *in-vitro* diagnostic device may be for diagnostic, monitoring or compatibility purposes. In some jurisdictions, some *in-vitro* diagnostic devices, including reagents and the like, may be covered by separate regulations.

1 ***APPENDIX B - Example of an Essential Principles Conformity Checklist***

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Essential Principle	Applicable to the device?	Method of Conformity[4]	Identity of Specific Documents
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.	Yes		
2. The solutions adopted by the manufacturer for the design and construction of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. In selecting the most appropriate solutions, the manufacturer should apply the following principles in the following order: • identify hazards and the associated risks arising from the intended use and foreseeable misuse, • eliminate or reduce risks as far as possible (inherently safe design and construction), • where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated, • inform users of the residual risks due to any shortcomings of the protection measures adopted.	Yes		
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.	Yes		
4. The characteristics and performances referred to in Clauses 1, 2 and 3 should not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the	Yes		

[4] Select from: recognised standard/other international standard/national standard/company standard/validated test/ etc.

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. 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 during transport and storage taking account of the instructions and information provided by the manufacturer.	Yes		
6. The benefits must be determined to outweigh any undesirable side-effects for the performances intended.	Yes		
7.1. The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Section I of the 'General Requirements'. Particular attention should be paid to: • the choice of materials used, particularly as regards toxicity and, where appropriate, flammability, • the compatibility between the materials used and biological tissues, cells and body fluids, 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.			
7.2. The devices should be designed, manufactured and packed in such a way as to minimise the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients, taking account of the intended purpose of the product. Particular attention should be paid to the tissues exposed and to the duration and frequency of exposure.			
7.3. Etc.			
8. Etc.			
9. Etc.			

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