Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

PROPOSED FINAL DOCUMENT

Title: Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices

Authoring Group: Work Group 2, Pre-market: IVDD

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Preface

This document is produced by the Asian Harmonization Working Party, based on the Global Harmonization Task Force Final Document GHTF/SG1/N046: 2008 of GHTF Study Group 1. The document is intended to provide non-binding guidance for use in the regulation of medical devices including In Vitro Diagnostic (IVD) medical devices, and has been subject to consultation throughout its development.

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1.0 Introduction

The objective of the Asian Harmonization Working Party (AHWP) is to encourage convergence at the worldwide level in the evolution of regulatory systems for medical devices, including In Vitro Diagnostic (IVD) medical devices in order to protect the public health by those regulatory means considered the most suitable.

The primary way in which the Asian Harmonization Working Party (AHWP) achieves its goals is through the production of harmonized guidance documents suitable for implementation or adoption by member Regulatory Authorities, as appropriate taking into account their existing legal framework, or by member economies with developing regulatory programmes. Eliminating differences between jurisdictions decreases the cost of gaining regulatory compliance and allows patients earlier access to new technologies and treatments.

This document should be read in conjunction with the AHWP document on *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*. The linked adoption of documents on classification and conformity assessment is important to ensure a consistent approach across all countries/regions adopting the global regulatory model recommended by the AHWP, so that premarket approval for a particular IVD medical device may become acceptable worldwide.

This document has been developed to encourage and support convergence of regulatory systems at the worldwide level. 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.

Regulatory Authorities that are developing conformity assessment schemes or amending existing ones are encouraged to consider the adoption of the system described in this document, as this will help to reduce the diversity of schemes worldwide and facilitate the process of harmonization.

Work Group 2 of the AHWP has prepared this guidance document. Comments or questions should be directed to the Chair of AHWP Work Group 2 whose contact details may be found on the AHWP web page (http://www.ahwp.info/).

2.0 Rationale, Purpose and Scope

2.1 Rationale

Regulatory systems are intended to ensure a high level of protection of public health and safety.

Public trust and confidence in IVD medical devices, and in the administrative systems by which they are regulated, are based on the safety and performance of such products throughout their life cycle.

Conformity assessment, conducted before and after an IVD medical device is placed on the market, and post-marketing surveillance of IVD medical devices in use are complementary elements of the AHWP global regulatory model. These complementary elements are intended to provide the objective evidence of safety and performance, benefits and risks, to maintain public confidence.

Conformity assessment is primarily the responsibility of the IVD medical device manufacturer. However, it is done in the context of the established regulatory requirements and both the process and conclusions are subject to further review by the Regulatory Authority and/or Conformity Assessment Body.

In general, the degree of involvement of the Regulatory Authority or Conformity Assessment Body in such reviews is proportional to the risks associated with a particular category of devices.

The inter-relationship between device class and conformity assessment is critical in establishing a consistent approach across all countries/regions adopting AHWP principles, so that the premarket approval process and evidence requirements for a particular IVD medical device are acceptable globally. This document provides guidance on the principles of conformity assessment for IVD medical devices. It should be read in conjunction with the AHWP document on *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification* that recommends rules to assist a manufacturer to allocate its IVD medical device to one of four risk classes. The procedures indicated in this document reflect the need to make conformity assessment more rigorous as the risk class of an IVD medical device increases.

2.2 Purpose

To describe:

- An overview of the available conformity assessment elements to demonstrate conformity to the *Essential Principles of Safety and Performance of IVD Medical Devices*;
- the conformity assessment elements that should apply to each class of device such that the regulatory demands are proportional to the risk class of the IVD medical device;

- the manufacturer's responsibilities to provide evidence that the IVD medical device is safe and performs as intended by the manufacturer;
- the responsibilities of a Regulatory Authority (RA), or Conformity Assessment Body (CAB) appointed by or acting on behalf of the RA, to confirm that the conformity assessment elements are properly applied by the manufacturer.

2.3 Scope

This document applies to all products that fall within the definition of an IVD medical device.

3.0 References

AHWP/WG1a/F001:2013 (now restructured to WG2) *AHWP Regulatory Framework for IVD Medical Devices*

AHWP/WG1a/F002:2013 (now restructured to WG2) *Essential Principles of Safety and Performance of IVD Medical Devices*

AHWP/WG2-WG8/F002:2014 *Role of Standards in the Assessment of Medical Devices*

AHWP/WG2_WG1/F001:2015 *Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device'*

AHWP/WG2/WD001:2016 *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*

AHWP/WG2/WD003:2016 *Submission Dossier for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices*

GHTF/SG2/N054:2006 *Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices*

GHTF/SG3/N010:2004 *Quality Management Systems – Process Validation Guidance*

GHTF/SG4/N028:1999 *Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers – Part1: General Requirements*

GHTF/SG4/N024:2002 *Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers: General Requirements – Supplement No. 4 – Compilation of Audit Documentation (Clause 5.7)*

4.0 Definitions

Audit: Systematic, independent, documented process for obtaining records, statements of fact or other relevant information and assessing them objectively to determine the extent to which specified requirements are fulfilled.

For the purpose of these guidelines, "audit" means audit of the auditee's quality management system to determine compliance with the relevant regulatory requirements.

Authorized Representative: means any natural or legal person established within a country or jurisdiction who has received a mandate from the manufacturer to act on his behalf for specified tasks with regard to the latter's obligations under that country or jurisdiction's legislation.

Conformity Assessment: the systematic examination of evidence generated and procedures undertaken by the manufacturer, under requirements established by the Regulatory Authority, to determine that a medical device is safe and performs as intended by the manufacturer and, therefore, conforms to the *Essential Principles of Safety and Performance of IVD Medical Devices.*

Conformity Assessment Body (CAB): a body engaged in the performance of procedures for determining whether the relevant requirements in technical regulations or standards are fulfilled. A CAB is authorized to undertake specified conformity assessment activities by a RA that will ensure performance of the CAB is monitored and, if necessary, withdraw designation.

Recognised Standards: standards deemed to offer the presumption of conformity to specific essential principles of safety and performance

Regulatory Authority (RA): a government body or other entity that exercises a legal right to control the use or sale of medical devices within its jurisdiction, and that may take enforcement action to ensure that medical products marketed within its jurisdiction comply with legal requirements.

Submission Dossier: a formatted compilation of documents and elements of the technical documentation to be submitted for conformity assessment purposes

Technical Documentation: the documented evidence, normally an output of the quality management system that demonstrates compliance of a device to the *Essential Principles of Safety and Performance of IVD Medical Devices*.

5.0 Conformity Assessment Elements

The conformity assessment elements that the RA may include in a conformity assessment system are:

- a quality management system
- a system for post-market surveillance
- a submission dossier

- a declaration of conformity
- the registration of manufacturers and their IVD medical devices by the RA.

All five elements are applicable to each of the device classes. The RA may provide alternatives within a conformity assessment element. When alternatives are provided, the manufacturer may choose the one that is appropriate.

The conformity assessment elements that appear in this Section describe the tasks of the manufacturer and, where appropriate, the responsibilities of the RA or CAB. Specific guidance on the conformity assessment elements for each device class is provided in the tables in Section 6.2.

5.1 Quality management system (QMS)

The requirements for a quality management system that is accepted by RAs for regulatory purposes and based on international recognised standards[1] for medical devices, such as the widely-adopted ISO 13485[2], combined with the other conformity assessment elements, are intended to ensure that IVD medical devices will be safe and perform as intended by the manufacturer.

A manufacturer needs to demonstrate its ability to provide IVD medical devices that consistently meet both customer and regulatory requirements. Manufacturers demonstrate compliance through an established and effectively implemented quality management system that meets the regulatory requirements.

The scope and complexity of the quality management system that a manufacturer needs to establish is influenced by varying needs, objectives, the products provided, processes employed, the size and structure of the organisation, and the specific regulatory requirements.

Processes required by the quality management system but carried out on the manufacturer's behalf by third parties remain the responsibility of the manufacturer and are subject to control under the manufacturer's quality management system. The RA/CAB should assess the adequacy of this control as part of the conformity assessment process.

The extent of the RA/CAB assessment of the manufacturer's quality management system is influenced by the class of the IVD medical device.

For Class B, C and D devices, the RA or CAB needs to be satisfied that the manufacturer has an effective quality management system in place, appropriate for the device under assessment. In doing this, the RA or CAB will consider any relevant existing certification and, if not satisfied, e.g. with its scope or with post-market performance history, may carry out an on-site audit of the manufacturer's facility. The RA may issue separate guidance on the acceptance by CABs of existing certification.

[1]AHWP/WG2-WG8/F002:2014 *Role of Standards in the Assessment of Medical Devices*
[2]AHWPTC/OB/R001:2014 *Asian Harmonization Working Party Playbook for Implementation of Medical Device Regulatory Frameworks*

Manufacturers of Class C and D devices should have a full quality management system that includes design and development. Manufacturers of Class B devices should have a quality management system also; however, the procedures incorporated within it may not necessarily include design and development activities. Manufacturers of Class A devices are expected to have the basic elements of a QMS in place but need not include design and development activities.

The QMS for manufacturers of Class A devices is normally not subject to premarket on-site audit by the RA or CAB.

5.2 System for post market surveillance

Prior to placing the product on the market, the manufacturer will put in place, as part of its quality management system, a process to assess the continued conformity of the device to the *Essential Principles of Safety and Performance* throughout the IVD medical device lifecycle. This process will include, at a minimum, complaint handling, vigilance reporting, and corrective and preventive action[3].

The RA or CAB may confirm that such a process is in place, usually at the time of the quality management system audit[4].

5.3 Technical documentation

The technical documentation provides the evidence that the IVD medical device meets the Essential Principles.

For the purposes of conformity assessment, the manufacturer will establish a submission dossier to be prepared and submitted as required by the class of the device. A description of the submission dossier is provided in the AHWP guidance document: *Submission Dossier for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices.* The scope and the required evidence in a submission dossier will be dependent on the class of the IVD medical device and its complexity.

The RA or CAB determines the adequacy of the documented evidence in support of the manufacturer's Declaration of Conformity to the Essential Principles through a review of the submission dossier. The depth and the timing of the review are likely to be influenced by the risk class of the IVD medical device and its complexity.

5.4 Declaration of conformity

One element of the AHWP regulatory framework for IVD medical devices requires that the manufacturer attest that its IVD medical device complies fully with all applicable *Essential Principles for Safety and Performance* as documented in a written 'Declaration of Conformity' (DOC).

[3] See AHWP/WG4 guidance documents
[4] Further details are provided in the AHWP guidance documents issued by Work Groups 6 and 7.

At a minimum, this declaration should contain the following information:

- A statement that each device that is the subject of the declaration:
  - complies with the applicable *Essential Principles for Safety and Performance*,
  - has been classified according to the classification rules[5], and
  - has met all the applicable conformity assessment elements.
- Information sufficient to identify the device/s to which the Declaration of Conformity applies.
- The risk class allocated to the device/s after following the guidance found in *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*.
- Which of the conformity assessment procedures described in Section 6.2 have been applied.
- The date from which the Declaration of Conformity is valid.
- The name and address of the device manufacturer.
- The name, position and signature of the responsible person who has been authorised to complete the Declaration of Conformity upon the manufacturer's behalf.

The RA or CAB may review and confirm the adequacy of the Declaration of Conformity, if required, by examining the supporting documents or other evidence.

5.5 Registration of manufacturers and their IVD medical devices by the Regulatory Authority

Registration of both the manufacturers and their IVD medical devices by the RA is considered to be the most basic level of regulatory control of devices in the market. This registration system will identify the IVD medical devices and the party responsible for the IVD medical devices within the particular jurisdiction, thereby facilitating any regulatory activity.

Prior to placing an IVD medical device on the market, the manufacturer, its local distributor or its Authorized Representative should provide the Regulatory Authority with the required information.

The RA will maintain the register.

6.0 Harmonized Conformity Assessment System

6.1 The relationship between conformity assessment and device classification

It is recommended that each IVD medical device be allocated to one of four classes, using a set of rules as defined in the AHWP document *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*. Class A devices are the lowest risk devices, Class B are moderate to low risk, Class C are moderate to high risk and Class D devices present the

[5] See AHWP/WG2 /WD001:2016 *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*.

highest risk. The level of scrutiny and evidence needed to demonstrate that the IVD medical device meets the *Essential Principles of Safety and Performance* and conformity assessment procedures should be proportional to the risk class of the IVD medical device.

This principle is illustrated in the tables that follow. The tables identify available conformity assessment elements and propose a combination of those elements that may be applied to different classes of IVD medical devices to construct a harmonized conformity assessment system that may be adopted as part of the AHWP regulatory framework for IVD medical devices. Where the RA provides alternatives within conformity assessment elements, e.g. the quality management system for a Class A or Class B device may be either a full quality management system or one without design and development control, the manufacturer may choose the one that it is appropriate.

6.2 Conformity assessment system

The four tables below summarise conformity assessment elements that apply to Class A, B, C and D devices.

CLASS "A" DEVICE

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS or a QMS without design and development controls.	Premarket regulatory audit not required.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to AHWP WG4 guidance.	May audit post-market to investigate specific safety or regulatory concerns.	5.2
Technical Documentation	Upon request prepare submission dossier.	Premarket submission of submission dossier not required. May be requested to investigate specific safety or regulatory concerns.	5.3
Declaration of Conformity	Prepare, sign and maintain.	On file with the manufacturer; available upon request.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.	5.5

CLASS "B" DEVICE

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS or a QMS without design and development controls.	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to AHWP WG4 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.	5.2
Technical Documentation	Upon request prepare submission dossier.	Premarket submission normally not required but if requested, receive and conduct a review of the submission dossier to determine conformity to Essential Principles.	5.3
Declaration of Conformity	Prepare, sign and submit.	Review and verify compliance with requirements.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.	5.5

CLASS "C" DEVICE

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS.	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to AHWP WG4 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.	5.2
Technical Documentation	Prepare and submit submission dossier for review.	Receive and conduct a premarket review of the submission dossier to determine conformity to Essential Principles.	5.3
Declaration of Conformity	Prepare, sign and submit.	Review and verify compliance with requirements.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.	5.5

Note: Although the RA/CAB responsibilities for Class C and Class D IVD medical devices are the same, it needs to be understood that the submission dossier for a Class C IVD medical device will contain less elaborate information than the submission dossier for a Class D device. The main difference for a Class D submission dossier would be in the level of details in the clinical/performance data and details of the manufacturer's QC release program. The RA/CAB should in the review process not normally require more elaborate information for a Class C device however this does not preclude the RA/CAB from requesting such information in specific cases.

CLASS "D" DEVICE

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS.	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to AHWP WG4 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.	5.2
Technical Documentation	Prepare and submit submission dossier for review. A submission dossier for this class should contain more extended information such as full performance evaluation reports.	Receive and conduct a premarket review of the submission dossier to determine conformity to Essential Principles.	5.3
Declaration of Conformity	Prepare, sign and submit.	Review and verify compliance with requirements.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.	5.5

Note: Although the RA/CAB responsibilities for Class C and Class D IVD medical devices are the same, it needs to be understood that the submission dossier for a Class C IVD medical device will contain less elaborate information than the submission dossier for a Class D device. The main difference for a Class D submission dossier would be in the level of details in the clinical/performance data and details of the manufacturer's QC release program. The RA/CAB should in the review process not normally require more elaborate information for a Class C device however this does not preclude the RA/CAB from requesting such information in specific cases.

6.3 Conformity assessment considerations

There are situations when characteristics of the device and/or its manufacturer may cause the RA or CAB, by exception, to modify particular requirements of the elements of conformity assessment.

For example:

- This may include deferring the review of the submission dossier for Class C/D devices until a subsequent regulatory audit.

- The RA or CAB may exempt the manufacturer from making a complete premarket submission and/or conduct an audit that is more limited in scope than would normally apply to a device of that class when:

  - the device incorporates well-established technology that is already present in the market;
  - the RA and/or CAB is familiar with the manufacturer's capabilities and its products;
  - the device is an updated version of a compliant device from the same manufacturer and it contains no substantive change;
  - the RA/CAB has particular experience with a comparable device;
  - internationally recognised standards[6] are available to cover the main aspects of the device and have been used by the manufacturer.

Similarly, the RA or CAB may require a more detailed premarket submission and/or require a more rigorous audit and/or the provision of more performance evaluation data than would normally apply to a device of that risk class when:

- the device incorporates innovative technology;
- an existing compliant device is being proposed for a new intended use;
- the manufacturer's experience level with the type of IVD medical device is limited;
- the device type tends to be associated with an excessive number of adverse events, including use errors;
- the device incorporates innovative or potentially hazardous materials;
- the device type raises specific public health concerns.

It should be emphasised that there must be a fully justified and documented case before the RA or CAB modifies in any way the relationship between device class and the associated conformity assessment procedure. Where there is justification for variation to the conformity assessment procedures normally applicable to a particular device class, a statement in this regard should be included in the submission dossier.

[6] AHWP/WG2-WG8/F002:2014 *Role of Standards in the Assessment of Medical Devices*