

**Section 3C**



**QCI - AIMED Voluntary Initiative on  
Medical Devices**

**Indian Certification of Medical Devices  
(ICMED) Scheme**

**Certification Criteria for  
ICMED 13485 Plus**

## Certification Criteria for ICMED 13485 Plus

### 1. Introduction

- 1.1 This document describes the requirements against which voluntary product certification can be obtained under the Indian Certification of Medical Devices (ICMED Plus) for Medical Devices to assure the safety, quality, and performance of medical devices.
- 1.2 All requirements of this document are generic and are intended to be applicable to all medical devices, regardless of type, size and intended use.
- 1.3 If any requirement(s) of this document is (are) not applicable due to the nature of the medical device or manufacturing method for which the requirements are applied, the manufacturer does not need to address such a requirement(s) and appropriate justification shall be recorded, provided such exclusions do not affect the device's ability, or manufacturer's responsibility, to provide a device that meets 'essential requirements for safety and performance', customer, and applicable statutory and regulatory requirements.

### 2. Scope

- 2.1 This document specifies the requirements, under clauses 4.0 to clause 20.00, for demonstrating the medical device/*in vitro* diagnostic medical device conformance to relevant essential safety and performance principles that when met, indicate a medical device is safe and performs as intended.
- 2.2 This document may also be used as guidance by medical device manufacturers, test and evaluation laboratories, standards development organizations, regulatory authorities, and conformity assessment bodies.

### 3. Definitions

#### 3.1 Medical Device

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purposes(s) of:

- i. diagnosis, prevention, monitoring, treatment or alleviation of disease,
- ii. diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- iii. investigation, replacement, modification, or support of the anatomy or of a physiological process,
- iv. supporting or sustaining life,
- v. providing information by means of *in vitro* examination of specimens derived from the human body,

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

The following products shall also be deemed to be medical devices:

- vi. devices for the control or support of conception,
- vii. products specifically intended for the cleaning, disinfection, or sterilization of devices.

### 3.2 ***In Vitro* Diagnostic (IVD) Medical Device**

'In Vitro Diagnostic (IVD) medical device' means a medical device, whether used alone or in combination, intended by the manufacturer for the *in vitro* examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes.

**Note 1:** IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.

### 3.3 **Basic standard (also known as horizontal standard)**

Standard that includes fundamental concepts or principles and specifies requirements with regard to general aspects applicable to a wide range of products, processes, or services

*Examples of basic standards include standards concerning risk management, clinical investigation and the quality management system for the manufacture of medical devices*

### 3.4 **Group standard (also known as semi-horizontal standard)**

Basic standard that specifies safety and performance criteria applicable to several or a family of similar products, processes, or services.

*Examples of group standards include safety standards or standards specifying requirements for a process, such as biological evaluation, general requirements for basic safety and essential performance for medical electrical equipment, sterilization, and usability.*

### 3.5 **Product standard (also known as vertical standard)**

Standard that specifies necessary safety and performance requirements for a specific or a family of product(s), process(es), or service(s) referring, as far as possible, to basic standards and group standards

*Examples of product standards include standards for defibrillators, hip implants, and respiratory gas monitors.*

***Refer Medical Device Rules 2017 for other definitions.***

## 4. **Classification of medical devices**

- 4.1 The determination of class shall be based on the potential of a medical device to cause harm to a patient or user as a combination of the probability of occurrence of harm and the severity of that harm (i. e. the risk it presents) and thereby on its intended use and the technologies it utilizes.

- 4.2 The manufacturer shall appropriately classify the medical device on the basis of GHTF risk class as determined using IAF ID13:2017 - IAF Medical Device Nomenclature (IAF MDN) including Medical Device Risk Classification, namely:
- 4.2.1. low risk - Class A
  - 4.2.2. low moderate risk- Class B,
  - 4.2.3. moderate high risk- Class C,
  - 4.2.4. high risk- Class D.
- 4.3 The risk classifications shall be assigned according to risk rules used in the document GHTF/SG1/N77:2012 - Principles of Medical Devices Classification. Further to these GHTF classification rules, EU MDR 2017 defines additional special rules (Refer Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017).
- 4.4 The manufacturer shall use the device name, category, and class of Medical Device as determined using IAF ID13:2017 - IAF Medical Device Nomenclature (IAF MDN).

## **5. Device Description and Product Specification, Including Variants and Accessories**

### **5.1 For other than *in vitro* medical devices**

- 5.1.1 The manufacturer shall define and document a device description, with following details:
- 5.1.2 general description including its generic name, model name, model no., materials of construction, intended use, indications, instructions for use, contraindications, warnings, precautions, and potential adverse effects.
- 5.1.2.1. the intended patient population and medical condition to be diagnosed or treated and other considerations such as patient selection criteria.
  - 5.1.2.2. principle of operation or mode of action.
  - 5.1.2.3. an explanation of any novel features.
  - 5.1.2.4. a description of the accessories, other medical device and other product that are not medical device, which are intended to be used in combination with it and it shall also be clarified whether these accessories or device are supplied as a system or separate components.
  - 5.1.2.5. a description or complete list of the various configurations or variants of the device that will be made available.
  - 5.1.2.6. Complete label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging.
  - 5.1.2.7. a general description of the key functional elements, e. g. its parts or components (including software if appropriate), its formulation, its composition, its functionality and where appropriate, this will include, labelled pictorial representations (e. g. diagrams, photographs, and drawings), clearly indicating key parts or components, including sufficient explanation to understand the drawings and diagrams.
  - 5.1.2.8. a description of the materials incorporated into key functional elements and those making either direct contact with a human body or indirect contact with the body, e.g., during extracorporeal circulation of body fluids. Complete chemical, biological and physical characterization of the material (s) of the medical device
  - 5.1.2.9. for medical devices intended to emit ionizing radiation, information on radiation source (e. g. radioisotopes) and the material used for shielding of unintended, stray, or scattered radiation from patients, users and other persons shall be provided.

- 5.1.3 The manufacturer shall define and document a device specification to be made available to the end user, e. g. in brochures, catalogues etc. The specification shall contain a list of the features, dimensions and performance attributes of the medical device, its variants, and accessories.
- 5.1.4 the rationale for the qualification of the product as a device; and the risk class of the device and the justification for the classification rule(s) applied in accordance.
- 5.1.5 The manufacturer shall provide information on:
  - 5.1.5.1. the manufacturer's previous generation of the device, if it exists,
  - 5.1.5.2. predicate devices available on the Indian and international markets, and
  - 5.1.5.3. comparative analysis to prove substantial equivalence to the predicate device(s), if claimed.

## 5.2 For *In Vitro* Diagnostic Medical Device

- 5.2.1 The manufacturer shall define and document a device description, with following details:
  - 5.2.1.1. it may include:
    - a. what is detected.
    - b. its function.
    - c. the specific disorder, condition, or risk factor of interest that it is intended to detect, define, or differentiate.
    - d. whether it is automated or not.
    - e. whether it is qualitative or quantitative.
    - f. the type of specimen required (e. g. serum, plasma, whole blood, tissue biopsy, urine).
    - g. testing population.
  - 5.2.1.2. the intended user.
  - 5.2.1.3. a general description of the principle of the assay method.
  - 5.2.1.4. the risk-based Class of the device.
  - 5.2.1.5. 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) where applicable.
  - 5.2.1.6. a description of the specimen collection and transport materials provided with the *in vitro* diagnostic medical device or descriptions of specifications recommended for use.
  - 5.2.1.7. for instruments of automated assays; a description of the appropriate assay characteristics or dedicated assays.
  - 5.2.1.8. for automated assays; a description of the appropriate instrumentation characteristics or dedicated instrumentation.
  - 5.2.1.9. a description of any software to be used with the *in vitro* diagnostic medical device.
  - 5.2.1.10. a description or complete list of the various configurations/ variants of the *in vitro* diagnostic medical device that will be made available.
  - 5.2.1.11. a description of the accessories, other *in vitro* diagnostic medical device and other products that are not *in vitro* diagnostic medical device, which are intended to be used in combination with the *in vitro* diagnostic medical device.
  - 5.2.1.12. complete label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging.

Reference to the manufacturer's previous device generation(s) or similar devices or device history.

## 6. Standards for Medical Device

### 6.1 Essential principles for safety and performance of medical devices

Medical device is required to meet the essential principles of safety and performance of medical devices as specified in following standard as applicable to the Device:

#### ISO 16142-1:2016

Medical devices -- Recognized essential principles of safety and performance of medical devices -- Part 1: General essential principles and additional specific essential principles for all non-IVD medical devices and guidance on the selection of standards.

#### ISO 16142-2:2017

Medical devices — Recognized essential principles of safety and performance of medical devices — Part 2: General essential principles and additional specific essential principles for all IVD medical devices and guidance on the selection of standards.

### 6.2 Product Standards for Medical Device

6.2.1 The medical device shall demonstrate conformance to relevant essential safety and performance principles by confirming to various relevant standards of Medical Devices.

6.2.2 The 'standard' for the purpose of the ICMED PLUS scheme refers to any National, International standards, or any published industry standards developed by any National or International associations of manufacturers. The manufacturer shall use following hierarchy while selecting standards:

6.2.2.1. Use of ISO 16142-1 and ISO 16142-2 for selection of standards in support of 'Essential Principles of Safety and Performance of Medical Devices'.

6.2.2.2. Basic Standards which cover the essential principles of safety and performance.

6.2.2.3. Group or Semi Horizontal standard – *Example - IEC 60601-1 - Medical electrical equipment - Part 1: General requirements for basic safety and essential performance.*

6.2.2.4. International Standards (ISO/IEC/ITU).

6.2.2.5. Established product or vertical standards, where available.

6.2.2.6. Validated manufacturer's standards, especially for new types of devices and emerging technologies, wherein, there are no established product standards nor product group standards. The manufacturer shall create valid scientific evidence for the medical device to demonstrate conformance to the essential principle in question.

6.3 The manufacturer shall define and document an essential principles checklist that identifies:

6.3.1. the essential principles of safety and performance.

6.3.2. whether each essential principle applies to the device and if not, why not.

6.3.3. the method used to demonstrate conformity with each essential principle that applies.

6.3.4. a reference for the method employed (e. g. standard)

- 6.3.5. the precise identity of the controlled technical document that offers evidence of conformity with each method used.
- 6.4 Methods used to demonstrate conformity shall include one or more of the following:
  - 6.4.1. conformity with standards through a recent test report from an ISO/IEC 17025 accredited or compliant laboratory.
  - 6.4.2. conformity with a commonly accepted industry test method.
  - 6.4.3. conformity with an in-house/ validated manufacturer's test method.
  - 6.4.4. the evaluation of pre-clinical and clinical evidence.
  - 6.4.5. comparison to a similar device already available on the market.
- 6.5 The essential principles checklist shall incorporate a cross-reference to the location of such evidence within the full technical documentation held by the manufacturer.
- 6.6 All devices containing electrical components shall also meet the Electrical Safety IEC 60601-1 - Medical electrical equipment - Part 1: General requirements for basic safety and essential performance and with electronic components EMC requirements as per IEC 60601-1-2.

## 7. Risk Management

- 7.1 The manufacturer shall perform a Risk Management Process complying with ISO 14971 for each Medical Device to be certified and record the results in a Risk Analysis Report. The manufacturer shall:
  - 7.1.1. establish a risk management process including a policy for determining acceptable risk
  - 7.1.2. establish acceptable levels of risk; and
  - 7.1.3. demonstrate that the residual risk(s) is acceptable (in accordance with the policy for determining acceptable risk)
  - 7.1.4. The risk analysis shall be periodically updated with the risks identified as per risk management plan.
- 7.2 The risk analysis shall address possible hazards for the *in vitro* diagnostic medical device such as the risk from false positive or false negative results, indirect risks which may result from *in vitro* diagnostic medical device associated hazards, such as instability, which could lead to erroneous results, or from user-related hazards, such as reagents containing infectious agents.

## 8. Design and development of Medical Device

- 8.1 The manufacturer shall define and document various stages of design and development as applied to the device. The manufacturer may refer to ISO 13485 for guidance.
- 8.2 For all **Class B, Class C, Class D** and any new medical device, other than new *in vitro* diagnostic, the following Design Analysis and validation data shall be maintained, including, (whichever applicable):
  - 8.2.1. design input and design output documents,
  - 8.2.2. mechanical and electrical tests,
  - 8.2.3. reliability tests,
  - 8.2.4. validation of software relating to the function of the device,

- 8.2.5. any performance tests,  
8.2.6. *in vitro* tests.
- 8.3 For all **Class B, Class C, Class D** and any new *in vitro* diagnostic medical device, which does not have predicate device, the following Design Analysis and validation data shall be maintained, including, (whichever applicable):
- 8.3.1. design input, design output documents, stability data;  
8.3.2. 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 *in vitro diagnostic* medical device  
8.3.3. device specification including specificity, sensitivity, reproducibility, and repeatability.  
8.3.4. product validation and software validation relating to the function of the device (if any);  
8.3.5. performance evaluation report from a laboratory - ISO/IEC 17025 accredited or compliant laboratory.
- 8.4 The manufacturer shall identify a controlling site if the design takes place at multiple sites.
- 8.5 Any major change in the Medical Device shall be brought to the notice of the Certification body. Changes in respect of following shall be considered as **major change**:
- 8.5.1. material of construction,  
8.5.2. design which shall affect quality in respect of its specifications, indication for use, performance and stability of the medical device,  
8.5.3. the intended use or indication for use,  
8.5.4. the method of sterilization,  
8.5.5. the increase in approved Shelf life,  
8.5.6. the name or address of,  
8.5.7. the domestic manufacturer or its manufacturing site,  
8.5.8. overseas manufacturer or its manufacturing site (for import only),  
8.5.9. authorised agent (for import only),  
8.5.10. label excluding change in font size, font type, colour, label design,  
8.5.11. manufacturing process, equipment or testing which shall affect quality of the device,  
8.5.12. primary packaging material.
- 8.6 Changes in respect of following shall be considered as minor change:
- 8.6.1. design which shall not affect quality in respect of its specifications, indication for use, performance, and stability of the medical device,  
8.6.2. in the manufacturing process, equipment, or testing which shall not affect quality of the device.  
8.6.3. packaging specifications excluding primary packaging material.

## 9. Manufacturing Processes

- 9.1 The manufacturer shall document specific information about the production and/or control of device manufacturing in respect of the medical devices under evaluation. It shall provide an overview of production from raw material to finished product, manufacturing environment, facilities and controls used for manufacturing, assembly, any final product testing, labelling and packaging and storage of the finished medical device. For this

purpose, the manufacturer shall submit an internal quality assurance plan covering all states of production, intended to ensure the final product conformity to the certification criteria and shall include measures for control over outsourced material and components, if applicable.

- 9.2 The manufacturer shall identify a controlling site if the manufacturing takes place at multiple sites.
- 9.3 The manufacturer shall allow any person authorized by the scheme owner or certification body to audit the manufacturing premise and to examine the process, procedure, and documents in respect of any manufacturing site or to take sample of certified medical device or the Medical Device for which the application for certification has been made.

If the manufacturer has stopped manufacturing activity or closed the manufacturing site for a period of thirty days or more, the same shall be intimated to the Certification body and the reason for the same shall be recorded.

## 10. Verification and Validation of Medical Device

### 10.1 General

- 10.1.1 The manufacturer shall undertake verification and validation studies to demonstrate conformity of the device with the essential principles that apply to it.
- 10.1.2 For other than *in vitro* diagnostic devices, the product verification and validation documentation shall include, wherever applicable:
- 10.1.2.1. engineering tests,
  - 10.1.2.2. laboratory tests,
  - 10.1.2.3. simulated use testing,
  - 10.1.2.4. any animal tests for demonstrating feasibility or proof of concept of the finished device,
  - 10.1.2.5. any published literature regarding the device or substantially similar devices.
- 10.1.3 For *in vitro* diagnostic medical devices, the product verification and validation documentation shall include, wherever applicable:
- 10.1.3.1. the study protocol,
  - 10.1.3.2. method of data analysis,
  - 10.1.3.3. study results and study report,
  - 10.1.3.4. study where appropriate, actual test result summaries with their acceptance criteria should be provided and not just pass/fail statements,
  - 10.1.3.5. any published literature regarding the device or substantially similar devices.
- 10.1.4 The product verification and validation documentation shall include or refer to one of the following:
- 10.1.4.1. test results indicating conformity to acceptance criteria of a recognized product or group standard,
  - 10.1.4.2. declaration or certificate of conformity to a recognized standard or group standard and with a summary of the data if no acceptance criteria are specified in the standard,

- 10.1.4.3. declaration or certificate of conformity to a published standard or group standard that has not been recognized, supported by a rationale for its use, and summary of the data if no acceptance criteria is specified in the standard,
- 10.1.4.4. declaration or certificate of conformity to a professional guideline, industry method, or validated manufacturer's standards, supported by a rationale for its use, a description of the method used, and summary of the data in sufficient detail to allow assessment of its adequacy,
- 10.1.4.5. a review of relevant published literature regarding the device / analyte (measurand) or substantially similar devices.
  
- 10.1.5 In addition, where applicable to the device, the manufacturer shall carry out following verification and validation activities on:
  - 10.1.5.1. biocompatibility studies as per prescribed standards,
  - 10.1.5.2. medicinal substances incorporated into the device, including compatibility of the device with the medicinal substance,
  - 10.1.5.3. biological safety of devices incorporating animal or human cells, tissues or their derivatives,
  - 10.1.5.4. sterilization,
  - 10.1.5.5. software verification and validation,
  - 10.1.5.6. animal studies that provide direct evidence of safety and performance of the device, especially when no clinical investigation of the device was conducted,
  - 10.1.5.7. clinical evidence.
  
- 10.1.6 Detailed test documentation shall describe test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions. Where no new testing has been undertaken, the documentation shall incorporate a rationale for that decision, e. g. biocompatibility testing on the identical materials was conducted when these were incorporated in a previous, legally marketed version of the device. The rationale shall be incorporated into the Essential Principles checklist.

## 10.2 Biocompatibility

- 10.2.1 For all invasive or implantable **Class B, Class C, Class D** medical device, Bio-compatibility tests and analysis shall be carried out and the following data shall be maintained:
  - 10.2.1.1 Bio-compatibility tests data,
  - 10.2.1.2 Report of biocompatibility study along with rationale for selecting specific tests carried out including conclusion of the study
  
- 10.2.2 ISO-10993, Biological Evaluation of Medical Devices, shall be followed for conducting bio-compatibility study for invasive medical devices.
  
- 10.2.3 Where biocompatibility testing has been undertaken (as per prescribed standards) to characterize the physical, chemical, toxicological and biological response of a material, detailed information shall be included on the tests conducted, standards applied, test protocols, the analysis of data and the summary of results. At a minimum, tests shall be conducted on samples from the finished, sterilized (when supplied sterile) device.

### **10.3 Medicinal Substances**

10.3.1 The manufacturer shall provide the identity and source of any medicinal substance incorporated in the medical device, justify the intended reason for its presence, and ensure its safety and performance in the intended application.

### **10.4 Biological Safety**

10.4.1 The manufacturer shall provide a list of all materials of animal or human origin used in the device. For these materials, detailed information shall be provided concerning the selection of sources or donors. The processes of harvesting, processing, preservation, testing and handling of tissues, cells and substances of such origin shall be defined, validated, and controlled.

10.4.2 Process validation results shall be included to substantiate that manufacturing procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents. Transmissible Spongiform Encephalopathies (TSE) or Bovine Spongiform Encephalopathy (BSE) Certificates shall be ensured.

10.4.3 Traceability from sources to the finished device shall be established through a system for record-keeping.

### **10.5 Sterilization**

10.5.1 Where the device is supplied sterile, the manufacturer shall ensure initial sterilization validation including sterilizer qualification, bioburden testing, pyrogen testing, testing for sterilant residues (if applicable) and packaging validation as per prescribed standards. The detailed validation documentation shall include the method used, sterility assurance level attained, standards applied, the sterilization protocol developed in accordance with prescribed standards, and a summary of results.

10.5.2 The manufacturer shall carry out ongoing revalidation of the process. Typically, this would consist of arrangements for, or evidence of, revalidation of the packaging and sterilization processes.

### **10.6 Software Verification and Validation**

10.6.1 The manufacturer shall implement IEC 62304, "Medical device software – Software life cycle processes" for safe and effective medical device software if the intended use qualifies the software as a medical device or if the software is part of a medical device.

10.6.2 The manufacturer shall validate the software, as used in the finished device. This includes summary results of all, validation and testing performed both in-house and in a simulated or actual user environment prior to final release. The validation shall also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

### **10.7 Animal Studies**

10.7.1 Depending on nature and intended use of the investigational medical device, device performance for its actions (including mechanical, electrical, thermal, radiation and any

other of this type) and safety shall be assessed, if possible, in healthy or diseased animal model (intended to be treated by such medical device), as appropriate, demonstrating reaction to active and basic parts of the devices on absolute tissue, local tissue as well as whole organ, clearly recording local, general and systemic adverse reactions, risks or potential risks and performance of device in line, if possible, with intended use. Wherever possible, histopathology, pathophysiology and path anatomy shall be carried out.

- 10.7.2 The manufacturer shall define the study objectives, methodology, results, analysis and conclusions and document conformity with Good Laboratory Practices. The rationale (and limitations) of selecting the particular animal model shall be documented.
- 10.7.3 Animal performance study data shall be maintained as evidence of safety and performance of the device, especially when no clinical investigation of the device is conducted.

## 10.8 Shelf Life of Medical Devices

- 10.8.1 The manufacturer shall determine and declare the shelf life of the medical devices, keeping in view the technical parameters and shall ordinarily not exceed sixty months from the date of manufacture, except in cases where satisfactory evidence is produced by the manufacturer to justify a shelf life of more than sixty months of a device.
- 10.8.2 If available, real-time aging data shall be collected to support the claimed shelf life. However, if real-time data is not available, accelerated stability data shall be collected and analyzed to support the claimed shelf life. The manufacturer shall initiate a real-time stability testing to validate the proposed shelf life. After completion of the real time stability analysis, real-time stability data shall be submitted in support of the claimed shelf life.

## 11. Analytical Studies for *in vitro* Diagnostic Medical Devices

The requirements in this section refer to all *in vitro* diagnostic 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 requirements for qualitative or semi-quantitative assays. Where possible, comments regarding instrumentation or qualitative assays appear in the requirements.

### 11.1 Specimen Type

- 11.1.1. The manufacturer shall identify the different specimen types that can be used. This shall include their stability and storage conditions. Stability includes storage and where applicable transport conditions. Storage includes elements such as duration, temperature limits and freeze/ thaw cycles.
- 11.1.2. The manufacturer shall establish the measurement procedure for comparison or determination of measurement accuracy for each matrix and anticoagulant when applicable. The procedure shall address specimen type tested, number of samples, sample range (using spiked samples as appropriate) or target concentrations tested, calculations and statistical methods, results, and conclusions.

### 11.2 Analytical Performance Characteristics

#### 11.2.1 Accuracy of Measurement

The manufacturer shall conduct both trueness and precision studies for measurement accuracy.

**Note:** 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.

### 11.2.2 Reproducibility

The manufacturer shall conduct reproducibility studies used to estimate, as appropriate, variability between days, runs, sites, lots, operators, and instruments. Reproducibility data shall be obtained for instrumentation in conjunction with an appropriate assay.

**Note:** 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.

### 11.3 Analytical Sensitivity

The manufacturer shall design the sensitivity study defining specimen type and preparation including matrix, analyte (measurand) levels, and how levels are established.

The number of replicates tested at each concentration shall also be defined as well as a methodology used to determine assay sensitivity. For example:

- 11.3.1. Number of standard deviations above the mean value of the sample without analyte (measurand), commonly referred to as limit of blank (LoB),
- 11.3.2. Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand), commonly referred to as limit of detection (LoD),
- 11.3.3. Lowest concentration at which precision and/or trueness are within specified criteria, commonly referred to as limit of quantitation (LoQ).

### 11.4 Analytical Specificity

11.4.1 The manufacturer shall conduct 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.

11.4.2 The manufacturer shall evaluate potentially interfering and cross-reacting substances/ agents on the assay. The test documentation shall include information on the substance/agent type and concentration tested, sample type, analyte (measurand) test concentration, and results.

11.4.3 The manufacturer shall plan and conduct Interference studies involving addition of 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. 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:

- 11.4.3.1. substances used for patient treatment (e. g. therapeutic drugs, anticoagulants, etc.).
- 11.4.3.2. substances ingested by the patient (e. g. over the counter medications, alcohol, vitamins, foods, etc.).
- 11.4.3.3. substances added during sample preparation (e. g. preservatives, stabilizers).
- 11.4.3.4. substances encountered in specific specimen's types (e. g. haemoglobin, lipids, bilirubin, proteins).
- 11.4.3.5. 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).

## 11.5 Metrological Traceability of Calibrator and Control Material Values

Where applicable, manufacturer shall ensure 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.

## 11.6 Measuring Range of the Assay

The manufacturer shall establish and document the measuring range (linear and non-linear measuring systems) including the limit of detection.

This documentation shall 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, a description of high dose hook effect and the data supporting the mitigation (e. g. dilution) steps shall be added.

## 11.7 Definition of Assay Cut-off

The manufacturer shall design a study including methods for determining the assay cut-off, and including:

- 11.7.1. the population(s) studied (demographics / selection / inclusion and exclusion criteria / number of individuals included),
- 11.7.2. method or mode of characterization of specimens,
- 11.7.3. Statistical methods e. g. Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey zone/equivocal zone.

## 11.8 Stability (Excluding Specimen Stability)

The manufacturer shall define, and document claimed shelf life, in use stability and shipping studies.

## 11.9 Claimed Shelf Life

The manufacturer shall conduct stability testing studies to support the claimed shelf life. Testing shall 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. Such detailed information shall describe:

- 11.9.1. the study report (including the protocol, number of lots, acceptance criteria and testing intervals).
- 11.9.2. when accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies.
- 11.9.3. conclusions and claimed shelf life.

### **11.10 In use Stability**

The manufacturer shall conduct 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, it shall be supported by data. The test documentation shall describe:

- 11.10.1. the study report (including the protocol, acceptance criteria and testing intervals).
- 11.10.2. conclusions and claimed in use stability.

### **11.11 Shipping Stability**

The manufacturer shall conduct 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 shall include variable shipping conditions such as extreme heat or cold. The test documentation shall describe:

- 11.11.1. the study report (including the protocol, acceptance criteria).
- 11.11.2. method used for simulated conditions.
- 11.11.3. conclusion and recommended shipping conditions.

## **12. Clinical Evaluation of Medical Device**

- 12.1 No manufacturer, person or sponsor shall conduct any clinical investigation in respect of investigational medical device in human participants except in accordance and with permission as per applicable statutory and regulatory requirements.
- 12.2 If a predicate device is available, the manufacturer shall carry out a substantial equivalence evaluation along with relevant published literature in accordance with rules.
- 12.3 The manufacturer shall furnish the clinical evidence that demonstrates conformity of the investigational medical device with the Essential Principles that apply to it.
- 12.4 Conformity with relevant general safety and performance requirements under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit-risk- ratio shall be based on clinical data providing sufficient clinical evidence.
- 12.5 Clinical investigations shall be performed on the basis of an appropriate plan of

investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims regarding the safety, performance and aspects relating to benefit-risk of devices.

- 12.6 The clinical investigations shall include an adequate number of observations to guarantee the scientific validity of the conclusions. The rationale for the design and chosen statistical methodology shall be presented.
- 12.7 The endpoints of the clinical investigation shall address the intended purpose, clinical benefits, performance, and safety of the device. The endpoints shall be determined and assessed using scientifically valid methodologies. The primary endpoint shall be appropriate to the device and clinically relevant.

### 13. System for Post-Marketing Surveillance

- 13.1 The manufacturer shall establish, maintain, and implement a post-marketing surveillance process for Class A (sold sterile or with measuring function), Class B, Class C and Class D medical devices.
- 13.2 This post-marketing surveillance process shall include complaint handling, post-market vigilance reporting, field corrective actions, recalls and any subsequent corrective & preventive actions.
- 13.3 The manufacturer shall collect and furnish the Post Marketing Surveillance or Vigilance Reporting procedures and data encompassing the details of the complaints received and corrective and Preventive actions taken for the same.
- 13.4 The manufacturer shall inform the Certification body and the Scheme Owner, of the occurrence of any suspected unexpected serious adverse event and action taken thereon including any recall within fifteen days of such event coming to the notice of the manufacturer.
- 13.5 Furthermore, manufacturers shall perform a specific post-marketing study of a particular type of device, and report the outcome to the Scheme owner, if so, required by the Scheme Owner.
- 13.6 Manufacturers shall undertake any additional action, if so, required after analyzing the outcome.

### 14. Testing

- 14.1 The testing and/or validation and verification of medical devices and/or analytical studies for *in vitro* diagnostic medical devices shall be carried out using an ISO/IEC 17025 accredited or compliant laboratory.
- 14.2 The manufacturer shall carry out acceptance (essential functional/performance) tests as described in its internal quality plan, technically, for the purpose of product release, in an ISO/IEC 17025 accredited or compliant laboratory.
- 14.3 The manufacturer shall maintain at least one unit of sample from each batch of invasive medical device and *in vitro* diagnostic medical device manufactured, for reference purpose for a period of one hundred and eighty days after the date of expiry of such batch. This requirement is generally applicable to the batch produced medical devices and not to medical equipment.

## 15. Quality Management System (QMS)

- 15.1 The manufacturer shall implement, document and maintain a QMS that ensures the medical devices it designs, manufactures and supplies to the market are safe, perform as intended and comply with the relevant provisions of the scheme at each manufacturing site of the device. The scope and complexity of the QMS shall be influenced by the range of different medical devices that are under QMS control, the processes employed, the size and structure of the organization, and the specific regulatory requirements.
- 15.2 Processes required by the QMS but carried out on the manufacturer's behalf by third parties remain the responsibility of the manufacturer and shall be subject to control under the manufacturer's QMS.
- 15.3 Manufacturers of **Class A** devices shall implement and maintain an effective QMS that complies with ICMED 13485 but have the option of excluding design and development controls from it.
- 15.4 Manufacturers of **Class B, C and D** devices shall implement and maintain an effective QMS that includes design and development controls (with option of excluding for some class B devices) and complies with full ICMED 13485.

## 16. Competence of Personnel

- 16.1 The manufacturing or testing activity of medical device shall be undertaken only under the direction and supervision of the competent technical staff.
- 16.2 The manufacturer shall appoint competent technical staff under whose direction and supervision the manufacturing activity of a medical device shall be undertaken, and such staff shall possess the educational qualification and experience as described in "ICMED-Certification Process for Systems Certification", Section 6.2.2.
- 16.3 The manufacturer shall appoint competent technical staff under whose direction and supervision the testing activity of a medical device shall be undertaken, and such staff shall possess the educational qualification and experience as described in "ICMED-Certification Process for Systems Certification", Section 6.2.2.

## 17. Technical Documentation (TD)

- 17.1 Manufacturers of all classes of device shall demonstrate conformity of the device to 'Essential Principles of Safety and Performance of Medical Devices' and other requirements described in this criteria, the applicable standards of Medical Devices through the preparation and holding of technical documentation that shows how each 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 shall be updated as necessary to reflect the current status, specification and configuration of the device.
- 17.2 The manufacturer may also establish a technical documentation detailing the following, as applicable:

- 17.2.1. The safety critical components used in the device.
- 17.2.2. The risk assessment carried out as per ISO 14971.
- 17.2.3. Usability engineering exercise carried out as per IEC 62366 (for Class C and Class D medical devices).
- 17.2.4. Internal compliance mechanism applied to regular production.

17.3 The extent of evidence in the TD shall increase with the class of the medical device, its complexity, and the extent to which it incorporates new technology.

17.4 When the TD is submitted to CB, it shall incorporate an attestation that the contents is truthful and accurate, and indicate the name, position and signature of the responsible person who has been authorized to submit it on the manufacturer's behalf.

## **18. Declaration of Conformity**

18.1 The manufacturer shall attest that its medical device complies fully with essential principles of safety and performance, all standard / technical and regulatory requirements and submit a written 'Declaration of Conformity', as per ISO/IEC 17050-1: Suppliers declaration of conformity.

18.2 The declaration shall contain the following information:

- 18.2.1. An attestation that each device that is subject to the declaration complies with the 'Essential Principles of Safety and Performance of Medical Devices' and applicable Safety/ Performance/standard and the applicable requirements of Labelling and Instructions for Use for Medical Devices.
- 18.2.2. Information sufficient to identify the device/s to which the Declaration of Conformity applies.
- 18.2.3. The classification of the device/s and the device name, code, and category as per IAF ID 13.
- 18.2.4. The date on which the Declaration of Conformity is issued.
- 18.2.5. The name and address of the device manufacturer.
- 18.2.6. The name, position, and signature of the responsible person who has been authorized to complete the Declaration of Conformity upon the manufacturer's behalf.

## **19. Recall of Medical Devices**

19.1 If the manufacturer considers or has reasons to believe that a medical device, which has been manufactured, sold or distributed, is likely to pose risk to the health of a user or patient during its use and therefore may be unsafe, the manufacturer shall immediately initiate procedures to withdraw the medical device in question from the market and patients, indicating reasons for its withdrawal and inform the regulatory authority, certification body and scheme owner the details thereof.

## **20. Labelling Requirements of Medical Devices**

### **20.1 Labelling**

20.1.1 Each 'Unit pack for sale' of the medical device shall be labelled / marked with following information.

- 20.1.1.1. Name / Trade Name of the device.
- 20.1.1.2. The Name & Address of manufacturer
- 20.1.1.3. Lot / Batch No.
- 20.1.1.4. Date of Expiry
- 20.1.1.5. Indication for single use (if applicable)
- 20.1.1.6. The word "STERILE" (For Sterile Devices)
- 20.1.1.7. Caution in event of damage to sterile pack
- 20.1.1.8. Max. Retail Price

20.1.2 In case of space constraint on the "unit pack for sale", the following information is also mandatory on secondary pack of Device. A user/ consumer can be cautioned by use of appropriate caution symbol on the unit pack.

- 20.1.2.1. Device description
- 20.1.2.2. Mfg. Lic. No. (if applicable)
- 20.1.2.3. Date of Mfg.
- 20.1.2.4. Storage / handling instruction
- 20.1.2.5. Operating instruction / Instruction for use, where appropriate
- 20.1.2.6. Method of sterilization (For Sterile Devices)
- 20.1.2.7. Warning / Precautions & Symbols (if applicable)
- 20.1.2.8. Customer- care –Contact Detail.

20.1.3 As far as it is practicable and appropriate, the information needed to identify and use the device safely shall be provided on the device itself, and/or on the packaging for each unit, and/or on the packaging of multiples devices. If individual packaging of each unit is not practicable, the information to be given in the leaflet/ Information to Use supplied with one or more Devices.

20.1.4 Each Device shall be accompanied by the information needed to use it safely and properly, taking account of the training and knowledge of the potential users, and shall identify the manufacturer.

20.1.5 Where appropriate, the information shall take the form of symbols. Any symbol or identification color used must conform to the harmonized Standards. In areas for which no Standards exist, the symbols and colors must be described in the documentation supplied with the Device". Graphical symbol as per ISO 15223 can be used as appropriate for all of above. Any additional labeling requirement specified in related product standard shall be included appropriately.

20.1.6 The unit pack may contain more than one number or type of medical devices.