



PROPOSED DOCUMENT

Global Harmonization Task Force

Title: Clinical Evidence for IVD medical devices – Scientific Validity
Determination and Performance Evaluation

Authoring Group: Study Group 5

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Preface

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

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

1.0 Introduction

GHTF would seek to evolve beyond convergence of regulatory requirements to embrace mutual acceptance of common data submissions, pre-market conformity assessment processes, quality systems, quality systems auditing results, and a broad sharing of post-marketing experience. The objective was to allow presentation of data that are acceptable in principle to relevant authorities as the basis for meeting regulatory requirements.

The broad goal for Study Group 5 is to promote the convergence of the regulatory requirements for the generation and presentation of evidence of the clinical safety and performance of medical devices. The Study Group 5 document SG5/NxRy recognizes that, in order to progress convergence of regulatory requirements and acceptance of common data, it is necessary to have a common understanding and application of terminology, concepts and principles.

Furthermore, a document was needed to describe the process used to demonstrate clinical evidence and to delineate when the elements of clinical evidence are appropriate for the IVD medical device.

In addition, a third document will provide guidance on clinical performance studies for IVD medical devices.

When placing an IVD medical device on the market the manufacturer must have demonstrated through the use of appropriate conformity assessment procedures that the device complies with the Essential Principles of Safety and Performance of Medical Devices. Generally, from a clinical perspective, it is expected that the manufacturer has demonstrated the device achieves its intended performance during normal conditions of use in the intended environment (e.g. blood-banks, hospitals, home environment). As IVD medical devices are used on specimens taken from the human body, the characteristics of clinical evidence are different from medical devices other than IVD medical devices.

2.0 Scope

The primary purpose of this document is to provide manufacturers with guidance on how to collect and document clinical evidence for an IVD medical device as part of the conformity assessment procedure prior to placing an IVD medical device on the market as well as to support its ongoing marketing. It is also intended to provide guidance to regulators and other stakeholders when assessing clinical evidence provided by manufacturers.

This document provides the following guidance:

- general principles of clinical evidence;

- how to determine scientific validity for an analyte (measurand), when is it expected and how to document it;
- on analytical performance and when is it expected;
- on clinical performance and when is it expected;
- how to demonstrate clinical performance (e.g. studies, literature);
- how to appraise and analyze the data; and
- on the content of the clinical evidence report.

The guidance contained within this document applies to devices that meet the definition of an IVD medical device as given in the GHTF document ‘Classification Principles of IVD medical devices’. It is not intended to apply to other medical devices.

3.0 References

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

GHTF/SG1/N45:2008 *Principles of In Vitro Diagnostic Medical Devices Classification*.

GHTF/SG1/N63:2011 *Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices*.

GHTF/SG1/N46:2008 *Principles of Conformity Assessment for In Vitro Diagnostic Medical Devices*.

GHTF/SG1/N41R9:2005 *Essential Principles of Safety and Performance of Medical Devices*.

SG5/NXXX Clinical Evidence for IVD medical devices – Key Definitions and Concepts.

4.0 Definitions

Diagnostic sensitivity

ability of an IVD examination procedure to identify the presence of a target marker associated with a particular disease or condition.

NOTE 1 : Also defined as percent positivity in samples from subjects where the target disease or condition is known to be present.

NOTE 2 : Diagnostic sensitivity is a number fraction, calculated as true positive values divided by the sum of true positive plus false negative values.

NOTE 3 : The disease or condition is defined by criteria independent of the examination procedure under consideration.

Source: ISO 18113-1:2009

Diagnostic specificity

ability of an IVD examination procedure to recognize the absence of a target marker associated with a particular disease or condition.

NOTE 1: Also defined as percent negativity in samples where the target analyte (measurand) is known to be absent.

NOTE 2: Diagnostic specificity is a number fraction, calculated as true negative values divided by the sum of true negative plus false positive values.

NOTE 3: The disease or condition is defined by criteria independent of the examination procedure under consideration.

Source: ISO 18113-1:2009

Examination

set of operations having the object of determining the value or characteristics of a property.

NOTE 1: In some disciplines (e.g., microbiology) an examination is the total activity of a number of tests, observations or measurements.

NOTE 2: Laboratory examinations that determine the value of a property are called quantitative examinations; those that determine the characteristics of a property are called qualitative examinations.

NOTE 3: Laboratory examinations are also called ‘assays’ or ‘tests.’

Source: ISO 18113-1:2009 modified

Predictive value

probability that a person with a positive examination result has a given condition under investigation, or that a person with a negative examination result does not have a given condition.

NOTE 1: In screening examinations, the predictive value is determined by the diagnostic sensitivity and diagnostic specificity of the examination procedure, and by the prevalence of the condition for which the examination is used.

NOTE 2: Prevalence means the proportion of persons with a particular disease within a given population at a given time.

NOTE 3: The positive predictive value indicates how effectively an examination separates true positive examination results from false positive examination results for a given attribute in a given population.

NOTE 4: The negative predictive value indicates how effectively an examination separates true negative examination results from false negative examination results for a given attribute in a given population.

Source: ISO 18113-1:2009 modified

In Vitro Diagnostic Medical Device

IVD medical device: a 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. This includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles.

GHTF SG1/N045:2008 Principles of IVD Medical Devices Classification.

Recognized Standards

Standards deemed to offer the presumption of conformity to specific Essential Principles of Safety and Performance.

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

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 Medical Devices (SG1/N041)*.

GHTF SG1/N046:2008 Principles of Conformity Assessment for IVD Medical Devices.

5.0 General principles of clinical evidence

To understand clinical evidence for IVD medical devices it must be taken into account that IVD medical devices differ from other medical devices in that the risks and benefits they pose are related to impact on patient management rather than direct contact between the device and the patient. A significant percentage of all healthcare decisions rely on clinical laboratory tests and these decisions can profoundly influence diagnosis and management of the patient.

Clinical evidence requirements will be influenced by the relative risk to the patient of an incorrect result from the IVD medical device, the degree of innovation reflected in the scientific/clinical recognition of the analyte (measurand) of interest, the assay technology, the novelty, the degree of variability of the subject population and disease state, and the intended user(s) of the device. While not intended to be unduly burdensome, the clinical

evidence must support the intended use of the IVD medical device as stated by the manufacturer while addressing the relative risks to the patient associated with the use of the device.

Gathering of information to support clinical evidence starts at the research phase for IVD medical devices and this process consists of two major phases: the identification of the scientific validity of the analyte (measurand) and the performance evaluation of the specific IVD medical device.

Once scientific validity of an analyte (measurand) is identified, the design process will lead to the development of an IVD medical device. The design process will be supported by a performance evaluation (this evaluation consists of analytical performance studies and where appropriate clinical performance studies).

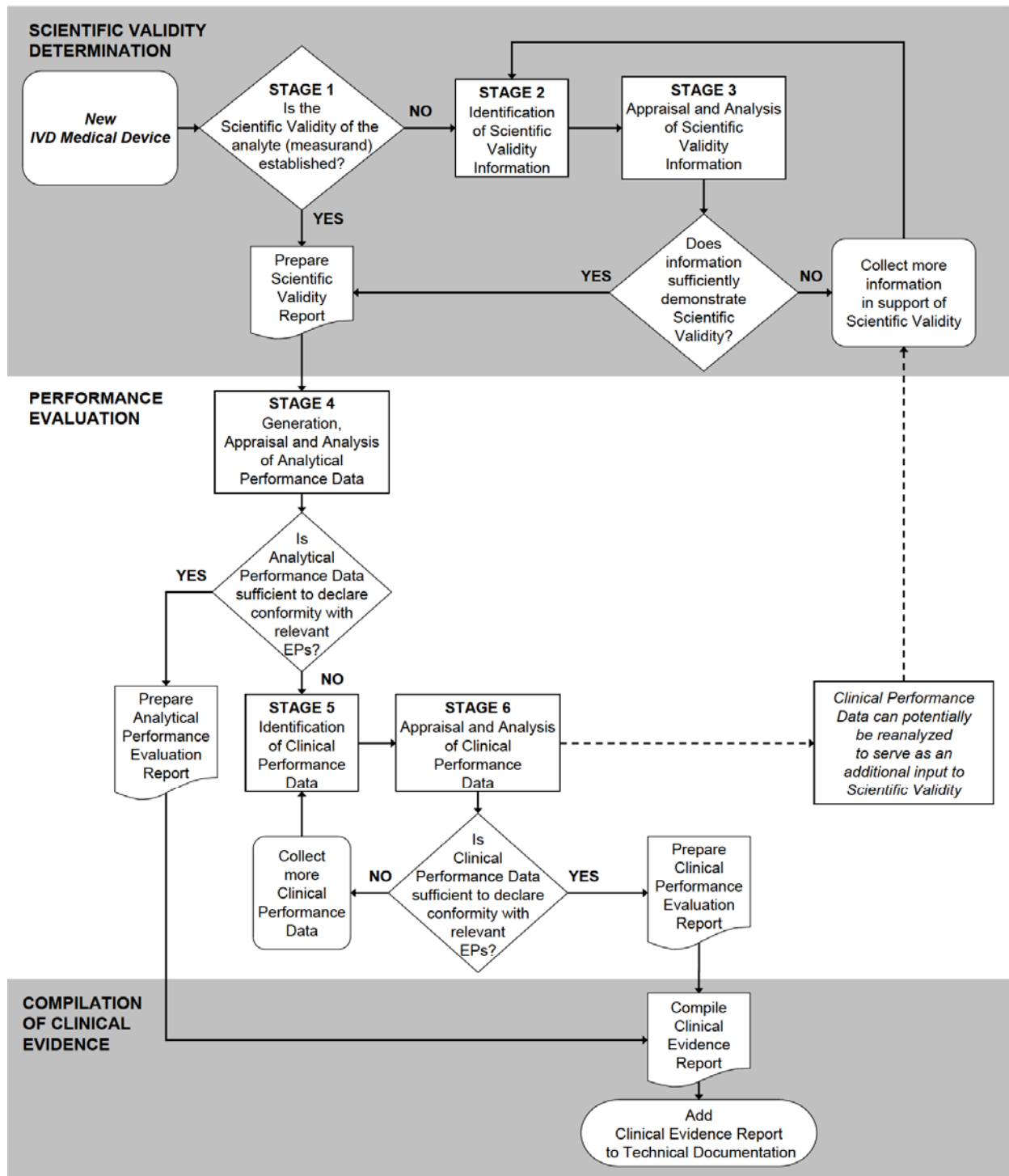
In the post-marketing phase data generated through clinical experience, where relevant, should be used to supplement the clinical evidence.

For IVD medical devices that have a new intended use, the existing clinical evidence report should be assessed as to its suitability to support the new intended use. If the new intended use is not supported by the existing evidence then addition to the scientific validity, the analytical and where appropriate, the clinical performance should be considered.

Stages of clinical evidence

Figure 1 on the next page provides an overview of the stages involved in the assessment of clinical evidence.

FIGURE 1



6.0 Scientific Validity Determination

Stage 1 - Is the Scientific Validity of the analyte (measurand) established?

Determination of scientific validity is not necessary where association of an analyte (measurand) to a clinical condition/physiological state is well known, based on available information such as peer reviewed literature, historical data and experience. For example it would not be reasonable to expect a manufacturer to demonstrate haemoglobin is associated with anaemia given the well established and recognized association. If the scientific validity is established, a brief rationale should be documented - proceed to Stage 4.

For a new analyte (measurand) and/or new intended use, scientific validity needs to be demonstrated. Proceed to Stage 2.

Stage 2 – Identification of scientific validity of the analyte (measurand)

Potential sources for the identification of scientific validity information are:

- Information on IVD medical devices that measure the same analyte (measurand) and with the same intended use that have marketing history (e.g. Instructions for Use)
- Literature searching: this information might be found in peer reviewed articles, regulatory guidance documents, conference proceedings, etc.
- Review of expert opinions: this information might be found in sources that include textbooks, clinical guidance documents, position statements from academic and professional organizations.
- Results from proof of concept studies: these studies are usually smaller scale scientific studies to identify the fundamental association of the analyte (measurand) with the clinical condition/physiological state.
- Results from clinical performance studies

Scientific validity will be based on one or more of these potential information sources.

Stage 3 – Appraisal and Analysis of scientific validity information

The purpose of the scientific validity appraisal is to select information based on its merits and limitations. Each piece of information is appraised to determine its relevance and quality for establishing the association between the analyte (measurand) and the clinical condition/physiological state.

To be relevant the information source should reference both the analyte (measurand) and the clinical condition/physiological state in question, and should show a clear link between the two.

The information provided should be of sufficient quality to enable a rational and objective assessment of the scientific validity.

The scientific validity analysis aims to collectively evaluate all of the appraised information, in terms of weight and significance.

The outcome of the analysis should be summarised in a report comprising references, justification and conclusion regarding whether there is a valid association between the analyte (measurand) and the clinical condition/physiological state.

The scientific validity data should be summarised in a scientific validity report which becomes part of the clinical evidence report.

7.0 Performance Evaluation

Performance evaluation for an IVD medical device is the process by which generated data are assessed and analyzed to demonstrate the performance (analytical and where appropriate clinical performance) of the envisioned IVD medical device for the intended use as stated by the manufacturer.

To address the appropriate requirements for performance evaluation, IVD medical devices may be segregated into three different categories:

a) Established and standardized tests

These tests have clinical guidelines or consensus for the use of the test, there is more than one commercial test available, and/or international standard or reference materials exist. These tests produce comparable results for the analyte (measurand) regardless of the method or the manufacturer.

Examples of this category include glucose, sodium, creatinine, hormones (HCG), biochemical tests for identification of microorganisms, blood gases.

b) Established and non standardized tests

These tests have clinical guidelines or consensus for the use of the test, there is more than one commercial test available. While international reference materials may exist, results obtained from different IVD medical devices might not be used interchangeably.

Examples of this category include infectious disease (Rubella, Hepatitis C), Hormones (SHBG), Cardiac markers (Troponin), Tumour markers (BCR-ABL, CEA, PSA), Cell markers (CD4, T-cells).

c) Novel tests

Such tests involves a new analyte, new technology, new target population, new application of an established technology, or a new intended use, and they are not established or standardized.

NOTE: New technology is defined as the practical application of a new technical process e.g. sequencing, immunoassay, gene amplification (e.g. blood grouping from agglutination to DNA amplification), mass spectroscopy to ELISA.

Examples of this category include newly identified cardiac markers (high sensitivity CRP) and tumour markers (CTC), vCJD, pharmacogenomics (CYP450, HLA typing for mutations, CCR5), emerging infectious diseases (SARS, H1N1).

7.1. Analytical Performance

Stage 4 – Generation, Appraisal and Analysis of Analytical Performance Data

Analytical performance is always expected for IVD medical devices. However for novel tests it may not be possible to demonstrate trueness since recognized reference materials or a suitable comparative method are not likely to be available. In this case, as an alternative, comparison to the current clinical standard practice would be appropriate.

For an established and standardized test information about analytical performance is sufficient to allow the product to be placed on the market as an IVD medical device. For an established and non-standardized test, information about analytical performance may be sufficient to allow the product to be placed on the market as an IVD medical device.

Analytical performance, which refers to technical test performance, may include data to demonstrate accuracy (trueness and precision), analytical sensitivity, analytical specificity, linearity, limit of detection and limit of quantitation, cut-off, measuring range, carry-over, as well as determination of appropriate specimen collection and handling, and endogenous and exogenous interference on assay results.

Analytical studies for trueness usually are based on one or more of the following:

- a) methods described in a recognized standard (e.g. ISO 15197: In vitro diagnostic test systems – Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus)
- b) comparison with an international reference method (e.g. atomic absorption for Calcium)
- c) Comparison with a reference material of a higher order (e.g. international reference materials)

Where the above described methods are not readily available, a comparison with an already available IVD medical device (method comparison) (e.g. in the field of immunoassays) or a recognized method, (e.g. Sanger sequencing for genotyping assays) may be used.

In most circumstances analytical performance testing using human specimens is needed. If specimens are of limited availability or do not cover the desired range of the assay or presence of the analyte (measurand), the use of contrived samples (e.g. spiked) would be acceptable.

The analytical performance data should be summarised in an analytical performance evaluation report which becomes part of the clinical evidence report.

7.2. Clinical Performance

For many IVD medical devices, clinical performance data are not required.

Clinical performance would not be expected for situations such as:

- Established and standardized tests
- Assay migration between instruments that share the same basic analytical technology but may for example vary in instrument throughput, whereby the formulation and the intended use of the assay do not change. There should be no expected change in clinical performance of the assay when run on the new instrument.
- Class A IVD medical devices.

When clinical performance is not expected, analytical performance is sufficient to allow the product to be placed on the market as an IVD medical device.

Clinical performance may be required for ‘established and non standardized tests’ while clinical performance will be typically required for ‘novel tests’. For high risk IVD medical devices (Class D), design changes that may affect the performance claims of the IVD medical device may also require clinical performance studies.

While not intended to be unduly burdensome, the clinical performance studies must provide evidence to support the intended use of the IVD medical device while addressing the relative risks/benefits associated with the use of the IVD medical device.

The clinical performance of an IVD medical device may be characterised by:

- diagnostic specificity, which indicates the effectiveness of an examination in correctly classifying patients that do not have a particular disease or condition, and

- diagnostic sensitivity, which indicates the effectiveness of the examination in correctly identifying patients who have a particular disease or condition.
- positive predictive value, which indicates the effectiveness of an examination in separating true positive results from false positive results for a given attribute in a given population.
- negative predictive value, which indicates the effectiveness of an examination in separating true negative results from false negative results for a given attribute in a given population.
- likelihood ratio, which refers to the likelihood that a given result would be expected in an individual with the target clinical condition/physiological state compared to the likelihood that the same result would be expected in an individual without that clinical condition/physiological state.
- expected values in normal and affected populations.

NOTE: The diagnostic sensitivity and diagnostic specificity depend on the choice of a cutoff value for the examination.

NOTE: Predictive value depends on the prevalence of the disease or condition in the population of interest.

Clinical performance of the device to be placed on the market is the relationship between the testing results and the clinical conditions of patients. Clinical performance studies could be retrospective or prospective. Such studies include, but are not limited to, diagnostic sensitivity and diagnostic specificity based on the true status of the patient, and negative and positive predictive values based on the prevalence of the condition or disease.

Clinical performance should only be performed once the analytical performance of the device has been established and determined to be acceptable. Clinical performance represents the true clinical assessment, where the test performance is evaluated in the target population. Ideally, the diagnostic sensitivity and specificity will be validated through studies conducted at multiple sites in different health care and geographical settings. The aim is to substantiate performance claims.

The clinical performance data should be summarised in a clinical performance evaluation report which becomes part of the clinical evidence report.

When the clinical performance includes a clinical performance study, the level of detail of the clinical performance study report will vary based on the class of the IVD medical device:

- Class A – not required.
- Class B – summary of study protocol, results and conclusion.
- Class C – detailed information on the complete study protocol, the method of data analysis, the complete study report and study conclusion.

- Class D - detailed information on the complete study protocol, the method of data analysis, the complete study report, study conclusion, and typically the individual data points (formatted raw data).

Stage 5 - Identification of Clinical Performance

Manufacturers are able to draw on one or more data sources to demonstrate clinical performance.

Potential sources for the identification of clinical performance data:

- Clinical Performance Studies
- Literature
- Experience gained by routine diagnostic testing

Data relevant to the clinical performance may be held by the manufacturer (e.g. manufacturer sponsored pre and post market study reports and adverse event reports for the IVD medical device in question) or in the scientific literature (e.g. published articles of clinical performance studies for the IVD medical device).

The manufacturer is responsible for identifying data relevant to the IVD medical device and determining the types and amount of data needed to establish clinical performance, giving consideration to the advantages and limitations of each data type.

7.2.1. Clinical Performance Studies

The guidance included within this section applies to clinical performance studies carried out by or on behalf of a manufacturer specifically for the purposes of conformity assessment in accordance with applicable regulations. Such studies are generally expected to be designed, conducted and reported in accordance and in compliance with local regulations and guidance.

Clinical performance studies should be designed, conducted, analyzed and evaluated so that the best possible representation is achieved with the target population in accordance with the intended use. Optimal clinical evaluation design, execution and analysis will ensure the greatest possible generalization of results, e.g. for different demographic or ethnic groups.

An IVD medical device may be designed for a variety of intended use/purposes with different diagnostic functions. The influence of diagnostic function on the design of clinical performance studies is described in detail in SG5/NxRx Clinical Performance Studies for IVD medical devices.

When conducting a performance study to establish the clinical performance of an IVD medical device, this testing is usually performed in parallel to the routine diagnostic testing performed for patient management care. In these cases, patient management decisions are based on the routine standard test.

In some instances, a performance study is carried out to establish the performance of an IVD medical device and even though testing may or may not be performed in parallel with a standard test, patient management decisions will be based on the results of the new IVD medical device. These are rare cases where it is known that the technology offered by the new IVD medical device is superior to routine testing or in cases where there is no routine test for the specific marker. These types of performance evaluations are subject to a variety of regulatory, legal and ethical requirements. Examples include, screening of blood donation with a NAT based assay for detection of West Nile Virus and the first PCR based test for SARS.

There should be careful selection of the routine diagnostic test(s) which will be used as the comparative method to evaluate the performance of an IVD medical device. Where possible, a reference test method should be included in the performance study protocol, and qualified with appropriate reference to the literature.

7.2.2. Literature

Literature searching can be used to identify published clinical performance data that is not in the possession of the manufacturer that may assist the manufacturer in establishing acceptable clinical performance of an IVD medical device. The data generated through literature searching should relate directly to the IVD medical device in question or earlier versions (e.g. reports of clinical studies that have been performed by third parties,).

When conducting a literature review, reasonable efforts should be made to conduct a comprehensive search. Refer for further guidance to Appendices A and B.

Once the literature search has been executed, a summary should be prepared and included in the clinical performance evaluation report. A copy of the methodology should be included and any deviations noted. It is important that the literature search is documented in sufficient detail so that the methods can be appraised critically, the results can be verified, and the search reproduced if necessary.

It is recognised that in cases where manufacturers source clinical performance data reported in the scientific literature (i.e. studies of the IVD medical device in question undertaken by a third party); the documentation readily available to the manufacturer for inclusion in the clinical performance evaluation is likely to be no more than the published paper itself.

7.2.3 Experience gained by routine diagnostic testing

These types of performance data are generated in actual use conditions that are outside the conduct of clinical performance studies. While much of the experience with diagnostic testing is found in literature, additional data may include:

- manufacturer-generated post market surveillance data,
- adverse events databases (held by either the manufacturer or regulatory authorities);
- data for the device in question generated from individual patients under emergency or compassionate usage programs prior to marketing of the IVD medical device (e.g. test for H1N1);
- details of clinically relevant field safety corrective actions (e.g. recalls, notifications, hazard alerts).

The value of routine diagnostic testing experience data is that it provides real world experience obtained in larger, heterogeneous and more complex populations (e.g. interfering substances). The data are most useful for identifying less common but potentially serious device-related adverse events. It is also a particularly useful source of diagnostic testing data for low risk devices that are based on long standing, well-characterized technology and, therefore, unlikely to be the subject of either reporting in the scientific literature or performance study.

The analyses of post-marketing data may, for some devices, provide reasonable assurance of performance.

If a manufacturer chooses to use experience data from routine diagnostic testing, it is important that any reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment of the information and make a conclusion about its significance with respect to the performance of the IVD medical device in question. Reports of such experience that are not adequately supported by data, such as anecdotal reports or opinion, should not be used.

Stage 6 – Appraisal and analysis of Clinical Performance Data

The purpose of the clinical performance appraisal is to select information based on its merits and limitations. Each piece of information is appraised to determine its relevance and quality to address questions about the IVD medical device, and its contribution to demonstrate the clinical performance of the IVD medical device (including any specific claims about performance).

To be relevant the information source should be specific to the IVD medical device in question and reflect its intended use.

The information provided should be of sufficient quality to enable a rational and objective assessment of the clinical performance.

The clinical performance analysis aims to collectively evaluate all of the appraised information, in terms of weight and significance. For the purpose of Clinical Performance evaluation, clinical performance study data is typically weighted higher than literature data which in turn is generally weighted higher than data gathered from clinical experience.

When weighting the results, particular attention should be given to circumstances where there are repeated publications on the same group of patients by the same authors, in order to avoid over-weighting the experience.

The different data sets should be reviewed for consistency of results across multiple sites and as appropriate, the intended target populations.

If the different data sets report comparable performance characteristics, certainty about the clinical performance increases. If different results are observed across the data sets, it will be helpful to determine the reason for such differences. Regardless, all data sets should be included.

As a final step the evaluator should consider the basis on which it can be demonstrated that the combined data show:

- the IVD medical device performs as intended by the manufacturer; and
- any risks associated with the use of the IVD medical device are acceptable when weighed against the benefits to the patient.

Such considerations should take into account:

- the intended users,
- the number and severity of adverse events,
- the adequacy of the estimation of associated risk for each identified hazard,
- the severity and natural history of the condition being diagnosed or treated, and
- the availability of alternative diagnostic tests and current standard of care.

The outcome of the analysis should be summarised in a report comprising references, justification and conclusion regarding the clinical performance of the IVD medical device.

The instructions for use should be reviewed to ensure they are consistent with the data and that all the hazards and other clinically relevant information have been identified appropriately.

8.0 Clinical Evidence Report

The clinical evidence report is a compilation of the scientific validity, analytical and clinical performance evaluation reports. If the analytical performance data is determined to be sufficient to declare conformity with the relevant Essential Principles without the need for clinical performance data, a brief rationale should be documented and included in the report. If the manufacturer concludes there is insufficient clinical evidence to be able to declare conformity with the Essential Principles, the manufacturer will need to generate additional data (e.g. conduct a clinical performance study, broaden the scope of

literature searching) to address the deficiency. In this respect development of clinical evidence, and in particular, clinical performance, should be an iterative process.

The clinical evidence report should contain sufficient information to be read as a stand alone document by an independent party (e.g. regulatory authority or notified body). It is important that the report outline:

- the justification for the approach taken to gather the clinical evidence
- the technology on which the medical device is based, the intended use of the device and any claims made about the device's clinical performance or safety;
- the nature and extent of the scientific validity and the performance data that has been evaluated; and
- how the referenced information (recognised standards and/or clinical data) demonstrate the clinical performance and safety of the device in question.

It should be noted that the level of detail in the report content can vary according to the scope of the scientific validity and the performance evaluation studies.

Appendices

Appendix A: Possible Format for the Literature Search Report

1. Device name/model

2. Scope of the literature search [should be consistent with the scope of the scientific validity and/or clinical performance]

3. Methods

- (i) Date of search
- (ii) Name of person(s) undertaking the literature search
- (iii) Period covered by search
- (iv) Literature sources used to identify data
 - scientific databases – bibliographic (e.g. MEDLINE, EMBASE);
 - specialised databases (e.g. MEDION)
 - systematic review databases (e.g. Cochrane Collaboration);
 - clinical trial registers (e.g. CENTRAL, NIH);
 - adverse event report databases (e.g. MAUDE, IRIS)
 - reference texts

[Include justification for choice of sources and describe any supplemental strategies (e.g. checking bibliography of articles retrieved, hand searching of literature) used to enhance the sensitivity of the search]

- (v) Database search details
 - search terms (key words, indexing headings) and their relationships (Boolean logic)
 - medium used (e.g. online, CD-ROM (including publication date and edition))[Attach copy of downloaded, unedited search strategy]
- (vi) Selection criteria used to choose articles

4. Outputs

- (i) Attach copy of literature citations retrieved from each database search
- (ii) Data selection process

[Attach flow chart and associated tables showing how all citations were assessed for suitability for inclusion in the clinical evidence (see Appendix B)]

Notes:

EMBASE Excerpta Medica published by Elsevier

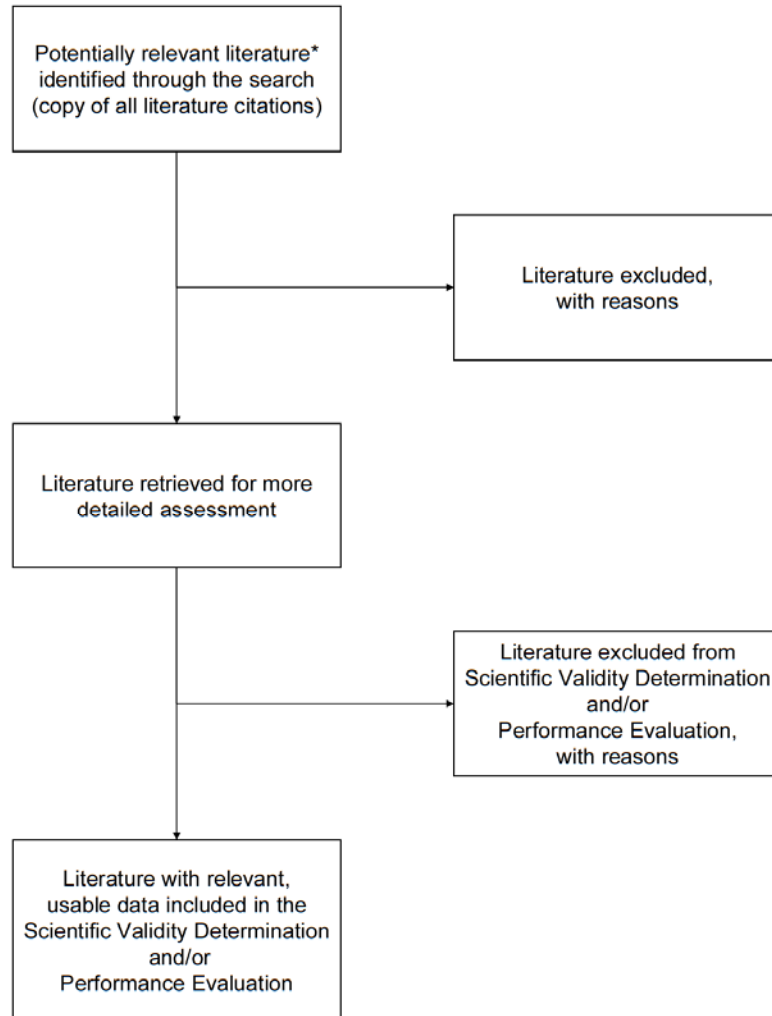
CENTRAL The Cochrane Central Register of Controlled Trials

IRIS The TGA's medical device Incident Report Investigation Scheme

MAUDE US FDA's Manufacturer And User Facility Device Experience database

Appendix B: Possible Methodology for Documenting and the Screening and Selection of Literature within a Literature Search Report¹

POSSIBLE METHODOLOGY FOR SCREENING AND DOCUMENTING LITERATURE



* Some literature for scientific validity may also address clinical performance if the data relates to the manufacturer's IVD medical device.

¹ Adapted from Moher, D., Cook, D. J., Eastwood, S., Olkin, I., Rennie, D., & Stroup, D. F. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUORUM statement. Quality of Reporting of Metaanalyses. *Lancet* 1999; 354: 1896-1900.