South African Health Products
Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

8 September 2025

GUIDELINES ON CLINICAL EVALUATION OF MEDICAL DEVICES

This guideline is intended to clarify the requirements of conducting a clinical evaluation of a medical device in South Africa. It represents the South African Health Products Regulatory Authority's (SAHPRA)'s current thinking on the safety, quality and performance of medical devices under clinical investigation. It is not intended as an exclusive approach. The Authority reserves the right to request any additional information to establish the safety, quality and performance of a medical device in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The Authority is committed to ensure that all registered medical devices will be of the required acceptable quality, safety and performance.

Document History

Final Version	Reason for Amendment	Effective Date [dd Month yyyy]
1	Published for public comment	15 November 2024
2	Published for implementation	25 August 2025

DR BOITUMELO SEMETE-MAKOKOTLELA
CHIEF EXECUTIVE OFFICER

Contents

Document History 1
Glossary 3
Definition of Terms 4
1. INTRODUCTION 5
1.1 Purpose 6
1.2 Scope 6
2. LEGAL PROVISION 6
3. GENERAL PRINCIPLES AND CONSIDERATIONS OF CLINICAL EVALUATION 6
3.1 Scope of a clinical evaluation 6
3.2 How is a clinical evaluation performed? 7
3.3 Who should perform the clinical evaluation? 7
3.4 Any consideration to vitro diagnostic devices (IVDs)? 8
3.5 Any considerations on Software as a Medical Device (SaMD)? 8
4. SOURCES OF DATA/DOCUMENTATION USED IN A CLINICAL EVALUATION 8
5. APPRAISAL OF CLINICAL DATA 11
6. ANALYSIS OF THE CLINICAL DATA 12
7. THE CLINICAL EVALUATION REPORT 13
8. REFERENCES 13
9. VALIDITY 13

Glossary

Abbreviation/ Term	Meaning
GHTF	Global Harmonization Task Force
IMDRF	International Medical Devices Regulatory Forum
ISO	International Organization for Standardization
SAHPRA	South African Health Products Regulatory Authority
SaMD	Software as a Medical Device

Definition of Terms

Adverse Event: Any untoward medical occurrence in patients/subjects, users or other persons. In the context of clinical investigation, for patients/subjects, this would include all untoward medical occurrences, whether or not related to the investigational device, that occurred in the course of the investigation. In the context of clinical experience, this would only include untoward medical occurrences that may be related to the medical device.

Clinical Data: Safety, clinical performance and/or effectiveness information that is generated from the clinical use of a medical device.

Clinical Evaluation: A set of ongoing activities that use scientifically sound methods for the assessment and analysis of clinical data to verify the safety, clinical performance and/or effectiveness of the device when used as intended by the manufacturer.

Clinical Evidence: The clinical data and its evaluation of a medical device.

Clinical Investigation: Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety, clinical performance, and/or effectiveness of a medical device.

Clinical Investigation Plan: Document that states the rationale, objectives, design, and pre-specified analyses, methodology, monitoring, conduct, and record-keeping of the clinical investigation.

Clinical Performance: The ability of a medical device to achieve its intended clinical purpose as claimed by the manufacturer.

Clinical Performance Study: Means a study undertaken to establish or confirm the clinical performance of a medical device, including IVD, focusing on the actual performance of the device in real-world clinical conditions, often involving the collection of data on how well the device performs its intended function and the clinical benefits it provides to patients.

Comparable Device: A medical device with a related function chosen by the manufacturer to inform the clinical evaluation of the device in question.

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.

Effectiveness: The ability of a medical device to achieve clinically meaningful outcome(s) in its intended use as claimed by the manufacturer.

Intended Use/Purpose: The objective intent of the manufacturer regarding the use of a product, process, or service as reflected in the specifications, instructions, and information provided by the manufacturer.

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

Safety: Acceptability of risks as weighed against benefits, when using the medical device according to the manufacturer's labelling.

Note: All other definitions are in alignment with Act 101 of 1965 and MD regulations

1. INTRODUCTION

Clinical evaluation is a set of ongoing activities that use scientifically sound methods for the assessment and analysis of clinical data to verify the safety, clinical performance, and/or effectiveness of the medical device when used as intended by the manufacturer. It is first performed during the development of a medical device in order to identify data that needs to be generated for regulatory purposes and will inform whether a new device clinical investigation is necessary, together with the outcomes that need to be studied. It is then repeated periodically as new safety, clinical performance and/or effective information about the medical device is obtained during its use.

When placing a medical device on the market, the manufacturer must have demonstrated, using appropriate conformity assessment procedures that the medical device complies with the Essential Principles of Safety and Performance of Medical Devices. it is expected that the manufacturer has demonstrated the medical device achieves its intended performance during use according to its labelling and that the known and foreseeable risks are minimised and acceptable when weighed against the benefits.

It is anticipated that manufacturers should periodically review performance, safety and the benefit-risk assessment for the medical device through a clinical evaluation and update the clinical evidence accordingly. This ongoing clinical evaluation process should allow manufacturers to communicate with conformity assessment bodies and SAHPRA in accordance with local reporting requirements any information that has an important bearing on the benefit-risk assessment of the medical device or that would indicate a need for labelling changes regarding contraindications, warnings, precautions or instructions for use.

1.1 Purpose

This document aims to provide manufacturers with guidance on how to conduct and document the clinical evaluation of a medical device as part of the conformity assessment procedure before placing a medical device on the market as well as to support its ongoing marketing. It is also intended to guide regulators and other stakeholders when assessing clinical evidence provided by manufacturers.

1.2 Scope

This document will cover general principles of clinical evaluation, identification of relevant clinical data to be used in a clinical evaluation, how to appraise and integrate clinical data into a summary, and how to document a clinical evaluation in a clinical evaluation report. The evaluation must also address any clinical claims made about the device, the adequacy of product labelling and product information (particularly contraindications, precautions/warnings), and the suitability of instructions for use. The details will be provided to all medical devices, excluding in vitro diagnostics, approved to be used in the Republic of South Africa.

2. LEGAL PROVISION

Regulations relating to medical devices

3. GENERAL PRINCIPLES AND CONSIDERATIONS OF CLINICAL EVALUATION

3.1 Scope of a clinical evaluation

Before a clinical evaluation is undertaken, the manufacturer should define its scope, based on the Essential Principles that need to be addressed from a clinical perspective. The clinical evaluation should cover any design features that pose special performance or safety concerns (e.g., presence of medicinal, human or animal components), the intended purpose and application of the medical device (e.g., target treatment group and disease, proposed warnings, contraindications and method of application) and the specific claims made by the manufacturer about the safety, clinical performance and/or effectiveness of the device. The

scope of the clinical evaluation will need to be informed by and cross-referenced to the manufacturer's risk management documents.

The risk management documents are expected to identify the risks associated with the medical device and how such risks have been addressed. The clinical evaluation is expected to address the significance of any risks that remain after designed risk mitigation strategies have been employed by the manufacturer.

3.2 How is a clinical evaluation performed?

Once the scope has been defined, there are three discrete stages in performing a clinical evaluation:

- Identification of pertinent standards and clinical data;
- Appraisal of each data set, in terms of its relevance, applicability, quality, and clinical significance; and
- Analysis of the individual data sets, whereby conclusions are reached about the safety, clinical performance, and/or effectiveness and presentational aspects (labelling, patient information and instructions for use) of the medical device.

At the end of the clinical evaluation, a report is prepared and combined with the relevant clinical data to form the clinical evidence for the medical device. 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 investigation, broaden the scope of literature searching) to address the deficiency

3.3 Who should perform the clinical evaluation?

The clinical evaluation should be conducted by a suitably qualified individual or individuals. A manufacturer must be able to justify the choice of the evaluator(s) through reference to qualifications and documented experience.

As a general principle, evaluators should possess knowledge of the following:

- The device technology and its application;
- Research methodology (clinical investigation design and biostatistics); and
- Diagnosis and management of the conditions intended to be treated or diagnosed by the medical device.

3.4 Any consideration of in vitro diagnostic devices (IVDs)?

Clinical evaluation should be performed for *in vitro* diagnostic devices as part of conformity assessment to the Essential Principles in a manner similar to other medical devices. The basic principles of objective review of clinical data will apply as described in this guidance document. However, this document will not cover in detail regarding establishment of clinical evidence of an in vitro diagnostic device. This is because IVDs offer some unique definitions and concepts, which will be defined in detail in another document developed named *Clinical Evidence for IVD medical devices*.

3.5 Any considerations on Software as a Medical Device (SaMD)?

SaMD can best be described as software that utilises an algorithm (logic, set of rules, or model) that operates on data input (digitised content) to produce an output that is intended for medical purposes as defined by the SaMD manufacturer. Like other medical devices, SaMD clinical evaluation should be consistent with this document.

4. SOURCES OF DATA/DOCUMENTATION USED IN A CLINICAL EVALUATION

Data relevant to clinical evaluation may be held by the manufacturer or a third party or be available in scientific literature, for the device in question or for comparable devices. The manufacturer is responsible for identifying data relevant to the medical device and determining the types and amount of data needed for the clinical evaluation.

4.1. Data generated through literature searching

Literature searching can be used to identify published clinical data that is not in the possession of the manufacturer, which may assist the manufacturer to establish acceptable safety, clinical performance and/or effectiveness of a medical device. The data generated through literature searching may relate directly to the device in question (e.g., reports of clinical investigations of the device in question that have been performed by third parties, adverse event reports) or to comparable devices.

Published data will need to be assessed concerning its possible contribution and weighting in establishing both the performance of the device in question and its safety. Papers considered unsuitable for demonstration of clinical performance and/or effectiveness because of poor study design or inadequate analysis may still contain data suitable for assessing the safety of the medical device.

4.1.1 The key elements of literature searching

The search strategy should be based on carefully constructed review questions. A protocol should be developed to identify, select and collate relevant publications to address these questions. This should be developed and executed by persons with expertise in information retrieval, having due regard to the scope of the clinical evaluation set out by the manufacturer. The involvement of information retrieval experts will help to maximise data retrieval.

Once the literature search has been executed, a report should be compiled to present the results of the search. A copy of the protocol should be included and any deviations noted.

4.1.2 What data/documentation from the literature search should be included in the clinical evaluation

The following documentation should be used in the clinical evaluation by the clinical evaluator:

- The literature search protocol;
- The literature search report; and
- Published articles and other references identified as being relevant to the device in question and suitable for evaluation.

The literature search protocol, the literature search report, and copies of relevant references become part of the clinical evidence and, in turn, the technical documentation for the medical device. With respect to the clinical evaluation, it is important that the clinical evaluator be able to assess the degree to which the selected papers reflect the intended application/use of the device, etc.

Copies of the actual papers and references are necessary to allow the evaluator to review the methodology employed (potential sources of bias in the data), the reporting of results and the validity of conclusions drawn from the investigation or report. Abstracts may lack sufficient detail to allow these issues to be assessed thoroughly and independently.

4.2. Data generated through clinical experience

These types of clinical data are generated through clinical use that is outside the conduct of clinical investigations and may relate to either the device in question or comparable devices. Such types of data may include:

- Post market surveillance reports, registries or medical records (which may contain unpublished long-term safety, clinical performance and/or effectiveness data);

- Adverse events databases (held by either the manufacturer or regulatory authorities); and
- Details of clinically relevant field corrective actions (e.g., recalls, notifications, hazard alerts).

How may clinical experience data/documentation be used in the clinical evaluation?

If a manufacturer chooses to use clinical experience data, 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 safety, clinical performance and/or effectiveness of the device. Reports of clinical experience that are not adequately supported by data, such as anecdotal reports or opinions, should not be used.

Post-marketing data about adverse events are generally more meaningful when related to usage but caution is needed because the extent of reporting may vary considerably between countries. The analyses of data within these reports may, for some medical devices, provide reasonable assurance of safety, clinical performance and/or effectiveness.

It may be helpful to provide a table summarising device-related adverse events, paying particular attention to serious adverse events, with comments on whether observed device-related adverse events are predictable on the basis of the mode of action of the medical device. Identified hazards not previously considered in the risk management documentation must be addressed, describing additional mitigation required (e.g., design modification, labelling changes, etc.).

4.3. Data from clinical investigations

This section applies to clinical investigations carried out by or on behalf of a manufacturer specifically for the purposes of conformity assessment in accordance with applicable regulations. Such clinical investigations are generally expected to be designed, conducted and reported in accordance with ISO 14155:2020, clinical investigation of medical devices for human subjects - good clinical practice, or to a comparable standard, and in compliance with the regulations in the Republic of South Africa.

It is recognised that where manufacturers source clinical investigation data reported in the scientific literature (i.e., investigations of either the device in question or comparable devices that are undertaken by a third party), the documentation readily available to the manufacturer for inclusion in the clinical evaluation is likely to be no more than the published paper itself.

What clinical investigation documentation/data should be used in the clinical evaluation?

Where a clinical investigation has been carried out by or on behalf of a manufacturer, it is expected that documentation relating to the design, ethical and regulatory approvals, conduct, results and conclusions of the investigation needed for the clinical evaluation will be available for consideration, as appropriate. These may include:

- The clinical investigation plan;
- Clinical investigation plan amendments and the rationale for these changes;
- The relevant Ethics Committee documentation, opinion(s) and comments for each investigation site, including a copy of the approved informed consent form(s) and patient information documents;
- Case report forms, monitoring and audit records;
- SAHPRA approvals and associated correspondence as required by applicable regulations;
- Documents related to financial disclosure, financial agreements or conflict of interests; and
- The signed and dated final clinical investigation report.

5. APPRAISAL OF CLINICAL DATA

The purpose of undertaking appraisal of the data is to understand the merits and limitations of the clinical data. Each piece of data is appraised to determine its suitability to address questions about the medical device, and its contribution to demonstrating the safety, clinical performance and/or effectiveness of the device (including any specific claims about safety, clinical performance and/or effectiveness).

What should the appraisal cover?

The data needs to be assessed for its quality and its relevance to the device in question, including its intended use (i.e., the data must be either generated for the device in question or for a comparable device). In addition, any reports or collations of data should contain sufficient information for the evaluator to be able to undertake a rational and objective assessment of the information and make a conclusion about its significance with respect to the safety, clinical performance and/or effectiveness of the device in question.

Further appraisal needs to be undertaken to determine the contribution of each data subset to establishing

the safety, clinical performance and/or effectiveness of the medical device. The evaluator should examine the methods used to generate/collect the data and assess the extent to which the observed effect (performance or safety outcome(s)) can be considered to be due to intervention with the medical device or due to confounding influences (e.g., natural course of the underlying medical condition, concomitant treatment(s)) or bias. The evaluator should also assess whether clinical data are collected in conformance with the applicable regulatory requirements or other relevant standards (ISO 14155:2020) and whether clinical data are applicable to the population for which the marketing authorisation is being sought.

There is no single, well-established method for appraising clinical data. Therefore, the evaluator should identify, in advance, the appropriate criteria to be applied for a specific circumstance. These criteria should be applied consistently.

6. ANALYSIS OF THE CLINICAL DATA

The goal of the analysis stage is to make a benefit/risk determination if the appraised data sets available for a medical device collectively demonstrate the safety, clinical performance and/or effectiveness of the device in relation to its intended use.

The methods available for analysis of clinical data generally are either quantitative or qualitative. Given the context within which most medical devices are developed (i.e., limited need for clinical investigations because of incremental changes in device design and therefore high use of literature and experience data), it is most likely that qualitative (i.e., descriptive) methods will need to be used.

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

- The medical device performs as intended by the manufacturer;
- The medical device does not pose any undue safety concerns to either the recipient or end-user;
- Any risks associated with the use of the device are acceptable when weighed against the benefits to the patient;
- Compliance with the relevant Essential Principles; and
- Whether post market clinical follow up or post approval study is necessary.

7. THE CLINICAL EVALUATION REPORT

At the completion of the clinical evaluation process a report should be compiled that outlines the scope and context of the evaluation; the inputs (clinical data); the appraisal and analysis stages; and conclusions about the safety, clinical performance and/or effectiveness of the device in question.

The clinical evaluation report should contain sufficient information to be read as a standalone document by an independent party (e.g., regulatory authority or conformity assessment body). **It is important that the report outlines:**

- The technology on which the medical device is based, the intended use of the medical device and any claims made about the device's safety, clinical performance and/or effectiveness;
- The nature and extent of the clinical data that has been evaluated; and
- How the referenced information (recognised standards and/or clinical data) demonstrates the safety, clinical performance and/or effectiveness of the device in question.

The clinical evaluation report should be signed and dated by the evaluator(s) and accompanied by the manufacturer's justification of the choice of evaluator.

8. REFERENCES

1. GHTF:2008-- Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED).
2. IMDRF:2019 Clinical Evidence – Key definitions and Concepts.
3. IMDRF: 2018- Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices.
4. IMDRF:2017- Software as a Medical Device (SaMD): Clinical Evaluation
5. IMDRF:2017 - Methodological Principles in the Use of International Medical Device Registry Data
6. ISO 14155: 2020 - Clinical investigation of medical devices for human subjects — Good clinical practice
7. ISO 14971:2019 - Medical devices - Application of risk management to medical devices

9. VALIDITY

This guideline is valid for a period of five (5) years from the effective date of revision. It will be reviewed on this timeframe or as and when required.