THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

GUIDELINES FOR CONDUCTING PERFORMANCE EVALUATION OF IN-VITRO DIAGNOSTIC DEVICES SUBMITTED FOR MARKETING AUTHORIZATION

JUNE, 2024

TMDA Headquarters, Plot No. 56/1, Block E, Kisasa B Centre, Hombolo Road, P. O. Box 1253, Dodoma - Tanzania, Tel: +255 (26) 2961989/2061990/ +255(22) 2450512/2450751/2452108, Email: info@tmda.go.tz, Website: www.tmda.go.tz, Toll free: 08001100834

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ABBREVIATIONS

CPSP	-	Clinical Performance Study Plan
EC	-	Ethical Committee
EU	-	European Union
EPs	-	Essential Principles
IC	-	Informed Consent
IMDRF	-	International Medical Devices Regulators Forum
ISO	-	International Organization for Standardization
IVD	-	In-vitro Diagnostic Device
IVDR	-	In-vitro Diagnostics Registration
MDCG	-	Medical Device Coordination Group
MoU	-	Memorandum of Understanding
NEC	-	National Ethics Committee
PQ	-	Pre-Qualification
QMS	-	Quality Management System
TMDA	-	Tanzania Medicines and Medical Devices Authority
WHO	-	World Health Organization

ACKNOWLEDGEMENTS

This first edition of the guidelines intends to establish a well-documented procedure for conducting performance evaluation of in-vitro diagnostics which have been identified to have higher risk to the public. It is my hope that the information included in these guidelines will assist manufactures and/or applicants to conduct performance evaluation studies in the United Republic of Tanzania and subsequent verification of the results by the Authority.

With this, I would like to extend my sincere gratitude to the TMDA staff and other experts who gave their valuable time and experience in the development of these guidelines. The acknowledgements are particularly extended to Ms. Rehema Mariki, Ms. Gudula Mpanda, Dr. Goodluck Gotora, Mr. Christian Kapinga, Mr. James Tanguye and Ms. Edina Zebedayo. Furthermore, it is with honor I appreciate the outstanding technical contribution offered by Prof. Willy Urassa, a World Health Organization (WHO) consultant, from the early stages of development of these guidelines.

I would also like to thank the International Medical Devices Regulators Forum (IMDRF), the World Health Organization (WHO) as well as Medical Device Coordination Group (MDCG) established by European Union (EU) for making their guidelines available for referencing.

The proper use and implementation of these guidelines will ensure that the in-vitro diagnostic devices which have been designated to be of public health importance will perform clinically as claimed by manufacturers.

Ms. Kissa W. Mwamwitwa

Director, Medical Devices and Diagnostics Control

FOREWORD

Performance evaluation is one of the critical steps in ensuring safety and performance of in-vitro diagnostics. Diagnostics that perform well provides assurance in obtaining positive or negative results in clinical practice. It is through this assertion that the TMDA has developed these guidelines. The guidelines outline requirements for applicants to design and execute performance evaluation studies in Tanzania. Data on performance evaluation is needed by TMDA as part of marketing authorization of in-vitro diagnostics to be used in Tanzania. This is one of the legal proceedings enshrined in the Tanzania Medicines and Medical Devices Act, Cap 219.

Applicants and/or manufactures are henceforth compelled to read the details as provided for in these guidelines to streamline and expedite the approval process of diagnostics targeting Tanzania market. Together with the existing legal framework including TMDA Act and Regulations in force, applicants will also be required to refer the ISO 20916 standard when conducting performance evaluation studies. Studies done comprehensively and pursuant to these guidelines will allow for generation of adequate data and subsequent authorization of in-vitro diagnostics for marketing in Tanzania.

It is envisaged that the guidelines will be helpful to our stakeholders and any suggestions for improvement of the same are likewise welcomed.

Dr. Adam M. Fimbo
Director General

DEFINITION OF TERMS

For the purpose of these guidelines the following terms or phrases are defined as follows;

Authority
Means the Tanzania Medicines and Medical Devices Authority or the acronym “TMDA” established under section 4(1) of the Act.

Applicant
Means any person or institution or company that applies formally for performance evaluation of IVD in Tanzania.

Clinical Performance
Means ability of an IVD to yield results that are correlated with a particular clinical condition/ physiological state in accordance to target population and intended use**.**

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

Diagnostic Sensitivity
Means the ability of a device to identify the presence of a target marker associated with a particular disease or condition.

Diagnostic Specificity
Means the ability of a device to recognize the absence of a target marker associated with a particular disease or condition.

Ethics Committee (EC)
Means an independent body composed of members with expertise in both scientific and non-scientific arenas which functions to ensure the protection of human rights and the well-being of research subjects based on six basic principles of autonomy, justice, beneficence, nonmaleficence, confidentiality and honesty.

Error rate
Means a measure of the degree of prediction error of a model made with respect to the true model.

In-Vitro Diagnostics Devices
Means a device whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body and animals principally to provide information for diagnostic, monitoring or compatibility purposes. IVD 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 and determination of physiological status.

Manufacturer
Means any person or a firm that is engaged in the manufacture of IVDs.

Negative likelihood ratio (LR-)
Means a probability that a person with the disease tested negative divided by the probability that a person without the disease tested negative.

Negative predictive value
Means the ratio of subjects truly diagnosed as negative to all those who had negative test results (including patients who were incorrectly diagnosed as healthy).

Performance evaluation
Means the assessment and analysis of data to establish or verify the performance (analytical performance and where applicable, clinical performance) of an IVD**.**

Positive predictive value
Means the ratio of patients truly diagnosed as positive to all those who had positive test results (including healthy subjects who were incorrectly diagnosed as patient).

Positive likelihood ratio (LR+)
Means probability that a positive test would be expected in a patient divided by the probability that a positive test would be expected in a patient without a disease.

Stringent assessment
Means assessment of safety, quality and performance of IVD as conducted by the WHO PQ (Pre-Qualification) programme or regional harmonization initiatives or as determined by the Authority.

Validation
Means confirmation by examination and provision of objective evidence that the requirements for a specific intended use have been fulfilled.

Verification
Means confirmation by examination and provision of objective evidence that the specified requirements have been fulfilled.

INTRODUCTION

Performance evaluation is a systematic process that assesses the analytical and clinical performance characteristics of an IVD device. This process involves a series of studies and analyses conducted according to TMDA regulatory guidelines and standards to determine the device's fitness for its intended use. Performance evaluation aims to validate the device's accuracy, precision, sensitivity, specificity, and other relevant parameters before the device can be placed on the market.

All IVDs which have higher risk to the public must undergo performance evaluation before being placed on the market. The performance evaluation is a continuous process conducted throughout the lifecycle of an IVD, that assesses the analytical and clinical performance as well as scientific validity which forms the clinical evidence for an IVD. The performance evaluation is an important aspect of the IVD registration, as it ensures that IVDs are safe, accurate, and effective for their intended use.

These Guidelines outline the requirements for the applicant/manufacture to design and execute performance evaluation studies in Tanzania. All IVDs which are not prequalified by WHO should undergo performance evaluation using sample from Tanzanian populations. Studies must be designed according to, and take into account scientific principles underlying the collection of clinical performance data along with accepted operational and ethical standards surrounding the use of human subjects. The data collection process must ensure patient safety and data integrity throughout the entire process of the study. At the end of the study applicants will be expected to provide report to the Authority for verification, assessment and approval.

These guidelines details the requirement on clinical performance study design type, ethical consideration for clinical performance study, clinical performance study protocol, conduct of clinical performance study and clinical performance study report.

The performance evaluation report (PER) is a crucial component in the technical documentation, consolidation of findings from the scientific validity analytical and clinical performance needed by TMDA as part of marketing authorization of in-vitro diagnostics in Tanzania.

1.0 Scope

The primary purpose of this guidelines is to provide guidance to applicants on the procedure for conducting performance evaluation studies of IVD medical devices which have not undergone stringent assessment as specified by TMDA.

Given the wide diversity of IVD medical devices and their associated risks, this document is not intended to provide comprehensive guidance for clinical performance studies of specific IVD medical devices.

Clinical performance studies are typically performed during the pre-market phase. However, this document may also apply to studies conducted during the post-market phase.

NOTE: This document should be read together with *the Guidelines for Submission of Documentation for Registration of In-Vitro Diagnostics Devices* together with ISO 20916 (In vitro diagnostic medical devices-clinical performance studies using specimens from human subjects).

2.0 Purpose of Clinical Performance Studies

The purpose of a clinical performance study is to verify performance claims as established by the manufacturer during analytical and validation studies.

3.0 Clinical Performance Study Design Type

Clinical performance studies should be designed in such a way as to maximize the relevance of the data while minimizing potential biases.

IVD medical device clinical performance studies will depend on class of IVD device. The design of the study should provide the data necessary to address the clinical performance of the IVD device. It should account for potential risks, follow appropriate ethical principles, and be compliant with all relevant legal and regulatory requirements.

The choice of the design for the clinical performance study will depend on the following considerations:

i. Study objectives

ii. Intended use, specifically

- test purpose(s) (e.g. diagnosis, screening, monitoring;
- target population(s) (e.g. age, race, gender, geography, clinical condition)
- specimen type(s) (e.g. serum, plasma, urine)
- intended user(s) (e.g. lay person)

iii. Analytical and clinical performance characteristics determined by the manufacturer

iv. Expected operational and clinical performance characteristics (e.g. sensitivity, specificity, error rate, reading time,)

v. Novelty of the technology and/or clinical use (e.g. relevant previous experience)

vi. Availability of an appropriate standard or reference method to establish presence or absence of the disease condition.

The following additional considerations will also need to be taken into account in designing the clinical performance study

i. Specimen collection and handling
ii. Characterization of the clinical samples to be used
iii. Clinical performance study site
iv. Statistical design
v. Potential risks
vi. Ethical approval requirements

3.1 Clinical Performance Study Design Considerations

An IVD medical device may be designed for a variety of intended uses such as establishment of a diagnosis, screening, monitoring of a disease condition. See table I in Appendix.

The test purpose will directly influence the subject sample size (N) and selection criteria (including inclusion and exclusion) when planning and designing the clinical performance study. For example, if the disease state prevalence is low and the intent of the assay is to screen asymptomatic individuals, specimens from a large number of subjects may be required to provide sufficient evidence of clinical performance. However, if the assay is to be used for diagnosis in symptomatic individuals, specimens from at least 100 subjects may be adequate.

Where appropriate, there should be consideration regarding the timing of specimen collection such as prior to treatment or during treatment. For example, a test for predisposition would require that the specimens should be drawn prior to the onset of the condition.

Where appropriate, the study should be designed to include patient follow-up to determine their clinical endpoint/outcome. This would be applicable for tests that identify future conditions such as tests for predisposition, prognosis and prediction.

Where appropriate, multiple test purposes might be evaluated simultaneously. In these cases, more than one design type can be combined into a single clinical performance study. Such clinical performance studies should be designed and involve patient populations (with known or readily identifiable clinical status) that would sufficiently validate all the potential test purposes.

3.2 Specimen Collection and Handling

Samples used in clinical performance studies are derived from specimens which may be obtained from relevant intended use population and may include purposefully-collected specimens, leftover specimens, or archived specimens.

Purposefully-collected specimens refer to specimens that were drawn from patients with the specific intention of using them in a particular clinical performance study. These specimens or their derived samples may be tested immediately after collection (i.e. fresh) or may be stored (e.g. refrigerated or frozen) for testing at a later date.

Leftover specimens are remnants of specimens collected for routine diagnostic testing that would otherwise have been discarded, or specimens that were previously collected for other research purposes (e.g. basic research studies, pharmaceutical clinical trials, previous IVD device clinical performance studies).

Archived samples refer to specimens or samples that were collected in the past and are obtained from repositories (e.g. blood banks, commercial vendor collections). While archived specimens or samples tend to be well-characterized whereby the analyte status and/or clinical status of the patient are known, some specimens or samples may be archived without first establishing their analyte/clinical status. Well-characterized archived specimens or samples are often the source for unique or rare specimens or samples in sufficient quantity, whereby without these specimens or samples, it would be difficult, if not impossible, to conduct the study in a reasonable timeframe.

For many IVD medical device clinical performance studies, it is appropriate to use leftover or archived specimens in lieu of purposefully-collected specimens provided that sufficient information concerning specimen characterization is available (e.g. anticoagulant, known patient treatment(s) that may influence test results, time of last treatment dose for therapeutic drug monitoring assays). Generally, clinical performance characteristics can be validated using leftover or archived specimens if they were collected, handled and stored appropriately (i.e. good integrity) and if the information available for the specimens meets the study design requirements.

Care must be taken to avoid introducing a selection bias through the use of leftover or archived specimens. Documentation should exist to support the integrity of the selected specimens in the clinical performance studies.

Attention needs to be given when using leftover or archived specimens to evaluate certain prognostic or predictive tests due to the potential that treatment regimens may bias results. It is generally more appropriate to use leftover or archived specimens when there is minimal treatment heterogeneity among the patient populations. Such an approach reduces the risk that variable treatment regimens will obscure the influence of prognostic or predictive markers on clinical outcomes.

3.3 Clinical Performance Study Site

Clinical performance studies for registration purposes will be conducted by laboratories specified in the TMDA standard operating procedures (SOP's) for performance evaluation studies, The selected laboratories should be independent and have a well-established and documented quality management system (QMS) based on ISO 15189 and ISO 17025 or equivalent. The clinical performance study Sites should have access to appropriate samples, ability to characterize the samples including reference methods specified in the protocol.

It is important to ensure that the collection and testing sites are reflective of the intended use environment and/or intended user.

The clinical performance site will adhere to memorandum of understanding (MoU) and confidentiality agreement signed with TMDA. The performance evaluation report will be sent to the sponsor or investigator and TMDA simultaneously.

The Authority will frequently monitor the performance of the identified study sites.

3.4 Statistical Analysis Considerations

In designing the study, appropriate statistical methods should be specified in advance and be based on sound scientific principles and methodology. Care must be taken in developing a statistical plan that includes following considerations:

- statistical significance levels,
- the power of the study
- appropriate sample size (N) for estimation of clinical performance parameters (e.g. sensitivity and specificity) with confidence intervals;
- appropriate sample size (N) for estimation of clinical performance measures (e.g. sensitivity and specificity) with confidence intervals;
- appropriate subject inclusion and exclusion criteria (e.g. age, disease status);
- minimization of bias such as selection bias, spectrum bias, verification bias (e.g. specimen/sample selection, collection, handling and storage; blinding of operator to clinical status of patient);
- criteria for re-examination and resolution of (equivocal results, discrepant results)
- criteria for data exclusion (e.g. protocol deviation);
- methods used for statistical analysis; and
- clinically relevant performance characteristics (e.g. sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value, negative predictive value, prevalence, percent agreement, correlation to clinical endpoints/outcomes, expected values).

3.5 Potential Risks

A variety of study factors influence the potential risks to patients when conducting clinical performance studies for IVD medical devices.

When study specimens are obtained from samples already taken for routine diagnostic testing there is no additional risk coming from the study. However, if the specimen is collected specifically for the study and involves invasive collection procedures the risks associated with these procedures should be taken into consideration. In doing so the level of invasiveness of the sampling procedures should also be considered (e.g. venipuncture versus spinal puncture).

Interventional studies carry higher risks as the results are used to manage patients. For these studies, appropriate procedures for adverse events monitoring and handling should

be in place. For clinical performance studies in which there is a risk to patients, clinical performance studies should only be performed once the analytical performance of the device has been established and determined to be acceptable.

For example, in clinical performance studies for companion diagnostics, the way in which the biomarker status impacts treatment decisions may pose a risk to the patients.

4.0 Ethical Considerations for Clinical Performance Studies

As a general principle, the rights, safety and well-being of subjects participating in IVD device clinical performance studies shall be protected in accordance with the ethical principles laid down in the Declaration of Helsinki

It is ethically important in deciding to conduct a clinical performance study that it should generate new data and answer specific safety and/or performance questions that remain unanswered by the current body of knowledge. The desire to protect human subjects from unnecessary or inappropriate experimentation must be balanced with the need to protect public health through the use of clinical performance studies where they are indicated based on scientific needs (e.g. specific mutations in a given population). In all cases, however, care must be taken to ensure that the necessary data are obtained in a scientific and ethical manner that does not expose subjects to undue risks or discomfort. The rights, safety and well-being of subjects are paramount, and appropriate clinical performance study design and conduct is essential to generate meaningful data.

4.1 Informed Consent

The requirement for patient-informed consent should be based on the risk posed to subjects participating in the clinical performance study. For IVD medical devices, informed consent is required for specimens specifically collected for the purpose of a clinical performance study.

If the clinical performance study will solely use leftover or archived specimens that are not individually identifiable (i.e. devoid of information that would otherwise permit traceability to the patient of origin), the requirement for informed consent may not apply or may be waived by the National Ethics Committee.

In some cases, informed consent may exist in a general form to cover the use of the specimens in any clinical performance studies.

The need for informed consent should be discussed with the Ethics Committee of each institution included in the study.

4.2 Ethics Committee Involvement

Prior to commencing a clinical performance study, the participating sites may require approval by national ethics committee (NEC). This independent committee is formally designated to review, approve and monitor studies involving human subjects with the aim of protecting their rights and welfare.

The ethics committee may choose to exempt certain IVD device clinical performance studies from their approval.

4.3 Communicating Test Results Outside of the Study

In some rare instances, there may be a need to communicate clinical performance study results to clinicians and/or public health institutions during or after the study. This can be the case when test results may have an immediate health impact (e.g. no routine testing exists) on the patient, the patient's relatives or the public.

The decision and the mechanism to report results to clinicians and or public health institutions should be discussed with the local ethics committee prior to beginning the clinical performance study.

Example: An IVD medical device for the detection of SARS is undergoing a clinical performance study. Specificity is assessed using prospectively-collected patient specimens. During testing of the specificity population, a sample is reported as positive. This result is confirmed by testing with an alternate method. It is ethically appropriate to communicate such unexpected results to ensure appropriate patient treatment.

5.0 Clinical Performance Study Protocol

The clinical performance study protocol sets out how the study will be conducted. It contains important information about the study design such as the purpose, objectives, study population, description of the test method(s) and interpretation of results, site training and monitoring, specimen type, specimen collection, preparation, handling and storage, inclusion and exclusion criteria, limitations, warning and precautions, data collection/management, data analysis, required materials, number of study sites and if applicable, clinical endpoints/outcomes, and requirements for patient follow-up.

In addition, the clinical performance study protocol identifies the key factors which may impact the completeness and significance of results, such as intended participant follow-up procedures, decision algorithms, discrepancy resolution process, masking/blinding, approaches to statistical analyses, and methods for recording endpoints/outcomes and, where appropriate, communication of test results.

TMDA will prepare appropriate performance evaluation protocols using experts in the specific analyte. The protocol will be shared with the applicant prior to commencement of the performance evaluation. The evaluation site will strictly adhere to the protocol unless after discussion and approval by the Authority.

6.0 Conduct of Clinical Performance Studies

A properly conducted clinical performance study, including compliance with the clinical performance study protocol and TMDA requirements (e.g. pre-study authorization for interventional studies by the TMDA), ensures the protection of subjects, the integrity of the data and that the data obtained is acceptable for the purpose of verification of manufacturer performance claims.
Considerations for the conduct of a clinical performance study may include:

- independence of study personnel
- qualification and training of study personnel
- adequate infrastructure
- appropriate calibration procedures and means of control

- relevant method for determining the true clinical status of patient specimens

Raw data of a clinical performance study should be maintained. Performance evaluation should be based on the implementation of an established Quality Management System (QMS) including ISO 15189 and/or ISO 17025 requirements or equivalent.

7.0 Clinical Performance Study Report

The protocol, results and conclusions of a clinical performance study should be documented in a Clinical Performance Study report. The results and conclusions should be transparent, free of bias, and clinically relevant. The report should contain sufficient information to enable it to be understood by an independent party without reference to other documents.

Such a report should also include as appropriate any protocol amendments or deviations, and data exclusions with the appropriate rationale.

The level of detail of the clinical performance study report will vary based on the class of the IVD medical device:

- Class A – A clinical performance study would not be expected hence a report would not be required.
- Class B – The study report would be limited to a summary of the study protocol, results and conclusion.
- Class C – The complete study report includes the method of data analysis, the study conclusion and relevant details of the study protocol.
- Class D – The complete study report includes the method of data analysis, the study conclusion, relevant details of the study protocol, and typically the individual data points (formatted raw data).

7.1 Clinical performance study report after close-out including premature termination

After the close-out of the clinical performance study, including premature termination, a report of the study shall be completed, containing the information listed below.

a) The clinical performance study report shall be in written form (including electronic or hard copy);

b) The title page should contain the following information:
   i. Title of the clinical performance study;
   ii. Identifiers of the clinical performance study (e.g. study number) where applicable;
   iii. Brief identification of the IVD medical device(s) under investigation, including names, models, etc., as relevant for complete identification;
   iv. When relevant, statement indicating whether the clinical performance study was performed in accordance with this document or any other applicable guidelines and applicable regulations;
   v. Date of report;
   vi. Author(s) of report.

c) A table of contents, where included, shall include the page number or locate information of each section; the introduction shall contain a brief statement placing the clinical performance study in the context of the development of the IVD medical device under investigation and relating the critical features of the clinical performance study (e.g. objectives and hypotheses, target population, treatment and follow-up duration) to that development.

Guidelines or standards that were followed in the development of the CPSP, or any: other agreements or meetings between the sponsor and regulatory authorities that are relevant to the particular clinical performance study, shall be identified or described.

d) A description of the IVD medical device under investigation, containing the following points:
   i. A description of the IVD medical device under investigation, including device identifier;
   ii. The intended use of the IVD medical device(s) under investigation;
   iii. Any changes to the IVD medical device while under investigation during the clinical performance study.

NOTE: Any change could be a critical change that invalidates the study when performance is affected.

e) A summary of or a reference to the CPSP, including any subsequent amendment(s) with a rationale for each amendment, shall be provided. The latest version of the CPSP may be appended to the report;

f) The results of the clinical performance study should cover the following points:
   i. the clinical performance study initiation date;
   ii. the clinical performance study completion/suspension date;
   iii. a listing of the clinical performance study sites where the study was conducted, dates for each, and details of conduct for each site, e.g. collection, testing;
   iv. a description of study-specific training received by site staff;
   v. the disposal of specimens and IVD medical devices under investigation;
   vi. the subject demographics/specimen characterization, when applicable;
   vii. CPSP conformity (including number and type of protocol deviations);
   viii. an analysis, which includes
      - a statistical analysis of the data resulting from the CPSP,
      - the statistical analysis method used and the acceptance criteria,
      - a summary of all adverse device effects,
      - a table compiling all observed device deficiencies that could have led to a serious adverse device effect, and any corrective actions taken during the clinical performance study, if any,

- any needed subgroup analyses for special populations (i.e. gender, racial/cultural/ethnic subgroups), as appropriate,
- an accountability of all subjects and specimens, as applicable to the study, with a description of how missing data or deviations(s) were dealt with in the analysis e.g. specimens not passing screening tests, invalid results.

g) A discussion of the study and overall conclusions. The conclusions shall include the following points:
   i. a critical appraisal of the study results to determine whether the aims of the study have been met;
   ii. the safety or performance results and any other endpoints;
   iii. any specific benefits or special precautions required for individual subjects or groups considered to be at risk;
   iv. any implications for the conduct of future clinical performance studies;
   v. any limitations of the clinical performance study.

h) A list of abbreviated terms, and definitions of specialized or unusual terms;

i) A section on ethics which shall include the following points:
   i. a confirmation that the CPSP and any amendments to it were reviewed by the ethics committee (when required);
   ii. a list of all ethics committees consulted in relation to the clinical performance study.

j) An overview of the administrative structure which shall include the following points:
   i. a brief description of the organization of the clinical performance study;
   ii. a list of investigators, including their affiliations and potential conflict of interests;
   iii. the names and complete contact details for any third parties that were directly involved in the conduct of the study.

When applicable, the clinical performance study report shall be made available in a documented manner to all principal investigators for review and comments recorded.

8.0 Appendix

The table below lists the most common test purposes and provides examples to illustrate their differences.

TABLE: DESCRIPTION OF COMMON TEST PURPOSES FOR IVD MEDICAL DEVICES		
Test Purpose	**Description**	**Examples**
Diagnosis	Diagnostic tests are used to determine, verify or confirm a patient's clinical condition as a sole determinant. This type of testing also includes sole confirmatory assays (to verify results of previous testing) and sole exclusion assays (to rule out a particular condition). These tests are designed to evaluate a patient's current state.	▪ HBs antigen confirmatory assay to verify positive screening results
Aid to Diagnosis	Aid to Diagnosis tests is used to provide additional information to assist in the determination or verification of a patient's clinical status. The test is not the sole determinant. These tests are designed to evaluate a patient's current state.	▪ troponin test as an aid in myocardial infarction diagnosis ▪ thyroid-stimulating hormone test to evaluate thyroid function ▪ toxoplasma IgG avidity assay to determine likelihood of active infection ▪ ANA test for autoimmune disease determination

TABLE: DESCRIPTION OF COMMON TEST PURPOSES FOR IVD MEDICAL DEVICES

Test Purpose	Description	Examples
Screening	Screening tests are used to determine the status of a disease, disorder or other physiological state in an asymptomatic individual. These types of tests include genetic screening assays, tests for physiological typing, and tests used to reduce the risk of infectious disease transmission, such as assays for prenatal screening and donor screening (transfusion or transplantation). Depending on the nature of the condition and the targeted patient population, screening tests may be used routinely or may be restricted to 'at risk' patients. These tests are designed to evaluate an individual's current state.	▪ test to detect hepatitis B surface antigen in donated blood ▪ test to detect HIV1/2 antibodies in donated blood ▪ test to detect syphilis antibodies in donated blood ▪ prenatal rubella IgG screening in pregnant women ▪ tests for the determination of HLA, blood groups and blood group factors for donor matching
Monitoring	Monitoring tests are used for the measurement of analyte levels for the purpose of adjusting treatments/interventions as required. Monitoring tests include the following: ▪ Assays which are used to ensure that an analyte remains within physiological levels or within an established therapeutic drug range. These types of monitoring tests are designed to evaluate an individual's current state. ▪ Assays which are used for serial measurement, whereby multiple determinations are taken over time. These types of monitoring tests are typically used for the detection/assessment of disease progression/regression, disease recurrence, minimum residual disease, response/resistance to therapy, and/or adverse effects due to therapy. These types of monitoring tests are designed to evaluate changes in an individual's state	▪ self-test glucose monitoring to allow for quick responses to hyperglycemia or hypoglycemia ▪ viral load testing of patients known to be infected with HIV to determine treatment response and adjust therapy if necessary

TABLE: DESCRIPTION OF COMMON TEST PURPOSES FOR IVD MEDICAL DEVICES

Test Purpose	Description	Examples
Predisposition	Predisposition assays are used to determine the likelihood of disease onset (i.e. assessing the risk of developing the disease in future) in presymptomatic patients. For patients at sufficient risk (as determined by test results), preventive interventions may be taken. These tests are designed to evaluate a patient's future state.	▪ genetic test for apolipoprotein E to assess the risk of developing Alzheimer's disease
Prognosis	Prognostic tests are used to measure factors linked to clinical outcome irrespective of treatment. Such tests may be used to estimate the natural progression of a disease (i.e. outcome in the absence of treatment), or to determine the likelihood of a clinical outcome irrespective of therapeutic intervention. These tests are designed to evaluate a patient's future state.	▪ highly sensitive C-reactive protein measurement for the risk stratification of patients with acute coronary syndromes to determine the likelihood of future cardiac events ▪ measurement of baseline HIV-1 RNA level to assess patient prognosis ▪ cancer gene expression profile testing for metastasis risk to tailor treatment aggressiveness
Prediction (of Treatment Response or Reaction)	Predictive tests are used to measure factors that determine the likelihood of patient responses or adverse reactions to a specific therapy. Predictive tests designed specifically for use with a targeted therapy are sometimes termed 'companion diagnostics' or 'Personalized medicine'. These tests are designed to evaluate a patient's future state.	▪ HER-2/neu testing in breast cancer patients to assess likelihood of response to hormone therapy ▪ identification of variations in cytochrome P450 genes (i.e. metabolizer status) to determine potential therapeutic benefits and/or adverse reactions to antiplatelet treatment
Determination of Physiological Status	Physiological status determination tests are used to evaluate the physiological state of an individual for the purpose of identifying a human condition or characteristic. These tests are designed to evaluate a patient's current state.	

Depending on its intended use, an IVD medical device may have one or more test purposes. For example, a nucleic acid-based infectious disease assay may be used for diagnosis (testing in patients suspected to be infected), screening (testing in asymptomatic patients) and monitoring (determination of viral load to assess effectiveness of treatment).
In some cases, it may be difficult to define a distinct test purpose, especially when one is dependent on (or linked to) another. For example, a single genetic test may be used to detect the genotype (i.e. screening) as well as providing the likelihood of developing the condition (i.e. predisposition).

9.0 Revision History

Revision No.	Date	Author	Description of change	Sections modified	Approvals

10.0 Bibliography

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