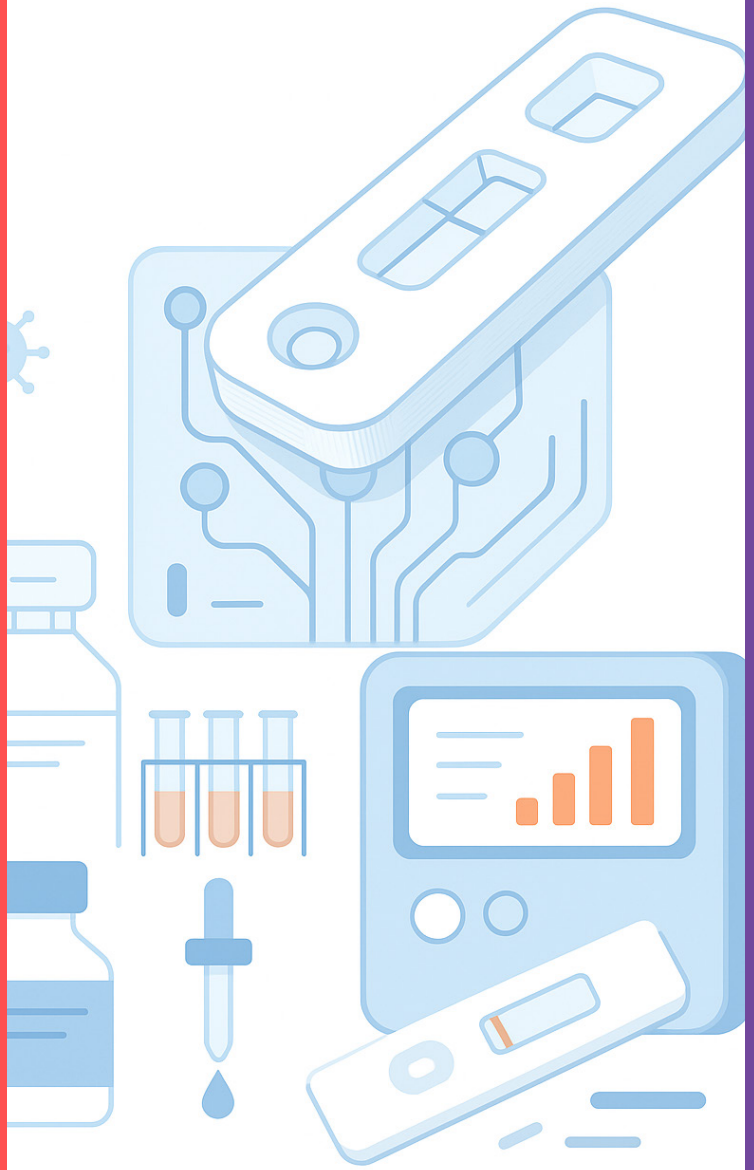


MedTech Mitra's

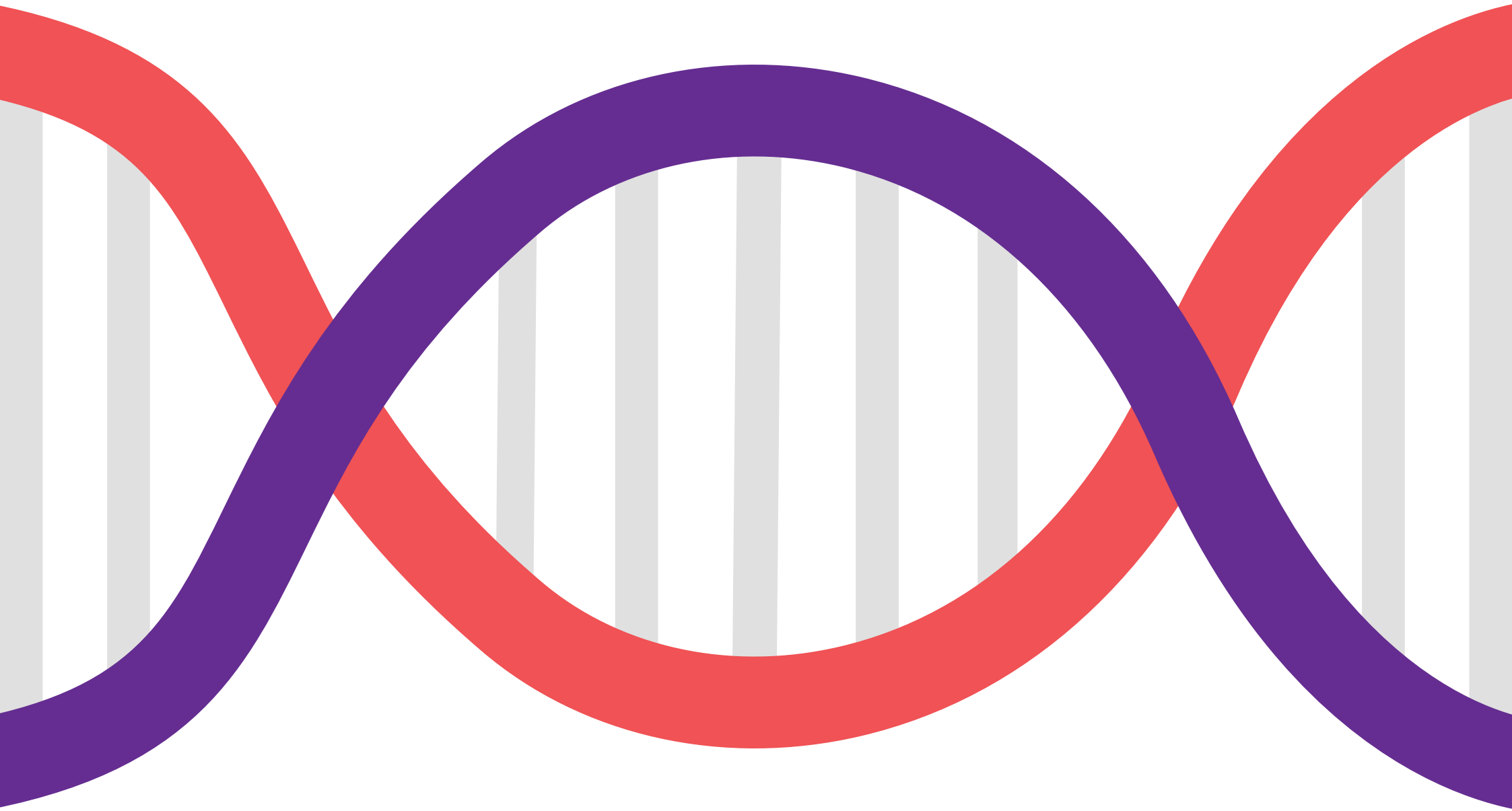
In-Vitro Diagnostic

INNOVATORS HANDBOOK

ICMR INDIAN COUNCIL OF MEDICAL RESEARCH
Serving the nation since 1911

MedTech mitra
Handholding MedTech innovators for clinical evaluation, regulatory facilitation and uptake of new products
A NITI Aayog-ICMR-CDSCO initiative

CDSCO



MedTech Mitra's In-Vitro Diagnostic Innovators Handbook

List of Contributing Institutes

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Foreword

November 11, 2025

India stands at a defining moment in the evolution of its healthcare innovation landscape. The demand for high-quality, affordable, and accessible medical devices and diagnostics is rising rapidly not only within our borders but across the global health ecosystem. This surge presents both a challenge and an unprecedented opportunity for Indian innovators, entrepreneurs, and researchers to design solutions that address pressing healthcare needs while advancing India's position as a trusted hub for medical technology innovation.

The Government of India, through initiatives has emphasized the importance of indigenous medical device manufacturing and the development of robust innovation ecosystems. Programs led by the Indian Council of Medical Research (ICMR), NITI Aayog, and academic institutions such as IITs and AIIMS have created unprecedented opportunities for innovators to access mentorship, funding, validation, and technology transfer support. Yet, the true impact of these initiatives depends on how effectively innovators can plan, execute, and scale their ideas ensuring that innovation does not remain confined to laboratories but reaches patients, hospitals, and communities.

This MedTech Mitra's In Vitro Diagnostic Innovators handbook for is a step towards institutionalizing that process. Organized into six comprehensive chapters, the workbook provides a structured roadmap for innovators, from identifying unmet clinical needs to developing, validating, and commercializing their technologies. It encourages innovators to think holistically, integrating scientific rigor with regulatory preparedness, quality systems, and market readiness.

As India moves towards becoming a global leader in affordable and high-quality healthcare technologies, it is imperative that our innovators adopt structured, time-bound, and mission-driven approaches to innovation. The Government, through its various institutions and platforms, will continue to provide the ecosystem, mentorship, and facilitation necessary to help these innovations thrive.

I commend the authors of this handbook for their effort in empowering India's MedTech innovators with a practical and visionary tool. I urge all readers scientists, clinicians, entrepreneurs, and policymakers to internalize the principles outlined here and apply them diligently in their innovation journeys. Together, let us transform India into a powerhouse of medical technology that not only meets domestic healthcare needs but also contributes meaningfully to global health security and well-being.

Jai Hind.

Dr Vinod K. Paul
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Foreword

India's healthcare ecosystem is evolving rapidly, and with it, the demand for reliable, high-quality, and accessible medical technologies continues to rise. Our nation is home to an exceptional pool of scientists, clinicians, and innovators who are contributing significantly to advancing healthcare research and innovation. The Indian Council of Medical Research (ICMR) has been at the forefront of supporting this ecosystem through a wide range of research programs and innovation-driven initiatives aimed at addressing national and global health priorities.

ICMR supports numerous medical research and product development projects representing the growing strength of India's scientific community and its potential to develop impactful medical technologies. However, for these innovations to achieve clinical and societal relevance, rigorous clinical validation is essential. Clinical validation ensures that every new diagnostic or medical device not only performs accurately and consistently but also meets the highest standards of patient safety and clinical utility.

The journey from laboratory discovery to patient care requires systematic planning, collaboration, and adherence to defined standards. Innovators and researchers must work closely with clinicians, hospitals, and industry partners to design and execute validation studies that reflect real-world clinical conditions. This evidence-based approach is crucial for building trust among healthcare professionals, regulatory authorities, and patients.

This MedTech Mitra's In Vitro Diagnostic Innovators Handbook developed jointly by ICMR and CDSCO (IVD Division) provides a structured pathway to help innovators understand and plan their clinical validation strategies effectively. By mapping key milestones and expectations across the innovation lifecycle, the workbook enables researchers to anticipate requirements, align with regulatory and ethical norms, and generate robust clinical evidence to support their product's safety and efficacy.

ICMR continues to extend strong support through initiatives such as the Medical Device and Diagnostics Mission Secretariat (MDMS) which provide mentorship, funding, and facilitation for innovators at different stages of their journey. Through these mechanisms, we aim to ensure that promising technologies are validated, scaled, and brought to market efficiently ultimately improving healthcare delivery for millions.

I encourage all innovators, researchers, and clinicians to embrace clinical validation as a vital step in the innovation process. By upholding the highest standards of science, ethics, and quality, we can ensure that India's medical devices and diagnostics stand among the best in the world. ICMR remain committed to supporting this journey through continuous engagement and handholding.

Together, let us work towards making India a global leader in developing safe, effective, and high-impact healthcare technologies for all.

Jai Hind.

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Foreword

India's medical technology landscape is witnessing an extraordinary transformation. A surge of innovation is emerging from our academic institutions, start-ups, and research centres. This reflects the creativity, scientific strength, and determination of our innovators. These innovations are addressing some of the most critical healthcare challenges faced by our nation, and increasingly, the world. As the medical device and in vitro diagnostic (IVD) sectors evolve rapidly, it becomes imperative for innovators to plan their regulatory journey as an integral part of their development roadmap.

In recent years, India's regulatory framework for medical devices has undergone significant strengthening and harmonization. The Medical Devices Rules, 2017 and subsequent amendments have aligned India's regulatory standards with global best practices. Today, our regulatory ecosystem stands among the most robust in the world emphasizing patient safety, product quality, and performance without impeding innovation. This progress reflects the Government's vision of ensuring that India not only innovates for itself but also contributes high-quality, globally acceptable medical technologies.

To translate innovation into market-ready products efficiently, innovators must understand, anticipate, and incorporate regulatory requirements at every stage from design and development to validation, manufacturing, and commercialization. Planning regulatory implementation early in the innovation cycle ensures that time-to-market is optimized and compliance gaps are minimized. This proactive approach transforms regulation from a perceived barrier into a strategic enabler of innovation.

In this context, the collaboration between ICMR and CDSCO (IVD Division) to develop this MedTech Mitra' s In Vitro Diagnostic Innovators Handbook is a commendable initiative. The workbook provides a structured, time-based framework to help innovators identify key regulatory milestones, documentation requirements, and quality management expectations across the product lifecycle.

CDSCO remains committed to supporting innovation through transparent processes, consultative engagement, and multiple facilitation mechanisms including the MedTech Mitra initiative and regular stakeholder interactions. Our goal is to ensure that every innovation emerging from India meets the highest standards of safety, efficacy, and quality, and that Indian products gain recognition and acceptance in global markets.

I extend my best wishes to all innovators, researchers, and entrepreneurs who are shaping the future of India's medical device ecosystem. Together, let us strive to build an innovation environment where regulatory excellence and scientific ingenuity work in harmony to deliver better healthcare outcomes for patients across the world.

Jai Hind.

RAJEEV SINGH RAGHUVANSHI
Digitally signed by RAJEEV SINGH RAGHUVANSHI
Date: 2025.11.11 10:51:01 +05'30'

Dr. Rajeev Singh Raghuvanshi
Drugs Controller General of India, CDSCO

Preface

The landscape of in vitro diagnostics (IVDs) is evolving at a remarkable pace, driven by scientific discovery, technological innovation, and the growing demand for accurate, timely, and accessible healthcare solutions. As diagnostics expand beyond traditional laboratory settings into point-of-care platforms, semi and auto analysing devices and software enabled tools, the need for clear, comprehensive, and practical regulatory guidance has never been greater.

This Innovators handbook has been developed with the aim of supporting all stakeholders such as manufacturers, developers, regulators, healthcare providers, and academic researchers in navigating the complex requirements associated with development of IVDs. It consolidates regulatory expectations, best practices, and internationally harmonized standards into a structured format designed to be both informative and actionable.

The preface also highlights the collaborative spirit behind this effort. Contributions have come from experts across multiple disciplines, reflecting the interdisciplinary nature of IVD development and evaluation. By presenting this document in a workbook format, we seek to provide not just static guidance but a dynamic tool that can be adapted and applied to real-world scenarios.

While this handbook is not legally binding, it is intended to complement existing regulations under the Medical Device Rules, 2017, and other applicable frameworks. Users are encouraged to apply its principles in conjunction with statutory requirements and institutional policies.

We envision that this handbook will serve as a practical companion throughout the product lifecycle from design and development through regulatory submission, manufacturing, and post-market surveillance. Above all, it aspires to promote patient safety, innovation, and quality in diagnostics, ensuring that IVDs remain a cornerstone of modern healthcare delivery.

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Scope

This innovators handbook serves as a comprehensive resource for first-time developers of In Vitro Diagnostic (IVD) medical devices, offering structured insights into step by step development of regulatory compliant IVD medical device production in India. By outlining key legal and procedural requirements, this document aims to minimize delays and reduce confusion among manufacturers, ensuring a more streamlined pathway from development to commercialization.

Recognizing the complexities of IVD medical device regulations, this guidance builds upon existing frameworks established by the Central Drugs Standard Control Organization (CDSCO) and the Indian Council of Medical Research (ICMR). By integrating the essential elements of these regulatory documents, it provides a simplified yet comprehensive roadmap to help innovators prepare for performance validation, regulatory submissions, and market entry.

A key feature of this document is the inclusion of To Do Lists at the end of each chapter, designed to support developers in understanding and fulfilling regulatory expectations. These To Do Lists provide a step-by-step breakdown of critical aspects such as device classification, performance evaluation, risk assessment, quality management system (QMS) compliance, and post-market surveillance. By following these structured guidelines, manufacturers can ensure that their IVD meet the required safety, efficacy, and quality standards mandated by regulatory authorities.

Furthermore, this handbook emphasizes the importance of early regulatory engagement and compliance planning, helping developers align their innovation with national and international best practices. It highlights the need for rigorous verification and validation of test methodologies, ensuring that the level of validation is proportionate to the risks posed by the IVD to the user, the patient, or public health.

Disclaimer

This handbook serves as a guidance resource and should not be considered a standalone regulatory reference. Manufacturers and innovators must refer to the official CDSCO website, as well as the ICMR MedTech Mitra portal, for the latest updates on IVD medical device regulations, approvals, and compliance requirements. Regulatory frameworks are subject to periodic revisions, and it is the responsibility of developers to stay informed about any changes that may impact their device approval and market authorization process.

Abbreviations

CDSCO	Central Drugs Standard Control Organization
NIB	National Institute of Biologicals
NHMRC	National Health and Medical Research Council
IVD	In Vitro Diagnostic
ISO	International Organization for Standardization
CLSI	Clinical and Laboratory Standards Institute
MD	Medical Device
MIA	Multivariate Index Assay
CMDTL	Central Medical Device Testing Laboratory
MDTL	Medical Devices Testing Laboratory
PCR	Polymerase Chain Reaction
NOC	No objection certificate
QC	Quality Control
QS	Quality System
INR	Indian National Rupee
RUO	Research Use Only
TGA	Therapeutic Goods Administration
CLA	Central Licensing Authority
SLA	State Licensing Authority
PMS	Post Marketing Surveillance
MvPI	Materiovigilance Program of India
PMCI	Post Marketing Clinical Investigation
PSUR	Periodic Safety Update Report
TRL	Technology Readiness Level
PoC	Proof of Concept
ICMR	Indian Council of Medical Research
MDMS	Medical Device and Diagnostics Mission Secretariat

Definitions

1. **Accuracy:** Closeness of agreement between a test result and the accepted reference value.

2. **Analytical performance:** The ability of an IVD medical device to detect or measure a particular analyte.

3. **Analytical Sensitivity:** The capability of the method to distinguish between two close concentrations of the target marker/analyte.

4. **Analytical Specificity:** The ability of an assay to measure in a sample a particular target measurand in the presence of for example other analyte/marker, matrix, interfering substances/organisms or cross-reactive species/agents.

5. **Assay Cut-off:** An assay cut-off is the predefined threshold value that determines whether a test result is positive, negative, or inconclusive. It serves as the critical point that distinguishes between different diagnostic outcomes, such as the presence or absence of an analyte (e.g., a pathogen, antibody, or biomarker) in a sample. The cut-off is essential in in-vitro diagnostic (IVD) assays because it ensures standardized interpretation of results across laboratories and clinical settings. It is often used in tests for infectious diseases (e.g., viral or bacterial infections), cancer biomarkers, or immunological conditions to provide actionable information for patient care.

6. **Bias:** Difference between the expectation of the test results and an accepted reference value.

7. **Biological reference Interval:** Specified interval of the distribution of values taken from a biological reference population.

8. **Calibrator:** A measurement reference material used in the calibration of a device.

9. **Clinical data:** Safety or performance information that is generated from the clinical use of a medical device.

10. **Clinical evaluation:** The assessment and analysis of a medical device's clinical data to verify the device's clinical safety and performance when used as intended by the manufacturer.

11. **Clinical evidence:** Clinical data and performance evaluation results, about a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s) when used as intended by the manufacturer.

12. **Clinical investigation plan:** A document that contains information about the rationale, aims and objective, design, and the proposed analysis, conduct, and methodology including performance, management, adverse event, withdrawal, and statistical consideration and record-keeping about clinical investigation.

13. **Clinical performance of an IVD medical device:** The ability of an IVD medical device to yield results that are correlated with a particular

clinical condition or physiological state by the target population and intended user.

14. **Clinical research organization:** Any entity to whom a sponsor may transfer or delegate one or more of its functions and duties regarding the conduct of a clinical investigation or clinical performance evaluation.

15. **Control material:** A substance, material or article intended by its manufacturer to be used to verify the performance characteristics of a device.

16. **Cross-reactivity:** Degree to which a substance other than the analyte binds to a reagent in a competitive binding immunochemical measurement procedure .

17. **Cut-Off Value:** Quantity value used as a decision limit to identify samples that indicate the presence or the absence of a specific disease, condition or measurand.

18. **Device for near-patient testing:** Any device that is not intended for self-testing but is intended to perform testing outside a laboratory environment, generally near, or at the side of, the patient by a health professional.

19. **Device for self-testing:** Any device intended by the manufacturer to be used by lay persons, including devices used for testing services offered to lay persons utilizing information society service.

20. **Diagnostic Sensitivity:** The ability of a device to identify the presence of a target marker associated with a particular disease or condition.

21. **Diagnostic Specificity:** The ability of a device to recognise the absence of a target marker associated with a particular disease or condition.

22. **Ethics committee:** An independent body established in a Member State by the law of that Member State and empowered to give opinions for this Regulation, taking into account the views of laypersons, in particular patients or patients' organizations.

23. **External Quality Assessment/ Proficiency Testing (EQA/PT):** Refers to a system in which the performance of a laboratory is assessed periodically and retrospectively by an independent external agency to indicate any shortcomings in the laboratory's performance through external Quality Assessment (EQA) program/ Proficiency Testing.

24. **Importer:** means any natural or legal person established within the Union that places a device from a third country on the Union market.

25. **Instructions for use:** The information provided by the manufacturer to inform the user of a device's intended purpose and proper use and of any precautions to be taken.

26. **Intended purpose**: The use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements, or as specified by the manufacturer in the performance evaluation.

27. **Intermediate Precision:** Precision under conditions intermediate between reproducibility conditions and repeatability conditions.

28. **Intermediate Precision Conditions:** Conditions where independent test results are obtained with the same method on identical test items in the same laboratory or location, but where other variables such as operators, equipment, calibration, environmental conditions and/or time intervals differ.

29. **Internal Quality Control (IQC):** Refers to the set of procedures undertaken by the laboratory personnel for the continuous and immediate monitoring of laboratory work to decide whether the results are reliable enough to be released.

30. **IVD Medical Device:** It is 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 **NOTE 1:** IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status. **NOTE 2:** In some jurisdictions, certain IVD medical devices may be covered by other national regulations.

31. **Kit:** A set of components that are packaged together and intended to be used to perform a specific in vitro diagnostic examination, or a part thereof.

32. **Label:** The written, printed, or graphic information appearing either on the device itself or on the packaging of each unit or on the packaging of multiple devices.

33. **Limit of blank (LoB):** Number of standard deviations above the mean value of the sample without analyte (measurand).

34. **Limit Of Detection (LoD):** Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand).

35. **Limit Of Quantitation (LoQ):** Lowest concentration at which precision and / or trueness are within specified criteria.

36. **Linearity:** The ability to provide measured quantity values that are directly proportional to the value of the measurand in the sample.

37. **Loan license:** A license issued for manufacturing a medical device by the State Licensing Authority or the Central Licensing Authority, as the case may be, to a person who intends to utilize the manufacturing site of another licence for manufacturing the same medical device as manufactured by the licence at that site.

38. **Manufacturer:** A natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured, or fully refurbished, and markets that device under its name or trademark.

39. **Market surveillance:** The activities carried out and measures taken by public authorities to check and ensure that devices comply with the requirements set out in the relevant Union harmonization legislation and do not endanger health, safety, or any other aspect of public interest protection.

40. **Medical device grouping:** A set of devices having the same or similar intended uses or commonality of technology allowing them to be classified in a group not reflecting specific characteristics.

41. **Metrological Traceability:** Property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty. The metrological traceability chain is a sequence of measurement standards and calibrations that is used to relate a measurement result to a reference.

42. **Negative predictive value:** The ability of a device to separate true negative results from false negative results for a given attribute in a given population.

43. **Performance evaluation:** An assessment and analysis of data to establish or verify the scientific validity, the analytical and, where applicable, the clinical performance of a device.

44. **Performance of a device:** The ability of a device to achieve its intended purpose as claimed by the manufacturer. It consists of the analytical and, where applicable, the clinical performance supporting that intended

purpose.

45. **Positive predictive value:** The ability of a device to separate true positive results from false positive results for a given attribute in a given population.

46. **Post-market surveillance:** All activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market, or put into service to identify any need to apply any necessary corrective or preventive actions immediately.

47. **Precision:** Closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions.

48. **Predicate device:** A device, first time and first of its kind, approved for manufacture for sale or import by the Central Licensing Authority and has a similar intended use, material of construction, and design characteristics as the device is proposed for a license in India.

49. **Primary Samples Specimen:** Discrete portion of a body fluid, breath, hair or tissue taken for examination, study, or analysis of one or more quantities or properties assured to apply for the whole.

50. **Quality Assurance (QA):** All planned or systematic actions necessary to provide adequate confidence that a service or product will satisfy given requirements for quality. QA is the comprehensive term that refers to all aspects of operation starting from preparation of the patient to sample collection, sample analysis, recording of the result, and its dispatch.

51. **Quality Control (QC):** Process of monitoring and evaluating work performance by measuring that performance against established standards.

52. **Quality Management System:** Requirements for manufacturing of medical devices as specified in the Fifth Schedule.

53. **Range:** A set of values of quantities of the same kind that can be measured by a given measuring instrument or measuring system with specified instrumental measurement uncertainty, under defined conditions.

54. **Reagent:** A chemical, biological, or immunological component, solution, or preparation intended by the manufacturer to be used as an in vitro diagnostic medical device.

55. **Recovery:** Proportion of the amount of analyte present in or added to a sample which is found by measurement.

56. **Repeatability:** Measurement under a set of conditions of measurement that includes the same measurement procedure, same operators, same measuring system ,same operating conditions and same location, and replicate measurements on the same or similar objects over a short period of time.

57. **Reproducibility:** Measurement under conditions that include different locations, operators, measuring systems and replicate measurements on the same or similar objects.

58. **Risk:** The combination of the probability of occurrence of harm and the severity of that harm.

59. **Recovery:** Proportion of the amount of analyte present in or added to a sample which is found by measurement.

60. **Robustness:** The robustness of an analytical procedure means the capacity of an analytical procedure to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

61. **Specimen receptacle:** A device, whether vacuum type or not, specifically intended by its manufacturer for the primary containment of specimens derived from human or animal bodies.

62. **Transmissible agent:** for classification of in vitro diagnostic medical device, means an agent capable of being transmitted to a person, which causes communicable, infectious, or contagious disease.

63. **TRL Analysis:** Technology Readiness Level - one of the assessment tools of the maturity level of a technology used by TTOs.

64. **Trueness:** Closeness of agreement between the average value obtained from a large series of test results and an accepted reference value.

65. **Unique Device Identifier:** A series of numeric or alphanumeric characters that are created through internationally accepted device identification and coding standards and that allow unambiguous identification of specific devices on the market.

66. **User:** Any healthcare professional or layperson who uses a device.

67. **Validation:** It is the documentary proof that the particular requirements for a specific intended use can be consistently fulfilled. it is an expectation that every lot of an IVD will behave as all other lots and will continue to meet design inputs. To ensure this, it is necessary to have validated test methods for measuring and/or monitoring specifications that will consistently produce results fit for purpose. The test methods must be validated to ensure that the results of measuring and/or monitoring are meaningful.

68. **Verification:** It is the documentary proof that particular specifications have been met. When designing and developing an IVD, relevant attributes such as cost, and those for performance such as precision, sensitivity and stability are identified and given numerical specifications in design input documentation. It is subsequently the role of the R&D department to design an IVD that will meet those specifications. The R&D department consequently identifies valid test methods to demonstrate that the specifications have been met (verified) in the new design. Once design has been established, further numerical specifications are produced by the R&D department to ensure that the specifications of each attribute will be met consistently in routine production and leading to quality manufacturing.

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CHAPTER

In-Vitro Diagnostic Innovation Journey & Proof of Principle

1.1 What is an In Vitro Diagnostic Medical Device?

IVD assay's are substances intended to be used outside human or animal bodies for the diagnosis of any disease or disorder.

- "is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination as intended by the manufacturer for the examination of specimens, including blood and tissue, derived from the human or animal body solely or principally to provide information for diagnostic, monitoring or compatibility purposes."
- IVD medical devices are any form of appliance, instrument, software, or device used by patients or healthcare professionals to perform tests using biological samples, such as blood, urine, or tissues, to determine a person's health status.

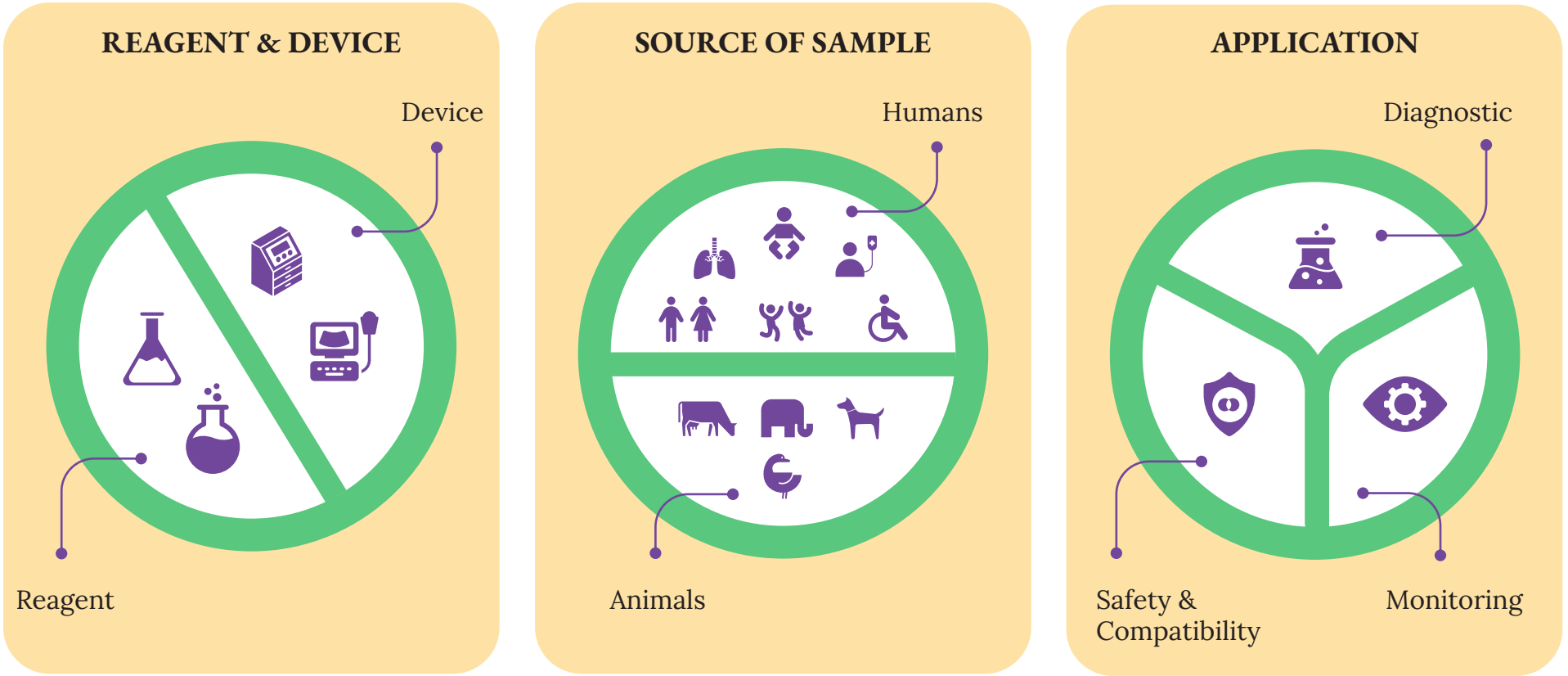


Figure 1: In-Vitro Diagnostic Medical Device overview

1.2 General Considerations

1.2.1 Intended use

The intended use describes how the test is to be used and by whom, for what condition, with what specimen type, for what patient or individual (e.g. age, race, gender, geography or clinical condition), and what is to be detected. The intended use also includes the function of the test that describes the circumstances under which an individual or patient would be tested. Functions may include:

- Screening (e.g. for surveillance or safety of blood supply)
- Monitoring patient therapy or following their progress after treatment
- Staging or aid to staging of disease
- Disease differentiation or prediction

1.3 IVD Medical Device Product Development Stage

The development process for an in vitro diagnostic (IVD) begins with the innovator or manufacturer conceptualizing an idea. This is followed by a comprehensive review of existing literature, publications, and intellectual properties to assess the novelty and viability of the concept. Subsequently, a proof-of-principle study is conducted to evaluate the scientific and technical feasibility of the idea. If feasible, the next step involves defining the methodological framework, such as biochemical, serological, or molecular assays etc., tailored to the diagnostic application. Finally, the intended use of the IVD is precisely defined to ensure its alignment with clinical and regulatory requirements.

The proof of priciple phase in the development of an in vitro diagnostic (IVD) product addresses four critical verticals to ensure a systematic and robust progression. First, assay development focuses on establishing diagnostic methodologies such as PCR, ELISA, or lateral flow assays (LFA), etc., this involves identifying and validating reagents and consumables to confirm their suitability for the intended application. Second, device development encompasses the design and integration of hardware, software, electronics, and optical components, ensuring these elements meet functional and technical requirements. Third, raw material used for manufacturing plays a pivotal role, with strict adherence to standard operating procedures (SOPs) for procurement, vendor qualification, and validation. This also includes the establishment of disposal protocols to comply with safety and environmental standards. Finally, the prototyping phase initiates with comprehensive documentation of the initial design, evolving through iterative development to the final validated design. All design modifications are controlled through a rigorous change management process to ensure that no deviations impact the intended use of the device. A Design Master File (DMF) is prepared to chronicle the entire design and development process. Throughout this phase, the implementation of a Quality Management System (QMS) in compliance with ISO 13485:2016 is essential, ensuring regulatory adherence and maintaining the highest product quality standards.

The design verification and validation phase is a critical stage in the development of an in vitro diagnostic (IVD) product, ensuring that all design specifications and requirements are met and that the device fulfils its intended use. Verification focuses on confirming that the design inputs such as functional, performance, and safety specifications are accurately translated into the final product without deviation. This involves rigorous testing to confirm that each component and system operates as expected in both isolated and integrated configurations. Validation, on the other hand, evaluates the overall product performance to ensure that it reliably delivers the desired outcomes in real-world applications and clinical settings.

This phase also emphasizes usability testing, which assesses whether the device is user-friendly and suitable for the intended operators, including laboratory professionals or healthcare providers. Usability studies identify potential challenges in handling, interpreting results, or integrating the device into existing workflows, ensuring that these issues are addressed before commercialization. By incorporating feedback from these assessments, the product is refined to maximize operational efficiency, minimize the likelihood of user error, and enhance overall satisfaction. Design verification and validation establish a robust foundation for regulatory approval and successful market entry.

With the technical aspects of the IVD product established, the innovator or manufacturer must now navigate the regulatory pathway to ensure compliance with Indian regulations. A critical first step in this process is determining whether the product has any existing predicates in India or if it qualifies as a completely novel innovator product. This evaluation informs the subsequent regulatory submissions.

To initiate the licensing process, the innovator or manufacturer must file Form MD 12 through the National Single Window System (NSWS) portal. Form MD 12 serves as an application for a license to manufacture medical devices intended for clinical investigations, tests, evaluations, demonstrations, or training. A checklist of required documents for this

application can be found on the “Online System for Medical Devices”, a Central Drugs Standard Control Organization (CDSCO) website.

Upon receiving approval for Form MD 12, the manufacturer can proceed to conduct performance evaluations as outlined in Form MD 13. If the IVD product has a predicate, the manufacturer may directly apply for a manufacturing license. In contrast, if the product is classified as an innovator product, the manufacturer must submit Form MD 24.

Once satisfactory performance evaluation results are obtained, the manufacturer can apply for a manufacturing license, which must align with the risk classification of the IVD. For Class A and B IVDs, the manufacturing license application is submitted using Form MD 3 or Form MD 4 in case of application for grant of loan license. Conversely, Class C and D IVD manufacturing licenses require submission of Form MD 7, or Form MD 8 in case of application for grant of loan license.

Following the submission, the regulatory agency will conduct a Quality Management System (QMS) audit. For Class A IVDs, this audit will occur post-approval of the manufacturing license, while for Classes B, C, and D, the technical audit or QMS audit will be carried out prior to the approval of the manufacturing license. This structured regulatory approach ensures that the IVD product adheres to the necessary safety and efficacy standards, facilitating its successful entry into the market.

Once the proof of concept is established, an industrial partner is onboarded, and the product design—encompassing electrical, mechanical, and/or software components, as applicable—is finalized, the manufacturer or innovator can proceed to to do list A. This to do list serves as a foundational tool to enhance their understanding of regulatory expectations, facilitating compliance with the applicable standards and guidelines.

1.4 Proof of Principle

1.4.1 Gap Analysis

The Proof of Principle (PoP) represents the foundational stage of pre - IVD development. At this stage, the manufacturer or innovator must undertake a comprehensive clinical need assessment a critical regulatory expectation and strategic imperative. This process involves a structured gap analysis to identify areas within the healthcare system where current diagnostic tools fall short and where improved clinical outcomes are achievable through innovative IVD solutions.

The assessment must be grounded in robust evidence, including but not limited to:

1. National and regional epidemiological data
2. Disease burden and surveillance reports (e.g., from ICMR, WHO)
3. Clinical workflow studies and hospital diagnostic pathway analysis
4. Stakeholder consultations with clinicians, laboratorians, and public health authorities
5. Review of existing treatment algorithms and diagnostic protocols

This ensures that the proposed IVD addresses a recognized public health priority and aligns with national health programs and clinical practice needs.

A comprehensive benchmarking of existing diagnostic solutions is a critical step in the Proof of Principle phase. This exercise enables the innovator to evaluate the current landscape of diagnostic products addressing the same or similar clinical conditions. The assessment should include both domestic and international products and cover key performance parameters such as sensitivity, specificity, positive and negative predictive values, time-

to-result, and throughput. Additional factors such as instrumentation requirements, ease of integration into existing laboratory workflows, and cost per test should also be considered. Benchmarking must extend beyond technical performance to include shelf life, ease of commercialization, and procurement data. By analyzing these aspects, innovators gain valuable insights into the strengths and limitations of existing technologies, identify gaps in performance or usability, and understand market expectations.

For an IVD to be successfully adopted and receive regulatory endorsement, it must demonstrate clear and clinically relevant differentiators. These may include:

1. Improved affordability and cost-effectiveness
2. Simplified sample-to-result workflow
3. Reduced training or technical expertise requirements
4. Portability for near-patient or decentralized testing
5. Faster turnaround times
6. Interoperability with existing diagnostic infrastructure

These differentiators should be clearly defined early in development to guide product design specifications, prototyping priorities, and go-to-market strategy. They also form a critical component of the regulatory submission narrative, demonstrating that the product fulfills an unmet need and offers a tangible advantage over existing solutions.

Furthermore, clearly articulated differentiators enhance the value proposition during funding discussions, procurement evaluations, and health technology assessments (HTAs).

1.4.2 Intended Use

During the proof of principle stage, it is essential to clearly define the intended use of the device. This forms a regulatory cornerstone and must describe the device's clinical purpose, the target population, the type of specimen, and the diagnostic application whether for screening, diagnosis, or monitoring. A well-crafted intended use statement ensures regulatory alignment and informs all subsequent development and performance evaluation activities.

Biomarker selection is the scientific basis of any IVD and must be biologically relevant, specific to the target condition, and consistently detectable in the selected specimen type. For infectious diseases, this may involve nucleic acids or antigens; for chronic conditions, enzymes or metabolites may be more appropriate. Selection should be justified through literature, clinical evidence, and feasibility of detection within the chosen specimen.

The specimen type significantly impacts diagnostic performance, usability, and regulatory classification. Factors such as analyte concentration, sample stability, collection ease, and biosafety must be considered. Specimen choice also affects kit design, reagent formulation, transport logistics, and clinical implementation.

Defining the target patient population is crucial for ensuring that performance claims are clinically meaningful. This includes specifying demographic and clinical subgroups (e.g., symptomatic adults in primary care). Such clarity supports ethical clinical study design, usability assessments, and accurate regulatory submissions.

Finally, the detection principle whether based on immunoassays, nucleic acid amplification, electrochemical signals, etc., must be clearly documented. This guides technical development, identifies applicable regulatory standards and supports analytical performance evaluation, risk management, and manufacturing scalability. Without this clarity, regulatory evaluation and product optimization are significantly compromised.

1.4.3 Target Product Profile

At the proof of principle stage, drafting a preliminary Target Product Profile (TPP) is essential to define the envisioned clinical, functional, operational, and regulatory characteristics of the IVD device. While not finalized, this early version of the TPP provides a strategic framework to align internal development goals and external stakeholder expectations, ensuring that subsequent efforts are clinically relevant, technically feasible, and regulatory compliant.

To begin with, it is important to describe the underlying detection principle that the assay will rely upon. This could include immunoassays, molecular amplification techniques such as PCR or LAMP, electrochemical sensing, fluorescence-based detection, or microfluidics. Documenting the detection approach at this stage helps assess feasibility, reagent compatibility, instrumentation needs, and potential limitations. It also informs early decisions on design complexity, integration with existing platforms, and suitability for point-of-care versus laboratory-based use.

Next, the TPP should specify sample requirements, such as the sample type (e.g., blood, urine, saliva), volume needed for detection, and any pre-processing steps like centrifugation, lysis, or filtration. Highlight whether any specialized equipment is required, as this directly impacts the practicality of the test in diverse clinical settings, especially in resource-limited environments. These early considerations also guide the layout of consumables (e.g., cartridges or cassettes), initial reagent formulations, and workflow simulations.

At this stage, developers must also outline anticipated analytical performance targets, including preliminary benchmarks for sensitivity, specificity, accuracy, and the expected Limit of Detection (LoD). These values should be realistic and informed by existing literature or early laboratory findings. Although exact performance claims will be refined in later stages, early targets provide a goalpost for assay optimization and help in selecting appropriate reference methods for future validation.

Equally important is defining the clinical performance expectations, including Positive Predictive Value (PPV), Negative Predictive Value (NPV), and diagnostic sensitivity and specificity. While these values are often context-dependent and influenced by disease prevalence, having an early estimate helps frame the clinical utility of the test—whether for screening, diagnosis, or monitoring and supports future decisions on sample size, patient recruitment, and study endpoints in clinical evaluations.

Operational feasibility must also be addressed by listing anticipated user profiles, target test settings (e.g., home, clinic, hospital lab), and turnaround time. These elements influence user interface design, packaging, instruction formats, and overall usability. For example, if a test is intended for primary care or self-testing, the TPP should anticipate simplified workflows and minimal operator training, while a lab-based test might prioritize throughput and integration with laboratory information systems.

Additionally, the TPP should provide a preliminary assessment of the regulatory classification under India's Medical Device Rules (MDR) 2017. This includes identifying the likely risk class (A to D) based on the intended use, test complexity, and clinical impact. It is also useful to list anticipated standards such as ISO 13485 for quality systems, ISO 14971 for risk management, and ISO 23640 for stability testing. Early classification planning ensures regulatory readiness and supports strategic alignment with Indian and global market entry requirements.

Finally, the TPP should propose a shelf-life estimate, informed by the anticipated reagent stability and storage conditions (e.g., refrigerated or ambient). Although formal data will be generated later, an early estimate is critical for planning accelerated stability studies, packaging design, and logistical feasibility, especially in public health programs or rural deployments.

By establishing a robust preliminary TPP during the proof of principle stage, developers lay a strong foundation for focused innovation, efficient

resource use, and regulatory alignment critical for translating an idea into a viable, impactful diagnostic product.

During the proof of principle stage, identifying a predicate or reference device is valuable. If a similar, legally marketed device (CDSCO-approved) exists, it should be used to define the parameters for performance evaluations and regulatory applications. The predicate's intended use, sample type, target condition, and result format should closely match the new assay. This allows the development team to benchmark performance expectations, anticipate regulatory documentation needs, and avoid reinventing performance evaluation frameworks.

It is important to verify similarity in intended use and assess whether both devices address comparable sample types and output formats (qualitative vs quantitative). Even subtle changes like switching from nasopharyngeal swabs to saliva can impact assay performance and require new studies. Similarly, if your device targets a different patient population or user profile (e.g., home use vs clinical lab), note this early, as it will influence risk classification and usability studies later on.

1.4.4 Pilot - Performance Data

The goal at the proof of principle stage is to demonstrate that the assay concept functions with real or contrived samples under controlled conditions. Begin by running a small panel of clinical or spiked specimens to confirm the test yields clear, interpretable results such as visible bands, fluorescence signals, or quantifiable curves. These experiments validate the core detection logic and surface issues like matrix interference or inconsistent signals.

Establish a rough estimate of Limit of Detection (LoD) and preliminary specificity using dilution panels or negative controls. While not definitive, this data helps frame design tolerances and identify the need for signal amplification or reagent tuning. Evaluate basic linearity, precision, and reproducibility using simple repeat testing across concentrations and conditions. This gives insight into protocol consistency and pinpoints variability that must be addressed before scaling.

All findings should be compiled into a concise technical summary, documenting sample sources, assay methods, performance plots, and key observations. Include limitations, anomalies, and potential next steps. This report will serve as the foundation for go/no-go decisions, stakeholder updates, and early dialogue with regulators or grant bodies.

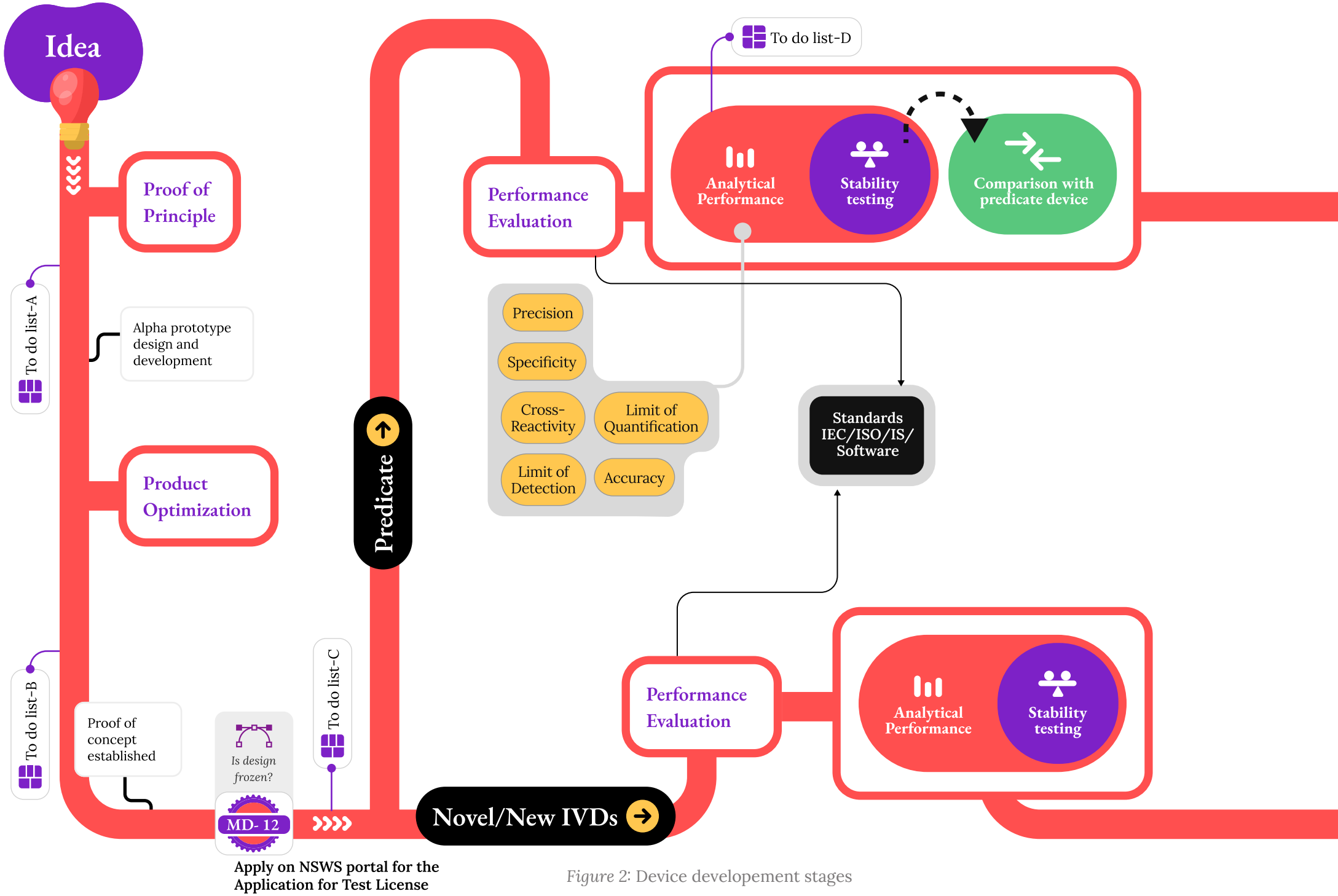
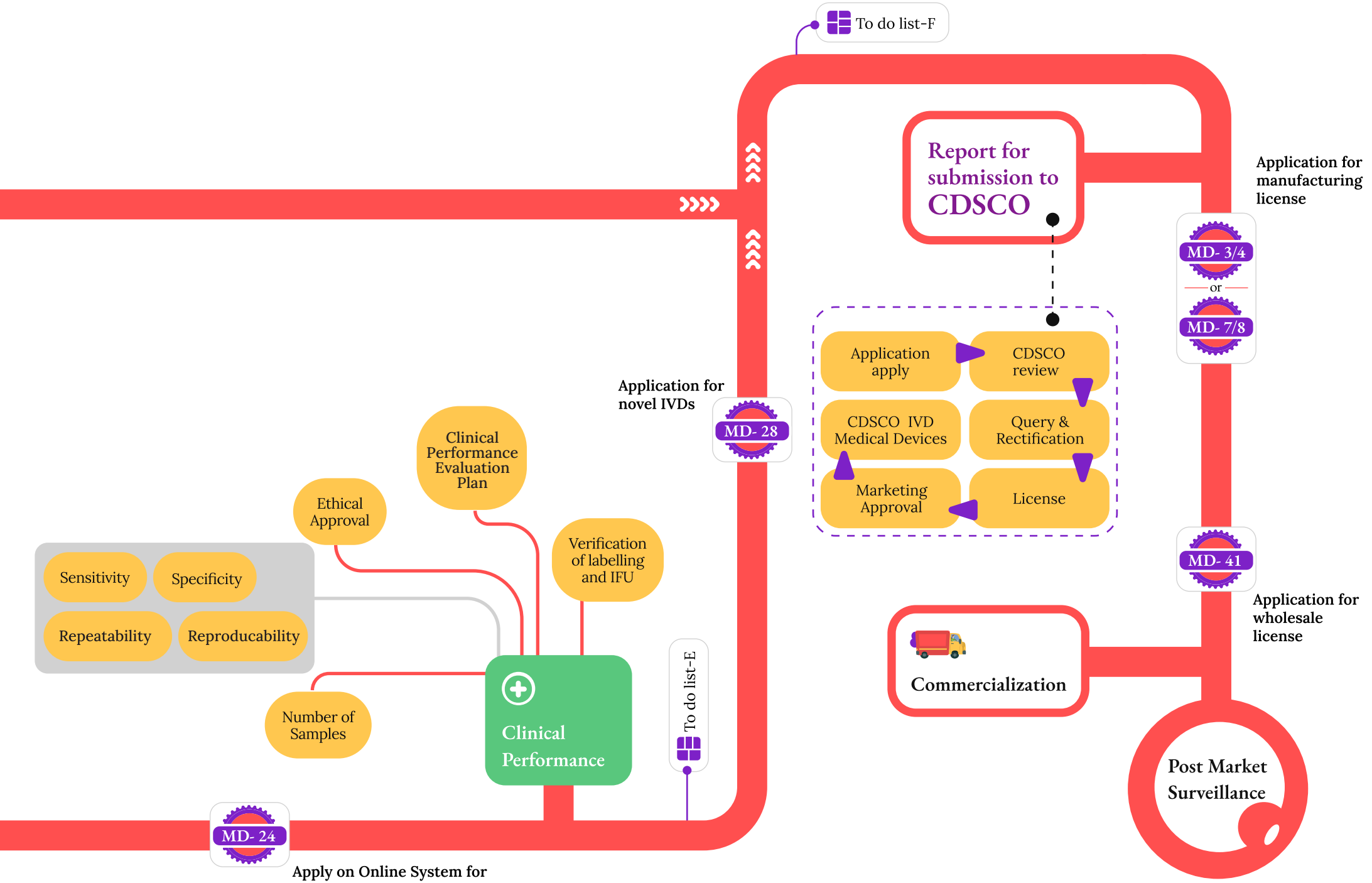


Figure 2: Device developement stages


To do list-F
Report for submission to CDSCO
Application for manufacturing license
MD- 3/4
or
MD- 7/8
Application apply
CDSCO review
CDSCO IVD Medical Devices
Query & Rectification
Marketing Approval
License
Application for novel IVDs
MD- 28
Clinical Performance Evaluation Plan
Ethical Approval
Verification of labelling and IFU
Sensitivity
Specificity
Repeatability
Reproducability
Number of Samples
Clinical Performance
To do list-E
MD- 41
Application for wholesale license
Commercialization
Post Market Surveillance
MD- 24
Apply on Online System for Medical Device Portal for MD-24

To do list A: Introduction to IVD & Proof of Principle

Gap Analysis: Identify and justify the clinical need for the IVD product. Benchmark existing solutions and define the opportunity for innovation and differentiation.

Sl. No	To do	Completed		Remarks
		Yes	No	
1.1	Conduct a clinical need assessment with supporting evidence			
1.2	Benchmark competing IVDs in India and globally (features, cost, performance).			
1.3	Define key differentiators for the new IVD (e.g., lower cost, ease of use, minimal calibration).			

Intended use: Define the clinical and diagnostic context in which the test will be used. Clarify target analyte, sample type, users, and the expected diagnostic outcome.

Sl. No	To do	Completed		Remarks
		Yes	No	
2.1	Identify the biomarker (e.g., pathogen, protein, nucleic acid, metabolite).			
2.2	Finalize the specimen type (e.g., blood, urine, saliva).			
2.3	Identify the use of the IVD (Diagnosis/Screening/ etc)			
2.4	Draft a clear and specific intended use statement.			
2.5	Define the target patient population (age, setting, disease state).			

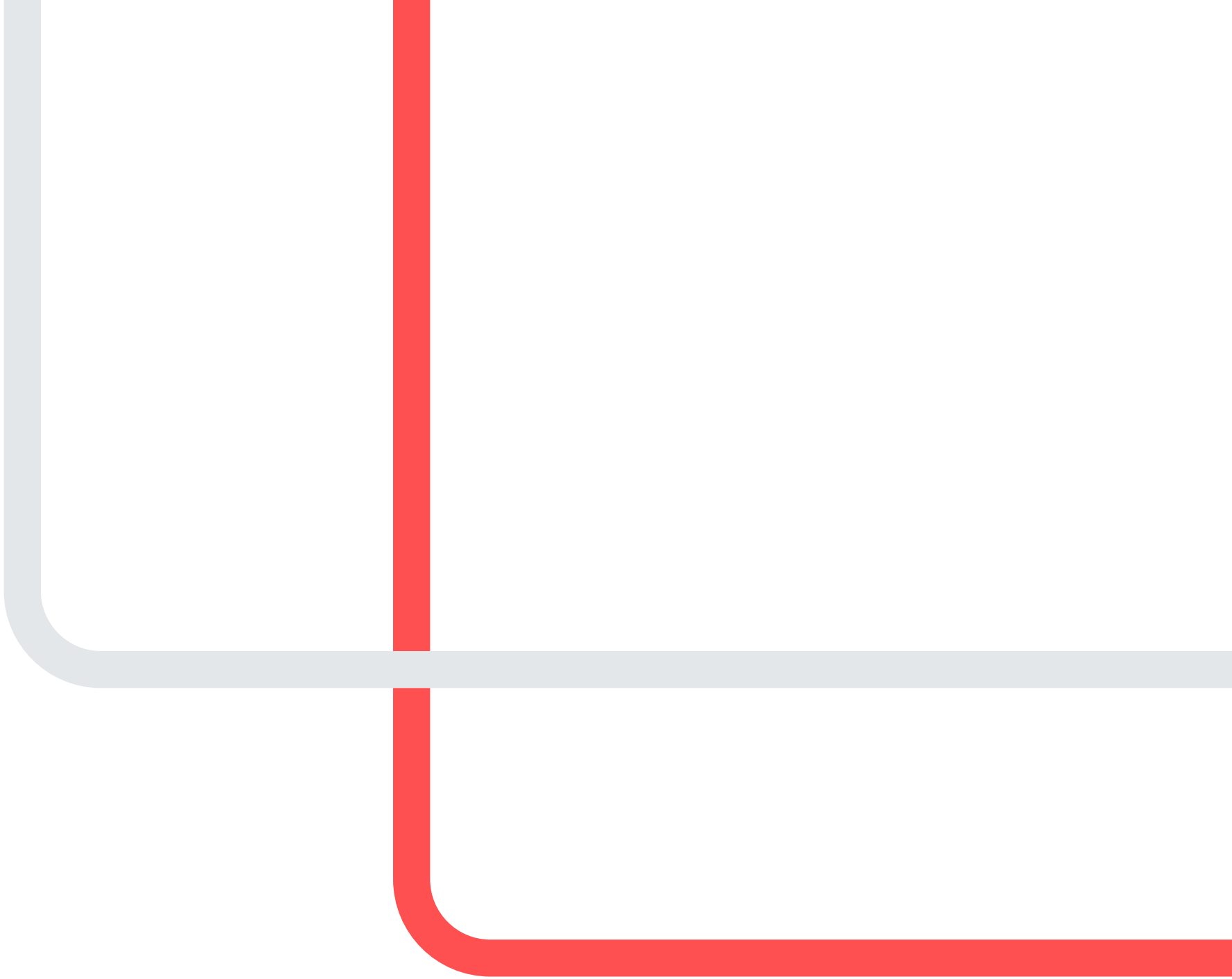
Sl. No	To do	Completed		Remarks
		Yes	No	
2.6	Specify the result type: qualitative or quantitative.			
2.7	Document the assay's core principle or technology.			

Target Product Profile: Define the product's functional, clinical, operational, and regulatory characteristics. This profile guides development priorities and aligns all stakeholders on expected outcomes.

Sl. No	To do	Completed		Remarks
		Yes	No	
3.1	Describe the underlying technology or detection principle.			
3.2	Specify sample requirements: volume, pre-processing, equipment needed.			
3.3	Define analytical performance targets (LoD, specificity, sensitivity, accuracy).			
3.4	Draft a clear and specific intended use statement.			
3.5	Define clinical performance targets (PPV, NPV, diagnostic sensitivity/specificity).			
3.6	List out Operational characteristics: turnaround time, user. lab test or home test			
3.7	Identify regulatory classification and applicable standards			
3.8	Set a shelf-life estimate based on reagent stability and storage conditions.			

Preliminary Data on Performance: Generate early functional data to demonstrate assay feasibility. Confirm signal detection, analytical range, and consistency using limited clinical specimens.

Sl. No	To do	Completed		Remarks
		Yes	No	
4.1	Demonstrate functional assay performance with limited clinical samples.			
4.2	Establish preliminary LoD and specificity.			
4.3	Evaluate assay linearity, reproducibility, and precision.			
4.4	Compile findings into a technical summary report.			



02

02

CHAPTER

Product Optimization

2.1 Classification of In-vitro Diagnostic Medical Devices:

Basic principles for the classification of in vitro diagnostic medical devices:

1. The intended use of the devices.
2. In combination with another device, the classification rules shall apply separately to each of the devices. Accessories are classified in their own right separately from the device with which they are used
3. Software, which drives a device or influences the use of a device, falls automatically in the same class.
4. Standalone software, which is not incorporated into the medical device itself and provides an analysis based on the results from the analyzer, shall be classified into the same category that of the in vitro diagnostic medical device where it controls or influences the intended output of a separate in vitro diagnostic medical device.
5. Calibrators intended to be used with a reagent should be treated in the same class as the in vitro diagnostic medical device reagent.

The classification of in vitro diagnostic (IVD) medical devices is based on their intended use and associated risks, as outlined below:

2.1.1 Class A (Lowest Risk)

a. IVDs used in in vitro diagnostic procedures:

1. Reagents or articles with specific characteristics intended for an IVD procedure.
2. Instruments designed specifically for an IVD procedure.
3. Specimen receptacles.

2.1.2 Class B (Low to Moderate Risk)

a. IVDs for Self-Testing:

1. Non-critical diagnostic results that do not determine a medically urgent status.
2. Preliminary test results requiring confirmation through laboratory testing.

b. Other IVDs:

1. Devices used for assessing the performance of an analytical procedure or its components without a quantitative or qualitative assigned value.
2. IVDs that do not fall under Class C or D categories.

2.1.3 Class C (Moderate to High Risk)

a. IVDs for Detecting Transmissible Agents:

1. Detecting sexually transmitted agents.
2. Detecting an infectious agent in cerebrospinal fluid or blood with limited risk of propagation (e.g., Cryptococcus neoformans, Neisseria meningitidis).
3. Identifying an infectious agent where an erroneous result may lead to death or severe disability (Chlamydia pneumoniae, Cytomegalovirus, MRSA).
4. Prenatal screening for immune status regarding transmissible agents (Rubella, Toxoplasmosis).
5. Determining infectious disease or immune status where errors could impact life-threatening patient management decisions.
6. Screening for disease stages, therapy selection, or cancer diagnosis.
7. Genetic testing (Cystic fibrosis, Huntington's disease).
8. Monitoring medicinal product levels, biological substances, or components where errors could lead to life-threatening management decisions (cardiac markers, cyclosporin, prothrombin time testing).
9. Managing patients with life-threatening infectious diseases (HIV or Hepatitis C viral load monitoring, HIV/HCV genotyping).
10. Screening for congenital disorders in fetuses (Down syndrome, spina bifida).
11. IVDs for Blood Grouping or Tissue Typing:
12. Ensuring immunological compatibility for transfusion or transplantation.

b. IVDs for Near-Patient Testing:

1. Blood gas analysis, blood glucose determination.
2. Anticoagulant monitoring, diabetes management, C-reactive protein, Helicobacter pylori testing.

2.1.4 Class D (Highest Risk)

a. IVDs for Detecting Transmissible Agents:

1. Detecting transmissible agents in blood, blood components, blood derivatives, cells, tissues, or organs to assess their suitability for transfusion or transplantation.
2. Detecting transmissible agents that cause life-threatening diseases with a high risk of propagation.

b. IVDs for Blood Grouping or Tissue Typing:

1. Blood grouping or tissue typing for critical systems (ABO, Duffy, Kell, Kidd, Rhesus, HLA, Anti-Duffy, Anti-Kidd).

2.2 Risk-based classification of IVD

IVDs are classified under Chapter II, Rule 4, Sub-rule (2) of Medical Device Rules 2017 on the basis of parameters specified in Part II of the First Schedule, in the following classes, namely:

The examples of risk-based classified In Vitro Diagnostic (IVD) medical devices outlined in Annexure 1. For the updated classification, please refer to the official CDSCO website.

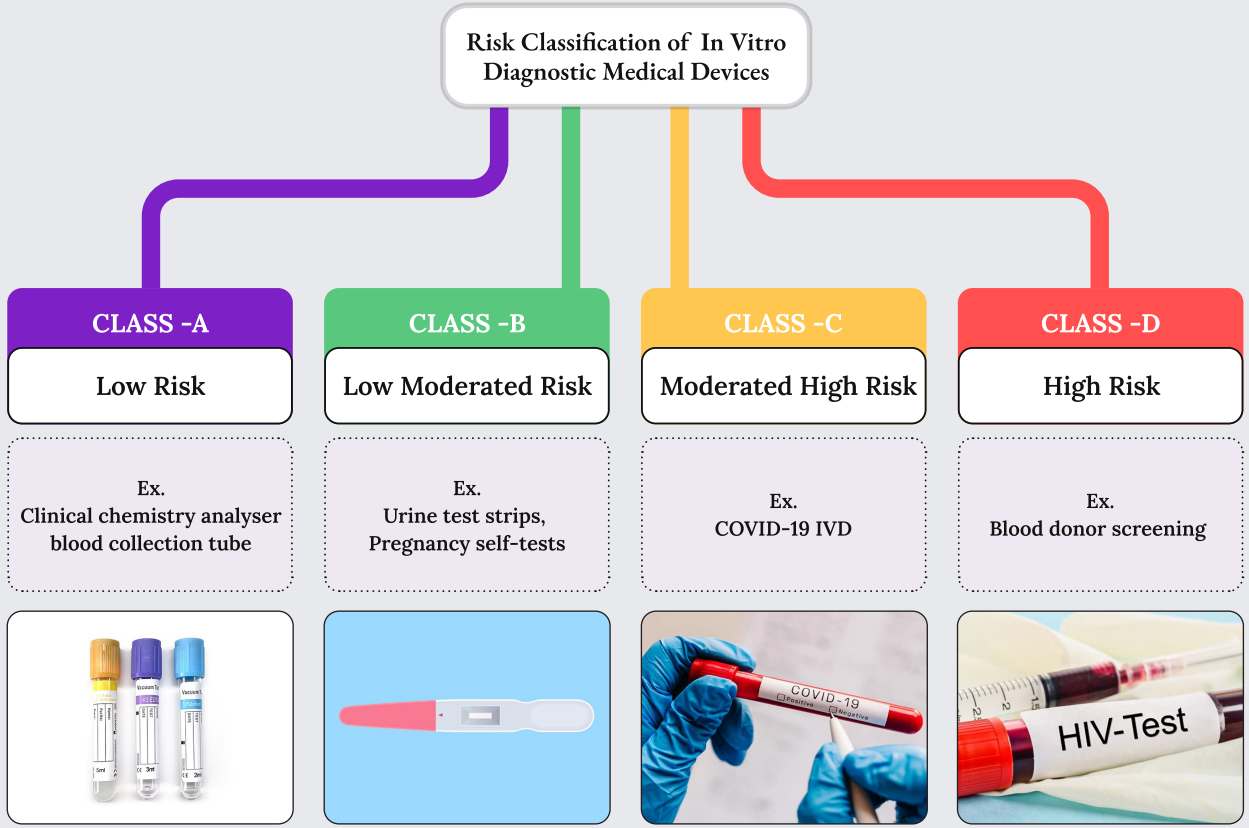


Figure 3: Risk-Based Classification of In Vitro Diagnostic Medical Devices

2.3 IVD Medical Device Regulatory Pathway (Predicate and Novel Devices)

The regulatory pathway for In Vitro Diagnostic (IVD) medical devices in India, governed by the Medical Device Rules (MDR), 2017, is designed to ensure that products entering the market are safe, effective, and of consistent quality. The pathway encompasses several stages from prototype development and evaluation to manufacturing, and commercialization under the oversight of the State Licensing Authority (SLA) and Central Licensing Authority (CLA) of the Central Drugs Standard Control Organisation (CDSCO).

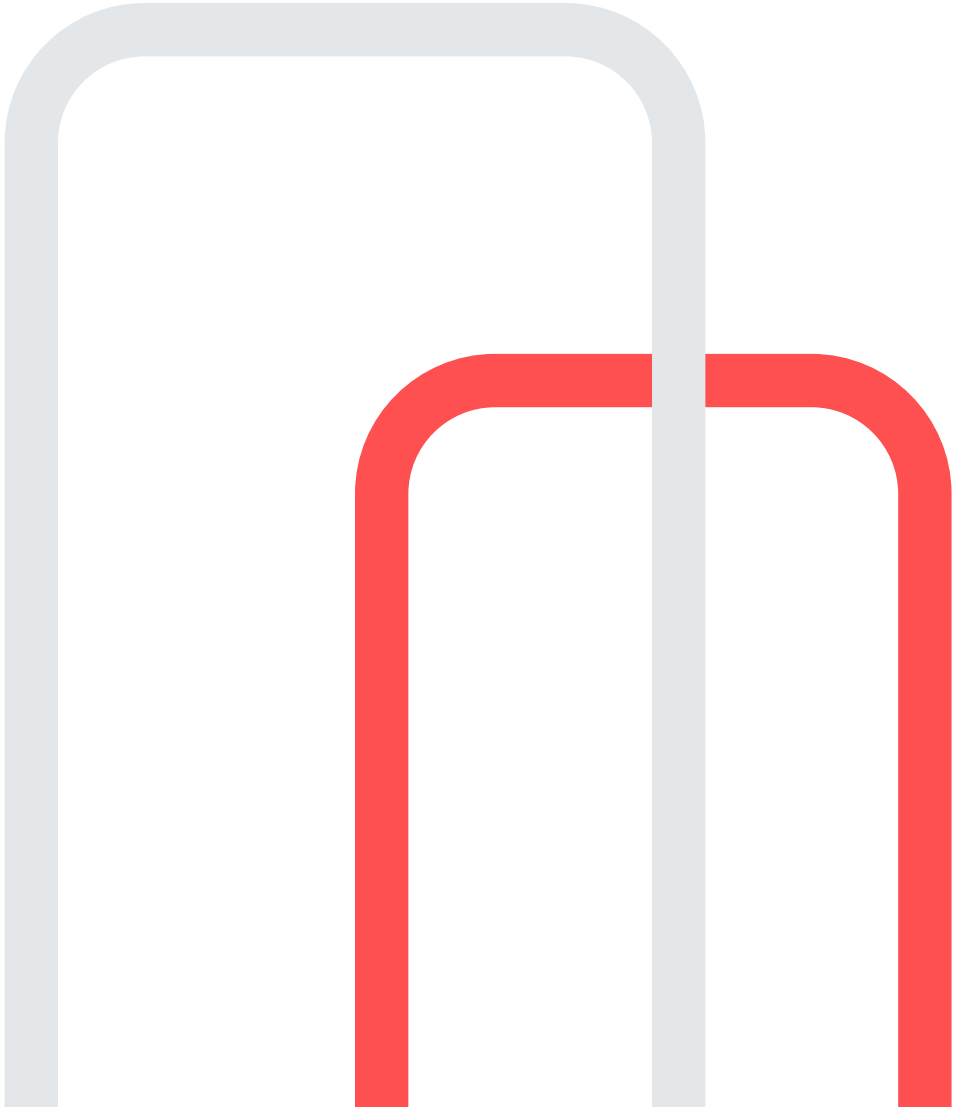
At the prototype stage, manufacturers are required to obtain a Test Licence (Form MD-13) after applying through Form MD-12. Form MD-12 is the application for License to Manufacture Medical Device for Purpose of Clinical Investigation, Test, Evaluation, Examination, Demonstration or Training. Compliance with an appropriate Quality Management System (QMS) is mandatory for devices intended for human use.

After receiving approval in Form MD-13, the manufacturer or innovator must conduct comprehensive performance evaluations of the IVD medical device to establish its safety, effectiveness, and consistent quality. These evaluations are typically performed to demonstrate conformity with the Essential Principles of Safety and Performance (EPSP) outlined under MDR, 2017.

It is important to note that academic and research institutions are not eligible to obtain a manufacturing license for IVD medical devices intended for commercial use. Therefore, a technology transfer to an industrial partner possessing a valid manufacturing facility and an established Quality Management System (QMS) is essential. The industry partner, upon receiving the transferred technology, can subsequently apply for the requisite manufacturing license under the appropriate regulatory pathway to enable commercial production and market authorization.

In cases of new In Vitro Diagnostic device, the applicant must seek prior approval by submitting Form MD-24. The Form MD-24 is the application for Grant of Permission to Conduct Clinical Performance Evaluation of a New In Vitro Diagnostic Medical Device. Upon satisfactory review of the application and supporting documentation, the regulatory authority issues the approval in Form MD-25.

Following approval, the applicant is responsible for conducting the clinical performance evaluation in accordance with the approved protocol and generating comprehensive data to demonstrate its performance of the IVD using clinical samples.



For novel IVD medical devices, where no predicate device exists, manufacturers or innovators must obtain prior permission to Import or Manufacture for sale or for distribution of new in vitro diagnostic medical device. This requires submission of an application in Form MD-28. It is the application for grant of permission to Import or Manufacture for sale or for distribution of new in vitro diagnostic medical device. The manufacturer receives the permission to Import or Manufacture New In Vitro Diagnostic medical device with the approval granted in Form MD-29.

The regulatory submissions at this stage must include supporting documentation as per Part IV of the Fourth Schedule of MDR 2017, which comprises the Device Master File (DMF), Plant/Site Master File (SMF), and relevant regulatory, technical, and clinical evidence. To demonstrate compliance with the Essential Principles of Safety and Performance (EPSP), manufacturers are expected to generate data from at least three test batches, encompassing Quality Control (QC) reports, stability studies, and performance evaluation results.

Upon successful completion of evaluations, the manufacturing is required for commercialization. For Class A and B devices (low to moderate risk), manufacturers must apply for manufacturing license through Form MD-3 (license issued in Form MD-5) or Form MD-4 (license issued in Form MD-6) for loan license to the SLA. For Class C and D devices (moderate to high risk), manufacturers must apply for manufacturing license through Form MD-7 (license issued in Form MD-9) or Form MD-8 (license issued in Form MD-10) for loan license to the CLA.

Throughout this process, both predicate and novel IVDs must undergo analytical and clinical performance evaluations substantiate their intended use and ensure compliance with applicable safety, performance, and quality standards. The regulatory review involves technical scrutiny and, when applicable, onsite audits by a Notified Body or expert evaluators, depending on device classification.

Figure 4 presents the regulatory pathway that an In Vitro Diagnostic (IVD) medical device manufacturer must follow to obtain approval for manufacturing and commercialization.

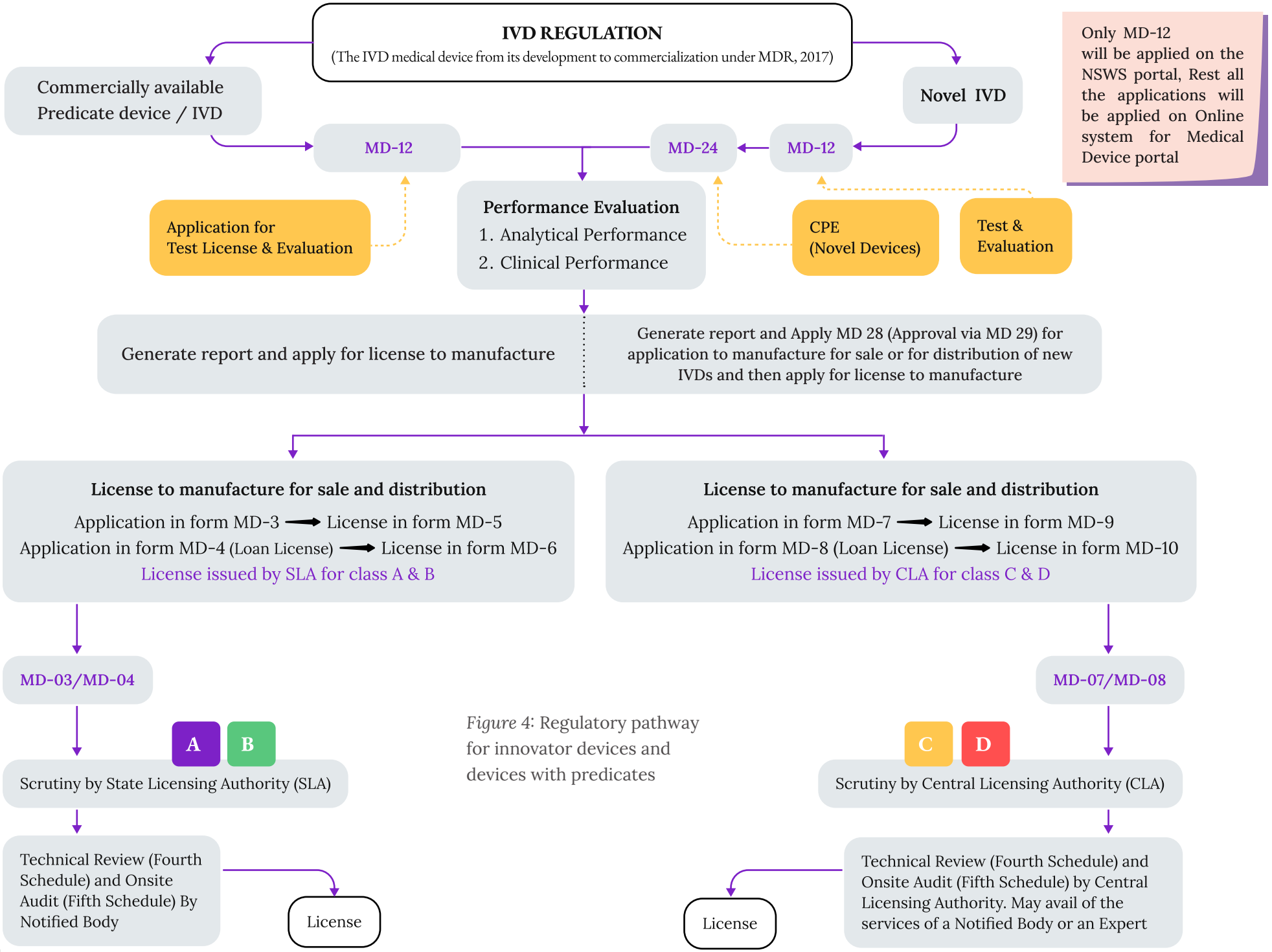


Figure 4: Regulatory pathway for innovator devices and devices with predicates

2.4 Export of medical devices:

Where a person intends to export any medical device, manufactured in India, and for that purpose, requests a certificate in the nature of free sale certificate or a certificate about quality, safety and performance in relation to that medical device as required by the authority concerned of the importing country, such person, may apply to the Central Licensing Authority [for Class C and Class D medical devices and State Licensing Authority for Class A and Class B medical devices] for the purpose along with a fee as specified in the Second Schedule and the said authority shall, if the /requirements are fulfilled, issue a certificate to the applicant.

2.4.1 Requirement for Free sale certificate:

1. Covering letter mentioning the name and address of the applicant, duly signed, and stamped by the head of organization.
2. Legal undertaking on 100 Rupees registered notarized stamp from the manufacturer stating that no action has been initiated against them or been convicted due to adverse events, market complaint, and Not of Standard Quality (NSQ) report of applied product
3. Copy of the respective Market License.
4. Fee Challan

Once the manufacturer has defined the intended use, identified the predicate device, and determined the appropriate classification, they can proceed with To do list B, C, D or E, which is specifically designed to assist manufacturers and innovators in selecting the most suitable regulatory pathway for their In Vitro Diagnostic (IVD) medical device.

2.5 Product Architecture & System Integration

The Product Optimization phase focuses on refining the system for regulatory compliance, manufacturability, and field readiness. This involves structured development across architecture, mechanical design, and electronic systems, Reagent and Assay Optimization, Process Optimization, Quality Management System Implementation, Risk Management reporting, Verification & Validation procedures, Change Management, Instructions for Use (IFU) Development, Packaging Design and Validation systems.

The process begins with developing a robust system architecture that integrates all functional domains such as, electronics, optics, software, and reagent pathways into a integrated system. This architecture must cohesively unify all critical subsystem mechanical, electronic, software, optical, and fluidic into a single, functionally coherent platform. The design must map the entire sample-to-result workflow, beginning from user interaction and specimen input to reagent handling, processing, detection, and result output. Each functional domain should operate in synchronization to ensure predictable, reproducible, and error-resilient system behavior.

User interaction points such as sample loading, touchscreen interfaces, sample applicator components, and result visualization must be ergonomically positioned and seamlessly integrated into the workflow. The architecture should clearly define how reagents are loaded, moved, mixed, and incubated across fluidic channels, valves, and chambers, with support from actuators, heaters, sensors, and optical modules. Optical detection systems such as fluorescence or absorbance-based readers must be precisely aligned and shielded to prevent ambient interference and ensure signal fidelity. Software subsystems should demonstrate the diagnostic sequence through embedded firmware, real-time control loops, user interface management, and secure data logging and export.

To meet quality and regulatory expectations, the architecture must provide a framework for full design traceability, enabling mapping between user needs, design inputs, subsystems, and verification outcomes. Hazards at the interface level such as electrical shock, fluid leaks, optical exposure, or mechanical pinching must be captured and mitigated within the risk management process, in line with ISO 14971 and IEC 62366. Furthermore, any changes to the architecture must follow a documented change control process with version management, impact assessments, and re-verification of affected components.

All architectural elements must be documented through comprehensive system block diagrams, workflow and sequence diagrams, control logic

charts, wiring and fluid routing schematics, and bill of material (BOM). These documents form a critical part of the Design History File (DHF), Device Master Record (DMR), and Device Master File (DMF), supporting regulatory submissions, internal audits, and ongoing product lifecycle management. The integrated system architecture, therefore, serves as the technical and regulatory spine of the product, enabling traceable, testable, and scalable diagnostic innovation.

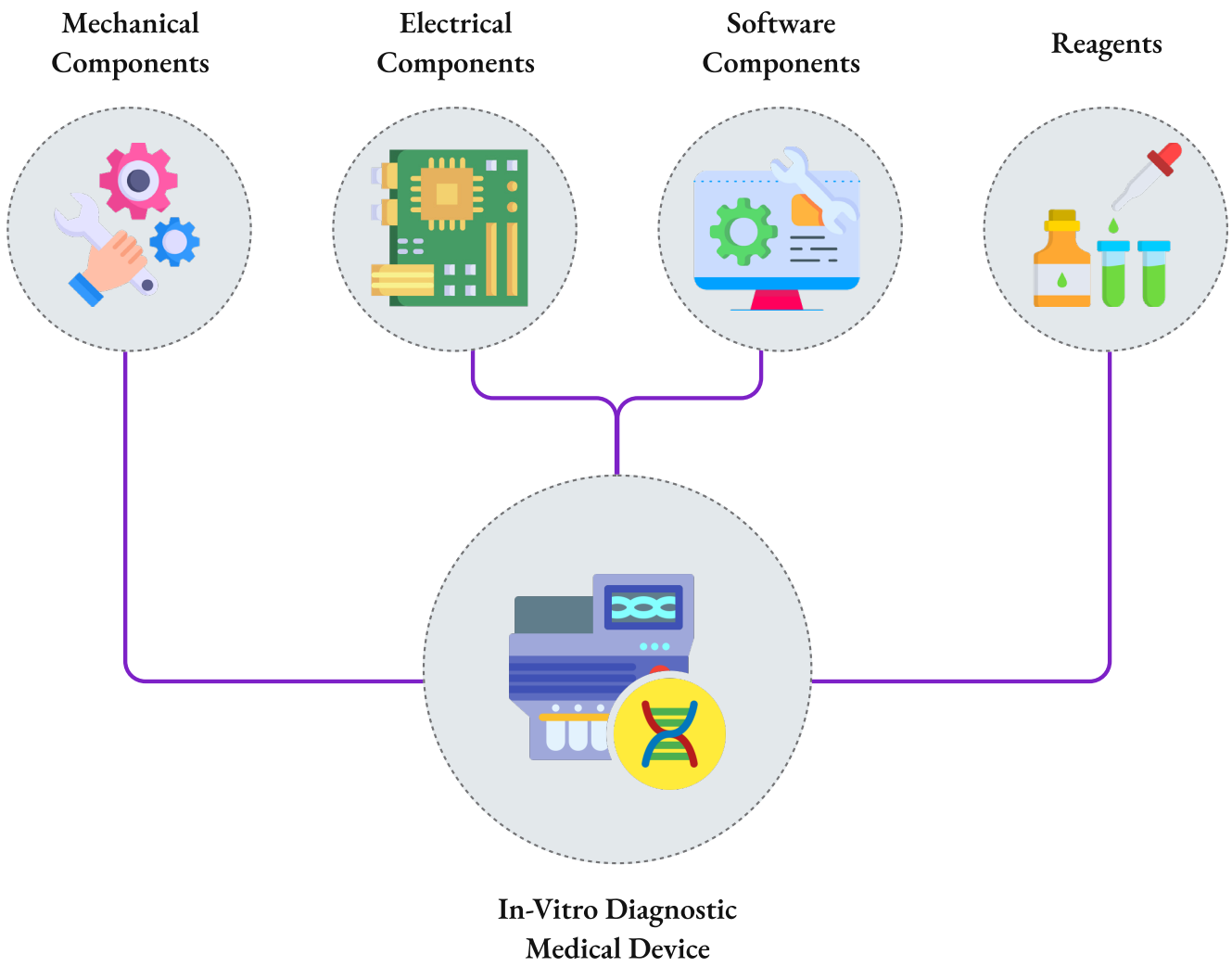


Figure 5: Product Architecture

2.6 Mechanical Components Optimization

Mechanical optimization requires designing durable, user-friendly components that can withstand the rigors of field deployment and high-throughput manufacturing environments. All mechanical subsystems must be engineered for longevity, ensuring reliable operation over extended use cycles in diverse and often harsh field conditions. Manufacturers must prioritize ergonomics and usability, ensuring that interfaces such as insertion points, lids, hatches, and control panels are intuitive and easy to handle even by minimally trained personnel. Material selection plays a critical role in this process i.e. components must be made from ISO 10993-compliant materials that are biocompatible, chemically inert to reagents, and sterilizable or resistant to common cleaning agents. These materials are essential for parts that come into contact with patients, clinical samples, or assay reagents, ensuring both user and assay safety.

Enclosures and structural parts must be robustly engineered to protect internal components from dust, splashes, shocks, and temperature fluctuations during storage, transport, and routine use. For devices intended for field use or decentralized testing environments, a minimum ingress protection (IP) rating is recommended to guard against environmental exposure. Proper sealing mechanisms, gaskets, and mechanical interlocks must be incorporated to ensure barrier integrity while allowing access for service and maintenance.

From a manufacturing perspective, mechanical designs must follow established Design for Manufacturability (DFM) principles. These include minimizing part count, favoring modular subassemblies, standardizing fasteners and connectors, and ensuring that components are moldable, machinable, or otherwise manufacturable at scale. Tool-friendly features such as alignment guides, self-locating tabs, and snap-fits can enhance assembly consistency and reduce production time. Tolerance stack-up analysis should be conducted across critical joints and interfaces to ensure precise alignment, especially where optical, fluidic, or electronic subsystems converge.

Thermal management is another essential design consideration. Mechanical structures must support the dissipation of heat generated by internal electronics, actuators, or biochemical reactions. This may involve integrating passive heat sinks, venting channels, or thermally conductive materials into the enclosure design to prevent localized overheating and to ensure stable assay performance.

All mechanical parts and assemblies must undergo extensive verification through stress analysis, fatigue testing, vibration simulations, and thermal cycling. These tests are critical for validating reliability under both normal and worst-case use scenarios. Components subject to movement or repetitive loading such as hinges, springs, and rotating mechanisms should be tested for wear resistance and operational longevity. The test data not only serve as design validation but also support risk management and regulatory submissions.

2.7 Electronics Optimization

Electronic system optimization is a critical pillar in the development of reliable and regulatory-compliant diagnostic devices, with the goal of achieving safe, robust, and high-performance operation across diverse use environments. The design must begin with the finalization of printed circuit board (PCB) layouts that integrate all necessary electronic components, sensors, actuators, power supplies, data acquisition modules, and communication interfaces. The circuitry must be engineered for electromagnetic compatibility (EMC) and immunity to external noise per IEC 61326 requirements, utilizing techniques such as multi-layer grounding, shielding, surge protection, and power line filtering to maintain signal integrity and operational stability. These provisions are vital to preventing malfunctions in the presence of electromagnetic interference, which is common in clinical and laboratory environments.

User-facing electronic features should be optimized for intuitive interaction and workflow efficiency. Interfaces may include capacitive or resistive touchscreens, status LEDs, tactile buttons, audio feedback elements, and integrated barcode or QR code scanners to support reagent tracking, sample identification, and operator authentication. These components must be seamlessly integrated into both the electronic and

mechanical design, with clearly defined communication protocols and power distribution to ensure consistent behavior. All hardware elements supporting human interaction must be tested for durability, clarity, and usability under various lighting and handling conditions.

Equally important is the safety and fault tolerance of the system. The electronics must incorporate protection features such as watchdog timers to recover from software hangs, over-voltage and reverse-polarity protection, electrostatic discharge (ESD) safeguards, and redundant power systems like uninterruptible battery backups or supercapacitors to maintain operation or support safe shutdown during power loss. Depending on the application, the design must conform to IEC 60601-1 (for patient-connected medical devices) or IEC 61010 (for diagnostic laboratory equipment), ensuring electrical isolation, mechanical robustness, and insulation from potential electrical hazards. These standards govern critical parameters such as leakage current, dielectric strength, enclosure safety, and creepage distances.

Integrated within the electronic system is the device's embedded software, which acts as the central nervous system controlling sensors, actuators, thermal modules, and user interface elements. This includes both low-level firmware (e.g., motor control loops, sensor sampling, timing logic) and high-level application software that coordinates workflows, data processing, diagnostics, and cloud integration. Firmware must be optimized for efficiency, stability, and real-time responsiveness, and should be architected in modular layers that facilitate updates, testing, and debugging. Safety-critical routines must incorporate redundancy and fallback behaviors, such as timeouts and error recovery modes, to minimize the impact of unexpected conditions.

Software control logic must be thoroughly verified, and aligned with the intended use scenarios. It should implement fault monitoring algorithms to detect hardware malfunctions (e.g., failed sensors, abnormal heating), system logs for auditability, and interlocks to prevent unsafe operations (e.g., preventing reagent heating in the absence of a sample). Device drivers, APIs, and communication stacks must be validated against known protocols (e.g., USB CDC, I2C, SPI, UART) and should support secure firmware-over-the-air (FOTA) or wired update mechanisms with cryptographic authentication and rollback capability.

Cybersecurity is a growing concern in connected medical devices and must be embedded into both the hardware and software design. Measures should include secure boot, encrypted data storage and transmission, role-based access control, audit trails, and periodic vulnerability scanning. Connectivity modules (Wi-Fi, BLE, Ethernet) must follow security best practices including WPA3 support, TLS for encrypted cloud communication, and hardened firmware to resist exploitation. Where cloud integration is supported (e.g., for data backup or remote diagnostics), the software should comply with regulatory frameworks such as ISO/IEC 27001 for information security and follow data privacy standards like India's Digital Information Security in Healthcare Act (DISHA) bill for health data management.

To support lifecycle maintenance and regulatory audits, diagnostic and calibration interfaces must be designed into the hardware and firmware. These interfaces can enable service engineers to perform routine device health checks, run calibration routines, access debug logs, and update firmware versions through secure, authenticated means. All test and calibration data should be version-controlled, time-stamped, and traceable to individual device IDs.

2.8 Reagent and Assay Optimization

Reagent and assay optimization is a cornerstone of successful in vitro diagnostic (IVD) product development, as it directly influences the analytical performance, stability, usability, and scalability of the diagnostic solution. Manufacturers must approach this phase with a systematic and data-driven strategy that aligns the biochemical performance of the assay with the operational constraints and requirements of the device platform.

The first priority is to develop robust Standard Operating Procedures (SOPs) for all reagent, buffer, and formulation processes to ensure reproducibility and batch-to-batch consistency. These SOPs should cover raw material preparation, reagent mixing, filtration, filling, aliquoting, labeling, and storage. All input chemicals whether enzymes, dyes, primers,

antigens, antibodies, stabilizers, or excipients must be sourced from qualified vendors with documented quality assurance. A valid and traceable Certificate of Analysis (CoA) must accompany each raw material batch, and vendor performance should be routinely audited to ensure adherence to quality standards.

Optimization of reagent formulations requires careful tuning of parameters such as pH, ionic strength, surfactant concentration, preservatives, stabilizers, and the concentration of active biological components. These parameters must be refined through Design of Experiments (DoE) approaches to maximize sensitivity, specificity, and reaction kinetics while minimizing matrix effects and variability. For nucleic acid-based assays, enzyme activity, primer-dimer formation, and amplification efficiency must be optimized. For immunoassays, antigen-antibody binding affinity, blocking conditions, and signal amplification systems should be validated. The formulation must be tested for robustness against common clinical interferents such as hemoglobin, lipids, urea, mucus, and medications, simulating real-world specimen variability. This ensures that diagnostic performance remains accurate across different patient profiles and sample types.

Assay studies must also include comprehensive cross-reactivity studies, particularly for infectious disease diagnostics, to confirm that the assay does not produce false positives due to the presence of non-target organisms or closely related pathogens. Similarly, internal positive and negative controls should be incorporated within each test to verify the integrity of the reagents and the overall workflow, ensuring that invalid results can be flagged automatically. Lot release specifications should be based on predefined acceptance criteria derived from analytical performance studies and must be validated with reference panels of known positive and negative samples.

Stability testing of reagent formulations must be performed under both real-time and accelerated conditions to determine the shelf life, storage conditions, and transport requirements. Based on these results, the storage format of reagents should be finalized—whether lyophilized, liquid, gel-based, or dried pellet. Lyophilization may be preferred for long-term stability without refrigeration, while liquid formats may offer convenience and ease of automation. Regardless of format, compatibility with packaging materials and cartridge substrates (e.g., polypropylene, cyclic olefin copolymer, silicone seals, or adhesives) must be verified to prevent leaching, adsorption, or degradation that may affect performance or reagent stability.

Another essential consideration is the reagent's compatibility with the device's automated dispensing, mixing, and detection subsystems. This includes optimizing viscosity, surface tension, and reconstitution characteristics to ensure smooth fluid handling and consistent reaction kinetics. Manufacturers must test reagents in situ, under simulated operational workflows, to validate performance across the full assay cycle from sample introduction to final readout.

To support regulatory readiness and manufacturing scalability, pilot-scale reagent production runs should be conducted using production-grade equipment and processes. These runs help identify formulation challenges, container-closure issues, fill volume precision problems, or yield inconsistencies early, before commercial scale-up. In-process controls, in-line weight or volume checks, and post-fill integrity testing (e.g., visual inspection, turbidity, leak testing) must be implemented and documented. A statistical sampling plan should be employed to validate homogeneity and performance across lots.

All optimization work must be documented in the Design History File (DHF) and cross-referenced in the Device Master Record (DMR) and Device Master File (DMF). Regulatory submissions should include analytical performance reports, stability data, raw material traceability records, and justification for chosen storage conditions and formats, as per CDSCO or other applicable regulatory bodies. Furthermore, reagent labeling should comply with biosafety and hazard communication requirements (e.g., GHS symbols) and reflect expiration, storage conditions, and reconstitution instructions clearly.

2.9 Risk Management

Risk management must be an integral part of the entire product lifecycle—from initial design through development, manufacturing, deployment, and post-market surveillance. This process should follow international standards, primarily ISO 14971 and ISO/TR 24971 for medical device risk management, as well as IEC 62366-1 for identifying and mitigating usability-related hazards. These standards ensure that the product is not only effective but also consistently safe for users, patients, and operators.

A structured and thorough Failure Modes and Effects Analysis (FMEA) must be conducted across all subsystems, including mechanical assemblies, electronic circuits, embedded and application software, assay reagents, optical systems, and human-machine interfaces. Each potential failure mode should be assessed for its severity, likelihood of occurrence, and ability to be detected before causing harm. This allows the team to prioritize risks and implement appropriate mitigation strategies—such as design modifications, software failsafes, user training, or labeling warnings.

To ensure comprehensive coverage, the risk management process must also include a usability-specific risk assessment. This is particularly important for devices used at the point of care or by non-professional users, such as patients, technicians, or caregivers. This assessment should evaluate the potential for use errors, confusion, or misuse stemming from unclear interfaces, ambiguous instructions, or environmental factors (e.g., lighting, noise, or urgency). These usability risks must be treated with the same rigor as technical hazards.

Each identified risk must have clearly defined acceptability criteria, based on the device's intended use, user population, and benefit-risk profile. All corresponding risk control measures whether through design changes, protective mechanisms, or information for safety must be documented and verified for effectiveness. Residual risks, if any, must be justified as acceptable and communicated appropriately.

A comprehensive Risk Management File (RMF) must be maintained and regularly updated. This file should include the risk management plan, risk analyses, evaluation of residual risks, records of risk control verification,

Figure 6: Risk Management as per ISO 14971

usability engineering outputs, and a risk-benefit analysis. It should serve as a central reference point during audits, regulatory submissions, and internal reviews.

Risk management is not a one-time activity. All identified risks must be reassessed whenever there are significant design changes, such as updates to hardware, firmware, or reagent formulations; or after receiving new inputs from clinical evaluations, usability studies, or post-market surveillance (e.g., complaints, incident reports, and service data). A robust change control process must be in place to trigger these reassessments automatically.

By embedding risk management across the design, development, and deployment pipeline, manufacturers can proactively identify and mitigate safety concerns, reduce the likelihood of adverse events, and ensure long-term compliance with international regulatory expectations.

To do list B: Product Optimization

Product Architecture & System Integration: Define and integrate all subsystems into a unified, functional architecture that supports reliable diagnostics. Ensure smooth interaction between fluidics, electronics, software, and reagent workflows.

Sl. No	To do	Completed		Remarks
		Yes	No	
5.1	Develop a system-level architecture integrating fluidics, electronics, optics, software, and reagent pathways.			
5.2	Map the complete user and sample workflow from sample input to result output.			
5.3	Define all module interfaces (mechanical, electrical, fluidic, data).			

Mechanical Components Optimization: Design robust, user-friendly mechanical parts that are compatible with manufacturing and sustained field use. Focus on materials, ergonomics, and performance under transport and usage conditions.

Sl. No	To do	Completed		Remarks
		Yes	No	
6.1	Design ergonomic components and user interaction features.			
6.2	Select ISO 10993-compliant, chemically inert, and sterilizable materials.			
6.3	Engineer enclosures with dust, splash, and thermal protection.			
6.4	Apply Design for Manufacturability (DFM) principles for scalable and repeatable production of components.			
6.5	Validate components under mechanical stress, transport, vibration, and temperature cycling.			

Electronics Optimization: Ensure reliable, safe, and regulatory-compliant electronics for signal acquisition, processing, and user interaction. Optimize PCB design and safety features for diagnostics and usability.

Sl. No	To do	Completed		Remarks
		Yes	No	
7.1	Finalize PCB design with sensors, actuators, power, and communication interfaces.			
7.2	Ensure EMI/EMC compliance (IEC 61326) with shielding and grounding.			
7.3	Integrate touchscreen, indicators, and QR/barcode readers for traceability.			
7.4	Implement fail-safes: watchdog timers, surge protection, and backup power.			
7.5	Align design with IEC 60601-1 or IEC 61010 for electrical safety compliance.			
7.6	Plan for diagnostics, calibration, and field servicing interfaces.			

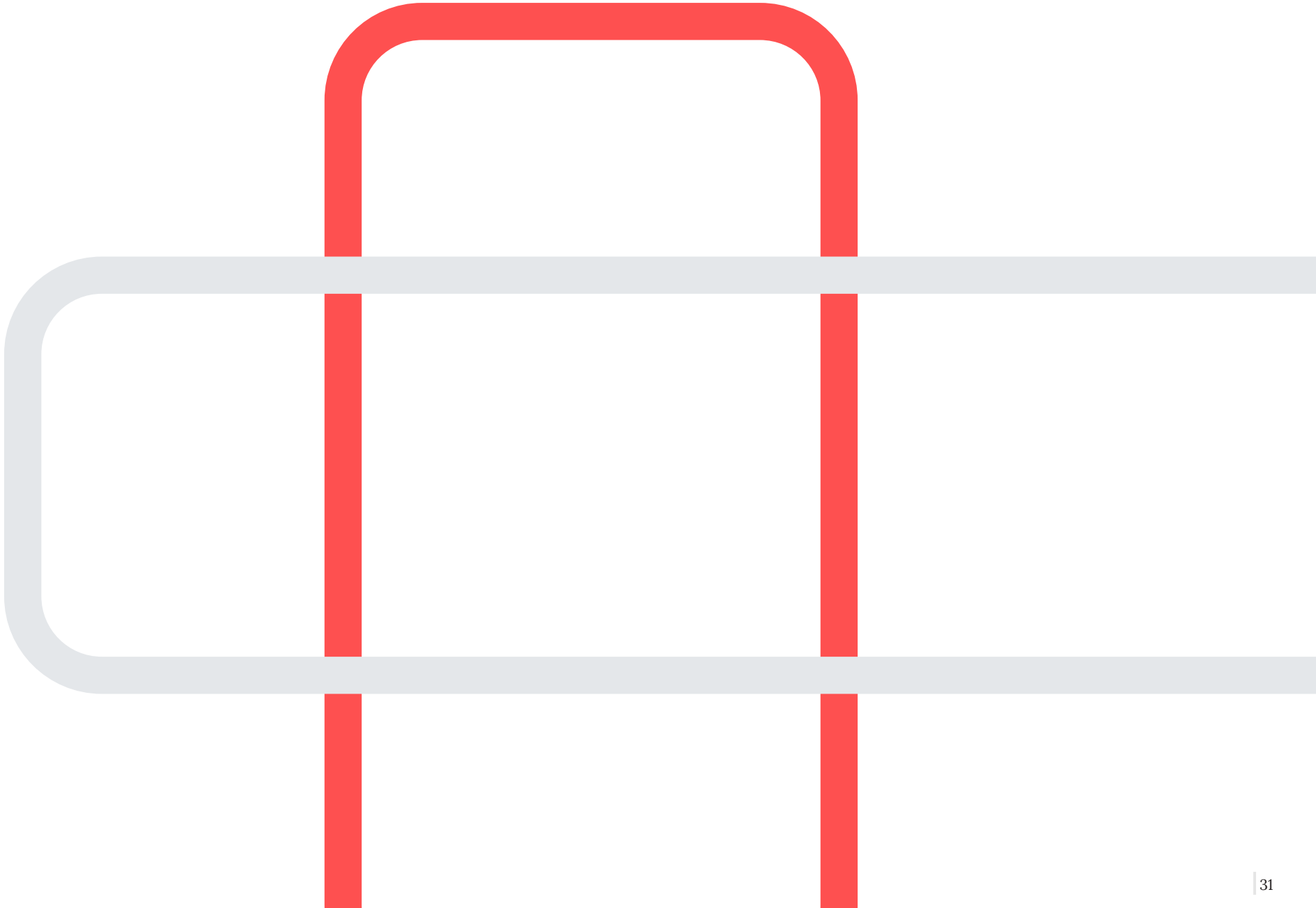
Reagent Optimization: Optimize reagents for stability, specificity, manufacturability, and compatibility with the device format. Ensure consistent assay performance under various environmental and sample conditions.

Sl. No	To do	Completed		Remarks
		Yes	No	
8.1	Develop SOPs for reagent and buffer formulation.			
8.2	Obtain Certificates of Analysis (CoA) for all chemicals.			
8.3	Optimize pH, salt, stabilizers, and active components for performance (LoD, specificity).			

Sl. No	To do	Completed		Remarks
		Yes	No	
8.4	Validate assay robustness against interferents (e.g., hemoglobin, bilirubin).			
8.5	Design internal controls and lot release criteria.			
8.6	Evaluate cross-reactivity with non-target organisms/analytes.			
8.7	Finalize reagent storage format (lyophilized, liquid, pellet).			
8.8	Test reagent compatibility with cartridge materials.			
8.9	Evaluate pilot-scale reagent manufacturing feasibility.			

Risk Management (ISO 14971): Identify, assess, and mitigate product risks across the device lifecycle. Ensure usability-related risks and regulatory requirements are continuously addressed.

Sl. No	To do	Completed		Remarks
		Yes	No	
9.1	Conduct detailed Failure Modes and Effects Analysis (FMEA) across the processess			
9.2	Define and document risk acceptability criteria and control strategies.			
9.3	Perform usability risk assessment as per IEC 62366-1.			
9.4	Maintain an up-to-date Risk Management File.			
9.5	Reassess risks after design changes, usability inputs, and field feedback.			



03

03

CHAPTER

QMS Manufacturing And Documentation

3.0 Quality Management System

The foundation of the QMS begins with well-defined document control processes, including creation, approval, revision, access, and archival of all quality-related documents. Procedures for Corrective and Preventive Actions (CAPA) must be established to systematically identify root causes of non-conformities and implement effective, sustainable resolutions. Internal audits should be conducted periodically to verify compliance with the QMS and to identify opportunities for improvement. A structured complaint handling process is required to capture, investigate, and resolve user feedback, ensuring timely escalation of serious incidents.

A complete Device Master Record (DMR) must be maintained for each medical device, containing all specifications, drawings, labeling, packaging, and assembly instructions necessary to produce the device consistently. Simultaneously, a comprehensive Design History File (DHF) must document the entire design and development journey, including design inputs, outputs, verification, validation, risk management, and design changes. These documents provide critical traceability and are indispensable during regulatory audits or product recalls.

To ensure ownership and accountability, organizational roles and responsibilities must be clearly assigned across functions such as R&D, manufacturing, quality assurance, regulatory affairs, and supplier management. This structure ensures that quality-related tasks are not only performed but also monitored and improved upon. Management reviews must be conducted at planned intervals to evaluate QMS performance, resource adequacy, risk controls, and customer feedback. These reviews should lead to actionable quality planning objectives and metrics that drive continuous improvement.

The QMS must extend to supplier qualification and monitoring processes, ensuring that materials, components, and outsourced services meet quality and regulatory expectations. This includes supplier audits, risk assessments, and quality agreements. Full traceability from raw materials and intermediate assemblies to final product release must be ensured through lot tracking, labeling, and serialization systems, especially for Class C and D devices.

Furthermore, Design and Development Planning must be thoroughly documented, including milestones, review gates, cross-functional responsibilities, and risk management integration. This plan ensures that design activities follow a controlled and auditable path. During Design Transfer, all essential information BOMs, specifications, process instructions, QC criteria, and training materials—must be transitioned from R&D to production without ambiguity, ensuring regulatory and quality compliance from the very first production lot.

Finally, for regulatory submissions, especially for obtaining manufacturing licenses or import licenses, a structured Device Master File (DMF) must be compiled in accordance with CDSCO's latest guidelines. This file should include device description, labeling, sterilization details, performance evaluation reports, risk analysis, clinical evidence, manufacturing process description, and post-market surveillance plan. The DMF serves as the backbone for CDSCO application review and must align with both national and international expectations.

In essence, an effectively implemented QMS not only satisfies regulatory requirements but also builds the foundation for delivering safe, reliable, and high-quality medical devices supporting both domestic and global market access.

To achieve consistent quality at scale, manufacturers must develop a robust and efficient manufacturing process that is both well-documented and validated. This process should be designed from the outset with scalability, reproducibility, and regulatory compliance in mind. The foundation begins with creating detailed Standard Operating Procedures (SOPs) for every step of the production lifecycle including the manufacturing of components, filling of reagents, mechanical and electronic assembly of the system, functional integration, and final packaging.

As production moves from the prototype phase to pilot and then commercial scale, workflows should be carefully reviewed and streamlined. The goal is to minimize manual interventions and reduce process variability by automating repetitive or error-prone tasks. This not only improves throughput and consistency but also enhances worker safety and lowers production costs over time.

For each production step, in-line Quality Control (QC) measures must be implemented. These include automated and manual checks such as visual inspections, dimensional checks, weight and volume verification, seal integrity testing, and barcode or data matrix scanning to confirm component identity and traceability. These controls should be strategically placed at critical control points to detect deviations early in the process and avoid costly rework or product rejection downstream.

In addition to in-line QC, batch-level quality assurance must be maintained through statistically sound sampling methods such as ISO 2859 based acceptance sampling plans. These ensure that each batch meets defined quality criteria before release, supporting both internal standards and external regulatory audits.

Figure 7: QMS Implementation

Manufacturers must also perform formal process validation, including Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ), to demonstrate control over critical operations. Process validation must also include documentation of Key Process Parameters (KPPs) such as temperature, pressure, fill volume, cycle time, and torque and their acceptable control ranges. These parameters should be continuously monitored through real-time data acquisition systems, where feasible, and supported by alarms or flags to detect out-of-spec conditions.

To support scalability, production layouts must be designed for modularity and flexibility, allowing for easy expansion as demand increases. Manufacturing should also incorporate lean production principles such as just-in-time inventory, batch traceability, and waste minimization to optimize resource use and reduce overhead. Workflow simulation tools and digital twins can be employed during process development to model scale-up scenarios, identify potential bottlenecks, and fine-tune layout efficiency before physical expansion.

Furthermore, supplier readiness must be assessed during scale-up. Key vendors must be qualified, monitored, and capable of supplying components or materials consistently at higher volumes without compromising on quality or delivery timelines.

Finally, all manufacturing data including raw material usage, production metrics, QC test results, deviations, and corrective actions must be recorded and securely stored in a traceable format, ideally within a Manufacturing Execution System (MES) or an integrated Quality Management System (QMS). These records support regulatory submissions, quality audits, and continuous improvement programs.

3.1 Change Management

In the development of medical and diagnostic devices, a structured and controlled design iteration process is essential to ensure safety, efficacy, regulatory compliance, and manufacturability. Design evolution must follow a defined lifecycle, with each phase clearly documented and reviewed to maintain traceability and quality oversight

The product design process should be divided into successive builds—typically including feasibility prototypes, alpha units, beta systems, and a final production-ready version. Each of these builds should serve a specific purpose:

1. Alpha builds focus on core functionality and feasibility testing.
2. Beta builds address refinements in usability, integration, and manufacturability.
3. The final build (pre-production) should be fully representative of the commercial version, meeting all design, performance, safety, and regulatory requirements.

A design freeze must be established as a formal milestone to lock the design configuration before initiating full-scale verification, validation, and manufacturing. After this point, no modifications should be made unless justified by testing outcomes, risk evaluations, or post-market requirements. This ensures stability in documentation, testing protocols, and regulatory filings.

Any changes to the design whether in hardware, software, firmware, materials, labeling, or documentation must be governed by a robust Change Control Process. This system should:

Capture the rationale for the change (e.g., performance improvement, cost reduction, risk mitigation).

Assess the impact of the change on safety, effectiveness, regulatory filings, risk profile, and previous verification and validation efforts.

Require a structured change request and approval workflow, involving cross-functional review by engineering, quality, regulatory, clinical, and manufacturing teams.

All approved changes must be logged in a version-controlled system such as a Design History File (DHF). Each modification should be traceable back to:

1. The initiating issue or improvement.
2. Associated input and output documents.

3. Revised risk assessments, test reports, and updated regulatory submissions.

To maintain design control, regular internal reviews should be held at predefined development milestones. These reviews function as Go/No-Go gates and ensure that:

1. Requirements are adequately met.
2. Test data supports the intended use.
3. Risk controls are properly implemented and validated.
4. Documentation is complete and aligned with QMS and regulatory requirements.

Each review should be documented with clear outcomes, action items, and decisions. Participants must include cross-disciplinary representatives to ensure all perspectives are considered technical, quality, regulatory, clinical, and end-user.

3.2 Labelling, Instructions for Use (IFU) Development, Packaging Design and Validation

Labeling is a critical component of product safety, regulatory compliance, and supply chain traceability in medical and in-vitro diagnostic (IVD) devices. Every device label must be carefully designed to convey all necessary product information in a clear, durable, and standardized format, ensuring that users can handle, store, and use the product safely and correctly across all intended settings—clinical laboratories, near-patient environments, or homes.

Manufacturers must develop clear, comprehensive, and regulatory-compliant Instructions for Use (IFU) to ensure that the IVD product can be used safely, correctly, and consistently by the intended user, whether healthcare professionals or laypersons. The IFU must include the manufacturer's name and full address, along with the product's intended use and user group. A detailed, step-by-step procedure should guide test execution, supported by illustrative diagrams if necessary. Interpretation criteria for results (positive, negative, and invalid) must be explicitly described. Instructions should also outline proper specimen collection, storage, and handling methods. All relevant warnings, biosafety precautions, limitations (e.g., interfering substances), and environmental constraints should be prominently included. The IFU must be developed in alignment with usability validation data and should be available in both printed and digital formats, following regulatory labeling requirements under CDSCO.

Packaging must be designed to maintain the functional integrity, sterility (if applicable), and usability of the IVD product throughout its shelf life and transport cycle. Selection of packaging materials should be based on chemical compatibility with reagents, mechanical protection against shock, vibration, and compression, and environmental durability under temperature, humidity, and light exposure. Regulatory-grade materials such as those meeting ISO 11607 for sterile barrier systems, should be used where required. The packaging system should be structured in layers: primary (e.g., pouch or vial), secondary (e.g., test kit box), and tertiary (e.g., shipping case), with appropriate labeling and tamper evidence. Validation must include container-closure integrity testing, leak testing, and compatibility with reagents or cartridges. Standard Operating Procedures (SOPs) should govern cleaning, visual inspection, sealing, and rejection criteria. Transport simulation and shelf-life testing should be performed under international protocols to ensure packaging resilience. The packaging process must be reproducible and well-documented to meet both quality assurance and regulatory expectations.

3.3 Verification & Validation

Verification and validation (V&V) activities form the foundation of a robust product development lifecycle, ensuring that the device meets both its design specifications and its intended clinical or diagnostic use. These processes must be planned, executed, and documented systematically to demonstrate conformance to regulatory and quality standards. The development of a comprehensive Verification and Validation Master Plan (VMP) is the first critical step. This plan should outline the overall V&V strategy, the scope of activities, individual test protocols, test environments, traceability to design inputs, and clearly defined acceptance criteria.

At the component level, verification activities must be performed for all major subsystems—mechanical, electrical, fluidic, optical, software, and reagent-related. Each component should be tested against its defined technical specifications, tolerances, and performance metrics to confirm it functions as intended in isolation. This includes dimensional checks, electrical continuity, firmware validation, chemical compatibility assessments, and interface testing.

System-level validation takes a broader approach, evaluating the complete, integrated device in conditions that closely mimic real-world use. These simulations should include environmental stresses such as temperature and humidity extremes, mechanical vibration, and power fluctuations to assess the system's resilience and consistency under variable field conditions. Operational testing should also evaluate the end-to-end sample-to-result workflow to verify performance across the entire diagnostic pathway.

Human factors and usability validation are particularly essential for point-of-care or near-patient devices, especially those intended for use by non-laboratory personnel or lay users. Formative studies should be conducted early to guide ergonomic and interface design, while summative studies must be carried out on final or near-final device configurations to confirm that intended users can operate the device safely and effectively without prior training. These studies should capture critical user tasks, failure points, and mitigation strategies, aligning with the requirements of IEC 62366-1 for usability engineering.

All verification and validation results must be thoroughly documented, including raw data, test reports, and pass/fail justifications. These records should be mapped to the design inputs via a traceability matrix and compiled into the Design History File (DHF) or Technical File. This documentation supports both internal quality assurance and external regulatory submissions, demonstrating that the product is safe, effective, and fit for its intended use.

3.4 Performance Study Protocol

All studies, analytical or clinical, must be based on a detailed and comprehensive study protocol. The specific content of a study protocol for different investigations will depend on the characteristics being validated, which in turn will depend on the risk management and planning that has been undertaken. However, most analytical and clinical performance studies share several common features. In general, protocols for studies investigating either analytical or clinical performance characteristics should include the following features, discussed below: study rationale, ethical considerations, study objectives and study method.

1. Study rationale
2. Ethical considerations
3. Study objectives
4. Study method
    a. Descriptions of test methods, test kits or other reagents and required materials, and how they will be used in the performance study
    b. A description of how results from tests will be recorded and interpreted
    c. The numbers and types of specimens or samples that will be used and how these were or will be acquired
        i. Specimens for analytical studies
        ii. Specimens for clinical studies

Labelling, Instruction for Use (IFU) & Packaging

Labelling

Ensure the label includes:

1. Device name
2. Model number or unique identifier
3. Lot/batch number
4. Manufacturing date and expiry date
5. Net quantity and pack size
6. Manufacturer's name and full address
7. Applicable CDSCO test manufacturing license numbers
8. Storage conditions (temperature, humidity)
9. Relevant safety symbols and pictograms according to ISO
10. UDI number
11. Ensure compliance with Legal Metrology (Packed Commodities) Rules, 2011

IFU

1. A detailed, step-by-step procedure for test execution
2. Instructions for interpreting test results, including definitions for positive, negative, and invalid outcomes
3. Illustrate or elaborate on proper specimen collection, handling, storage, and processing
4. Include warnings and precaution

Packaging

1. Ensure packaging provides adequate protection against microbial and chemical contamination, as well as physical damage
2. Ensure packaging protects against physical damage (drop, shock, crush) and environmental factors (temperature, humidity, UV).
3. Maintain product integrity, sterility (if applicable), and cleanliness until point of use.
4. Conduct and document container-closure integrity and compatibility testing with final product formats
5. Validate packaging performance through simulated transport and shelf- life stability studies
6. Ensure packaging process validation and maintain relevant records
7. Ensure compliance with Legal Metrology (Packed Commodities) Rules, 2011

Figure 8: Labeling, IFU, Packaging

d. Testing protocol

e. Data collection and management

f. Data analysis

g. Study oversight and monitoring

3.5 Performance study outputs

The output of a performance study, whether analytical or clinical, will be one or more study reports (e.g. one or more interim progress reports, culminating in a final report at the completion of testing). The study report (whether interim or final) should provide at least the following:

1. An executive summary: this should include a summary of the experimental protocol (as described in detail above) as it was intended and as it was actually performed, to ensure that it aligns with the study validity principles outlined in the study protocol.

2. For clinical performance study reports: A discussion on the study population demographics, to allow a clear understanding of limitations of the studies – this will be part of the limitations on the use of the test (e.g. age limits) and will also address study bias.

3. Lot numbers involved and the location of the manufacturing documentation.

4. Criteria for all the testing (including physical, chemical and QC panels at the start and end of the assigned life of the components), and location of the records of all original testing data and records of storage conditions.

5. Any deviations from, or additions to, the study protocol, and justifications for these, including specimen exclusions, collection procedure as it was actually performed, and so on.

6. Tabulated or graphical summaries of the evidence in support of the performance claim being validated – any such table or graph should be accompanied by an explanation of how the experimental evidence supports the performance claim, as well as any inherent limitations to conclusions that can be drawn from the study

7. Full study data (as an addendum) to support any summary evidence – annexes should be included, giving raw or intermediate results that allow verification of the summary (statistical) results.

8. Final conclusion stating whether or not the study's stated objectives had been satisfactorily addressed and the consequences this has for product development and validation.

Retention of photographic records, machine printouts and electronic data, or physical retention of membranes from opened cassettes is encouraged. Records should be retained for the period of time equivalent to the commercial lifetime of the IVD, but not less than 2 years.

3.5.1 Example table, clinical performance study: Diagnostic Sensitivity

Table 1: Summary of results for clinical trial Xxxx, for determination of diagnostic sensitivity

Study site	Number of specimens tested	Number of specimens reactive by reference method	Number of valid tests	Number of specimens reactive in the IVD	Number of specimens falsely nonreactive	% sensitivity	95% confidence interval

3.5.2 Example table, clinical performance study: Diagnostic specificity

Table 2: Summary of results for clinical trial Xxxx, for determination of diagnostic specificity

Study site	Number of specimens tested	Number of specimens reactive by reference method	Number of valid tests	Number of specimens nonreactive in the IVD	Number of specimens falsely reactive	% specificity	95% confidence interval

3.5.3 Example table, analytical performance study: precision

Table 3: Summary of assay precision (Repeatability)

Qc Panel Member	Number Of Replicate Test	Signal To Cut-Off Ratio		Within-condition % CV
		Mean	Standard Deviation	
Negative control				
QC-1 (low-titre positive)				
QC-2 (mid-range positive)				
QC-3 (high-titre positive)				

QC quality control, S/Co signal to cut-off ratio, SD standard deviation, CV coefficient of variation

Table 4: Summary of assay precision (reproducibility) for QC panel member QC-1 (low-titre positive)

Qc Panel Member	Number Of Replicate Test	Signal To Cut-Off Ratio		Within-condition % CV
		Mean	Standard Deviation	
Overall reproducibility				
Between-day				
Between-operator				
Between-lot				
Between-instrument				

QC quality control, S/Co signal to cut-off ratio, SD standard deviation, CV coefficient of variation

3.5.4 Example table, analytical performance study: interfering substances

Table 1: Summary of test results for determination of analytical specificity: endogenous substances

Specimen ID	Test results			
	Unspiked specimen	Specimen spiked with substance-1 (xx g/mL)	Specimen spiked with substance-2 (x/mmol)	Specimen spiked with substance-3 etc.
ID 1				
ID 2				
ID 3				
ID 4				

3.6 Contents of a site or plant master file

The IVD medical device manufacturer shall prepare a succinct document in the form of site master file containing specific information about the production and/or control of device manufacturing carried out at the premises. It shall contain the following information:

3.6.1 General Information

1. Brief information on the site (including name and address), relation to other sites
2. Manufacturing activities
3. Any other operations carried out on the site
4. Name and exact address of the site, including telephone, fax numbers, web
5. Site URL and e-mail address
6. Type of medical devices handled on the site and information about
7. Specifically toxic or hazardous substances handled, mentioning the way they are handled and precautions taken
8. Short description of the site (size, location and immediate environment and other activities on the site)
9. Number of employees engaged in production, quality control, warehousing, and distribution
10. Use of outside scientific, analytical or other technical assistance in relation to the design, manufacture and testing
11. Short description of the quality management system of the company
12. Devices details registered with foreign countries
13. Brief description of testing facility

3.6.2 Personnel

1. Organisation chart showing the arrangements for key personnel
2. Qualifications, experience and responsibilities of key personnel
3. Outline of arrangements for basic and in-service training and how records are maintained
4. Health requirements for personnel engaged in production
5. Personnel hygiene requirements, including clothing

3.6.3 Premises and Facilities

1. Layout of premises with indication of scale
2. Nature of construction, finishes/fixtures and fittings
3. Brief description of ventilation systems. More details should be given for critical areas with potential risks of airborne contamination (including schematic drawings of the systems). Classification of the rooms used for the manufacture of sterile products should be mentioned
4. Special areas for the handling of highly toxic, hazardous and sensitizing materials;
5. Brief description of water systems (schematic drawings of the systems are desirable) including sanitation
6. Maintenance (description of planned preventive maintenance programmes for premises and recording system)

3.6.4 Equipment

1. list of the equipment is required)
2. maintenance (description of planned preventive maintenance programmes and recording system)
3. qualification and calibration, including the recording system.
4. Arrangements for computerized systems validation.

3.6.5 Sanitation

Availability of written specifications and procedures for cleaning the manufacturing areas and equipment.

3.6.6 Production

1. Brief description of production operations using, wherever possible, flow sheets and charts specifying important parameters
2. Arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage
3. Arrangements for reprocessing or rework
4. Arrangements for the handling of rejected materials and products
5. Brief description of general policy for process validation.
6. Brief description of sterilisation facility

3.6.7 Quality Assurance

Description of the quality assurance system and of the activities of the quality assurance department. Procedures for the release of finished products.

3.6.8 Storage

Policy on the storage of medical devices.

3.6.9 Documentation

Arrangements for the preparation, revision and distribution of necessary documentation, including storage of master documents.

3.6.10 Medical Device Complaints and Field Safety Corrective Action

1. Arrangements for the handling of complaints
2. Arrangements for the handling of field safety corrective action.

3.6.11 Internal Audit

Short Description of the internal audit system.

3.6.12 Contract Activities

Description of the way in which the compliance of the contract acceptor is assessed.

3.7 Device Master File for In Vitro Diagnostic Medical Devices (Executive Summary)

An executive summary shall be provided by the manufacturer and shall contain:

3.7.a

Introductory descriptive information on the in vitro diagnostic medical device, the intended use and risk Class of in vitro diagnostic medical device, novel features (if any), claimed shelf life and a synopsis on the content of the dossier.

3.7.b

Regulatory status of the similar device in India (approved or new in vitro diagnostic medical device).

3.7.c

Domestic price of the in vitro diagnostic medical device in the currency followed in the country of origin.

3.7.d

Marketing history of the in vitro diagnostic medical device from the date of introducing the in vitro diagnostic medical device in the market.

3.7.e

List of regulatory approvals or marketing clearance obtained in below format (submit respective copy of approval certificate)

S.N.	Name of the country	Approved indication	Approved shelf life	Composition	Risk Class	Date of first approval

3.7.f

Status of pending request for market clearance

Regulatory Agency of the country	Intended use	Indication for use	Registration status and date	Reason for rejection/ withdrawal, if any

3.7.g

Safety and performance related information on the in vitro diagnostic medical device:

i. Summary of reportable events and field safety corrective action from the date of introduction

For adverse event (false diagnosis or any other hazard during its use)

Adverse event (false diagnosis)	Frequency of occurrence during the period (number of report/total units sold)

For Field Safety Corrective Action (FSCA)

Date of FSCA	Reason for FSCA	Countries where FSCA was conducted	Description of the action taken

ii. If the in vitro diagnostic medical device contains any of the following then descriptive information on the following need to be provided.

(1) Animal or human fluids or derivatives thereof, rendered non-viable.

(2) Cells, tissues and/or derivatives of microbial recombinant origin.

3.7.1 Documentation

Description and specification, including variants and accessories of the in vitro diagnostic medical device

3.7.1.1 Description

The device master file should include the following device descriptive information:

a. It may include:-

   1. What is detected
   2. Its function (for example screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease)
   3. The specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate
   4. Whether it is automated or not
   5. Whether it is qualitative or quantitative
   6. The type of specimen required (eg. Serum, plasma, whole blood, tissue biopsy, urine)
   7. Testing population

b. The intended user (lay person or professional);

c. A general description of the principle of the assay method;

d. The risk based Class of the device;

e. A description of the components (e.g. reagents, assay controls and calibrators) and where appropriate, a description of the reactive ingredients of relevant components (such as antibodies, antigens, nucleic acid primers) where applicable

f. A description of the specimen collection and transport materials provide with the in vitro diagnostic medical device or descriptions of specifications recommended for use

g. For instruments of automated assays; a description of the appropriate assay characteristics or dedicated assays

h. For automated assays; a description of the appropriate instrumentation characteristics or dedicated instrumentation

i. A description of any software to be used with the in vitro diagnostic medical device

j. A description or complete list of the various configurations/variants of the in vitro diagnostic medical device that will be made available

k. A description of the accessories, other in vitro diagnostic medical device and other products that are not in vitro diagnostic medical device, which are intended to be used in combination with the in vitro diagnostic medical device.

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

3.7.1.2

For a new in vitro diagnostic medical device: Where relevant to demonstrating conformity to the essential principles, and to provide general background information, the device master file may provide a summary of Clinical Performance Evaluation reports.

3.7.1.3 For an in vitro diagnostic medical device already available on the market in India

1. This information may include a summary of the number of adverse event reports related to the safety and performance of this in vitro diagnostic medical device in relation to the number of in vitro diagnostic medical devices placed on the market.
2. External certificates and documents which give written evidence of

conformity with the essential principles may be annexed to the device master file.

3. Comparative analysis to prove substantial equivalence to the predicate device(s), if claimed in the application.

3.7.2 Essential principles checklist

1. The device master file should include an essential principles checklist that identifies:
    a. The essential principles of safety and performance
    b. Whether each essential principle applies to the in vitro diagnostic medical device and if not, why not
    c. The method used to demonstrate conformity with each essential principle that applies
    d. The reference to the actual technical documentation that offers evidence of conformity with each method used.
2. The method used to demonstrate conformity may include one or more of the following:-
    a. Conformity with recognized or other standards;
    b. Conformity with a commonly accepted industry test method (reference method);
    c. Conformity with appropriate in house test methods that have been validated and verified;
    d. Comparison to an in vitro diagnostic medical device already available on the market.
3. The essential principles checklist should include a cross-reference to the location of such evidence both within the full technical documentation held by the manufacturer and within the Device master file.

3.7.3 Risk analysis and control summary

The device master file should contain a summary of the risks identified during the risk analysis process and a description of how these risks have been controlled to an acceptable level. Preferably, this risk analysis should be based on recognised standards and be part of the manufacturer's risk management plan.

The summary should address possible hazards for the in vitro diagnostic medical device such as the risk from false positive or false negative results, indirect risks which may result from in vitro diagnostic medical device associated hazards, such as instability, which could lead to erroneous results, or from user-related hazards, such as reagents containing infectious agents. The results of the risk analysis should provide a conclusion with evidence that remaining risks are acceptable when compared to the benefits.

3.7.4 Design and manufacturing information

3.7.4.1 Device design:

The Device master file should contain information to allow a reviewer to obtain a general understanding of the design applied to the in vitro diagnostic medical device. It should include a description of the critical ingredients of an assay such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the in vitro diagnostic medical device, This section is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. If design takes place at multiple sites, a controlling site must be identified.

3.7.4.2 Manufacturing processes

The device master file should contain information to allow a reviewer to obtain a general understanding of the manufacturing processes. It is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. The information may take the form of a process flow chart showing, for example, an overview of

production including the technologies used, assembly, any in-process and final product testing, and packaging of the finished in vitro medical device.

3.7.4.3 Manufacturing sites

The device master file should identify the sites where these activities are performed (this does not include the sites of all suppliers of raw materials but only the sites that are involved in critical manufacturing activities). If Quality Management System certificates, or the equivalent, exist for these sites, they may be annexed to the device master file.

3.7.5 Product validation and verification

The information provided in the product validation and verification section of the device master file will vary in the level of detail as determined by the class of the device. The device master file should summarize the results of validation and verification studies undertaken to demonstrate conformity of the in vitro diagnostic medical device with the essential principles that apply to it. Where appropriate, such information might come from literature.

For the purpose of the device master file document, summary and detailed information are defined as follows:

i. Summary information: A summary should provide enough to assess the validity of that information by the regulatory authorities. This summary should contain a brief description of:

    a. Study Protocol

    b. Study Results

    c. Study Conclusion

This summary may include:

    a. Where a recognized standard exists, a declaration/certificate of conformity to a recognized standard can be provided with a summary of the data if no acceptance criteria are specified in the standard;

    b. In the absence of a recognized standard, a declaration/certificate of conformity to a published standard that has not been recognized might be provided if it is supported by a rationale for its use, and summary of the data, and a conclusion, if no acceptance criteria are specified in the standard;

    c. In the absence of a recognized standard and non-recognized published standards, a professional guideline, industry method, or in-house standard may be referred to in the summarized information. However, it should be supported by a rationale for its use, a description of the method used, a summary of the data in sufficient detail and a conclusion to allow assessment of its adequacy;

    d. A review of relevant published literature regarding the device/analyte (measurand) or substantially similar in vitro diagnostic medical devices.

ii. Detailed information should include:

    a. Complete Study Protocol

    b. Method Of Data Analysis

    c. Complete Study Report

    d. Study Conclusion

For detailed information, when a recognized standard exists that contains the protocol and the method of data analysis, this information can be substituted by a declaration or certificate of conformity to the recognized standard along with a summary of the data and conclusions. where appropriate, actual test result summaries with their acceptance criteria should be provided and not just pass/fail statements.

3.7.6 Analytical Studies

The statements and descriptions in the following sections refer to all in vitro diagnostic medical devices. It must be noted however that there are applicability differences between instrumentation and reagent-based assays, and that the assays themselves may be quantitative, semi-quantitative or qualitative in nature. There may be limited applicability of some of the following subsections for qualitative or semi-quantitative assays. Where possible, comments regarding instrumentation or qualitative assays appear in the subsections.

While measurement trueness, affected by systematic error, is normally expressed in terms of bias, measurement precision, affected by random error, is naturally expressed in terms of standard deviation, Accuracy is affected by a combination of systematic and random effects that contribute as individual components of the total error of measurement.

3.7.7 Specimen type

a. This section should describe the different specimen types that can be used. This should include their stability and storage conditions. Stability includes storage and where applicable transport conditions. Storage includes elements such as duration, temperature limits and freeze/thaw cycles.

b. This section should include summary information for each matrix and anticoagulant when applicable, including a description of the measurement procedure for comparison or determination of measurement accuracy. This includes information such as specimen type tested, number of samples, sample range (using spiked samples as appropriate) or target concentrations tested, calculations and statistical methods, results and conclusions.

3.7.8 Analytical performance characteristics

3.7.8.1 Accuracy of measurement

This section should describe both trueness and precision studies.

Explanation - The general term measurement accuracy is currently used to cover both trueness and precision, whereas this term was used in the past to cover only the one component now named trueness.

3.7.8.2 Reproducibility

This section should include reproducibility estimates and information about the studies used to estimate, as appropriate, variability between days, runs, sites, lots, operators and instruments. Such variability is also known as “Intermediate Precision”. Reproducibility data is obtained for instrumentation in conjunction with an appropriate assay.

Note 1.- Such studies should include the use of samples that represent the full range of expected analyte (measurand) that can be measured by the test as claimed by the manufacturer.

Note 2.- If a recognized standard is used, a declaration/certificate of conformity to the recognized standard along with a summary of the data and conclusions.

3.7.9 Analytical sensitivity

This section should include information about the study design and results. It should provide a description of specimen type and preparation including matrix, analyte (measurand) levels, and how levels were established. The number of replicates tested at each concentration should also be provided as well as a description of the calculation used to determine assay sensitivity. For example:

a. Number of standard deviations above the mean value of the sample

without analyte (measurand), commonly referred to as limit of blank (LoB).

b. Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand), commonly referred to as limit of detection (LoD).

c. Lowest concentration at which precision and/or trueness are within specified criteria, commonly referred to as limit of quantitation (LoQ).

For Class C and D in vitro diagnostic medical devices, detailed information would be provided.

3.7.10 Analytical specificity

1. This section should describe interference and cross reactivity studies to determine the analytical specificity, defined as the ability of a measurement procedure to detect or measure only the analyte (measurand) to be detected, in the presence of other substances/ agents in the sample.

2. Provide information on the evaluation of potentially interfering and cross reacting substances/agents on the assay. Information should be provided on the substance/agent type and concentration tested, sample type, analyte (measurand) test concentration, and results.

3. Interferents and cross reacting substances/agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources such as:

    a. Substances used for patient treatment (e.g. Therapeutic drugs, anticoagulants, etc.)

    b. Substances ingested by the patient (e.g. Over the counter medications, alcohol, vitamins, foods, etc.)

    c. Substances added during sample preparation (e.g. Preservatives, stabilizers);

    d. Substances encountered in specific specimens types (e.g. Hemoglobin, lipids, bilirubin, proteins)

    e. Analytes of similar structure (e.g. Precursors, metabolites) or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that may mimic the test condition (e.g. For a hepatitis a assay: test specimens negative for hepatitis a virus, but positive for hepatitis b virus).

Explanation - Interference studies involve adding the potential interferent to the sample and determining any bias of the test parameter relative to the control sample to which no interferent has been added.

3.7.11 Metrological traceability of calibrator and control material values

Where applicable, summarize the information about metrological traceability of values assigned to calibrators and trueness control materials. Include, for example, methods and acceptance criteria for the metrological traceability to reference materials and/or reference measurement procedures and a description of value assignment and validation.

Precision control materials, used when establishing the reproducibility of a measurement procedure do not require the assessment of metrological traceability to a reference material or a reference method.

3.7.12 Measuring range of the assay

This section should include a summary of studies which define the measuring range (linear and non-linear measuring systems) including the limit of detection and describe information on how these were established. This summary should include a description of specimen type, number of samples, number of replicates, and preparation including information on matrix, analyte (measurand) levels and how levels were established. If applicable, add a description of high dose hook effect and the data supporting the mitigation (e.g. dilution) steps.

3.7.13 Definition of Assay Cut-off

This section should provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, including:

a. The population(s) studied (demographics / selection / inclusion and exclusion criteria / number of individuals included);

b. Method or mode of characterization of specimens; and

c. Statistical methods e.g. Receiver Operator Characteristic (roc) to generate results and if applicable, define gray-zone/equivocal zone.

3.7.14 Stability (excluding specimen stability:

This section should describe claimed shelf life, in use stability and shipping studies.

3.7.15 Claimed Shelf life

This section should provide information on stability testing studies to support the claimed shelf life. Testing should be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these lots do not need to be consecutive lots). Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies. Such detailed information should describe:

a. The study report (including the protocol, number of lots, acceptance criteria and testing intervals)

b. When accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies;

c. Conclusions and claimed shelf life.

Explanation - Shelf life can be derived from the lot with the longest real time stability data as long as accelerated or extrapolated data from all three lots are comparable.

3.7.16 In use stability

This section should provide information on in use stability studies for one lot reflecting actual routine use of the device (real or simulated). This may include open vial stability and/or, for automated instruments, on board stability. In the case of automated instrumentation if calibration stability is claimed, supporting data should be included. Such detailed information should describe:

a. The study report (including the protocol, acceptance criteria and testing intervals)

b. Conclusions and claimed in use stability.

3.7.17 Shipping stability

This section should provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated shipping conditions. Shipping studies can be done under real and/or simulated conditions and should include variable shipping conditions such as extreme heat or cold. Such information should describe:

1. The study report (including the protocol, acceptance criteria)

2. Method used for simulated conditions

3. Conclusion and recommended shipping conditions

3.7.18 Clinical Evidence

The device master file should contain the Clinical Evidence, Evaluation report that demonstrates conformity of the in vitro diagnostic medical device to the Essential Principles that apply to it.

3.7.19 Labelling

The device master file should typically contain a complete set of labeling associated with the in vitro medical device as described in Chapter VI.

3.7.20 Post marketing surveillance data (vigilance reporting)

The dossier should contain the post marketing surveillance or vigilance reporting procedures and datacollected by the manufacturer encompassing the details of the complaints received and corrective and Preventive actions taken for the same.

3.7.21 Information required to be submitted for the in vitro diagnostic medical device

1. The details of source antigen or antibody as the case may be and characterization of the same. Process control of coating of antigen or antibody on the base material like Nitrocellulose paper, strips or cards or ELISA wells etc. Detailed composition of the in vitro diagnostic medical device and manufacturing flow chart process of the in vitro diagnostic medical device showing the specific flow diagram of individual components or source of the individual components.
2. Test protocol of the in vitro diagnostic medical device showing the specifications and method of testing. In house evaluation report of sensitivity, specificity and stability studies carried out by the manufacturer.
3. In case of imported diagnostic in vitro diagnostic medical devices, the report of evaluation in details conducted by the National Control Authority of country of origin.
4. Specimen batch test report for at least consecutive 3 batches showing specification of each testing parameter.
5. The detailed test report of all the components used/packed in the finished in vitro diagnostic medical device.
6. Pack size and labeling.
7. Product inserts.
8. Specific evaluation report, if done by any laboratory in India, showing the sensitivity and specificity of the in vitro diagnostic medical device.
9. Specific processing like safe handling, material control, area control, process control, and stability studies, storage at quarantine stage and finished stage, packaging should be highlighted in the product dossier.

NOTE:

1. All the test reports submitted as a part of the dossier should be signed and dated by the responsible person.

2. Batch Release Certificates and Certificate of Analysis of finished product for minimum 3 consecutive batches should be submitted.

3. All certificates submitted must be within the validity period.

4. Any information which is not relevant for the subject in vitro diagnostic medical device may be stated as 'Not Applicable' in the relevant sections/ columns of the above format, and reasons for non-applicability should be provided.

Once the innovator or manufacturer is ready to implement Quality Management System (QMS) manufacturing practices, it's crucial to understand the frameworks that govern these activities.

To do list C: QMS Manufacturing and Documentation

Quality Management System (ISO 13485 Implementation): Establish a documented, auditable QMS in line with ISO 13485 and CDSCO expectations. Ensure consistent quality, compliance, and traceability throughout development.

Sl. No	To do	Completed		Remarks
		Yes	No	
10.1	Develop and document a Quality Management System (QMS) as per ISO 13485 and CDSCO guidelines.			
10.2	Implement document control and maintain DMR/DHF.			
10.3	Assign and document organizational roles and responsibilities.			
10.4	Ensure traceability from raw materials to final product.			
10.5	Document design and development planning			
10.6	Prepare Device Master File (DMF) as per CDSCO.			
10.7	Preparing SOPs for manufacturing			
10.8	Establish in-process QC (visual, volume, weight, seal, barcode)			
10.9	Standardize batch QC with valid sampling.			
10.10	Perform process validation (IQ, OQ, PQ).			
10.11	Define and document Key Process Parameters (KPPs) and control ranges.			
10.12	Implement CAPA, internal audits, and complaint handling.			

Change Management: Manage changes and continuous improvements with design control and traceability. Ensure that all design iterations are justified, documented, and verified.

Sl. No	To do	Completed		Remarks
		Yes	No	
11.1	Define iterative loops: alpha -> beta builds -> design freeze.			
11.2	Implement a formal change control process (impact review, approval, traceability).			
11.3	Maintain a version-controlled change log linked to verification outcomes.			
11.4	Re-test and re-verify impacted modules after approved changes.			
11.5	Conduct internal design review checkpoints (Go/No-Go) before freezing designs.			

Labeling, Instruction for use and Packaging: It is recommended that you ensure all product labeling, instructions for use (IFU), and packaging are developed to be clear, compliant, and supportive of product safety and traceability. Make sure labeling meets CDSCO and ISO standards, with all critical information visible and traceable throughout the supply chain. Develop standardized IFUs to enable users to operate the IVD product safely and correctly, ensuring these instructions align with regulatory requirements and are validated through usability testing. Additionally, design and validate packaging to protect product integrity, using approved materials and processes that meet regulatory, environmental, and transportation requirements.

Sl. No	To do	Completed		Remarks
		Yes	No	
12.1	Ensure the label includes the device name.			
12.2	Include the model number or unique identifier on the label.			
12.3	Display the lot or batch number.			
12.4	Indicate the manufacturing date and expiry date.			

Sl. No	To do	Completed		Remarks
		Yes	No	
12.5	State the net quantity and pack size.			
12.6	Provide the manufacturer's name and full address.			
12.7	List applicable CDSCO test/manufacturing license numbers.			
12.8	Specify storage conditions (temperature, humidity).			
12.9	Add relevant safety symbols and pictograms according to ISO 15223-1.			
12.10	Clearly display warnings (e.g., single use only, do not reuse).			
12.11	State the intended use and intended user (e.g., healthcare professional, lay user).			
12.12	Develop and provide clear, standardized Instructions for Use (IFU) that include: 1. A detailed, step-by-step procedure for test execution. 2. Instructions for interpreting test results, including definitions for positive, negative, and invalid outcomes. 3. Guidance on proper specimen collection, handling, storage, and processing. 4. All relevant warnings, limitations, and precautions (e.g., biosafety, interfering substances).			

Sl. No	To do	Completed		Remarks
		Yes	No	
12.13	Select and validate packaging materials and design: 1. Use regulatory-grade materials with chemical compatibility (no reagent interaction). 2. Ensure environmental durability (temperature, humidity, UV resistance). 3. Ensure mechanical resistance (drop, shock, crush). 4. Define packaging layout (primary, secondary, tertiary). 5. Conduct container-closure integrity and compatibility testing with final reagents and formats.			
12.14	Establish and implement SOPs for: 1. Cleaning containers before filling. 2. Leak testing. 3. Visual inspection and rejection criteria.			
12.15	Validate packaging performance through: 1. Simulated transport testing. 2. Shelf-life stability studies.			

Verification & Validation (V&V): Verify functional performance and validate clinical safety, reliability, and usability. Ensure regulatory submission readiness through well-documented V&V.

Sl. No	To do	Completed		Remarks
		Yes	No	
13.1	Develop a Verification and Validation Master Plan (VMP).			
13.2	Conduct component-level verification (mechanical, electrical, reagent, software).			
13.3	Perform system-level validation under real-use and stress scenarios.			
13.4	Validate human factors through formative and summative usability studies.			
13.5	Test failure and error-handling performance (e.g., invalid samples, power cuts).			

04

04

CHAPTER

Performance Evaluation

4.0 General

Performance evaluation of an In Vitro Diagnostic (IVD) medical device assesses its ability to achieve the intended use as specified by the manufacturer. This evaluation ensures that the device meets the claimed analytical and clinical performance standards, demonstrating its reliability, accuracy, and suitability for diagnostic applications.

- Analytical performance studies evaluate "the ability of an IVD medical device to detect or measure a particular analyte".
- Clinical performance studies demonstrate "the ability of the IVD medical device to yield results that are correlated with a particular condition/physiological state in accordance target population and intended user".

The process of performance evaluation is intended to demonstrate that a test method consistently delivers results that are accurate, reliable, and suitable for its intended use. This entails verifying that when the performance evaluation is conducted by a qualified analyst using appropriate equipment, reagents, and environmental conditions and strictly adhering to the protocol it yields results that meet predefined performance criteria.

The performance of an IVD medical device encompasses the essential characteristics that determine how well the device can detect, measure,

or monitor specific biological markers or analytes. It ensures that the diagnostic tool functions as intended and delivers results that are accurate, reliable, and reproducible, ultimately influencing clinical decisions and patient outcomes. Analytes can range from infectious agents like viruses and bacteria to proteins, nucleic acids, or metabolites used for disease detection, monitoring.

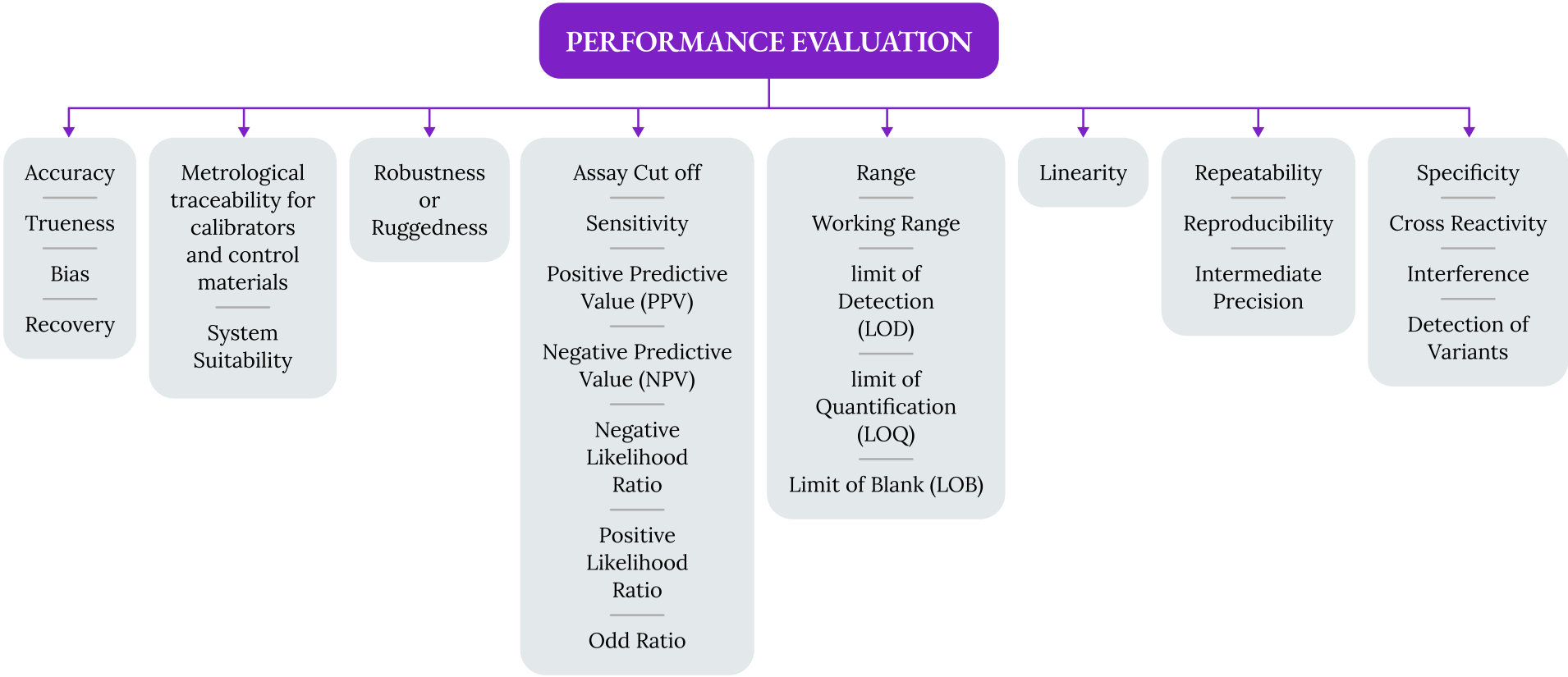
4.1 Performance characteristics

The analytical performance evaluation of an in vitro diagnostic (IVD) device includes a comprehensive assessment of the following elements:

1. Specimen Type Evaluation: Assessment of the suitability of the sample type, including procedures for collection, storage conditions, and transport stability.
2. Equivalence of Specimen Types: Verification of consistency in performance across different accepted specimen types.
3. Core Analytical Performance Characteristics:
    a. Accuracy
    b. Trueness and Bias
    c. Precision, including repeatability and reproducibility
    d. Analytical Sensitivity, such as limit of detection and detection of genetic or antigenic variants
    e. Analytical Specificity, including evaluation of potential interferences and cross-reactivity
    f. Measuring Range (Linearity and Reportable Range)
4. Assay-Specific Studies
    a. Cut-off Validation for qualitative or semi-quantitative assays
    b. Validation of Assay Reading Time to ensure consistent interpretation within specified time windows
    c. Traceability of calibrators and control materials to certified reference materials or international standards
    d. Validation of Assay Procedure to confirm robustness of steps under normal and stressed conditions
5. Stability Studies
6. Robustness Testing
7. Human Factors Assessment
8. Verification of Labelling and Instructions for Use (IFU)

The Clinical performance evaluation of an in vitro diagnostic (IVD) device includes a assessment of the following elements (Non Exhaustive):

1. Clinical sensitivity
2. Clinical specificity
3. Positive Predictive Value (PPV)
4. Negative Predictive Value (NPV)
5. End-user verification of labelling and IFU (self-testing)



Note: The figure below outlines various performance evaluation parameters. However, not all of these parameters are applicable to every device. This list is not exhaustive, and devices under evaluation may also be assessed against additional parameters as required.

Most in vitro diagnostic (IVD) test methods are designed to produce quantitative, numerical results however, certain assays yield only qualitative outcomes typically binary interpretations such as "analyte present" or "analyte absent" relative to a predefined cut-off value. While some IVDs are intentionally designed to deliver only qualitative results at the point-of-care or in user environments, the underlying methods used during development and manufacturing often generate quantitative data.

In many cases, qualitative assays can be adapted to generate semi-quantitative or fully quantitative results through instrumental readings (e.g., enzyme immunoassays) or comparison with graded reference standards.

If quantitative output is not feasible, the performance evaluation should be designed using appropriate qualitative statistical methods to ensure reliability and reproducibility.

Simply reporting a result as "positive" or "negative" without an accompanying assessment of uncertainty is generally insufficient, especially when the assay is used for purposes such as stability testing, sensitivity analysis, precision characterization, or release-to-market decisions.

The following table outlines the analytical performance parameters that should be evaluated based on the nature of the IVD result qualitative or quantitative.

Table 6: Performance evaluation parameters for qualitative versus quantitative IVDs

Characteristics	Quantitative	Qualitative
Selectivity/specificity	Yes	Yes (True negative rate)
Sensitivity	Yes (LOD/LOQ)	Yes (True positive rate)
Limit of detection	Yes	Yes
Limit of quantitation	Yes	No
Linearity (or other calibration model)	Yes	No
Working Range	Yes	No
Accuracy	Yes	No
Precision	Yes	Yes
Robustness / Ruggedness	Yes	Yes
Recovery/Trueness	Yes	No
Traceability	Yes	No
Stability	Yes	Yes

4.2 General considerations for analytical performance studies

4.2.1 Specimen type, collection and handling

The numbers and types of specimens used in performance studies will depend largely on the studies themselves, particularly on whether it is analytical or clinical performance that is being investigated. International guidance also provides recommendations. Consideration should be given to the ability of an IVD to detect all claimed analytes; for example, for an IVD intended to detect HIV-1 including Group O and HIV-2, performance should not consist solely of testing using HIV-1 antibody-positive specimens.

Specimens used in analytical studies will vary depending on the study objectives, but each study should make use of specimens that provide a level of reactivity that demonstrates how well the test performs at its limits. Ideally, specimens should be of the same matrix intended for use with the test (e.g. serum, plasma, finger-prick whole blood or oral fluid). However, low-reactive specimens close to the cut-off value, which can be of the greatest value in testing the limits of performance, may be difficult to obtain or be in short supply. If this is the case, contrived specimens (e.g. negative specimens in the corresponding matrix spiked to a low level of reactivity with the test analyte, or dilutions of a high-concentration specimen) may be used in a study, provided that the approach has a comprehensive scientific justification.

The choice of sample specimen type will be dictated by the intended use of the IVD (and the intended specimen for use with the IVD). Clinical evidence must be presented for all claimed specimen types. If a full clinical study is performed on only one of several claimed specimen types, this approach must be justified. Specimens for clinical performance studies typically come from three possible sources:

- Specimens taken prospectively from patients with appropriate disease signs and symptoms, with the intention that the specimens be used in a particular clinical performance study. These specimens may be tested immediately (fresh) or may be aliquoted and stored refrigerated or frozen for testing at a later time. If tested at a later time, specimen storage conditions (e.g. temperature, duration and the effect of specimen freeze-thaw cycles on the specific test analyte) must be consistent with those determined as part of analytical studies conducted during earlier stages of product development.
- Leftover specimens collected for routine diagnostic testing that would otherwise be discarded, or specimens collected for research purposes. Knowledge of specimen storage and handling before use of leftover or research-use specimens is important, as are any ethical considerations related to the patient source.
- Archived specimens that were collected in the past and were stored for extended periods of time in repositories. These specimens would be made available for use by those conducting analytical and clinical performance studies, or for use in product research and development. As above, specimens should only be used if their storage has been consistent with storage requirements (e.g. duration, temperature and freeze-thaw cycles) determined for specimens during analytical testing of the IVD.

Regardless of the route of acquisition, particular care must be taken to ensure both that specimen integrity is maintained during the course of a study, and that the acquisition of specimens does not introduce one or more types of bias such as selection bias.

4.3 Component analysis

The manufacturer or innovator plays a critical role in ensuring the safety, performance, and compliance of a IVD medical device. A well-structured approach to device design, component review, software evaluation, usability analysis, and regulatory compliance is essential to meet industry standards and regulatory expectations. The manufacturer must adopt a systematic approach to designing the device, ensuring all components and subsystems are carefully identified, evaluated, and documented. This process involves creating a detailed Bill of Materials (BoM), listing all parts, including mechanical, electronic, and software components, with

specifications such as material type, dimensions, tolerances, and supplier details.

A comprehensive design specification should outline the functionality, intended use, safety features, power requirements, and user interface details. Furthermore, the manufacturer should define the device architecture, establishing how different components interact to achieve the intended function.

4.4 Review of Mechanical and Electronic Components

A detailed review of mechanical and electronic components is necessary to ensure device reliability, durability, and compliance with regulatory standards. For mechanical components, manufacturers must focus on materials selection. The manufacturer or innovator should conduct structural integrity testing, including tensile strength, fatigue analysis, and impact resistance, to assess durability. If the device involves fluidics or microfluidic components, optimal flow dynamics, leak-proof connections, and precise control over reagents are essential, especially for devices like nucleic acid extraction systems.

For electronic components, a thorough review should include circuit design and PCB analysis to verify compliance with IEC 60601-1 (Medical Electrical Equipment – General Requirements for Safety and Performance). Electromagnetic Compatibility (EMC) testing is crucial to ensure that the device does not emit or get affected by electromagnetic interference as per IEC 60601-1-2. Additionally, manufacturers must evaluate battery and power management for safety and energy efficiency. Finally, sensor calibration and validation are necessary to ensure accuracy and repeatability in detecting biological or chemical signals.

4.5 Software verification and validation

If the IVD incorporates software (embedded or standalone), the manufacturer must ensure that it meets regulatory requirements for performance, cybersecurity, and reliability. Key steps in software evaluation include software verification, software validation and software risk management, which involves identifying potential software failures and their impact as required by ISO 14971. The manufacturer should follow the Software Development Lifecycle (SDLC) as outlined in IEC 62304, which defines best practices for software design, coding, validation, and maintenance. The dossier should contain information on the software design and development process and evidence of the validation of the software, as used in the finished device.

Software validation and verification are crucial processes that include unit testing, integration testing, and system testing to ensure software reliability. Additionally, user interface (UI) testing must be conducted to verify that the software is intuitive, responsive, and free of critical usability issues.

4.6 Usability Engineering

Usability testing, although not a compulsory requirement, plays a crucial role in ensuring that medical devices are easy to operate and effectively mitigate risks associated with human error. This practice is guided by IEC 62366 (Usability Engineering for Medical Devices), which provides a framework for manufacturers to design devices that are not only safe and effective but also user-friendly. To achieve this, manufacturers should engage in simulated use testing, allowing for the observation of user interactions with the device in realistic scenarios. This methodology is instrumental in identifying potential usability issues and facilitating improvements based on real-world user experiences. Additionally, a thorough assessment of labeling and instructions for use (IFU) is essential to guarantee that all warnings, step-by-step guides, and troubleshooting tips are presented in a clear and comprehensible manner.

Moreover, it is imperative for manufacturers to concentrate on minimizing cognitive load through simplified design strategies, particularly for point-of-care testing devices. By reducing complexity, manufacturers can help alleviate user confusion and enhance overall usability. Effective usability engineering is paramount in preventing user errors that could compromise test accuracy or jeopardize patient safety. Thus, prioritizing usability

not only aligns with regulatory standards but also fosters better clinical outcomes and user satisfaction.

4.7. Basic principles for stability testing

A well-designed stability study must generate evidence of the stability of each of the critical constituents in the IVD (risk-evaluated critical constituents), evidence of stability for each of the claimed analytes, and evidence for any particular level of performance, including the precision, sensitivity and specificity of the kit. It is a manufacturer's responsibility to ensure that all claims made regarding the stability of the IVD performance are supported by objective, scientifically-sound evidence.

The domestic manufacturer or authorized agent (in case of Import) shall submit the duly signed detailed information pertaining to stability of applied product in Device Master File as specified in point 15.0 -18.0 of Appendix III of Part III of Fourth Schedule of MDR-2017. Manufacturer should describe claimed shelf life, in use stability and shipping stability studies and should provide information on stability testing studies to support the claimed shelf life.

4.7.1 Claimed Shelf life

This section should provide information on stability testing studies to support the claimed shelf life. Testing should be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these lots do not need to be consecutive lots).

Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies. Such detailed information should describe:

a. The study report (including the protocol, number of lots, acceptance criteria and testing intervals)

b. When accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies

c. Conclusions and claimed shelf life.

Shelf life can be derived from the lot with the longest real time stability data as long as accelerated or extrapolated data from all three lots are comparable.

4.7.2 In use stability

This section should provide information on in use stability studies for one lot reflecting actual routine use of the device (real or simulated). This may include open vial stability and/or, for automated instruments, on board stability. In the case of automated instrumentation if calibration stability is claimed, supporting data should be included. Such detailed information should describe:

a. The study report (including the protocol, acceptance criteria and testing intervals)

b. Conclusions and claimed in use stability.

4.7.3 Shipping stability

This section should provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated shipping conditions. Shipping studies can be done under real and/or simulated conditions and should include variable shipping conditions such as extreme heat or cold. Such information should describe:

a. The study report (including the protocol, acceptance criteria)

b. Method used for simulated conditions

c. Conclusion and recommended shipping conditions.

4.7.4 Suitability for use in India

The stability studies submitted to CDSCO should accurately reflect the expected environmental conditions and the normal usage conditions/ methods encountered by the users in India's States, such as:

a. Extremes of temperature for in-use conditions and during transportation

b. Extremes of humidity encountered during in-use conditions, transportation and storage

c. Dust

d. Light, both the amount required for accurate testing/results interpretation and any affects that light may have on the IVD functionality

e. Micro-organisms

4.7.5 Standards

CDSCO recommends the following latest standards, guidelines for the use in establishment of stability claims for IVD medical device:

- CDSCO's Guidance on Stability Studies of In-Vitro Diagnostic Medical Device (IVDMD)
- ISO 23640 (In vitro diagnostic medical devices - Evaluation of stability of in vitro diagnostic reagents)
- CLSI-EP25-A
- ASTM:D4169-14
- ASTM F-1980-21
- WHO TGS-2

It is recommended that manufacturers be familiar with the standard and consider them when designing and planning their stability studies.

4.7.6 Finalized product presentation

During stability testing, all IVD components (including the device, calibrator and / or control material, etc.) must be made and tested to the finalized manufacturing documentation and in the finalized packaging including intended labels and containers. All presentations (e.g. different buffer volumes used for different kit sizes) must be used during stability testing.

4.7.7 Minimum number of lots

The design of stability studies must take into consideration lot-to-lot variability, with a risk assessment conducted to identify the most important sources of variability. Although existing standards recommend the use of a single lot for certain stability studies, the impact of lot-to-lot variability must be taken into consideration and the use of additional lots may be necessary. Three lots, at a minimum, must be used to establish or verify shelf-life, in-use claims require testing on a minimum of one lot. To ensure that the potential for lot-to-lot variability is addressed, independent lots must be used i.e., lots containing different batches of critical constituents such as nitrocellulose membranes, recombinant antigens, peptides, nucleic acids and the enzymes used in nucleic acid test- based (NAT-based) testing technologies.

4.7.8 Assessment of liquid components

The orientation of the product during storage (that is, upright versus inverted or horizontal) may need to be included in a protocol where contact of the product with the different parts of the container (such as the closure system or the body of the container) may be expected to affect the stability of the products contained (for example, liquid component). This is sometimes referred to as "inverted container stability". The product orientation may need to be moved occasionally during the stability study to ensure that there is direct contact between the liquid contents and all parts of the container. This aspect requires particular attention during in-use stability studies of components that are diluted or reconstituted from a freeze-dried state before use.

4.7.9 Stability testing protocol

As part of an approved study plan for the determination of IVD stability, a detailed testing protocol should be prepared (including the following as a minimum, as appropriate.

1. QMS identifiers (e.g. experiment name, document references, etc.) that allow traceability to both the overarching study plan and to subsequently generated records/documents such as result worksheets
2. Responsibilities, name of operator and their training requirements.
3. The dates and times when the stability study will be performed
4. Name, designation and Signatures of the operator and supervisor
5. The objectives of the study (i.e. determination of shelf-life, determination of in-use stability of a component, etc.)
6. The name and lot number of the IVD and/or components being subjected for stability studies.
7. How the components/finished product will be sampled from the production department
8. Stability testing panel members and their characterization to be used, including valid test methods which reflect the IFU claims. Note: IVDs should be tested with samples at several different analyte concentrations, including samples at low concentration near the cut-off level of the assay.
9. The experimental method that will be used for testing. This must follow the finalized testing method from the IFU. It must describe clearly how the experiment was performed in terms of: Required storage and/or challenge conditions
    a. The duration of storage/challenge
    b. The schedule of testing intervals
    c. The stability testing panel
    d. The numbers of replicate tests performed for each stability testing panel member.
10. How and where results are to be recorded
11. Acceptance criteria
12. How aberrant, discordant or invalid results will be dealt with
13. How storage/challenge conditions are to be applied

4.8 Test batch Device manufacturing

Performance Evaluation Phase is a critical component of an IVD product's technical documentation and regulatory submission, aimed at verifying and validating the device's analytical reliability, reproducibility, stability, and clinical comparability. The process begins with test batch manufacturing, where traceable, well-characterized lots are produced under GMP-aligned workflows. A comprehensive Test Batch Manufacturing Plan must be developed, and Batch Manufacturing Records (BMRs) should be created for each lot. All components and reagents used in the evaluation must pass incoming quality control (IQC), and calibration and maintenance records of the equipment involved must be archived. Personnel assigned to the manufacturing process should be qualified and documented for traceability. In-process quality control (IPQC) checks such as for fill volume, reagent integrity, and seal integrity—must be recorded, and each lot must undergo post-manufacturing release testing. Lot-to-lot reproducibility is assessed using performance metrics, and Device History Records (DHRs) must be compiled in compliance with ISO 13485 and maintained for audit readiness.

4.9 Analytical Performance Evaluation

Following manufacturing, the analytical performance evaluation is conducted to characterize the technical limits, detection capability, and precision of the device. Key analytical parameters include Limit

of Detection (LoD), Limit of Quantification (LoQ), Linearity, Accuracy, Precision (Repeatability and Reproducibility), Specificity, Cross-reactivity, and Robustness. Relevant standards such as CLSI EP17 (for LoD), EP06 (for Linearity), EP05 (for Precision), and ISO 15197 must be referenced, and a statistically powered analytical plan must be drafted with predefined acceptance criteria. Reference materials such as inactivated pathogens, nucleic acids, proteins, or clinical sample pools—should be selected or acquired. Known spiking concentrations must be determined, and all spiking, dilution, and assay runs must be performed using calibrated and validated equipment, with documented calibration records. Testing should include multiple replicates, randomized and blinded sample handling, and be performed by different operators across multiple days to simulate real-use variability. Acceptance criteria for each parameter must be defined in advance (e.g., CV ≤ 20% for precision, $R^2 \geq 0.95$ for linearity), and statistical methods such as ANOVA, regression analysis, and confidence intervals must be used to evaluate results. All deviations or non-conformities should be documented with corrective actions, and findings should be compiled into a formal Analytical Performance Evaluation Report.

4.10 Stability Performance Analysis

Next, stability performance analysis must be performed to demonstrate that the IVD device and its reagents maintain functional integrity under all expected conditions of storage, transport, and use. Components requiring stability evaluation should be clearly identified, and a Stability Master Plan must be drafted in accordance with ISO 23640 and ICH Q1A(R2) guidelines. This plan should define the study duration, time intervals, number of lots (minimum of three independently manufactured lots), and environmental conditions to be tested—including storage stability, shipping simulation, in-use stability, and open-vial or post-reconstitution stability. Both accelerated and real-time stability studies must be conducted. Functional testing at specified time points (e.g., 0, 3, 6, 12, and 18 months) should include assessments of signal strength, reagent appearance, pH, and buffer integrity. Data must be recorded and statistically trended in real time. Interim and final reports should be generated to support shelf-life claims and to validate product labeling with appropriate expiry dates and storage instructions.

4.11 Comparator Study with Predicate Device

Finally, a comparator study with a legally marketed predicate device or gold standard reference method must be conducted to establish clinical and functional equivalence. The comparator device's identity, model, version, and Instructions for Use (IFU) must be documented. Study design must define the type of samples, target analyte range, and handling protocol. Comparative testing may be structured as a side-by-side, randomized blinded comparison or retrospective panel study. Both devices must undergo calibration and QC verification before use. The study must predefine agreement metrics such as Positive Percent Agreement (PPA), Negative Percent Agreement (NPA), Cohen's Kappa, ROC curve analysis, and or Bland-Altman plots where applicable. Any discordant results should be resolved through third-party testing or adjudicated consensus. Blinding procedures must be enforced, and all operators must be trained appropriately. Raw outputs and interpretation methods should be recorded with full traceability. Statistical analysis should be conducted in accordance with a pre-approved plan, and results compiled into a Comparative Performance Report aligned with CDSCO submission requirements.

Collectively, this phase ensures that the IVD product demonstrates scientific validity, robust analytical performance, and clinical reliability. Each element must be meticulously documented and included in the product's technical file to support regulatory review and eventual market authorization.

To do list D: Performance Evaluation

Test batch Device manufacturing: Produce well-characterized, traceable batches for performance testing under controlled conditions using GMP-aligned workflows.

Sl. No	To do	Completed		Remarks
		Yes	No	
14.1	Prepare a detailed Test Batch Manufacturing Plan with defined objectives.			
14.2	Create Batch Manufacturing Record (BMR) template			
14.3	Verify incoming quality control (IQC) for all components and reagents.			
14.4	Assign trained personnel and record their roles (traceability logs).			
14.5	Create and archive calibration and maintenance records of all production equipment.			
14.6	Conduct in-process QC (e.g., fill volume, reagent integrity, seal testing).			
14.7	Perform post-manufacturing lot-release testing for each batch.			
14.8	Assess lot-to-lot reproducibility using performance metrics.			
14.9	Compile full device history records (DHRs) for all lots used in evaluation.			
14.10	Ensure documentation complies with ISO 13485 and regulatory record-keeping.			

Analytical spiked samples: Establish the assay's technical limits, variability, and detection capability using reference materials, simulated specimens, and spiking studies.

Sl. No	To do	Completed		Remarks
		Yes	No	
15.1	Identify and document applicable standards			
15.2	Draft a statistically powered Analytical Performance Plan with predefined objectives and pass/fail criteria.			
15.3	Define analytical endpoints: 1. LoD 2. LoQ 3. Linearity 4. Precision (Repeatability & Reproducibility) 5. Accuracy 6. Specificity 7. Cross-reactivity 8. Robustness			
15.4	Acquire or prepare certified reference materials or well-characterized clinical pools.			
15.5	Define sample randomization and blinding procedures.			
15.6	Assign minimum number of replicates and independent operators.			
15.7	Use calibrated equipment and validated procedures for spiking and assay runs.			
15.8	Conduct testing under simulated real-use conditions (e.g., variable pipetting, lot differences).			
15.9	Analyze data using appropriate statistical methods (ANOVA, regression, confidence intervals).			

Sl. No	To do	Completed		Remarks
		Yes	No	
15.10	Document non-conformities, deviations, and corrective actions.			
15.11	Generate a comprehensive analytical performance report for internal and regulatory use.			

Reagent stability study: Demonstrate stability of reagents and devices under all conditions that the product is likely to encounter — storage, shipping, and use.

Sl. No	To do	Completed		Remarks
		Yes	No	
16.1	Identify all product components requiring stability evaluation.			
16.2	Define environmental parameters for: 1. Storage stability 2. Shipping stability 3. In-use stability 4. Open-vial or reconstitution stability			
16.3	Draft and approve a Stability Master Plan including study duration, intervals, and number of lots.			
16.4	Conduct Accelerated and Real-Time studies			
16.5	Establish acceptance criteria for performance over time			
16.6	Include performance tests (e.g., signal strength, appearance, pH, buffer integrity)			
16.7	Ensure stability testing covers at least three independently manufactured lots.			

Sl. No	To do	Completed		Remarks
		Yes	No	
16.8	Conduct functional testing at defined time points (e.g., 0, 3, 6, 12, 18 months			
16.9	Document and trend all data in real-time with statistical summaries.			
16.10	Generate interim and final stability summary reports supporting shelf life claims.			
16.11	Validate labeling with appropriate expiry date and storage instructions.			

Comparison with predicate device: Compare performance against a legally marketed device using well-defined endpoints and standard statistical methods.

Sl. No	To do	Completed		Remarks
		Yes	No	
17.1	Identify all product components requiring stability evaluation.			
17.2	Define environmental parameters for: 1. Storage stability 2. Shipping stability 3. In-use stability 4. Open-vial or reconstitution stability			
17.3	Draft and approve a Stability Master Plan including study duration, intervals, and number of lots.			
17.4	Conduct Accelerated and Real-Time studies			
17.5	Establish acceptance criteria for performance over time			

Sl. No	To do	Completed		Remarks
		Yes	No	
17.6	Include performance tests (e.g., signal strength, appearance, pH, buffer integrity)			
17.7	Ensure stability testing covers at least three independently manufactured lots.			
17.8	Conduct functional testing at defined time points (e.g., 0, 3, 6, 12, 18 months			
17.9	Document and trend all data in real-time with statistical summaries.			
17.10	Generate interim and final stability summary reports supporting shelf life claims.			
17.11	Validate labeling with appropriate expiry date and storage instructions.			

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CHAPTER

Performance Evaluation Using Clinical Samples

5.0 General

Clinical performance studies shall be conducted in a manner in which every precaution has been taken to protect the rights and the health and safety of the subject, user and other persons, considering all regulatory and ethical requirements, using valid scientific principles. When conflict of interest or bias cannot be avoided, there shall be full disclosure that is appropriately documented and justified. Clinical performance studies shall be undertaken under an effective quality management system to ensure that these principles are met. The study sponsor shall take responsibility for ensuring that these principles are met.

The sponsor shall define the roles and responsibilities of all parties including those of the sponsor, monitor, principal investigator and study team members in accordance with this document.

All parties participating in the conduct of the clinical performance study shall be qualified to perform their tasks by education, training or experience, and this shall be documented appropriately.

Quality assurance and quality control principles shall apply to the processes of the clinical performance study. The sponsor shall

a. Implement and maintain written procedures to ensure that

   i. The Clinical Performance Study Is Designed, Conducted And Monitored

   ii. All Devices And Other Study-Related Materials Are Properly Accounted For

   iii. Data generated are documented, recorded, reported and archived in conformity with this document and the clinical performance study protocol (CPSP). all subsequent amendments to the CPSP.

b. Maintain records to document the conformity of all parties involved in the clinical performance study.

c. Ensure that the auditing requirements of are met, when applicable, and

d. Justify and document significant exceptions to the requirements of this document.

Quality assurance and quality control aspects for clinical performance studies can be integrated in the sponsor's overall quality system.

In certain circumstances, it might be appropriate to perform the testing only at the manufacturer's site, in this case, a justification for this decision should be documented. For example, a study to determine reference values can often be performed entirely at the manufacturer's site. Studies conducted internally at a manufacturer's site can rely upon the manufacturer's quality system policies, processes, and procedures to meet the applicable requirements of this document. When used, these quality system documents should be referenced within the CPSP.

The sponsor can transfer any or all of the duties and functions related to the clinical performance study, including monitoring, to an external organization (such as a contract research organization or individual contractor), but the ultimate responsibility for the quality and integrity of the clinical performance study data shall reside with the sponsor. All the requirements in this document applying to a sponsor shall also apply to the external organization in as much as this organization assumes the clinical performance study-related duties and functions of the sponsor.

The sponsor shall specify in a written agreement any clinical performance study-related duty or function assumed by the external organization, retaining any clinical performance study-related duties and functions not specifically transferred to, and assumed by, the external organization.

The sponsor shall be responsible for verifying the external organization has and adheres to written study-related procedures.

As a substantial percentage of healthcare decisions rely on information provided by IVDs, results from IVDs can significantly influence patient diagnosis, management, treatment and overall clinical outcomes. As such, the clinical evidence of an IVD should demonstrate that the defined clinical benefit is achieved and that the IVD is safe.

The clinical evidence must also support the intended purpose and performance of the IVD, as stated by the manufacturer while addressing the residual risks to the patients, users or other persons associated with the use of the device. To determine and justify the level of clinical evidence, the amount and quality of supporting data should be evaluated. The evidence should be assessed by taking into the account strength, robustness, and quality of data in order to draw meaningful conclusions. All in all, the clinical benefit of the IVD should always outweigh the overall residual risk.

5.1 Clinical Performance

Clinical performance means the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user.

The clinical performance aims to demonstrate that IVD can achieve clinically relevant outputs through predictable and reliable use by the intended user. The manufacturer should demonstrate that the IVD has been tested for the intended use, target population, use condition, operating

and use environment and with all the intended user groups. Indicators of clinical performance vary and depend strongly on the intended purpose and performance claims.

Clinical performance may not be required for certain devices Such as Class A and few Class B IVDs. For example, clinical performance data may not be expected for non-sterile specimen receptacles, microscopy glass slides, or some general reagents. In such cases and where due justification is given, a clinical performance report would not be expected. Nevertheless, the remaining aspects of the performance evaluation report including other elements of clinical evidence would still be required unless due justification is given.

For those devices demonstrating clinical performance, the following principles are highlighted as potential sources of clinical performance data:

1. Data from scientific peer-reviewed literature,
2. Data from published experience gained by routine diagnostic testing,
3. Data from clinical performance studies,
4. Other sources of clinical performance data.

Clinical performance can be characterised by the demonstration and evaluation of applicable aspects of clinical performance for the device in question, such as (non-exhaustive):

1. Diagnostic sensitivity
2. Diagnostic specificity
3. Positive predictive value
4. Negative predictive value
5. Number needed to treat/diagnose (average number of patients that need to be treated/diagnosed in order to have an impact on one person)
6. Number needed to harm/misdiagnose (number of patients that need to be diagnosed/ treated in order have an adverse effect on one patient)
7. Positive likelihood ratio
8. Negative likelihood ratio
9. Odds ratio
10. Usability /user interface.

Other parameters may be determined by the manufacturer to be applicable when demonstrating the clinical performance characteristics of the IVD in the intended use environment and may be included in the clinical performance report. It is important that aspects of clinical performance are assessed in terms of their statistical relevance, e.g. inclusion of confidence interval and interpretation of the impact on robustness of the result with regards to the intended purpose.

5.2 Clinical Performance Studies

When determining what data is needed to demonstrate the safety and performance of IVDs, it is important to consider available existing data and how to bridge any deficits. In the event that data is not available in either sufficient quality or quantity it will need to be generated. Clinical performance studies should be conducted in line with well-established international guidance in this field, such as the international standard ISO 20916 on clinical performance studies using specimens from human subjects, regardless of the classification of the device.

5.3 Design of the Clinical Performance Study

Clinical performance studies shall be carried out using product representative of the final manufactured IVD medical device intended for commercialisation, using controlled and accepted processes and procedures, though scale up might not yet be completed.

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

1. Study objectives
2. The outcome of the risk evaluation
3. Intended use, specifically
    a. Test purpose (e.g. diagnosis, screening, monitoring)
    b. Target population (e.g. age, race, gender, geography, clinical condition, treatment status)
    c. Specimen type (e.g. serum, plasma, urine, whole blood)
    d. Intended user/operator (person performing the test e.g. lay person)
4. Specimen/sample handling and storage conditions (e.g. sample cannot be frozen)
5. Sample size estimate, and description of planned statistical analysis
6. Quality, availability and accessibility of specimens (e.g. limited number of leftover specimens available)
7. Testing location (e.g. point-of-care setting, central laboratory)
8. Intended use setting's environmental conditions
9. Established analytical performance characteristics (e.g. precision, interference, measuring interval (range), cut-off, limit of detection, limit of quantification)
10. Intended clinical performance characteristics (e.g. sensitivity, specificity, positive predictive value, negative predictive value, reference intervals, cut-off)
11. Prevalence of the clinical condition/physiological or pathological state
12. Novelty of the technology and/or clinical use (e.g. relevant previous experience)
13. Availability of appropriate method to establish the clinical status of the subject
14. Availability of quality control material
15. Mechanisms to avoid bias

5.4 Permission to Conduct Clinical Performance Evaluation

No individual or sponsor shall conduct a clinical performance evaluation of a new In Vitro Diagnostic (IVD) medical device using specimens such as blood or tissue derived from the human body without obtaining prior approval from the Central Licensing Authority (CLA). This permission shall be granted in accordance with the conditions and procedures outlined in the Medical Device Rules 2017.

The CLA may, in public interest, abbreviate, defer, or waive the requirement for a clinical performance evaluation, provided that the reasons are recorded in writing.

If the application meets all regulatory requirements, the Central Licensing Authority may grant permission in Form MD-25 within 90 days of submission. If the application is rejected, the decision, along with the reasons, will be communicated to the applicant.

5.4.1 Conditions for Conducting Clinical Performance Evaluation

Once permission is granted under Rule 59(5) of MDR 2017, the sponsor must comply with the following conditions:

1. The clinical performance evaluation must be conducted according to the approved clinical performance evaluation plan and Good Clinical Practice (GCP) Guidelines.
2. The evaluation shall commence only after obtaining approval from a registered Ethics Committee.
3. The study must be registered with the Clinical Trial Registry of India

(CTRI) before enrolling the first participant.

4. An annual status report indicating whether the evaluation is ongoing, completed, or terminated must be submitted to the CLA. In the event of termination, the detailed reasons must be reported within 30 days.
5. All laboratories, institutions, sponsors, and associated personnel involved in the evaluation shall be subject to inspection by the CLA, which may include representatives from the State Licensing Authority or external experts.
6. The evaluation must begin within one year from the date of permission; otherwise, prior approval from the CLA is required for initiation.
7. The CLA may impose, modify, or exempt certain conditions regarding the objectives, design, subject population, eligibility criteria, assessment, conduct, and treatment procedures of the clinical performance evaluation.

5.4.2 Suspension or termination of a clinical performance study

If a sponsor fails to comply with the conditions of the granted permission, the CLA may suspend or cancel the approval partially or entirely, for a duration it deems appropriate.

Any aggrieved party may file an appeal with the Central Government within 30 days of the suspension or cancellation. The appeal will be reviewed, and a decision will be communicated within 60 days after providing the appellant an opportunity to be heard.

a. Procedure for suspension/termination

A principal investigator, ethics committee, or regulatory authority can suspend or prematurely terminate participation in a clinical performance study at the study sites for which they are responsible.

When suspicion of an unacceptable risk to subjects arises during the clinical performance study, the sponsor shall suspend the clinical performance study while the risk is assessed. The sponsor shall terminate the clinical performance study when an unacceptable risk is confirmed.

The sponsor shall consider terminating or suspending the participation of a particular study site or investigator when monitoring or auditing identifies serious or repeated deviations on the part of an investigator.

When suspension or premature termination occurs, the terminating party shall justify its decision in writing and promptly inform the other parties with whom they are in direct communication. The principal investigator and sponsor shall keep each other informed of any communication received from either the ethics committee or the regulatory authority.

When, for any reason, the sponsor suspends or prematurely terminates the clinical performance study at an individual study site, the sponsor shall ensure that the ethics committee is notified, either by the principal investigator or by the sponsor. When the suspension or premature termination was in the interest of safety, the sponsor shall inform all other principal investigators.

When suspension or premature termination occurs,

1. The sponsor shall remain responsible for providing resources to fulfil the obligations from the CPSP and existing agreements for following up the subjects enrolled in the clinical performance study, and
2. The principal investigator or authorized designee shall promptly inform the enrolled subjects at his/her study site, when applicable.

b. Procedure for resuming the clinical performance study after temporary suspension

When the sponsor concludes an analysis of the reason for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the sponsor shall inform the relevant parties of the rationale and provide them with the relevant data supporting this decision.

When subjects have been informed of the suspension, the principal investigator or authorized designee shall inform them of the reasons for resumption.

The sponsor shall promptly report any deviation from the CPSP that affects the rights, safety or well-being of the subject or the scientific integrity of the clinical performance study, including those that occur under emergency circumstances.

5.5 Clinical Performance Study Protocol (CPSP)

The purpose of the CPSP is to ensure the clinical performance study is performed to yield high-quality, accurate and reliable data for the IVD medical device under investigation. The CPSP shall be developed by investigators or sponsors appropriately qualified by education, training, or experience. An appointed representative of the sponsor shall sign and date the protocol, indicating sponsor acceptance. The CPSP and all subsequent amendments to the CPSP shall be agreed upon between the sponsor and all principal investigators and shall be recorded with a justification for each amendment.

5.5.1 Principal investigator responsibilities

The principal investigator (PI) plays a crucial role in conducting clinical performance studies. The PI is responsible for managing the day-to-day conduct of the study, ensuring ethical compliance, and adhering to the clinical performance study plan (CPSP). They must indicate their acceptance of the CPSP in writing and maintain all necessary documentation, including agreements, contracts, and source documents. The PI is tasked with using the IVD medical device under investigation as per the CPSP and instructions, while also managing device and specimen accountability. They must not implement modifications to the CPSP without proper approval and should document any deviations, adverse events, and corrective actions taken. Ensuring data accuracy, integrity, and timeliness is a key responsibility, as is supporting monitoring and auditing activities by the sponsor and ethics committee. The PI must be accessible to monitors, retain all study-related records, disclose potential conflicts of interest, and document relevant communications. This comprehensive set of responsibilities ensures the proper conduct and ethical integrity of clinical performance studies for IVD medical devices.

5.5.2 Contents of the CPSP

1. General: The Clinical Performance Study Plan (CPSP) should encompass all relevant information outlined in this section. It must include a detailed description of each specified topic, ensuring clarity, particularly for those topics that are not self-explanatory. Any amendments to the CPSP should also address all listed topics comprehensively.
2. Identification of the clinical performance study protocol:
    a. Title of the clinical performance study.
    b. Reference number identifying the specific clinical performance study, if any.
    c. Version or date on each page of the CPSP.
    d. Summary of the revision history in the case of amendments.
    e. Page number and the total number of pages on each page of the CPSP
3. Identification and description of the IVD medical device under investigation
    a. Summary description of the IVD medical device under investigation and its intended use.
    b. Name of the IVD medical device, including software and accessories, if any, intended use including populations and indications of the IVD medical device under investigation in the proposed clinical performance study.
    c. Summary of the necessary training and experience needed to use the IVD medical device under investigation, when applicable.
4. Sponsor: Name and address of the sponsor of the clinical performance study, when testing is occurring externally to the sponsor's site.
5. Study site: Individual sites need not be identified in the CPSP, however, the sponsor shall maintain an updated CDSCO approved list of study sites, and institutions.

6. Overall synopsis of the clinical performance study: A summary or overview of the clinical performance study shall include all the relevant information regarding the clinical performance study design, such as inclusion/exclusion criteria, number of specimens and, when applicable, subjects, duration of the clinical performance study, objective, endpoint.

7. IVD medical device under investigation and comparator: When used, list the comparator. When the comparator is a commercial assay, include name and manufacturer, and when applicable, the version or catalogue number. When the comparator is a reference method or "gold standard", provide adequate published references supporting the methodology.

8. Specimens and when applicable, subjects providing specimens:

    a. Validated specimen type (for example only plasma collected using validated anticoagulant).
    b. Inclusion criteria.
    c. Exclusion criteria.
    d. Information necessary to characterise the subject/specimen (e.g. status of other analytes, concomitant medications).
    e. Number of specimens and/or subjects.
    f. Specimen storage, handling, transport, and disposal

9. Procedures: If applicable, a detailed description should be provided of all study-related procedures that the specimens will undergo during the clinical performance study. Additionally, when relevant, the procedure for determining when and how incidental findings should be communicated to subjects or physicians must be outlined.

10. Monitoring plan

11. Data management:

    a. Procedures used for data review, database cleaning, and issuing and resolving data queries.
    b. Procedures for verification, validation, and securing of electronic clinical data systems, when applicable.
    c. Procedures for data retention.
    d. Specified data retention period.
    e. Other aspects of quality assurance, as appropriate

12. Statistical considerations

    a. The description of and justification for
    b. Statistical design, method and analytical procedures,
    c. Sample size
    d. Level of significance and power of the clinical performance study,
    e. Pass/fail criteria to be applied to the results of the clinical performance study,
    f. Provision for an interim analysis, when applicable,
    g. Procedures that ensure that all the data is taken into account, treatment of missing, unused or spurious data.

13. Deviations from clinical performance study protocol

    a. Statement specifying that the investigator is not allowed to deviate from the CPSP, except when a deviation is necessary to protect subject's rights, safety and well-being, or the scientific integrity of the clinical performance study.
    b. Procedures for recording, reporting and analysing CPSP deviations.
    c. Descriptions of procedures for corrective and preventive actions for repeated and/or major CPSP deviations.

14. Accountability of IVD medical devices under investigation: The procedures for ensuring accountability of IVD medical devices under investigation should include controlled access and use strictly within the clinical performance study as per the CPSP. The sponsor must maintain records tracking the devices' physical location from shipment to return or disposal. The principal investigator or an authorized designee must document the receipt, use, return, and disposal of these devices, including details such as receipt date, device identification

(e.g., batch/serial number), expiry date, usage dates, and return or disposal dates, as applicable.

The manufacturer or innovator must select a CDSCO-approved laboratory to conduct the clinical performance evaluation. Once the laboratory is identified, the manufacturer or innovator is expected to prepare all prerequisite documentation and appoint a qualified investigator to oversee the clinical performance evaluation.

To facilitate compliance, To do list E has been designed to assist manufacturers and innovators in structuring and submitting the clinical performance evaluation report to CDSCO for further regulatory approval.

5.6 Performance Evaluation strategy

Clinical performance evaluation is the final and most critical phase in the assessment of an IVD device. It provides real-world evidence of the device's effectiveness, reliability, and safety when used on intended clinical specimens within the target population. This phase confirms that the analytical performance translates into meaningful diagnostic utility, measured through sensitivity, specificity, predictive values, and other clinical metrics. Regulatory authorities such as the CDSCO, USFDA , and EU IVDR require comprehensive clinical data to support product claims. Proper documentation, ethical compliance, and statistical analysis are essential to ensure that the evidence is scientifically robust and suitable for regulatory approval under Form MD-24.

The process begins with the development of a Clinical Performance Evaluation Plan (CPEP), which must clearly define:

1. Study objectives (e.g., to establish clinical sensitivity and specificity)
2. Target population (e.g., symptomatic, asymptomatic, high-risk)
3. Study endpoints (e.g., true positive, true negative rates, predictive values)
4. Timelines and milestones (including pilot and main study phases)

Sites selected for clinical evaluation should be NABL-accredited laboratories, ICMR-recognized, or CDSCO-registered clinical facilities to ensure data reliability and regulatory acceptability. The clinical study protocol must be submitted to an Institutional Ethics Committee (IEC) for review and approval. Parallelly, the study must be registered in the Clinical Trial Registry of India (CTRI) as a matter of ethical and regulatory compliance.

Well-defined inclusion and exclusion criteria must be set based on clinical indications and intended user groups. Ethical considerations, such as informed consent, data privacy, and vulnerable population safeguards, must be integrated and documented in the protocol. Clinical site personnel must be trained and certified on procedures for sample collection, device operation, test interpretation, data entry, and adverse event reporting.

Before commencing full-scale evaluation, a pilot study may be executed to validate logistics, protocol feasibility, user interactions, and data capture tools. Insights from the pilot can be used to revise SOPs, redefine endpoints, or improve usability features.

The main clinical evaluation should be carried out under real-world use conditions, using traceable and auditable data capture systems (e.g., electronic CRFs, barcode tracking). Devices under evaluation should be used strictly per their Instructions for Use (IFU) to simulate end-user handling. The clinical performance must be benchmarked against a predicate or gold standard method such as RT-PCR, ELISA, or microbiological culture, depending on the target analyte.

The following key clinical performance metrics must be computed:

1. Sensitivity (True Positive Rate)
2. Specificity (True Negative Rate)
3. Positive Predictive Value (PPV)
4. Negative Predictive Value (NPV)
5. Likelihood Ratios (Positive and Negative)

6. 95% Confidence Intervals

Stratified Analysis (e.g., age, sex, symptomatic/asymptomatic)

Special attention should be given to discordant results, which must be resolved using predefined methods such as a third independent method or clinical adjudication by experts.

For in vitro diagnostic devices intended for use by laypersons, such as self-tests, or for deployment in decentralized settings like point-of-care (POC) clinics, usability and field performance assessments are essential components of clinical performance. These studies ensure that the device can be operated reliably and safely by its intended users, under realistic environmental and operational conditions. Usability studies must be designed to evaluate the ease of understanding the Instructions for Use (IFU), the correct execution of test procedures, interpretation of results, and the rate of handling errors or invalid outcomes. Lay users should be representative of the target population and must not receive assistance beyond what is described in the IFU. Observational data should be collected to identify any issues related to sample collection, reagent handling, test timing, or result reading. For professional-use devices, assessments should consider workflow integration, technician fatigue, and variation in skill levels.

In addition to usability, field performance testing evaluates how the device withstands environmental stress and real-world handling scenarios. Devices should be exposed to conditions such as high temperature, humidity, mechanical vibration, and potential delays between sample collection and testing. Simulations of transportation stress, including drop tests or shipping validation, may be required to confirm durability. Operational variations—such as different sample types, inconsistent pipetting, or extended open-vial time—must be accounted for to ensure that the device maintains accuracy and reliability under variable field conditions. In-use stability must be confirmed by testing the same reagents and devices over their claimed usage window (e.g., after opening or reconstitution). Together, usability and field performance data provide critical evidence that the device performs as intended across a range of real-world scenarios and user competencies. These findings must be documented in the clinical performance report and submitted as part of the regulatory dossier.

5.7 Clinical Documentation

Comprehensive clinical documentation is a cornerstone of regulatory compliance for in vitro diagnostic (IVD) devices. It ensures traceability of all clinical activities, supports reproducibility of results, and facilitates transparency during regulatory audits and inspections. All elements of the clinical performance evaluation must be meticulously recorded, verified, and archived in line with Good Clinical Practice (GCP), ISO 20916, and CDSCO requirements.

To begin, manufacturers must obtain Institutional Ethics Committee (IEC) approval prior to study initiation. A valid CTRI registration number (Clinical Trial Registry of India) must be secured, and all approvals and regulatory correspondence must be maintained in the trial master file. Documentation should clearly define the study duration, geographical locations, and a comprehensive description of the study population, including age, gender, risk group, or other relevant demographic data.

Details of the sample types used—such as fresh clinical specimens, archived or leftover samples, contrived panels, or spiked matrices—must be documented, along with total sample count and subgroup distributions. All Case Report Forms (CRFs) should be completed for each sample tested and signed off by authorized clinical personnel. Study site logs must track critical activities such as shipment receipts, temperature monitoring, and daily logs of testing events.

Principal Investigator (PI) attestation letters are required to confirm the integrity of the study, and signed data summaries must validate that the PI has reviewed, approved, and certified the findings. Training records for all personnel involved in sample collection, handling, and device operation must be maintained to confirm competency and protocol adherence. All protocol deviations, adverse events, and incidents must be logged with details of investigation and corresponding Corrective and Preventive

Actions (CAPA) undertaken.

Before statistical analysis is performed, a formal data lock must be executed. This step prevents any retrospective alteration of the dataset and establishes the integrity of the final analysis. Data should be analyzed using validated statistical software by qualified personnel, preferably under the guidance of a biostatistician. Analyses should include sensitivity, specificity, positive and negative predictive values (PPV and NPV), likelihood ratios, and confidence intervals. If applicable, stratified analyses based on demographic or clinical subgroups should be presented. The method used for discordant resolution (e.g., adjudication panel, third test) must also be transparently reported.

All findings must be compiled into a Clinical Performance Evaluation Report, which must follow the structure outlined in MDR 2017.

To do list E : Performance Evaluation Using Clinical samples/ Clinical Performance Evaluation

Performance Evaluation strategy: Validate diagnostic accuracy and usability in intended users and real-world clinical settings.

Sl. No	To do	Completed		Remarks
		Yes	No	
18.1	Develop a Clinical Performance Evaluation Plan (CPEP) with objectives, population, endpoints, and timeline.			
18.2	Select study sites with necessary infrastructure (NABL-accredited or CDSCO-registered labs).			
18.3	Prepare and submit protocol to Institutional Ethics Committee.			
18.4	Register the clinical study with CTRI (Clinical Trial Registry of India).			
18.5	Define inclusion/exclusion criteria and sample flow.			
18.6	Document patient/sample consent procedures and ethical safeguards.			
18.7	Train clinical personnel on sample collection, test execution, and data logging.			
18.8	Conduct pilot study to test protocol and usability issues.			
18.9	Conduct the main clinical evaluation with traceable data capture systems.			

Sl. No	To do	Completed		Remarks
		Yes	No	
18.10	Identify and measure: 1. Sensitivity 2. Specificity 3. PPV 4. NPV 5. Likelihood Ratios 6. Confidence Intervals and stratified subgroup analyses			
18.11	Document adverse events, protocol deviations, and incident reporting.			
18.12	Compile in-house clinical performance data on: 7. Usability 8. Analytical stability under field use 9. Environmental stress conditions			
18.13	Prepare study site logs, PI attestations, and case report forms			
18.14	Perform data lock, analysis, and generate a clinical performance report.			
18.15	Align all reports with the requirements of Form MD-24 or Form MD-28 for regulatory submission.			

Clinical Documentation:

Sl. No	To do	Completed		Remarks
		Yes	No	
19.1	Obtain Ethics Committee approval			
19.2	Document parameters for inclusion/exclusion criteria			
19.3	Document study duration, location, and number of laypersons (for self-test devices)			
19.4	Document the sample type used, number of samples use, number of left over samples			
19.5	Generate statistical data to establish performance evaluation data compliance with the regulatory standards			
19.6	Generate a Clinical Performance report			

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06

CHAPTER

Submission of Documents

6.0 Pre- requisite Regulatory certification requirements

The submission of documents phase marks the final step in the regulatory journey for an In Vitro Diagnostic (IVD) medical device. This stage is crucial for securing manufacturing licenses, marketing approvals, and wholesale distribution license. It requires a comprehensive and organized submission of technical, clinical, and quality-related documentation that demonstrates the device's safety, efficacy, and compliance with MDR, 2017. This phase includes three primary pillars: pre-requisite certifications and final report submissions

To begin, manufacturers must ensure that all necessary regulatory certifications and authorizations are in place. This includes compiling documentation for licenses already received for test batch production, analytical performance evaluation, and clinical performance evaluations, if applicable. A Final Risk Management Report must be prepared in accordance with ISO 14971, confirming that all potential risks have been systematically identified, assessed, and mitigated. Additionally, the manufacturer must ensure compliance with environmental safety standards relevant to medical devices, as outlined in Annexure A of the Fifth Schedule of the MDR 2017. This involves documentation related to biomedical waste, chemical disposal, and plastic management, all of which are essential for regulatory approval. A comprehensive Device Master File

(DMF) must also be assembled to provide a detailed technical overview of the device's design, intended use, manufacturing process, testing, and labeling. Furthermore, implementation of a robust Quality Management System (QMS) aligned with ISO 13485 across the organization is mandatory to ensure consistent product quality and regulatory adherence. A copy of the most recent inspection or audit report conducted by a Notified Body, CDSCO, or another competent authority within the last three years should also be included to demonstrate ongoing compliance and manufacturing readiness.

The next step involves submission of final performance evaluation reports. An organizational chart should be included to delineate the roles and responsibilities of all personnel involved in IVD manufacturing and regulatory functions. Final design and manufacturing files must be submitted, detailing the finalized product configuration, specifications, change history, and production workflow. These should be supplemented with a comprehensive Plant Master File outlining the facility's layout, environmental controls, HVAC systems, utility infrastructure, and manufacturing capabilities. The final Product Validation and Verification Report must demonstrate that the product fulfills design inputs, user needs, and regulatory specifications through actual testing outcomes and documented evidence. A Performance Evaluation Report issued by the Central Medical Device Testing Laboratory (CMDTL) must be included. If third-party analytical evaluations were conducted at any NABL-accredited laboratory, the resulting reports showcasing device sensitivity, specificity, and overall analytical performance should also be appended to support the product claims.

6.1 License documentation strategy

Finally, manufacturers must establish a comprehensive Regulatory Lifecycle Management Plan to maintain compliance post-approval. This begins with an undertaking from the manufacturer, signed and stamped, confirming that there has been no change in the constitution of the firm during the application period. Documents necessary for license retention should be prepared in accordance with the renewal timelines outlined under MDR 2017. Provisions should be made for follow-up audits by regulatory authorities or third-party bodies to ensure continual compliance. The manufacturer must also compile Post-Market Surveillance (PMS) data, including complaint logs, vigilance reports, adverse event investigations, and field safety corrective actions (FSCAs), to demonstrate ongoing monitoring of product safety and effectiveness.

Any changes made after product approval such as updates to labeling, alterations in raw materials, or shifts in manufacturing locations must be formally documented and submitted to CDSCO as Post Approval Change (PAC) Applications. Each submission should include detailed supporting data and a clear scientific or technical justification to demonstrate continued compliance and product integrity.

This chapter provides a comprehensive collection of checklists tailored for various applications required to be submitted to the Central Drugs Standard Control Organization (CDSCO). Each checklist is designed to ensure compliance with regulatory requirements, streamline the submission process, and facilitate the approval of in-vitro diagnostics medical devices.

6.2 Checklist for manufacturing Class A & B IVD Medical Devices (Form MD 3)

Checklist for Form MD 3	
Sl. No	**Mandatory requirements**
1	Cover letter
2	Constitution Details of Manufacturer
3	Site or plant master file as specified in Appendix I of Fourth Schedule of MDR 2017, (Part 1)
4	Device master file as specified in Appendix III of Fourth Schedule of MDR 2017, (Part 1)
5	Essential principles checklist for demonstrating conformity to the essential principles of safety and performance of the in vitro medical device
6	Undertaking signed by the manufacturer stating that the manufacturing site is in compliance with the provisions of the Fifth Schedule of MDR 2017
7	Labelling and Pack Size
8	Fee Challan
9	Legal Form

6.3 Checklist for Loaned Site Manufacturing Class A & B IVD Medical Devices (Form MD 4)

Checklist for Form MD 4	
Sl. No	**Mandatory requirements**
1	Cover letter
2	Constitution of the Firm
3	The Establishment /Site ownership /Tenancy Agreement

Checklist for Form MD 4	
Sl. No	**Mandatory requirements**
4	Copy of Certificate supporting quality management system (ISO: 13485), if any
5	(PMF) Plant Master file from the Manufacturer as Plant Master file from the Manufacturer as specified in Appedix 1 of Forth Schedule of Medical Devices Rules (Part 1,2,3,4, & 5)
6	Device Master file from the Manufacturer as specified in Appendix II (only for Medical Devices) of Forth Schedule of Medical Device Rules. Note: In case of Class A devices, Appendix II is not required. For Class A devices upload information as specified in Part II of Forth Schedule for Medical Devices or IVDs, as the case may be. (Part 1,2,3,4, & 5)
7	Performance Evaluation Report of IVDs only
8	Test License obtained for testing and generation of quality control data
9	Undertaking signed stating that the manufacturing site is in compliance with provision of Fifth schedule
10	Fee Challan
11	Legal Form

6.4 Checklist for manufacturing Class C & D IVD Medical Devices (FORM MD 7)

Checklist for Form MD 7	
Sl. No	**Mandatory requirements**
1	Cover letter
2	Constitution Details of Manufacturer (Part 1 & 2)
3	Site or plant master file as specified in Appendix I of the Fourth Schedule of MDR 2017. (Part 1, 2, 3, 4 & 5)
4	Quality Management System as per Fifth Schedule of Medical Devices Rules, 2017 (Part 1, 2, 3, 4, 5, 6, 7, 8, 9, & 10)
5	Undertaking signed by the manufacturer stating that the manufacturing site complies with the provisions of the Fifth Schedule of MDR 2017
6	Copy of latest inspection or audit report carried out by Notified bodies or National Regulatory Authority or Competent authority within the last 3 years. (if any)

Checklist for Form MD 7	
Sl. No	**Mandatory requirements**
7	Copy of NOC from Department of Animal Husbandry, Ministry of Agriculture, In Case of Veterinary IVD Kits (if available)
8	Copy of NOC from Bhabha Atomic Research Centre (BARC), Mumbai, In case Radio Immuno Assay Kits (if available)
9	Valid copy of Quality Management System certificate (ISO:13485) certificate issued by the competent authority .(if any)
10	Copy of Test licence obtained for testing and generation of quality control data, if any
11	Self attested copy of valid Whole sale licence or manufacturing licence if any
12	Device Master File for In Vitro Diagnostic Medical Devices as per Appendix – III of Part III of Fourth Schedule of Medical devices Rules, 2017 (Part 1-18)
13	Table the areas showing the environmental requirement for Medical Devices as per Annexure A of the Fifth Schedule of Medical Devices Rules, 2017.
14	Fee Chalan
15	Legal Form

6.5 Checklist for Loaned Site Manufacturing Class C & D IVD Medical Devices (FORM MD 8)

Checklist for Form MD 8	
Sl. No	**Mandatory requirements**
1	Cover letter
2	Constitution of the Firm
3	The Establishment /Site ownership /Tenancy Agreement
4	Copy of Certificate supporting quality management system (ISO 13485), if any

Checklist for Form MD 8	
Sl. No	**Mandatory requirements**
5	Plant Layout of the premise with an indication of the scale
6	Organization chart showing the arrangements for key personnel
7	Qualification, Experience and responsibilities of key Technical Persons
8	List of Equipment and Instruments
9	Contract Activities if any
10	Quality Management System as per Fifth Schedule of Medical Devices Rules, 2017
11	Quality Manual
12	Quality Policy
13	Control of Documents
14	Control of Records
15	Management Responsibility
16	Internal Audit System
17	Preventive and Corrective Action
18	Procedure for identifying training needs and ensuring that all persons are trained to adequately perform their assigned responsibilities.
19	Table the areas showing the environmental requirement for Medical Devices as per Annexure A of the Fifth Schedule of Medical Devices Rules, 2017.
20	Device Master file from the Manufacturer as specified in Appendix II (only for Medical Devices) of Forth Schedule of Medical Device Rules. Note: In case of Class A devices, Appendix II is not required. (Part 1-14)
21	Essential principles checklist for demonstrating conformity to the essential principles of safety and performance of the in vitro medical device
22	Performance Evaluation Report of IVDs only

Checklist for Form MD 8	
Sl. No	**Mandatory requirements**
23	Test License obtained for testing and generation of quality control data
24	Undertaking signed stating that the manufacturing site is in compliance with provision of Fifth schedule
25	Fee Chalan
26	Legal Form

6.6 Checklist for license to manufacture medical device for purpose of clinical investigations, test, evaluation, examination, demonstration, or training of IVD (Form MD 12)

Checklist for Form MD 12	
Sl. No	**Mandatory documents**
1	Cover letter
2	Brief description of the medical device including intended use, material of construction, design
3	Undertaking stating that the required facilities including, equipment, instruments, and personnel have been provided to manufacture such medical devices
4	List of equipment, Instruments
5	List of competent personnel
6	Justification of quantity proposed to be manufactured
7	Schematic plan of premises
8	Certification of the site with a detailed raw component
9	Detailed description of how the raw material will be procured so that the entire process is scrutinized

Checklist for Form MD 12	
Sl. No	**Mandatory documents**
10	Test protocols
11	Fee Challan
12	Legal Form

6.7 Checklist for Clinical performance evaluation of new IVD (FORM MD 24)

Checklist for Form MD 24	
Sl. No	**Mandatory requirements**
1	Cover letter
2	Constitution of the Firm
3	Device description including specification of raw material and finished product, data allowing identification of the device in question, proposed instruction for use, labels and regulatory status in other countries, if any.
4	In-house performance evaluation data used to establish stability, specificity, sensitivity, repeatability and reproducibility.
5	Approval from an Ethics Committee
6	Clinical performance evaluation plan
7	Case Report Form
8	Undertaking by investigators
9	An undertaking that the device in question conforms to the requirements of these rules, apart from aspects covered by evaluation and apart from those specifically itemised in the undertaking, and that every precaution has been taken to protect the health and safety of the patient, user and other persons.
10	Performance evaluation report from a laboratory designated under sub-rule (1) of rule 19.

Checklist for Form MD 24	
Sl. No	**Mandatory requirements**
11	Fee Challan
12	Legal Form

6.8 Checklist for grant of permission to import or manufacture for sale or for distribution of a new In-Vitro Diagnostic Medical Device (FORM MD 28)

Checklist for Form MD 28	
Sl. No	**Mandatory documents**
1	Cover letter
2	Power of Attorney (Original) authenticated in India either by a Magistrate of First Class or by Indian Embassy in the country of origin or by an equivalent authority through apostille along with under taking from the authorized agent as specified in Part I of Forth Schedule
3	Constitution details of domestic manufacturer
4	Self attested copy of valid Whole sale licence or manufacturing licence
5	Notarized and valid copy of overseas manufacturing site or establishment or plant registration, by whatever name called, in the country of origin issued by the competent authority
6	Notarized and valid copy of Free Sale Certificate issued by the National Regulatory Authority or equivalent competent authority of the country of orgin.(if any)
7	Notarized and valid copy of Free Sale Certificate issued by the National Regulatory Authority or equivalent competent authority of the any of the countries namely United States of America, Australia, Canada, Japan, and European Union Countries
8	Copy of latest inspection or audit report carried out by Notified bodies or National Regulatory Authority or Competent Authority within last 3 years, if any.
9	Copy of NOC from Department of Animal Husbandry, Ministry of Agriculture, In Case of Veterinary IVD Kits
10	Copy of NOC from Bhabha Atomic Research Centre (BARC), Mumbai, In case Radio Immuno Assay Kits

Checklist for Form MD 28	
Sl. No	**Mandatory documents**
11	Notarized and valid copy of Quality Management System certificate (ISO 13485) certificate issued by the competent authority
12	Notarized and valid copy of Production Quality Assurance certificate or Full quality Assurance certificate issued by the competent authority.(if any)
13	Notarized and valid copy of CE design certificate issued by the competent authority.(if any)
14	Undertaking signed by the manufacturer stating that the manufacturing site is in compliance with the provisions of the Fifth Schedule of MDR 2017
15	Site or plant master file as per Appendix I, Fourth Schedule of MDR 2017
16	Device master file as per Appendix III, Fourth Schedule of MDR 2017
17	Device data
17.1	Design input, Design output documents, Stability data
17.2	Device specification including specificity, sensitivity, reproducibility, and repeatability
17.3	Product validation and software validation (if any)
18	Risk Management Data
19	Clinical Performance Evaluation data carried out in India and in other countries (if any)
20	Regulatory status and restrictions on use in other countries (if any)
21	Essential principles checklist for demonstrating conformity to the essential principles of safety and performance of the in vitro medical device
22	Product Insert
23	Labelling and Pack Size
24	Fee challan

Checklist for Form MD 28	
Sl. No	**Mandatory documents**
25	Legal form
26	Copy of performance evaluation report issued by the central medical device testing laboratory or medical device testing laboratory registered under sub-rule (3) of rule 83 of MDR 2017 for three batches.
27	Stability
27.1	Claimed Shelf-life stability study report (3 lots)
27.2	In-use stability study report (1 lot)
27.3	Shipping stability study report (1 lot)
28	Specific evaluation report (from Indian lab, if available)
29	Specimen batch test report for at least 3 consecutive batches
30	Correlation chart with respect to products list mentioned in MD-28 and FSC submitted
31	Testing method preferably in Video (if available)

To do list F : Submission of Documents

Pre- requisite Regulatory certification requirements

Sl. No	To do	Completed		Remarks
		Yes	No	
20.1	Compile the list of licenses received for production of test batches, performance evaluation and clinical performance evaluation (If applicable)			
20.2	Compile the Final risk management report as per ISO 14971			
20.3	Compile certification required to comply with environmental requirement for Medical Devices as per Annexure A of Fifth Schedule of Medical devices Rules, 2017			
20.4	Prepare Device Master file for submission			
20.5	Implement QMS across organization for regulatory compliant IVD manufacturing			
20.6	Attach copy of latest inspection or audit report carried out by Notified bodies or National Regulatory Authority or Competent Authority within last 3 years			
20.7	Prepare an Organizational chart defining the roles and responsibilities of personnel involved in the IVD manufacturing			
20.8	Compile the final device Design and Manufacturing files			

Sl. No	To do	Completed		Remarks
		Yes	No	
20.9	Compile final Plant master file for submission			
20.10	Prepare Device Master file for submission			
20.11	Prepare final Product validation and verification report			
20.12	Copy of performance evaluation report issued by the central medical device testing laboratory			
20.13	Specific evaluation report, if done by any NABL accredited laboratory in India, showing the sensitivity and specificity of the in vitro diagnostic medical device			

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The preparation of this innovatos handbook is the result of a collective effort by experts and institutions dedicated to advancing in vitro diagnostic (IVD) practices in India in alignment with global best standards. It reflects not only technical knowledge but also a shared commitment to innovation, quality, and public health.

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ANNEXURE

The list of Annexure are uploaded on MedTech Mitra's website

Annexure 1: Examples (Risk Classification) of In-Vitro Diagnostic Medical Device under provisions of subrule(2) rule 4 of the MDR, 2017

Annexure 2: Essential Principles for safety and performance of medical devices guidelines

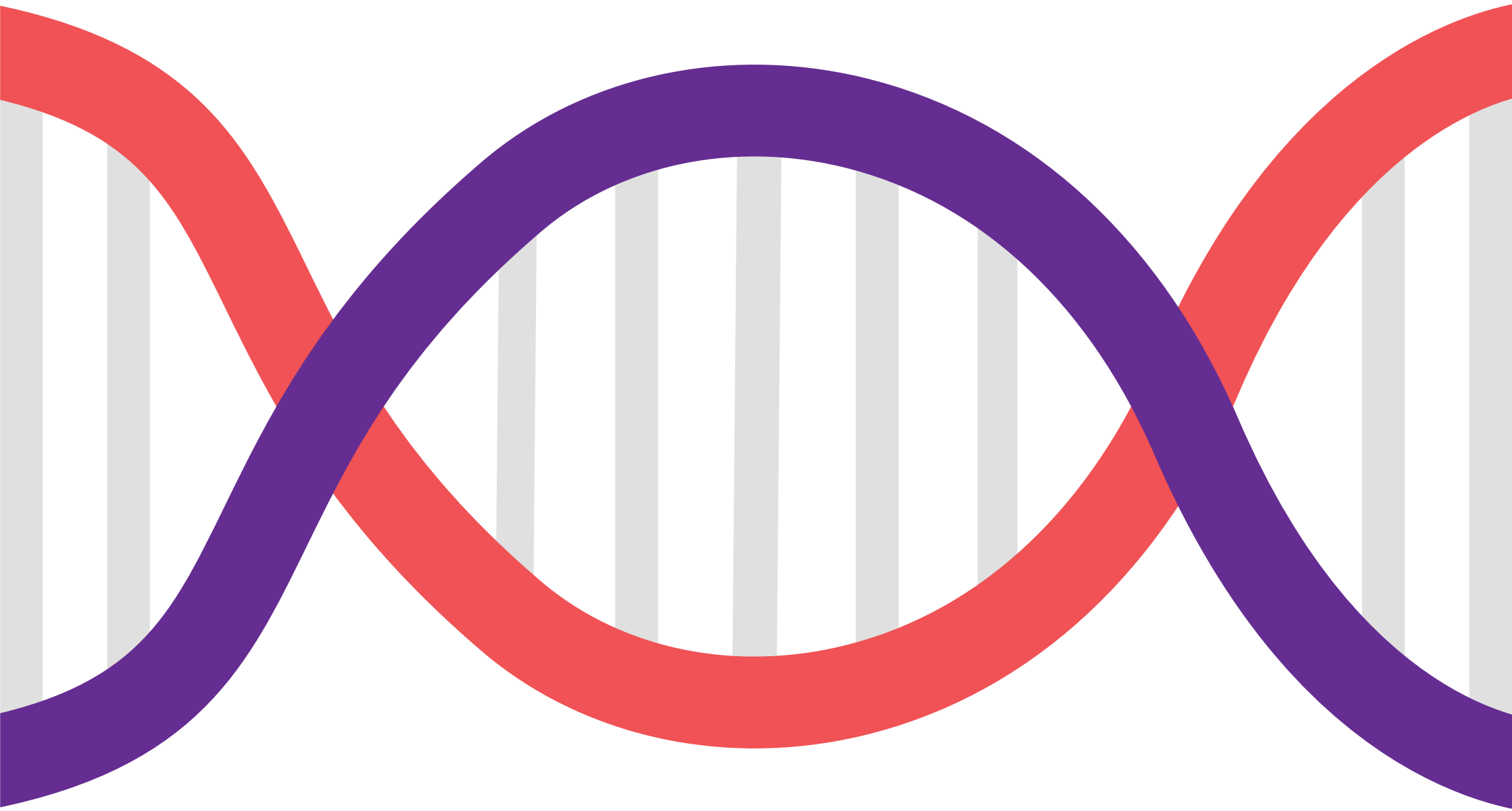
Annexure 3: CDSCO updated list of Laboratories for conducting Performance Evaluation of In - Vitro Diagnostic Medical Device

Annexure 4: List Of Standards

Annexure 5: List of Forms for IVD Medical Devices under MDR, 2017

Annexure 6: Checklist For Free Sale Certificate Or Export

Annexure 7: CDSCO's IVD Frequently asked Questions



The Indian Council of Medical Research (ICMR), is an autonomous organization under the Department of Health Research (DHR) for the planning, promoting, coordinating and conducting biomedical research in India. Medical Device and Diagnostics Mission Secretariat (MDMS), under Division of Development Research, was established to foster indigenous manufacturing of medical device and diagnostic technologies for an AtmaNirbhar Bharat. MDMS aims to support and catalyze research, development and indigenous manufacturing of both innovative & cost effective medical device & diagnostic technologies to strengthen healthcare sector in India through a Mission mode consortia approach.

MedTech Mitra, launched on December 25, 2023, is a joint initiative by ICMR and Central Drugs Standard Control Organization (CDSCO) under the guidance of NITI Aayog coordinated by MDMS, ICMR. It serves as a 'highway' for medtech innovators, offering personalized handholding support for regulatory facilitation, clinical evaluation and uptake of new products, across the product development lifecycle—bridging gaps between innovation, regulation, validation, and commercialization. The initiative aims to overcome critical challenges, often termed "valleys of death," including ideation to commercialization.

The key knowledge partner organizations of MedTech Mitra are CDSCO, NITI Aayog-Atal Innovation Mission, Bureau of Indian Standards (BIS), Kalam Institute of Health & Technology, (KIHT)/ Andhra Pradesh MedTech Zone (AMTZ), DHR-Health Technology Assessment in India (HTAIn), DHR-Centre for Guidelines, ICMR-Indian Clinical Trial & Education Network (INTENT) Network & ICMR- MDMS, Government e-Marketplace (GeM), Atomic Energy Regulatory Board (AERB) and National Health Systems Resource Centre (NHSRC).