Australian Commission on Safety and Quality in Health Care

NPAAC National Pathology Accreditation Advisory Council

Requirements for the Development and Use of In-house In Vitro Diagnostic Medical Devices

sixth edition

2026

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Acknowledgement

We acknowledge the Traditional Owners and Custodians of Country throughout Australia. We recognise their continuing connection to land, waters and community and acknowledge their ongoing contribution to the health system and community. We pay our respects to Elders past and present.

We recognise that knowledge about healthy Country, community and culture has been developed by Aboriginal and Torres Strait Islander peoples over tens of thousands of years and has been shared for generations. We are committed to partnering with and learning from Aboriginal and Torres Strait Islander peoples through the work that we do.

Updates

Requirement Edition	Year	Changes
First Edition	2004	First published.
Second Edition	2007	Introduced ISO 15189 aligned requirements.
Third Edition	2014	Reprinted and reformatted to be read in conjunction with the *Requirements for Medical Pathology Services.*
Fourth Edition	2018	Revised for alignment with the Therapeutic Goods Administration in-house IVD regulatory framework.
Fifth Edition	2025	Introduced a new companion diagnostics (CDx) framework, including CDx validation and clinical trial assay equivalence requirements (Standard 8), and updates to the new Commission template with removal of references to the *Requirements for Medical Pathology Services.*
sixth edition	2026	Introduction of new IVD Software requirements (**Standard 9**) including specific requirements for Artificial Intelligence (AI) and Machine Learning (ML) enabled software. Change to CDx - C8.1 b An in-house IVD must not include, in its intended purpose or patient reports any recommendation for the use of a ~~specific~~ corresponding medicine or biological product unless it has been validated as a companion diagnostic.

Contents

Background

The Australian Commission on Safety and Quality in Health Care leads and coordinates national improvements in health care safety and quality.

About the Australian Commission on Safety and Quality in Health Care

The Australian Commission on Safety and Quality in Health Care (the Commission) partners with the Australian Government, state and territory governments and the private sector to achieve a safe, high-quality, sustainable health system. It also works closely with patients, carers, clinicians, medical scientists, managers, healthcare organisations and policymakers.

Key functions of the Commission include:

- developing National Safety and Quality Standards
- developing Clinical Care Standards to improve the implementation of evidence-based health care
- coordinating work in specific areas to improve outcomes for patients
- providing information, publications and resources about safety and quality.

The Commission works in four priority areas.

- **High-quality care in an evolving environment** – so that high-quality health care is delivered consistently, reliably and equitably for all Australians.
- **Strong outcome focused clinical governance** – so that clinical governance, integrated standards and accreditation drive better patient outcomes
- **Empowered patients, families, carers and communities** – so that health care is designed and delivered with patients and communities.
- **An improvement-driven workforce culture** – because better health care is everyone's responsibility, every day.

About the National Pathology Accreditation Scheme

The National Pathology Accreditation Scheme (NPAS) requires pathology practices to meet relevant standards for their pathology services to be eligible for Medicare benefits. The *Health Insurance (Accredited Pathology Laboratory-Approval) Principles 2017* (the Approval Principles) underpin NPAS. The Approval Principles set the categories of accredited pathology laboratories, specify the standards to be met and the kind of pathology services provided.

The Approval Principles ensure that pathology practices providing Medicare eligible pathology services meet and maintain compliance with the standards. The Approval Principles objectives include:

- supporting the diagnosis and treatment of illness by linking Medicare benefits to pathology services that provide reliable results
- reducing the risk of misdiagnosis from pathology services that provide unreliable results
- maintaining public confidence in pathology services.

The Commission administers the NPAS behalf of the Australian Government Department of Health, Disability and Ageing (the Department). The Department manages the policy and regulatory framework for pathology practice accreditation that are approved to provide Medicare eligible pathology services.

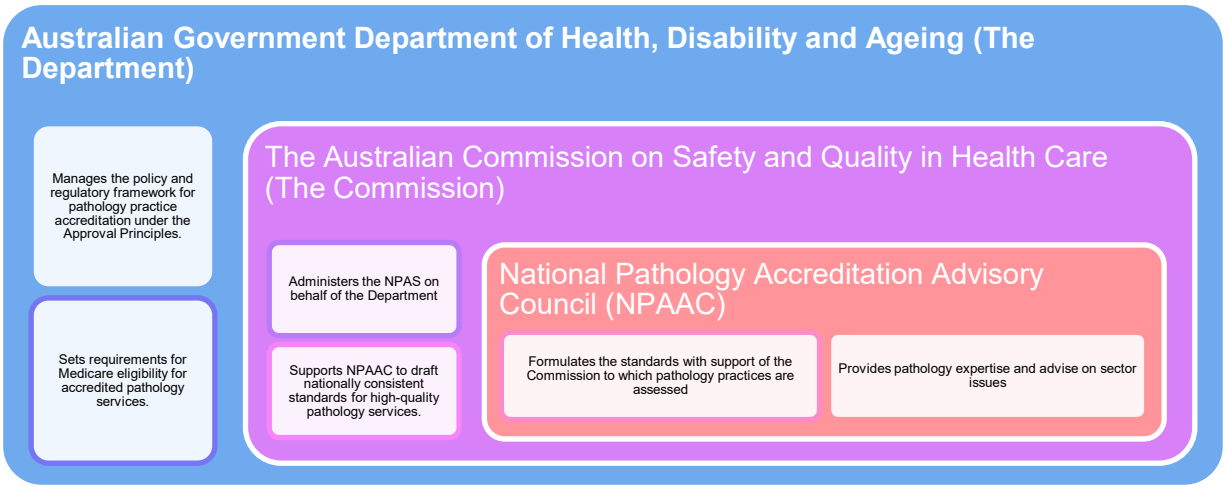
About the National Pathology Accreditation Advisory Council

The National Pathology Accreditation Advisory Council (NPAAC) was established in 1979 to consider and make recommendations to the Australian, state and territory governments on:

- matters related to the accreditation of pathology practices
- the introduction and maintenance of uniform standards of practice in pathology practices throughout Australia.

NPAAC, supported by the Commission, is responsible for formulating standards which pathology practices are assessed against. The Approval Principles give effect to NPAAC-endorsed standards by listing the standards and accreditation materials pathology practices seeking approval to provide Medicare eligible pathology services must meet. The pathology practice's conformity with the standards is assessed by the accrediting agencies defined in the Approved Principles.

Roles and Responsibilities – National Pathology Accreditation Scheme



Introduction

The *Requirements for the Development and Use of In-house In Vitro Diagnostic Medical Devices (IVDs) (sixth edition, 2026*) is a Tier 3B NPAAC document. It sets out the minimum requirements for best practice in the development and/or use of in-house IVDs.

Core principle

The fundamental principle of this document is that all in-house tests must be produced in a manner that ensures they are safe and perform as intended. This Standard supports that principle by introducing requirements for the design, production, verification, and validation of in-house IVDs.

Regulatory alignment

The document has been reviewed to reflect current regulatory requirements for in-house IVDs. These Requirements have been developed with reference to Australian legislation and international standards, including:

- **AS ISO 15189** – Medical laboratories – Requirements for quality and competence
- **ISO 13485** – Medical devices – Quality Management Systems – Requirements for Regulatory Purposes
- **ISO 14971** – Medical devices – Application of Risk Management to Medical Devices.

Related documents and compliance

This document should be read within the national pathology accreditation framework, including current versions of the following NPAAC documents:

- All Tier 2 and Tier 3 documents
- Tier 4 documents, including:
    - Requirements for Laboratory Testing for Antibodies to HIV and HCV
    - Requirements for Medical Testing of Human Nucleic Acids
    - Requirements for Medical Testing of Microbial Nucleic Acids.

Laboratories must also comply with relevant state and territory legislation, including any reporting requirements.

Document structure

Each section identifies key points for practice as either Standards (S) or Commentaries (C).

- **Standard**: The minimum requirement for procedures, methods, staffing, or facilities. Standards required before a laboratory can attain accreditation are prefaced with an ‘S’ (for example, S2.2). The use of “must” indicates a mandatory requirement.
- **Commentary**: Provides clarification to the standards, examples and guidance. Prefaced with a ‘C’ (for example, C1.2). Commentaries may be normative or informative. If a commentary uses “must”, it is considered normative and holds the same weight as a Standard.

Appendices may also be normative or informative and are considered integral to the document.

Context

In Australia, all in vitro diagnostic medical devices (IVD medical devices or IVDs) intended for therapeutic use are regulated under the *Therapeutic Goods Act 1989*.

A new regulatory framework for IVDs was implemented on 1 July 2010, following amendments to the Therapeutic Goods (Medical Devices) Regulations 2002 to include IVDs as a subset of medical devices.

Regulatory Requirements for IVDs

These legislative changes apply to all IVDs, including in-house IVDs, and require that all manufacturers certify their products as:

- safe
- fit for their intended purpose
- manufactured to a high standard of quality.

This is achieved through compliance with a set of Essential Principles (EPs), which establish requirements relating to device performance, risk management, and the identification and mitigation of hazards. The EPs form the foundation of the regulatory framework for in vitro diagnostic (IVD) medical devices, setting out the overarching safety and performance criteria that must be met. These principles are legislated in Schedule 1 of the *Therapeutic Goods (Medical Devices) Regulations 2002*[1].

Risk Classification of IVDs

The level of regulatory review required for each IVD is determined by assessing the risk posed to individual or public health. Classification rules consider the likelihood and severity of harm, assigning products to one of four risk categories.

[1] Australia, *Therapeutic Goods (Medical Devices) Regulations 2002*, Schedule 1 (Federal Register of Legislation), https://www.legislation.gov.au/F2002B00237/latest/text

- Class 1 IVD – No public health risk or low personal risk.
- Class 2 IVD – Low public health risk or moderate personal risk.
- Class 3 IVD – Moderate public health risk or high personal risk.
- Class 4 IVD – High public health risk.

Manufacturer Responsibilities

It is the manufacturer's responsibility to determine the classification of each IVD, based on its intended use and the significance of the result. These rules apply to both commercially supplied and in-house IVDs. If more than one classification rule applies, the IVD must be assigned the highest applicable classification.

Conformity Assessment Procedures

The classification of an IVD determines the minimum conformity assessment procedures required to demonstrate compliance with the Essential Principles (EPs). These procedures differ depending on whether the IVD is commercially supplied or manufactured in-house.

The classification rules for IVDs are detailed in Schedule 2A of the Regulations[2]. It is the manufacturer's responsibility to determine the classification of each IVD and consideration must be given to its intended use and the overall significance of the final result. The classification rules are relevant to both commercially supplied and in-house IVDs, and except in those cases where a special rule exists, if more than one classification rule applies the IVD must assume the highest classification level.

The classification of the IVD will determine the minimum conformity assessment procedure(s) that a manufacturer must apply to demonstrate compliance with the EP. The appropriate conformity assessment procedure is further established based on either commercial or in-house manufacture. More detailed information relating to classification of IVDs is available in the guidance document *Classification of IVD Medical Devices* available on the TGA website.[32]

In-house IVDs

In-house IVDs are separated into two groups for the purposes of determining the appropriate conformity assessment procedure.

- Class 1–3 in-house IVDs.
- Class 4 in-house IVDs.

Manufacturers of in-house IVDs that are classified as a Class 1 in-house IVD, Class 2 in-house IVD or Class 3 in-house IVD are required to follow the set of conformity assessment procedures detailed in Schedule 3 Part 6A of the Regulations, and as outlined in the guidance document *The Regulatory Requirements for In-House IVDs in Australia*.[4]

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[2] Australia, *Therapeutic Goods (Medical Devices) Regulations 2002* (Federal Register of Legislation, last modified March 21, 2026), https://www.legislation.gov.au/F2002B00237/latest/text

[3] *Therapeutic Goods (Medical Devices) Regulations 2002: Schedule 2A – Classification rules for IVD medical devices*. Canberra (AU): Australasian Legal Information Institute. Available: https://www.austlii.edu.au/cgi-bin/viewdoc/au/legis/cth/consol_reg/tgdr2002400/sch2a.htm l

[4] Therapeutic Goods Administration. *Regulatory requirements for in-house IVDs*. Version 3.0. Canberra (AU): TGA; 2024 May. Available from: https://www.tga.gov.au/sites/default/files/regulatory-requirements-in-house-ivds.pdf

Responsibility for review of each laboratory's compliance with the requirements rests principally with the accrediting agency, National Association of testing authorities and will be carried out in conjunction with their routine laboratory accreditation visits.

Class 1-3 in-house IVDs are exempt from inclusion in the Australian Register of Therapeutic Goods (ARTG) subject to certain conditions.

- Laboratories manufacturing in-house IVDs are required to notify the TGA by 1 July 2017 of all in-house IVDs manufactured. After 1 July 2017, laboratories are required to re-notify the TGA only when new in-house IVDs are introduced (by 1 July of the next financial year). The details will be maintained by the TGA in a repository.
- Laboratories manufacturing in-house IVDs must be accredited as a medical testing laboratory and must meet *AS ISO 15189 Medical laboratories – Requirements for quality and competence.* NATA may be able to assess certain laboratories (that are outside the scope of ISO 15189) that manufacture Class 1-3 in-house IVDs against ISO/IEC 17025*, General requirement for the competence of testing and calibration laboratories.* Requests for assessment against ISO/IEC 17025 will be considered by NATA on a case-by-case basis and only in exceptional circumstances (for example, veterinary laboratories that primarily perform testing on animals but may also perform testing on human samples on request).
- A laboratory that manufactures (or develops) in-house IVDs must meet the NPAAC *Requirements for the Development and Use of In-house IVDs.*
- Laboratories must maintain suitable documentation that can be used to demonstrate that each in-house IVD complies with the applicable provisions of the NPAAC Standards, including the *Requirements for Medical Pathology Services*. Information must include details of the design, development, production, validation and monitoring for each device.
- Laboratories must maintain a post-marketing system that monitors the performance of each in-house IVD, implements corrective action as appropriate to address deficiencies in design and production, and notify the TGA of any adverse events arising from the use of the in-house IVD.

Laboratories that manufacture Class 4 in-house IVDs need to include these in the ARTG, unless otherwise exempt. To do this, laboratories have a choice of two pathways:

- obtaining TGA conformity assessment certificates prior to applying for inclusion of their Class 4 in-house IVDs in the ARTG; or
- using their existing NATA accreditation to ISO 15189, or their TGA manufacturing licence, to apply directly for inclusion of their Class 4 in-house IVD in the ARTG.

Further information about conformity assessment procedures for Class 4 in-house IVDs is available on the TGA website.

Criteria for assessment of in-house IVDs

Standards outlined in this document are listed in **Table 1**.

Table 1 Criteria for assessment of in-house IVDs

1.	General requirements
2.	Design
3.	Production and contracted services

4. Analytical performance
5. Scientific validity
6. Clinical performance
7. Clinical utility
8. Companion diagnostics
9. IVD software requirements
10. Multivariate index assays
11. Monitoring, analysis and improvement
12. Adverse events and recalls
13. Documentation

The requirements outlined in Sections 2 to 13 are intended to ensure that the quality system implemented by all accredited laboratories under AS ISO 15189, extends to the requirements surrounding the production or manufacture of an in-house IVD.

Laboratories that design, produce, and use in-house IVDs need to ensure that their current Quality System (QS) covers these requirements. The extra requirements of the QS to cover activities surrounding in-house IVDs may be summarised as:

- management responsibility
- resource management
- planning and production
- monitoring, analysis and improvement.

It is expected that most of these requirements will be met by modification of the existing QS within the laboratory. Extension of the QS requirements to cover in-house IVDs is considered in Sections 2 to 13.

1. General requirements

No.	Standard and commentary
S1.1	The work environment must be conducive to ensuring that the design, production, and utilisation of in-house IVDs meet the regulatory requirements of this document.
S1.2	An in-house IVD must not be used in the provision of any service by a laboratory unless it has been validated according to these Requirements (except as outlined in S1.3 below). C1.2 a In-house IVDs, or commercial tests endorsed by the manufacturer as 'for research use only' or 'not for diagnostic use', or elements of such tests that are supplied as 'analyte-specific reagents' must be validated in accordance with this document if they are to be used in the management of a specific patient, or used to produce a result on a specific patient that may be used for patient management. C1.2 b An IVD is considered to be for research use only when the results produced using that IVD are neither used for nor intended to be used for patient management.
S1.3	If an in-house IVD cannot be fully validated, and there is no reasonable access to an alternative validated assay, and it is used in one or more of the circumstances described in C1.3a, then the report issued with the test result must contain the following statement: *"The test used cannot be fully validated to the current NPAAC Requirements because (insert a brief reason) and the results should be interpreted accordingly. For further information please contact the laboratory."*

No.	Standard and commentary
	C1.3 a Incompletely validated in-house IVDs must only be used clinically in the following circumstances: i. for a new or uncommon condition where its rarity precludes the laboratory from fulfilling all validation requirements ii. an uncommon application where it is not possible to fulfil all validation requirements iii. a matter of urgency for a disease that poses a serious risk to public health
	C1.3 b The laboratory must have a documented plan for validation.
	C1.3 c Where an in-house IVD has been used in the circumstances described in S1.3, validation records must be available to the fullest possible extent
	C1.3 d Where an in-house IVD has been used in the circumstances described in C1.3 a, validation must be completed as soon as possible
S1.4	If any modification is made to a commercially supplied IVD or an existing in-house IVD, it must be treated as a new in-house IVD, and the modification must be validated in accordance with these Requirements
	C1.4 a This must include changes to intended use (including sample type) or indications for use
	C1.4 b Where an IVD has been modified, the validation steps required are determined by the nature of the modification. It must be demonstrated that the changes have been properly assessed and show that the assay continues to perform safely and effectively
S1.5	Where a laboratory develops an in-house IVD, that IVD must only be used in that laboratory or its own laboratory network.
	C1.5 a If a laboratory supplies an in-house IVD that has been manufactured in-house to a laboratory outside of its own laboratory network, then that IVD must be assessed as a commercially supplied IVD, and as such, must meet the requirements for commercially supplied IVDs as set out in the *Therapeutic Goods (Medical Devices) Regulations 2002*[5]
	C1.5 b This Standard does not prevent collaboration in the design and development of IVDs or exchange of clinical samples as these are not captured by the definition of an in-house IVD

[5] *Therapeutic Goods (Medical Devices) Regulations 2002*. Canberra (AU): Federal Register of Legislation; 2025 Oct 1. Available from: https://www.legislation.gov.au/F2002B00237/latest/text

2. Design

No.	Standard and commentary
S2.1	The laboratory must have and maintain a QS that ensures that all phases in the design, production, utilisation, storage, packaging and transport of in-house IVDs within the laboratory are sufficient and fully documented to ensure that any in-house IVD produced is suitable for purpose C2.1 a For each in-house IVD, there should be a file containing documents defining IVD specifications, production processes and QS requirements
S2.2	The IVD must be designed and produced so that when used under the conditions and for the purposes intended, all reasonable measures have been taken to minimise the risk of compromising the health and safety of the patient, the user or any other person
S2.3	The design and construction of the IVD must conform to the *Essential Principles on the safety and performance of medical devices | Therapeutic Goods Administration (TGA)*, (refer to Appendix A) and consider best practice, where this includes identifying and eliminating risks associated with use (including disposal), and ensuring that adequate protection measures are in place C2.3 a The laboratory must ensure that the safety of the patient, the operator, and other staff is not compromised by the design, production, or the use of the validated IVD, through compliance with all state and territory occupational health and safety requirements C2.3 b ISO 14971 Medical Devices - *Application of Risk Management to Medical Devices*. Annex H: Guidance on risk management for in vitro diagnostic devices provides useful information on identification, evaluation and control of risk
S2.4	The IVD must be designed and produced in a way that ensures it is safe to use for the entire intended life of the device
S2.5	Where parts of the in-house IVD are to be purchased from an external source, the laboratory must ensure that the products purchased will meet the requirements as specified in the design protocol

3. Production and contracted services

Planning, scheduling resources, and purchasing are all part of the manufacture of in-house IVDs as are procedures for monitoring these processes.

No.	Standard and commentary
S3.1	The laboratory must establish documented procedures to ensure that products sourced for use in the routine production of in-house IVDs conform to specified requirements and are traceable
S3.2	The laboratory must ensure that sub-contracted services that affect the in-house IVD are controlled
S3.3	Where work environment conditions are critical for the development, production, validation, or use of the in-house IVD, the laboratory must monitor and control these work environment conditions
S3.4	Senior staff must have significant diagnostic or research experience with new test development and validation. The depth and complexity of this experience must be commensurate with the range and complexity of IVD development undertaken in the laboratory C3.4 a The presence of experienced supervisors and trainers is essential, given their critical involvement in error detection, error correction and problem solving
S3.5	The laboratory must plan and carry out the production of in-house IVDs under controlled conditions from design, manufacture and validation of the proposed product to its release for routine use

No.	Standard and commentary
	C3.5 a Controlled conditions include: i. identification of different stages of assay development, including routine production ii. implementation of review, verification and validation of the above by designated personnel iii. documented requirements (e.g. batch size, acceptable performance limits) iv. identification and use of reference materials and reference measurement procedures v. identification and use of suitable equipment (i.e. appropriate for use and calibrated) vi. identification and use of monitoring and measuring processes and devices vii. planned and documented specifications and processes for the release of the product, and for the receipt of the product at the site of routine storage before product use viii. planned and documented specifications and processes for any packaging and labelling of the final product, accessories or components ix. planned and documented specifications, processes and records if cleanliness of the environment is critical (e.g. production step where sterilisation is required)
S3.6	The laboratory must establish procedures to verify the suitability of the in-house IVD for use in the setting in which it will normally be used
S3.7	Records relating to production batches and the status of an in-house IVD, or a component thereof, must be traceable and retained for a minimum of 4 years beyond the date of their valid use or 5 years from the date of manufacture and: a. the laboratory must maintain records of each batch produced. This must include records of all components of the batch, and any other information relevant to the successful use of the batch in the routine environment b. each batch, and each component within the batch, must be assigned a unique identifier and must be available for the purposes of traceability c. at each stage of production, the product status must be identifiable. A batch of an in-house IVD awaiting final release validation must be clearly identified as such. A batch that has been deemed acceptable for routine use (i.e. validation criteria have been passed) should be identified as such d. if a component within a batch is changed, then that batch must be considered as a new batch and will require re-validation
S3.8	The laboratory must establish documented procedures to ensure that conditions preserving the effectiveness of an in-house IVD are not compromised

No.	Standard and commentary
S3.9	The laboratory must ensure that any validation and monitoring measures required for verification of the processing steps are identified, validated and documented
S3.10	If a batch, or part thereof, is distributed within a laboratory network, then procedures or instructions must also be issued relating to the transport, receipt and use of the test at its destination. Such instructions should refer to the packaging, transport, handling, storage and identification of the in-house IVD

4. Analytical performance

The analytical performance of an in-house IVD medical device is its ability to detect or measure a particular analyte.

No.	Standard and commentary
S4.1	The stability of the analyte being measured must be determined under the sample storage conditions being used
S4.2	The suitability of an IVD must be demonstrated for use with each specimen type to be tested under the collection and transport conditions used by the laboratory
S4.3	The minimum specimen handling and IVD storage conditions must be determined and documented for the end-users of the in-house IVD
S4.4	The accuracy and imprecision of in-house IVDs must be determined by at least one of the following methods applicable to the relevant biological material: a. The use of certified reference material b. Comparison with a definitive method or a reference method c. Performance of recovery experiments d. Use of validated in-house reference material e. Performance in external proficiency-testing programs or laboratory sample exchange programs C4.4 a The materials used in this analysis may include known positive and negative control samples or proficiency material or be from patients of known clinical states. The threshold for detection of an analyte can be determined by the repeat analysis of samples with results near the cut-off of sensitivity for the IVDs
S4.5	Sufficient numbers of specimens and appropriate statistical tools must be employed in the development phase to achieve the confidence levels required to satisfy both the analytical performance and the required clinical utility of the test

No.	Standard and commentary	
	C4.5 a	In general, validation of analytical performance requires that the reference interval, analytical sensitivity, limits of detection, analytical specificity, accuracy, imprecision, linearity, and freedom from interference be addressed. Laboratories should strive to achieve the best test performance relevant to the intended clinical use of the IVD
	C4.5 b	It is not possible to be prescriptive about the required sensitivity and specificity, nor about the number of specimens involved, because these will vary with the intended use and with the significance of false results. Where there are significant guidelines available, these should be taken into consideration when assessing IVD performance. An example of this would be use of the PHLN guidelines for gonococcal PCR[64]
	C4.5 c	Consideration should be given to seeking statistical advice if required
S4.6	The source and number of specimens tested during the validation phase must be documented	
	C4.6 a	Relevant legislative and organisational policies on the use of clinical samples for validation purposes must be followed
S4.7	An estimate of measurement uncertainty of the in-house IVD must be determined where relevant and possible	
S4.8	The detectable and measurable range and limit of detection of the IVD must be determined where it yields a quantitative or, where appropriate, a semi-quantitative result	
	C4.8 a	In general, validation of quantitative, semi-quantitative and qualitative IVD procedures should include a comparative evaluation of the IVD against the definitive method, a reference method, or an established procedure with known analytical performance and clinical utility. Where there are discrepancies between the new in-house IVD and its comparator, then an analysis of discrepant results should be performed using other test modalities, review of clinical and other information, and/or referral to another laboratory for testing
	C4.8 b	Cut-off values for determination of positivity and/or negativity should be derived for an IVD where it yields a semi-quantitative or qualitative result
	C4.8 c	Where appropriate, it should be demonstrated that IVDs for genetic tests are capable of distinguishing between homozygotes, heterozygotes and hemizygotes for the alleles in question
S4.9	There must be an investigation to detect possible interference of performance of the IVD, where applicable. The laboratory must be able to show that at least the most likely interfering substances have been eliminated as a source of error	

[6] Australian Centre for Disease Control. *PHLN guidelines for the use and interpretation of nucleic acid detection tests for Neisseria gonorrhoeae in Australia*. Canberra (AU): CDC; 2005 Available: https://www.cdc.gov.au/resources/publications/phln-guidelines-nucleic-acid-tests-neisseria-gonorrhoeae

No.	Standard and commentary	
	C4.9 a	It is important to know whether the IVD responds uniquely to the analyte that it was designed to measure or detect, or whether there are any other analytes that may also react with the test system to give unexpected or invalid results. This is particularly important in nucleic acid amplification for viral or bacterial markers, where highly conserved areas of DNA may cross many species boundaries
S4.10	Measurement of robustness must be performed by determining the impact of expected changes in conditions.	
	C4.10 a	Expected changes may include operator, equipment (where more than one instrument may be used), different source of reagent, or changes in parameters such as pH, temperature and/or humidity. This is particularly important where the in-house IVD is distributed within a laboratory network. Measurement can be done by use of controls and an evaluation panel that best tests the critical components of technical performance, particularly the sensitivity and specificity of the test
S4.11	Reagent stability must be monitored and recorded over time, and comparable performance of the IVD from batch to batch must be demonstrated. Expiry dates, if relevant, must be documented.	
	C4.11 a	The internal QC and/or external proficiency testing programs will assist with this process
S4.12	Equipment must be used in its intended manner or, the performance of the equipment must be verified as part of the in-house IVD validation	
S4.13	Laboratories must verify the performance of their in-house IVDs for the intended specimen types and conditions	
	C4.13 a	Types of specimens used for validation should be as similar as possible to the specimens expected to be routinely received for testing.
	C4.13 b	Specimens should also be chosen to yield results that cover at least the range of possible results expected from patient samples
S4.14	Laboratories must determine appropriate specimen handling, storage conditions, and specimen types, where applicable, and inform collection staff and staff performing the medical testing with the in-house IVD of these limitations	

5. Scientific validity

The scientific validity of an analyte is the association of that analyte with a clinical condition or physiological state.

Explanatory note

Scientific validity is often identified from academic research and is supported by studies evaluating the analyte for potential clinical applications. The generation and assessment of clinical evidence is an ongoing process. Information related to clinical evidence should be monitored routinely once the in-house IVD is being used for patient testing by the laboratory

No.	Standard and commentary
S5.1	A clinically useful association between the clinical condition and the interpretation of the in-house IVD must be demonstrated. Level 1 or Level 2 published evidence must be cited based on either NHMRC[5], EGAPP[6], Eurogentest Gene cards[7] or other guidelines for the evaluation of such evidence. C5.1 a A single retrospective study or a case-control study (evidence Level 3), whilst important in establishing proof of concept should not necessarily be considered sufficient to clinically validate a new biomarker assay
S5.2	Requirements of clinicians and other relevant parties, including their expectations relating to the level of service and the type and extent of interpretation, must be considered when designing an in-house IVD

6. Clinical performance

The clinical performance of an in-house IVD medical device is its ability to yield results that are correlated with a particular clinical condition/ physiological state according to a target population and an intended user.

No.	Standard and commentary
S6.1	The clinical sensitivity and specificity as well as positive and negative predictive values must be available for the relevant condition
	C6.1 a Such data can be derived from multiple sources such as clinical performance studies, published studies from other groups, or experience gained by routine diagnostic testing
	C6.1 b Further information on clinical performance study design may be found in the GHTF document GHTF/SG5/N8:2012 entitled Clinical Evidence for IVD medical Devices – Clinical Performance Studies for In Vitro Diagnostic Medical Devices[7]

[7] please note that GHTF documents are now published through the *International Medical device Regulators Forum* which can be found on International Medical Device Regulators Forum

7. Clinical utility

The clinical utility of any new in-house IVD medical device is the usefulness of results obtained from testing with the IVD and the value of the information to the individual being tested and/or the broader population.

No.	Standard and commentary
S7.1	New in-house IVDs for novel tests, or established IVDs for a novel use, must only be offered in the clinical setting (as opposed to the research setting) where there is sufficient evidence of clinical utility for the specific population of patients in which the assay is intended for use. C7.1 a Levels of evidence must be assessed in accordance with relevant criteria, such as NHMRC[5], EGAPP[6], Eurogentest Clinical Utility Gene Cards[7], or other guidelines for evaluating such evidence. The source of the criteria must be cited C7.1 b The pre-test probability of a positive or negative result—and the risks associated with false positive or false negative results—can vary significantly between populations (e.g. symptomatic vs asymptomatic patients) C7.1 c Assessment of evidence for clinical utility should focus on: i. supporting data from clinicians explaining why the test is needed and how it will be used in clinical decision-making ii. the quality of individual studies, the overall body of evidence, and the quantity of relevant data iii. the consistency and generalisability of findings
S7.2	The introduction of an in-house IVD must be a planned activity designed to produce a test that is fit for purpose in terms of clinical performance and clinical utility. The laboratory must demonstrate that the product's design and development process was directed towards meeting these criteria

No.	Standard and commentary
C7.2 a	Relevant considerations may include: i. the prevalence of the clinical condition. ii. the expected number and frequency of referrals iii. the need for out-of-hours testing iv. whether a reference laboratory service is required v. whether a lower level of service is sufficient

Example

A qualitative assay for BCR–ABL mRNA may be suitable for diagnosing chronic myeloid leukaemia, while a quantitative assay is needed for monitoring residual disease.

8. Companion diagnostics

A companion diagnostic IVD provides essential information for the safe and effective use of a medicine or biological product.

For a device to be considered a companion diagnostic, the medicine must be approved in Australia and include within its product information that companion testing is essential for the safe and effective use for the relevant medicine or biological product. The TGA's Understanding regulatory requirements for in vitro diagnostic (IVD) companion diagnostics (CDx)[8] provides further information on companion diagnostics.

No.	Standard and commentary
S8.1	Companion diagnostics that have not been approved for diagnostic use by the TGA must be considered an in-house IVD for the matching medicine or biological product and evaluated in accordance with these requirements before being used for diagnostic or therapeutic purposes
	C8.1 a The intended purpose of a companion diagnostic must clearly state that it is to be used for one or both of the following, where the product information for the medicine or biological states that companion testing is essential for: i. selecting patients for treatment with a medicine or biological product ii. monitoring patients who are being treated with the medicine or biological product
	C8.1 b An in-house IVD must not include, in its intended purpose or patient reports any recommendation for the use of a corresponding medicine or biological product unless it has been validated as a companion diagnostic

[8] Therapeutic Goods Administration (TGA). *Understanding regulatory requirements for in vitro diagnostic (IVD) companion diagnostics (CDx)* [Internet]. Canberra (AU): Department of Health and Aged Care; 2019, Available: https://www.tga.gov.au/resources/guidance/understanding-regulatory-requirements-vitro-diagnostic-ivd-companion-diagnostics-cdx

No.	Standard and commentary
	C8.1 c The clinical utility of a companion diagnostic is demonstrated by one or more pivotal clinical studies (the clinical trial assay) that align with the TGA's approval of the medicine or biological product
	C8.1 d Where a pathology laboratory is seeking accreditation of a companion diagnostic, but the in-house IVD was not the IVD used in the pivotal studies, the laboratory must demonstrate clinical utility by showing clinical comparability to the clinical trial assay The process includes: i. a direct clinical comparability study conducted on samples from the pivotal clinical study; or ii. a direct clinical comparability study conducted on samples from patients like those enrolled in the pivotal clinical study; or iii. an indirect clinical comparability where there is: a) strong evidence that the scientific validity, analytical and clinical performance of the companion diagnostic is highly comparable to the clinical trial assay b) a scientific and clinical justification that the companion diagnostic will deliver clinically comparable outcomes to those in the pivotal clinical study and therefore a clinical comparability study is not required **Direct clinical comparability example** When no 'gold standard' biomarker exists, a clinical comparability study may be conducted using samples from the pivotal study or similar patients, comparing the in-house IVD to the clinical trial assay or a validated equivalent. **Indirect clinical comparability example** When the in-house IVD detects the same biomarker in samples similar to those used in the clinical trial, with comparable analytical performance and within an accredited external quality assessment program, clinical comparability may be inferred.

9. In vitro device software requirements

Section 9 applies to all IVD software, including embedded/integrated software, software that drives or influences other devices, and standalone software or software as medical device (SaMD) with or without Machine Learning or AI components.

The definition of an IVD medical device in the Therapeutic Goods (Medical Devices) Regulations 2002 applies regardless of the technology used in the product. In house IVDs that are software or that include software must meet the regulatory requirements for in house IVDs.

All the relevant general in-house IVD requirements also apply to IVD software. However, additional software requirements apply as detailed below.

Laboratories that design, produce, and use in-house IVD software need to ensure that their current Quality System (QS) covers the design of the in-house IVD software including details of the processes, systems and measures used for controlling, monitoring and verifying that at each stage of the design process, compliance with the applicable provisions of the *Essential Principles*[9] (see also section 2 Particular requirements – design) is achieved. *Essential Principle 12.1* applies to commercial IVD software and outlines regulatory requirements for software design and production.

[9] Therapeutic Goods Administration (TGA). *Demonstrating evidence to comply with the Essential Principles* [Internet]. Canberra (AU): Department of Health and Aged Care; 2022 Aug 25 Available: https://www.tga.gov.au/resources/guidance/demonstrating-evidence-comply-essential-principles

No.	Standard and commentary
S 9.1	In-house IVD software that is intended to make use of data and information must be designed and produced in a way that ensures that: a. the safety, performance, reliability, accuracy, precision, useability, security and repeatability of the device are appropriate for the intended purpose of the device b. any consequent risks, or impairment of performance, associated with one or more fault conditions is eliminated or appropriately reduced c. the device is resilient with respect to interactions that could occur during the use of the device and that could result in unsafe performance of the device d. the device provides suitable warnings in a timely manner if there is a risk to patient or operator safety including: i. following the disruption to services upon which the device is dependent for the device's operation ii. following the performance of the device being adversely affected e. when relevant to safety, the device enables users to verify correct operation f. data privacy is preserved where applicable
S 9.2	The development of the in-house IVD occurs within a risk management framework to promote the safety and effectiveness of the device throughout its product life cycle
S 9.3	In-house IVD software must be developed and maintained using contemporary, evidence-based methods for design, development life cycle, development environment, version control, quality and risk management, security, verification and validation, change and configuration management and problem resolution C 9.3 a. IEC 62304 provides an example of an appropriate medical device software life cycle standard
S 9.4	The pathology practice must ensure coordinated involvement of appropriately qualified experts from relevant disciplines at each stage of the in-house IVD software lifecycle, with roles and responsibilities clearly defined and documented
S 9.5	In-house IVD software that is intended to be used with computing platforms must be designed and developed considering the platform capability, resource and configuration limitations of the platforms and external factors including technology environments that may affect safe and effective use

No.	Standard and commentary
S 9.6	Risks to patient safety from the use of the device in clinical decision making must be minimised through appropriate integration into clinical workflow C 9.06 a Integration of the software into existing clinical workflows ensures that outputs are delivered at the correct point in clinical decision-making, are clearly understood by users, and do not disrupt established procedures C 9.06 b Alignment with real-world clinical practice workflows supports safe and high-quality decisions and reduces the risk of misinterpretation, delays, or inappropriate reliance on the software
S 9.7	Instructions and information for the in-house IVD software must be available to the relevant workforce and include requirements for hardware, software, information technology environments and security controls necessary to operate the device as intended
S 9.8	In-house IVD software must be designed, produced and maintained using contemporary evidence-based practice for software engineering and cyber security practice, including where relevant and appropriate: a. protection against unauthorised access or manipulation b. minimisation of risks from known cyber security vulnerabilities (including either or both remediation of known vulnerabilities and application of compensating controls) c. regular review and implementation of updates and patches d. disclosure of known vulnerabilities in the device or its components and associated mitigations e. provision of information to support decisions about applying updates or controls
S 9.09	A data governance framework must address quality management, privacy, storage, security and cybersecurity practices. Risk management within that framework must address versioning, traceability, auditability, authenticity, confidentiality, and integrity of data C9.09 a Data sets, validation data and audit records must be kept for the life of the device and not less than two years
S 9.10	The safety and performance of in-house IVD software post implementation into clinical use is monitored. Processes must be established for system failure and adverse events reporting to the designated person and the TGA aligned with legislative requirements C 9.10 a The reportability requirements for IVD software are the same as for all IVDs. This includes the threshold for reportable changes, regardless of whether it is considered by the laboratory as a minor or major change. For further information see Ongoing responsibilities | Manufacturing or supplying in-house in-vitro

No.	Standard and commentary
	diagnostic medical devices (IVDs) | Therapeutic Goods Administration (TGA)[10].
S 9.11–S 9.17 apply where machine learning is used to develop or train an AI model that is deployed in a locked state for clinical use. Models that continue to learn or adapt after deployment are outside the scope of this Standard	
S 9.11	The pathology practice must implement an AI management system consistent with relevant international standards, such as ISO 42000
S 9.12	The model outputs are established from the performance of the device in the context of the clinical workflow. The risks of interaction between humans and the device that could influence clinical decisions such as automation bias, over-reliance, and user interface design are considered
C 9.12 a	The outputs are clearly documented and provide transparency on the AI decisions, so that users can understand, in broad terms, how the model arrived at its result, and indicate the limitations and biases[11] of the model and the reliability of the result
S 9.13	When model development or training is completed, an algorithm lockdown[12] must be applied to ensure the model operates only within its validated scope. Where the model is retrained or modified, lockdown must be re-applied, performance re-verified, and risks to safety and performance managed and documented before clinical use
S 9.14	The laboratory must ensure that any data used to influence or assess how the in-house IVD software performs is suitable for its intended purpose and

[10] Therapeutic Goods Administration (TGA). *Manufacturing or supplying in-house in-vitro diagnostic medical devices (IVDs)* [Internet]. Canberra (AU): Department of Health and Aged Care; c2024, Available: https://www.tga.gov.au/products/medical-devices/vitro-diagnostic-devices/manufacturing

[11] **Bias** is a systematic and non-random error in an AI model or its outputs that results in unequal, inaccurate, or unintended performance across different individuals, populations, sample types, or clinical contexts, in a way that is not clinically justified by the intended purpose of the device.
In the context of AI-enabled in-house IVD software, bias may arise from:

- the data used to train, test, or validate the model
- the design or optimisation of the algorithm
- the clinical workflow or user interaction with the software
- changes over time in populations, practice, or data quality

and may lead to differences in sensitivity, specificity, accuracy, or reliability for particular subgroups or use conditions.

[12] **Algorithm lockdown**
A documented control state in which a software algorithm or machine-learning model is frozen for clinical use, such that its logic, parameters, weights, structure, and operating thresholds cannot change without formal change control, re-verification, and re-authorisation.
Algorithm lockdown ensures that:

- the deployed model operates only within the scope for which safety and performance have been assessed and validated.
- any retraining, updating, or modification is treated as a controlled change.
- the impact of changes on safety, performance, bias, and clinical utility is formally assessed; and
- traceability between the validated model, deployed version, and clinical outputs is maintained.

No.	Standard and commentary
	based on contemporary evidence-based practice. Data that influences the performance of the device must be: a. representative b. of sufficient quality c. maintained to ensure integrity d. managed to reduce bias C 9.14 a Data sets are representative of the intended patient population, and the sample is of sufficient diversity and size to assess clinical performance C 9.14 b Data collection protocols describe the different requirements for training, testing and monitoring data sets C 9.14 c Training datasets must be independent of test datasets. All sources of potential dependence, including those related to patients, sites, and data acquisition processes, must be identified and addressed to assure independence
S 9.15	Test performance is evaluated on data independent of the training data set according to standard criteria for medical devices and compared to current accepted standard practice C 9.15 a Performance is audited across relevant subgroups to detect and mitigate bias and drift and regularly monitored. Monitoring is proportional to clinical risk and human oversight
S 9.16	Reference standards used to train and validate the model are fit-for-purpose and the source and rationale for their selection, is clearly documented
S 9.17	In addition to the general requirements for software, the laboratory holds specific evidence for AI-enabled software. This includes (but is not limited to): a. how AI contributes to the intended purpose of the device b. a description of the algorithm and model design including information on the training and testing phases of the AI model and how this relates to the intended purpose c. information about the data used for training and testing, including: i. a statistically informed justification for dataset sizes ii. a description of the populations represented in the data, for example, age, gender, and ethnicity iii. a justification for how this data would be generalisable or appropriate for the Australian population and sub-populations for whom the AI is intended to be used, in the context of the relevant Australian clinical practice standard for which the device is used d. reference to relevant independent international consensus standards or guidance, where available, used to structure or support the development and documentation of the AI-enabled software

No.	Standard and commentary
	e. risk management evidence to show how risks have been addressed including AI specific risks such as (but not limited to) overfitting, bias and performance degradation such as data drift f. evidence to show how the device meets requirements for clinical evidence

10. Multivariate index assays

A Multivariate Index Assay (MIA) is an IVD medical device that:

- combines the values of multiple variables using an interpretation function to yield a final, patient-specific result (such as a score or an index etc.) that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, and
- provides a result whose derivation is non-transparent and cannot be independently derived or verified by the end user

In other words, the requesting clinician requires information from the test developer, rather than generally accepted information from the clinical community, to interpret the MIA result for use in patient management.

No.	Standard and commentary
S10.1	Multivariate Index Assays that have not been approved for diagnostic use by the TGA (or are sold as RUO) must be considered an in-house IVD and evaluated in accordance with these Requirements before being used for diagnostic or therapeutic purposes
	C10.1 a In particular, validation, verification and documentation of the algorithm in relation to clinical utility of the assay must be subject to the same level of rigor as other analytical aspects of the assay

11. Monitoring, analysis and improvement

Monitoring the performance of in-house IVDs and the analysis of such monitoring is to ensure that there are processes in place to demonstrate the conformity of the IVD (i.e. its suitability for purpose).

The laboratory should be able to identify and implement any changes necessary to maintain the quality and suitability of the IVD for its intended purpose, and to ensure continued suitability and effectiveness.

No.	Standard and commentary
S11.1	Previously defined and documented performance characteristics of the IVD must be monitored and measured to verify that product requirements have been met
	C11.1 a Where laboratories generate their own in-house quality control material then such material is also an in-house IVD and must be validated as such and must also be included on the TGA in-house IVD notification database
	C11.1 b Where available, laboratories should use well-characterised and standardised control material that is available to a range of laboratories. However, if necessary, laboratories may generate their own quality control material. If so, they must verify stability of such material under the storage and any inter-laboratory transport conditions used
	C11.1 c Where possible, preventive action should be taken to eliminate causes of potential non-conformities to prevent their occurrence, as identified through the risk analysis undertaken during the design phase of the IVD
S11.2	The organisation must establish documented procedures to analyse appropriate data to demonstrate the conformity of the in-house IVD to product specifications
	C11.2 a Data should be sourced from multiple sources such as internal audits, user feedback, nonconformity to internal QC or external quality assurance, and feedback from suppliers on specific reagents or products incorporated into the in-house IVD

12. Adverse events and recalls

The act of reporting information about an adverse event is not an admission of liability for the event or its consequences. Examples of adverse events and requirements are outlined in Table 1.

No.	Standard and commentary	
S12.1	Information about an adverse event resulting from the use of an in-house IVD, must be reported to the laboratory's designated person and to the Therapeutic Goods Administration (TGA) as soon as practicable but within the timeframes specified	
	C12.1 a	Laboratories must have documented procedures for reporting adverse events to the designated person and the TGA
	C12.1 b	Information about an adverse event that presents a serious public health threat, or concern must be reported to the TGA within 48 hours of the laboratory becoming aware of the event
	C12.1 c	Information about an adverse event that led to the death or serious deterioration in the state of health of a patient, a user of the in-house IVD or another person must be reported to the TGA within 10 days of the laboratory becoming aware of the event
	C12.1 d	Information about an adverse event that might lead to the death or serious deterioration in the state of health of a patient, a user of the in-house IVD or another person must be reported to the TGA within 30 days of the laboratory becoming aware of the event
	C12.1 e	Adverse events may arise from malfunction or deterioration in the characteristics or performance of the in-house IVD, inadequacy in the design, production, labelling or instructions for use of the in-house IVD, or use of the in-house IVD that is contrary to the intended use

No.	Standard and commentary	
	C12.1 f	Adverse events that lead to a serious deterioration in the state of health of a patient, a user of the in-house IVD or another person include: i. a life-threatening illness or injury ii. permanent impairment of a body function iii. permanent damage to a body structure iv. a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure
	C12.1 g	Adverse events include 'near misses' that did not result in any harm but might have led to the death or serious deterioration in the health of a patient or user of an in-house IVD on another occasion
	C12.1 h	Reporting of information about adverse events to the TGA should occur through the Medical Device Incident Report Investigation Scheme (IRIS)[8]
	C12.1 i	Reporting of information about adverse patient outcomes to the TGA is not required where the adverse outcome resulted from known limitations in the design of the in-house IVD and the in-house IVD performed within its accepted design parameters[13], for example: i. A false negative result leads to a patient not being treated ii. The analytical sensitivity of the in-house IVD is known to be 95% and is clearly stated in the instructions for use/method iii. The in-house IVD was performing within its design parameters, as evidence by results of positive controls performed with the patient's sample
	C12.1 j	All adverse event reporting procedures must be documented in the quality management system
S12.2 Recalls	A laboratory must report to its designated person and the TGA, information relating to any malfunction or deterioration of a Class 4 in-house IVD, or inadequacy in its design, production, labelling or instructions for use, that has led the laboratory to take steps to recover devices of that kind that have been distributed for use in that laboratory or other laboratories within that laboratory network.	
	C12.2 a	Laboratories must have documented procedures in place for reporting any such recalls for Class 4 in-house IVDs to its designated person and the TGA

[13] Although not initially considered an adverse event that requires reporting to TGA, such incidents must be recorded and monitored by the laboratory (as per S10.2) to ensure the in-house IVD is operating within expected limitations. Multiple incidences may identify a problem with an in-house IVD that subsequently could require reporting to the TGA as an adverse event.

No.	Standard and commentary	
	C12.2 b	Reporting of recalls to the TGA Recalls Unit can be made by mail, fax or email and should be done in accordance with the requirements of Uniform Recall Procedure for Therapeutic Goods (URPTG). Contact information for the Recalls Unit can be found on the Procedure for recalls, product alerts and product corrections (PRAC) | Therapeutic Goods Administration (TGA)[14]

Table 2 - Examples of adverse events and requirements

Adverse event	Requirement
A false negative result associated with the malfunction of an in-house IVD that presents a serious public health threat (e.g. false negative HIV donor screening result due to a malfunction of the in-house IVD).	Report to TGA within 48 hours of the laboratory becoming aware of the event.
A false negative result associated with the deterioration in the performance of an in-house IVD that has led to the death or serious deterioration in the state of health of a patient (e.g. false negative result for bacterial meningitis due to deterioration in the sensitivity of the in-house IVD).	Report to TGA within 10 days of the laboratory becoming aware of the event
A false negative or false positive result associated with an inadequacy in the design or manufacture of an in-house IVD which might lead to the death or serious deterioration in the health of a patient (e.g. incorrect genotype identification due to an inadequacy in the design of the in-house IVD that has resulted in inappropriate patient treatment).	Report to TGA within 30 days of the laboratory becoming aware of the event

[14] Therapeutic Goods Administration. *Procedure for recalls, product alerts and product corrections (PRAC)* [Internet]. Canberra (AU): TGA; 2026 Feb 24 [updated 2026 Feb 24]. Available from: https://www.tga.gov.au/safety/recalls-and-other-market-actions/procedure-recalls-product-alerts-and-product-corrections-prac

13. Documentation

No.	Standard and commentary
S13.1	The laboratory must establish documented procedures for the design, development, production, validation and monitoring of an in-house IVD.

C13.1 a This documentation on method establishment must include where relevant:

i. description of the analytical method

ii. selection criteria for reagents and their source(s)

iii. quality and identity of standards used

iv. description of experiments to determine accuracy, imprecision and any other performance characteristics

v. an estimate of measurement uncertainty

vi. description of stability studies

vii. information on sample processing and storage

viii. summary tables of analytical runs, including any method deviations

ix. any calculations applied to results

x. summary information on QC samples

xi. post-implementation monitoring and improvement

xii. the use of assays for non-validated criteria

xiii. any other relevant information relating to the assay

This documentation on method establishment may include where relevant:

i. criteria for acceptance or rejection of the standard or calibration curve

ii. criteria for acceptance or rejection of QC

No.	Standard and commentary
	iii. criteria for variability of duplicate assays.
C13.1 b	The laboratory must produce a report on method validation that shows the successful completion of appropriate validation studies for the in-house IVD in question. The method-validation report must include: i. summary information ii. method development and establishment iii. risk analysis iv. application of the method to routine sample analysis v. management approval for implementation vi. references vii. other relevant information
C13.1 c	Documentation relating to design, development and validation must be retained for a period of not less than 4 years after cessation of use of the in-house IVD
C13.1 d	The summary should list all method-validation studies, verification and revalidation signed by a Laboratory Director or delegate. Any changes to the method over time, including subsequent revalidation and verification, should be added to the summary report
C13.1 e	Where full validation data is not readily accessible for in-house IVDs produced before the NPAAC Requirements for the Development and Use of In-House IVDs (Second Edition 2007), evidence to support the analytical and clinical performance of an in-house IVD may be provided in the form of ongoing monitoring and surveillance, which may include historical EQA data, QC reports or clinical correlation
C13.1 f	It is recommended that the following data should be added to the validation file over time: i. QC monitoring of sensitivity and specificity ii. uncharacteristic changes to detection limits

Glossary

Term	Definition
Accuracy	The closeness of the agreement between the result of a measurement and a true value of the measurement. If the true value cannot be determined, then an accepted value may be used as a substitute.
Adverse event	An event arising from the use of an IVD medical device that might lead, or might have led, to the death or serious deterioration in the state of health of a patient, a user of the IVD medical device or another person.
Algorithm	A defined set of computational rules used to transform input data into outputs.
Algorithm lockdown (Locked AI model)	A controlled state where an AI model cannot change after deployment except through formal change processes, re-verification, and approval.
Analytical performance	The ability of an IVD to detect or measure an analyte, including sensitivity, specificity, accuracy, precision, and robustness.
Artificial Intelligence (AI)	Software-based systems using computational methods to perform tasks requiring human intelligence (e.g. recognition, prediction, decision support). Includes ML-based IVD systems.
Bias	A systematic, non-random error causing unequal or inaccurate performance across populations or contexts without clinical justification. The laboratory must demonstrate that potential sources of bias are identified, performance is evaluated across subgroups, limitations are documented and communicated, and risks are managed. Elimination is not required, but unrecognised or unjustified bias is not acceptable. Includes data, algorithmic, measurement/label, deployment/workflow, and temporal bias.
Bias	For the purposes of this Standard, addressing bias means that the laboratory must be able to demonstrate that: • potential sources of bias have been identified and considered • performance has been evaluated across relevant subgroups, where applicable • any limitations are documented, justified, and communicated • risks arising from bias are managed within the risk management framework. Elimination of all bias is not required; however, unrecognised, unmanaged, or clinically unjustified bias is not acceptable. Bias may include, but is not limited to: • Data bias When training or test data are not representative of the intended patient population (e.g. under representation of certain age

	groups, ethnicities, disease subtypes, or specimen characteristics). • Algorithmic bias When model design or optimisation disproportionately favours performance for some cases or groups over others without clinical justification. • Measurement or label bias When reference standards, annotations, or outcome labels used for training or validation are inconsistent or inaccurate across subgroups. • Deployment or workflow bias When real world use differs from the conditions under which the model was validated (e.g. different instruments, operators, settings, or pre analytical conditions). • Temporal bias (including drift) When model performance degrades over time due to changes in populations, practices, or data characteristics.
Change management	A controlled process for proposing, approving, implementing, and documenting changes to an in-house IVD, including AI/software updates.
Clinical evidence	All information supporting scientific validity, analytical performance, clinical performance, and clinical utility.
Clinical evidence for an IVD	All the information that supports the scientific validity and performance for its use as intended by the manufacturer.
Clinical performance	The ability of an IVD medical device to yield results that are correlated with a particular clinical condition/physiological state in accordance with the target population and the intended user.
Clinical utility	The usefulness of the results obtained from testing with the IVD medical device and the value of the information to the individual being tested and/or the broader population.
Conformity assessment	A process by an accreditation body to assess the competence of a laboratory against standards for a defined scope.
Continuous (adaptive) learning AI model	An AI model that updates itself after deployment; not covered under this Standard.
Data drift	Changes in data characteristics over time that may reduce AI model performance.
Data governance	Policies and controls ensuring data quality, integrity, privacy, security, and traceability.
Deployment	The release of an IVD or software into routine clinical use.
Imprecision	The dispersion of independent results of measurements obtained under specified conditions. Imprecision is expressed numerically as standard deviation or coefficient of variation. Note: The term ‘imprecision’ is used rather than ‘precision’ because the common measures used, such as standard deviation and coefficient of variation, are in fact measures of imprecision.

In house IVD	An IVD developed/used within a lab or network and not supplied externally.
In vitro diagnostic medical device (IVD)	A device intended for the in vitro examination of specimens derived from the human body, such as blood or tissue, to provide information on physiological or pathological states, health, or disease. (TGA)
In-house IVD	An IVD developed, modified, or used within an Australian laboratory/network (including off-label use) and not supplied outside that network.
In-house IVD	The same as the definition in the Therapeutic Goods (Medical Devices) Regulations 2002. This an IVD medical device that is, within the confines or scope of an Australian laboratory or Australian laboratory network: • developed from first principles; or • developed or modified from a published source; or • developed or modified from any other source; or • used for a purpose, other than the intended purpose assigned by the manufacturer; and • not supplied for use outside that laboratory or laboratory network.
Intended purpose	The use intended by the manufacturer as stated in documentation, instructions for use, advertising, and technical documentation. The defined use of an IVD, including clinical application, population, specimen type, output, and users.
Intended purpose	The same as the definition in the Therapeutic Goods (Medical Devices) Regulations 2002§1 and is the purpose for which the manufacturer of the device intends it to be used, as stated in: • the information provided with the device; or • the instructions for use of the device; or • any advertising material applying to the device; and • technical documentation describing the mechanism of action of the device.
IVD software	Software functioning as an IVD (including standalone or embedded), with or without AI.
Machine learning (ML)	A subset of AI where algorithms learn patterns from data rather than explicit programming.
Medical laboratory network	A group of laboratories under a single Approved Pathology Authority with one quality system, operating across fields or multiple sites.
Medical laboratory network	A network of laboratory organisations that operate under a single Approved Pathology Authority (APA) with a single quality management system for which: • the activities of the network span more than one field of testing or program; or • the network operates at multiple sites within a field or involves a combination of multiple sites and programs.

Method validation	The process of defining an analytical requirement and confirming that the method under consideration has performance capabilities consistent with that requirement.
Method verification	Testing whether manufacturer validation data can be reproduced in the end-user's environment.
Method verification	Procedures to test to what extent the performance data obtained by manufacturers during method validation can be reproduced in the environments of end-users.
Model testing	Evaluating a trained model on independent data to assess performance and limitations.
Model training	The process where an ML model learns from data.
Modified IVD	An IVD used outside its intended purpose or not in accordance with manufacturer instructions, affecting performance and requiring validation.
Monitoring (post-implementation)	Ongoing surveillance of IVD performance, safety, and clinical impact after deployment.
Multivariate Index Assay (MIA)	An IVD medical device that: • combines the values of multiple variables using an interpretation function to yield a final, patient-specific result (such as a score or an index etc.) that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, and • provides a result whose derivation is non-transparent and cannot be independently derived or verified by the end user.
Overfitting	When a model performs well on training data but poorly on new data due to excessive adaptation.
Performance degradation	A decline in accuracy or usefulness over time or under changed conditions.
Quality system (QS)	Framework governing management, processes, resources, and continuous improvement for in-house IVDs.
Risk management	A lifecycle process for identifying, analysing, controlling, and monitoring risks.
Scientific validity	The established association of an analyte with a clinical condition or physiological state.
Software as a Medical Device (SaMD)	Software performing medical functions independently of hardware devices.
Usability	The extent to which an IVD can be used effectively, efficiently, and safely in its intended setting.
Validation (software)	Confirmation that software/AI performs as intended in its clinical context.
Verification (software)	Confirmation that software outputs meet specified development requirements.

Appendices

Appendix A

Essential Principles

Normative

The Essential Principles are set out in Schedule 1 of the *Therapeutic Goods (Medical Devices) Regulations 2002* and provide information about the safety and performance levels required, hazards to be addressed, or issues to be considered when manufacturing medical devices. Readers are encouraged to review the current Regulations from the Federal Register of Legislation noting that the legislation may be subject to amendment from time to time.

Appendix B

Classification rules for IVDs

Normative

The classification rules applicable for IVDs are located in Schedule 2A of the *Therapeutic Goods (Medical Devices) Regulations 2002*, and set out the assigned risk classification for an IVD medical device. Readers are encouraged to review the current Regulations on the Federal Register of Legislation noting that the legislation may be subject to amendment from time to time.

Appendix C

Procedures applying to in-house IVD medical devices

Normative

The conformity assessment procedures in Schedule 3, Part 6A of the *Therapeutic Goods (Medical Devices) Regulations 2002* set out the minimum requirements to be met by laboratories manufacturing Class 1-3 in-house IVDs.

The conformity assessment procedures in Schedule 3, Part 6B of the *Therapeutic Goods (Medical Devices) Regulations 2002* set out the minimum requirements to be met by laboratories manufacturing Class 4 in-house IVDs. Alternatively, if preferred, laboratories that manufacture Class 4 in-house IVD have the choice of applying the conformity assessment procedures set out in Schedule 3, Part 1 of the *Therapeutic Goods (Medical Devices) Regulations 2002* (i.e. same conformity assessment procedures as those for manufacturers of commercially supplied IVDs).

A copy of the current Regulations that may be subject to change from time to time can be accessed from Federal Register of Legislation.

Appendix D

Frequently asked questions and examples for guidance

Informative

The following guidance is provided in response to frequently asked questions relating to in-house IVDs.

If a laboratory makes up its own culture media, are these in-house IVDs?

If a laboratory utilises their own formulation to make microbiological culture media from general laboratory reagents (e.g. dehydrated powders and agar bases) with the intention of using them for a diagnostic purpose, then they are considered Class 1 in-house IVDs.

If a laboratory makes up its own stains, are these in-house IVDs?

If a laboratory utilises their own formulation to make stains, dyes or other staining solutions (e.g. fixatives, decolourising agents) with the intention of using them for a diagnostic purpose, then those stains are considered in-house IVDs.

What are the requirements for validating stains that are prepared in-house?

The validation of staining solutions that have been prepared 'in-house' should consider the following aspects:

- Physical properties of the individual components used as well as the finished product (e.g. pH, ionic concentration, water quality – deionised/filtered).
- Testing of the finished stain using a range of specimens as appropriate to the stain type (tissue sections, organisms, control slides etc).
- The test slides should cover the range of features in tissue or cells that are expected to be seen under routine conditions of use.

When validating the performance of an in-house IVD, what constitutes statistically significance numbers?

Because circumstances can vary so much, even between similar IVDs, it is not possible to specify the minimum numbers of samples required to be tested in any situation, but ideally every effort should be made to make the evaluation of sensitivity and specificity of the assay statistically significant.

Each variable aspect of an assay which *may* have an impact on assay performance should be considered, including (but not limited to):

- The range and number of samples tested should be selected to cover the entire measuring range – i.e., the upper, middle lower concentrations of the target analyte, with consideration given to the upper and lower extremes for quantitative or semi-quantitative assays, or for qualitative assays the limit of detection (i.e., near cut off).
- Samples should be selected from a population range similar to the intended setting of use (adults, elderly, children, neonates, endemic persons (important for some infectious diseases).
- The recommended specimen types (serum, plasma, urine, saliva etc), and storage stability; specimen characterisation should include enough samples to cover likely variants of the target analyte, including different serotypes, sub-types, weakly reacting specimens, or if there is more than one analyte, a number of mixed targets across the selection of specimens tested. If there is difficulty in availability of suitable specimens, every effort should be made to obtain them from alternative sources (other laboratories, commercially sourced specimens, spiked).
- A selection of samples representing similar or commonly cross-reacting clinical conditions or infectious diseases should be included.

What aspects of my in-house assay do I need to validate?

- The classification and intended purpose of the in-house IVD will determine depth of validation required and the aspects to be validated.
- An in-house IVD developed from first principles or developed (or modified) from a published source would require more validation than an in-house IVD based on changes made to a commercially supplied IVD.
- Where a commercially supplied IVD has been modified, validation should focus principally on the effects of that change.
- Factors to be considered include the target analyte of the IVD, whether it is a qualitative or quantitative assay, complexity of methodology, the availability and range of characterised samples, the availability of published (peer-reviewed) articles relating to that IVD or other similar IVDs. Each performance characteristic should be considered (as appropriate) and may include sensitivity and specificity (both analytical and clinical); accuracy (trueness); precision (reproducibility and repeatability); measuring range; linearity; and assay cut-off.

How are assays that are labelled research use only (RUO), including components such as primers or probes to be treated?

- If a laboratory is utilising primers and probes as components for use in an in-house IVD, or if they utilising a RUO marked kit which they intend to use for a diagnostic purpose (i.e. reporting of patient results) then the assay they have developed meets the definition of an in-house IVD and the laboratory is required to validate in accordance with this document.
- The suppliers of kits marked RUO should be aware that under the Therapeutic Goods Act, the definition of a therapeutic good includes *goods that are represented in any way to be, or that are, whether because of the way in which the goods are presented or for any other reason, likely to be taken to be for therapeutic use.*
- Representation for therapeutic use includes verbal or written statements made in relation to products as part of their labelling, advertising or promotion (regardless of the RUO label).

A laboratory performs flow cytometry on blood, bone marrow and tissue samples for the diagnosis of haematological malignancies. There is considerable heterogeneity between these malignancies and therefore the number of permutations for each panel

of antibodies is considerable and is sample dependent. Does each panel of antibodies need to be validated and considered to be an in-house IVD?

- The test should be considered to be an in-house IVD for the identification of the most appropriate immunophenotype to assist with the accurate diagnosis of the malignancy. The in-house IVD may therefore be notified to the TGA as a single test "Immunophenotyping of haematological malignancy" and not as each component (e.g. CD3, CD19 etc). Validation should include the performance of each individual component singly and when used in a cocktail as well as the ability to accurately determine the immunophenotype.

Appendix E

Additional resources for IVD software requirements

IEC 462304:2006 Medical device software – Software life cycle processes[15] and *ISO 13485:2016 Medical devices Quality management systems - Requirements for regulatory purposes* [16]provide information about technical and quality management system requirements applicable to IVD software. These standards (or equivalent) apply to commercial IVD software developers and can be used by laboratories developing in-house IVD software to support compliance with these requirements.

For IVDs enabled by machine learning AI, the IMDRF *'Good Machine Learning Practice for Medical Device Development: Guiding Principles'* and, the TGA web guidance Evidence requirements for software using AI should be implemented.

[15] International Electrotechnical Commission (IEC). *IEC 62304:2006 — Medical device software: Software life cycle processes* [Internet]. Geneva (CH): IEC; 2006 Available (Pay): https://www.iso.org/standard/38421.html

[16] International Organization for Standardization (ISO). *ISO 13485:2016 — Medical devices: Quality management systems — Requirements for regulatory purposes* [Internet]. Geneva (CH): ISO; 2016 Available (Pay): https://www.iso.org/standard/59752.html

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