

NATIONAL PATHOLOGY ACCREDITATION ADVISORY COUNCIL

**REQUIREMENTS FOR LABORATORY
TESTING FOR HUMAN
IMMUNODEFICIENCY VIRUS (HIV)
AND HEPATITIS C VIRUS (HCV)**

(Third Edition 2013)

NPAAC Tier 4 Document

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Requirements for Medical Pathology Services

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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 laboratories and the introduction and maintenance of uniform standards of practice in pathology laboratories throughout Australia. A function of NPAAC is to formulate Standards and initiate and promote education programs about pathology tests.

Publications produced by NPAAC are issued as accreditation material to provide guidance to laboratories and accrediting agencies about minimum Standards considered acceptable for good laboratory practice.

Failure to meet these minimum Standards may pose a risk to public health and patient safety.

Scope

The *Requirements for Laboratory Testing for Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV)* is a Tier 4 NPAAC document and must be read in conjunction with the Tier 2 document *Requirements for Medical Pathology Services*. The latter is the overarching document broadly outlining standards for good medical pathology practice where the primary consideration is patient welfare, and where the needs and expectations of patients, Laboratory staff and referrers (both for pathology requests and inter-Laboratory referrals) are safely and satisfactorily met in a timely manner.

Whilst there must be adherence to all the Requirements in the Tier 2 document, reference to specific Standards in that document are provided for assistance under the headings in this document.

The *Requirements for Laboratory Testing for Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV)* sets the minimum Standards for good pathology practice in Australia for testing for HIV and HCV. This document applies to Australian pathology Laboratories testing for HIV and HCV. Additional requirements may exist for Laboratories that test under the conditions of a licence to the Code of Good Manufacturing Practice (GMP) for Human Blood and Tissues issued by the Therapeutic Goods Administration (TGA). These Requirements do not attempt to incorporate requirements for GMP licensure.

The Requirements, in broad principle, apply to the use of all types of HIV and HCV assays including immunoassays used for diagnosis and confirmatory testing (e.g. western blot), qualitative nucleic acid testing, quantitative nucleic acid testing, genotyping and resistance testing.

Abbreviations

ARTG	Australian Register of Therapeutic Goods
AS	Australian Standard
bDNA	Branch Chain DNA test
GMP	Good Manufacturing Practice
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ISO	International Organization for Standardization
IVD	In Vitro Diagnostic Medical Device
MBS	Medicare Benefits Schedule
NAT	Nucleic Acid Testing
NATA	National Association of Testing Authorities, Australia
NHMRC	National Health and Medical Research Council
NPAAC	National Pathology Accreditation Advisory Council
NRL	National Serology Reference Laboratory, Australia
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
QMS	Quality Management System
RCPA QAP	Royal College of Pathologists of Australasia Quality Assurance Programs
TGA	Therapeutic Goods Administration

Definitions

Confirmatory Testing	<p>means -</p> <ol style="list-style-type: none"> 1. A procedure performed to verify the truth or validity of something thought to be true or valid. 2. Testing performed to assure that a result achieved is the correct result or is the final test performed to achieve the true diagnosis.
Diagnostic test/assay	<p>means a measurement or examination of a diagnostic Specimen for the purpose of diagnosis, prevention, or assessing treatment of any disease or the assessment of health or impairment of health of an individual patient.</p> <p>NOTE: Laboratory tests are often called "in vitro diagnostic tests."</p>
Management test/assay	<p>means a test to guide the selection of treatment or to monitor treatment/s in subjects known to have the disease.</p>
Nucleic Acid Testing	<p>means Nucleic Acid Tests such as target amplification, polymerase chain reaction (PCR), signal amplification, Branch Chain DNA (bDNA) assay and DNA sequencing are testing methods for the detection and/or characterisation of DNA and RNA.</p>
Post exposure prophylaxis	<p>means a treatment that is designed to protect an individual against a disease agent to which the individual has been recently exposed.</p>
Standard Testing	<p>means the standard or most common examination performed in the Laboratory for a particular area of testing. This examination will most often be the most frequently performed examination for a particular testing area and will consequently generate the highest volume in that testing area.</p>
Reference measurement procedure	<p>means a thoroughly investigated measurement procedure, described in detail in a written document, shown to yield values having a measurement uncertainty commensurate with its intended use, especially in assessing the trueness of other measurement procedures for the same quantity and in characterising reference materials.</p>
Reference procedure	<p>means a procedure with established high quality of results, which can be used for assessment of other procedures i.e. a procedure of testing, measurement or analysis, thoroughly characterised and proven to be under control, intended for:</p> <ol style="list-style-type: none"> (a) quality assessment of other procedures for comparable tasks; or (b) characterisation of reference materials including reference objects; or (c) determination of reference values.

	<p>The uncertainty of the results of a reference procedure must be adequately estimated and appropriate for the intended use.</p> <p>The term "reference procedure" applies to testing, measurement and analysis, i.e. all procedures for determining characteristics of materials, products and processes. These characteristics can be of quantitative or qualitative kind, and they can be defined independently or by the procedure itself.</p> <p>Reference procedures are used to validate other procedures, to characterise reference materials or reference objects as well as for determining reference values of materials characteristics. Another application field is testing, measurement or analysis as a basis for important decisions, e.g. for authoritative evidence.</p> <p>The definition of a "reference procedure" presumes the existence of several procedures for a specified task or of different realisations of the same methodology. Given this, a reference procedure is qualified by the uncertainty of results, proven to be fit for an agreed purpose. Moreover, it has to be accepted as such by the relevant target groups.</p> <p>In the case of quantitative results the uncertainty comprises trueness and precision combined in the sense of measurement uncertainty [1]. In the case of qualitative results the uncertainty is an estimate of the probability of erroneous results. Where possible the assessment of uncertainty includes traceability to the International System of Units (SI) or to other recognised reference systems.</p>
Reference testing	<p>means a thoroughly investigated test, described in detail in a written document, shown to yield results having an uncertainty commensurate with its intended use, especially in assessing the trueness of other tests for the same analyte and in characterising Specimens containing that analyte.</p>

Requirements for Medical Pathology Services (RMPS)	<p>means the overarching document broadly outlining standards for good medical pathology practice where the primary consideration is patient welfare, and where the needs and expectations of patients, Laboratory staff and referrers (both for pathology requests and inter-Laboratory referrals) are safely and satisfactorily met in a timely manner.</p> <p>The standard headings are set out below –</p> <p>Standard 1 – Ethical Practice Standard 2 – Governance Standard 3 – Quality Management Standard 4 – Personnel Standard 5 – Facilities and Equipment A – Premises B – Equipment Standard 6 – Request-Test-Report Cycle A – Pre-Analytical B – Analytical C – Post-Analytical Standard 7 – Quality Assurance</p>
Screening test/assay	<p>means –</p> <ol style="list-style-type: none"> 1. a test to systematically detect the presence or absence of a drug or a substance <p>NOTE: Screening is generally a qualitative procedure and results are described as reactive or nonreactive depending on whether they are greater or less than a designated cut-off value. Nonreactive results can be reported as “antibody negative”</p> <ol style="list-style-type: none"> 2. a test to systematically identify individuals at sufficiently high risk of a specific disorder to benefit from further investigation or direct preventive action, among persons who have not sought medical attention on account of symptoms of that disorder 3. a test given to defined populations (e.g. newborns) to detect increased risk of a specific condition 4. a method used to evaluate large populations of individuals for the presence of a disease or analyte 5. testing of asymptomatic subjects 6. checking for disease when there are no symptoms.
Supplemental testing	<p>means any examination other than the standard testing procedure(s) performed in a given testing area to increase the accuracy of diagnosis (or status).</p>
Window period	<p>means the period (following infection) when tests in use do not identify the infection is present.</p>

Introduction

Requirements for Laboratory Testing for Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) is the Tier 4 NPAAC document that sets the minimum standards for good pathology practice in Australia for testing for HIV and HCV. Assays for these viruses are registrable under the *Therapeutic Goods Act (1989)* and are therefore subject to pre- and post-market monitoring to assure their ongoing safety and performance. These Requirements recognise that principles and processes involved in using these assays reflect those for other pathology tests but the considerable public health significance of the results warrants greater attention and may need the provision of additional information to doctors and their patients and the facilitation of surveillance activities. The implementation of these Requirements is necessary to avoid public health risks.

The purpose of this document is to assist medical and scientific Laboratory professionals in finding relevant information and to reduce the need for constant cross referencing of other documents.

These Requirements are intended to serve as minimum standards in the accreditation process and have been developed with reference to current and proposed Australian regulations and other standards from the International Organization for Standardization including:

AS ISO 15189 *Medical laboratories – Requirements for quality and competence*

These Requirements should be read within the national pathology accreditation framework including the current versions of the following NPAAC documents:

Tier 2 Document

- *Requirements for Medical Pathology Services*

All Tier 3 Documents

Tier 4 Document

- *Requirements for the Medical Testing of Human Nucleic Acids*

In addition to these Standards, Laboratories must comply with all relevant state and territory legislation (including any reporting requirements).

These Requirements are written as specific principles and are designed to serve without alteration until the next revision date. The following principles cover the entire document:

- Laboratories must be able to demonstrate continued compliance with NPAAC Standards in their assessment history.
- Failure to meet these minimum Standards poses a potential risk to public health and patient safety.

In each section of this document, points deemed important for practice are identified as either ‘Standards’ or ‘Commentaries’.

- A Standard is the minimum requirement for a procedure, method, staffing resource or facility that is required before a Laboratory can attain accreditation – Standards are printed in bold type and prefaced with an ‘S’ (e.g. **S2.2**). The use of the word ‘**must**’ in each Standard within this document indicates a mandatory requirement for pathology practice.
- A Commentary is provided to give clarification to the Standards as well as to provide examples and guidance on interpretation. Commentaries are prefaced with a ‘C’ (e.g. C1.2) and are placed where they add the most value. Commentaries may be normative or informative depending on both the content and the context of whether they are associated with a Standard or not. Note that when comments are expanding on a Standard or referring to other legislation, they assume the same status and importance as the Standards to which they are attached. Where a Commentary contains the word ‘**must**’ then that Commentary is considered to be **normative**.

Please note that Appendix A is **normative** and should be considered to be an integral part of this document.

Please note that all NPAAC documents can be accessed at www.health.gov.au/internet/main/publishing.nsf/Content/health-npaac-publication.htm

While this document is for use in the accreditation process, comments from users would be appreciated and can be directed to:

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1. Laboratory ethics

(Refer to Standard 1 in *Requirements for Medical Pathology Services*)

2. Quality management system

(Refer to Standard 3 in *Requirements for Medical Pathology Services*)

3. Staffing, supervision and consultation

(Refer to Standard 3 and Standard 4 in *Requirements for Medical Pathology Services*)

S3.1 The staff must have an understanding of the regulatory framework for HIV and HCV test kits and mechanisms for reporting problems with those kits.

4. Facilities

(Refer to Standard 5 in *Requirements for Medical Pathology Services*)

S4.1 Storage and handling of HIV/HCV Specimens must minimise the risk of cross-contamination of Specimens.

S4.2 The level of security in the Laboratory must ensure the confidentiality of HIV/HCV results.

5. Pre-analytical phase

(Refer to Standard 1 and Standard 6A in *Requirements for Medical Pathology Services*)

Tests for HIV and HCV are conducted with the aim of making a diagnosis for the purpose of treatment, patient management or are supported as routine public health measures by a jurisdictional department of health (e.g. sexual health screening). These tests require verbal consent of the individual being tested (or their legal guardian). Obtaining appropriate consent is the responsibility of the health care practitioner requesting the test, and does not require specific pre-test discussion with pathology personnel.

S5.1 Where tests are undertaken at the request of a third party (e.g. life insurance or visa applications) rather than for screening of a person at risk, the Laboratory must ensure that the individual being tested or a third party requester has nominated a medical practitioner who will take responsibility for receiving the result in the case of a reactive result.

C5.1(i) Jurisdictions may have individual legal requirements for emergency situations regarding the management of collection of pathology Specimens from a patient unable to provide consent. When the request form indicates the reason for referral is a result of a biohazard injury, Laboratories must have a policy in place for automated or cascading (sequential testing based on preceding results) reflex testing associated with biohazard injury that includes the following:

- permission from the source individual and exposed individual (this involves a combined policy with the infection control committee of a recognised hospital/health centre [or equivalent] or direct liaison with the referring medical practitioner)
- identification of the appropriate individual/medical practitioner to advise of results.

C5.1(ii) In emergency situations patient consent may not be possible to obtain (e.g. if a person were unconscious). In such circumstances, a medical practitioner acting as an “agent of necessity” should arrange for any test which is clinically relevant.

S5.2 The primary Specimen collection manual used by the Laboratory and/or Specimen reception must include instructions for the use and production of patient identifiers used in the processing of Specimens in a coded manner. This document must be part of the document control system.

C5.2(i) The request form **must** contain unique identifiers for the individual being tested, whether this is a combination of the individual’s name, date of birth, a unique code or other unique identifier. It will allow identification of the individual being tested to the medical practitioner originating the request. The Laboratory **must** ensure that it has sufficient information to link the Specimen and request form accurately.

- C5.2(ii) To ensure that patients and their Specimens are correctly identified, three unique identifiers should be provided where possible.
- C5.2(iii) It is the right of any patient to request deidentified testing for HIV status. In the pre-analytical phase, discussion about the need for testing should constitute implicit consent. Importantly, at the time of Specimen collection, pathologists recognise the right of the patient to refuse the collection of the Specimen unless the patient is subject to a legal directive requiring the Specimen to be collected.
- C5.2(iv) 'Code books' that contain the patient's true identity and their 'coded' identity are not the responsibility of medical Laboratories.
- C5.2(v) NPAAC acknowledges that the issue of HIV and HCV pre-test discussion with patients is outlined in the relevant policy document and notes that discussion requirements are unable to be addressed by the staff of medical Laboratories.

6. Analytical phase

(Refer to Standard 6B in *Requirements for Medical Pathology Services*)

S6.1 Only methods included or registered on the ARTG must be used.

C6.1 An updated list of test kits registered/included on the ARTG is available from the TGA website*.

S6.2 Confirmation of reactive results must be carried out as specified in the National HIV and HCV Testing Policies.

C6.2(i) Procedures **must** be in place to confirm initially reactive and repeat reactive screening results.

C6.2(ii) Test kits for HIV and HCV are evaluated prior to registration by the TGA and their ongoing performance is assessed during their use. The TGA's review of these kits includes the assignment of a testing status based on a combination of the assay's stated intended purpose and the outcomes of performance testing. This status is either as a standard test or as a reference test for diagnostic purposes.

C6.2(iii) Algorithms for the use of supplemental or follow-up testing methods should be based in knowledge of their antigenic composition along with that of the screening assay. Standard text should be developed to accompany an HCV antibody positive PCR negative result and HCV antibody positive PCR positive result.

C6.2(iv) Seroconversion and window periods:

- Anti-HIV tests are presently available as third and fourth generation tests. Fourth generation tests include the facility to identify both antigen and antibody
- The window period or time between infection and when a test's target analyte(s) can first be detected, varies from test to test. The window period for third and fourth generation anti-HIV tests is 3-5 weeks after infection. For qualitative NAT the window period is approximately 2 weeks.
- For anti-HCV tests the window period is 9-11 weeks. For combination tests the window period is approximately 6 weeks and for qualitative NAT the average is 3 weeks.
- If an individual is suspected to be at risk for seroconversion and the first test result is negative or equivocal, a reporting comment should be included suggesting testing should be performed again on a Specimen drawn 1-2 weeks following the first Specimen for HIV and after 3-12 weeks for HCV depending on when the exposure occurred

* <http://tga.gov.au/docs/html/artg.htm>

relative to the first test. If there is no change, testing should be performed again at 12 weeks after the exposure for HIV and in approximately 24 weeks for HCV where the chance of conversion is 3 SD outside the mean seroconversion time (or the chance of seroconversion is less than 1%).

7. Post-analytical phase

(Refer to Standard 6C in *Requirements for Medical Pathology Services*)

S7.1 There must be no written reports of reactive or equivocal screening results for HIV or HCV issued until supplemental test results are available.

C7.1(i) When HIV antibody test results are reactive or equivocal in an individual for the first time, the Laboratory should undertake confirmatory testing to confirm or resolve the result. The responsible referring medical practitioner must be contacted by telephone, at an appropriate time, to discuss the results. (Note: in some jurisdictions, medical boards have stipulated communication must be between medical practitioners). There should also be an arrangement between referring and referral Laboratories to ensure the referring medical practitioner can be contacted to discuss HIV results that are reactive or equivocal.

C7.1(ii) The event of a Specimen being confirmed positive should trigger provision to the requesting doctor information about the result, further information and/or referral information for the patient.

S7.2 Final validation of a reactive or equivocal result must be by the specialist pathologist or senior scientist.

C7.2 Laboratory Directors should have available the means to control access to HIV results through written policies.

8. Health and safety

(Refer to Standard 3 and Standard 4 in *Requirements for Medical Pathology Services*)

9. Audit and assessment

(Refer to Standard 7 in *Requirements for Medical Pathology Services*)

10. Requirements for Laboratories providing reference testing

(Refer to Standard 4 and Standard 7 in *Requirements for Medical Pathology Services*)

S10.1 The supervising pathologists and scientific staff must have extensive experience in the diagnostic testing for HIV and HCV, and must maintain their knowledge and expertise in the relevant areas of specialised testing.

- C10.1(i) The pathologists, pathologist trainees and experienced scientific staff **must** provide expert advice on test interpretation, and be able to directly assist with patient counselling and further patient management, or be able to provide information on suitable referral services.
- C10.1(ii) Laboratories conducting reference testing should include Nucleic Acid Testing (NAT) as part of their testing for corroboration of difficult diagnostic assessments. Nucleic acid tests such as PCR are not validated for formal confirmation of a diagnosis of HIV infection. However, they are useful supplementary tests to assist in diagnosis.
- C10.1(iii) Reference tests are used by Laboratories to conduct supplemental and/or confirmatory testing for HIV and HCV. Reference testing is performed in facilities that provide higher level testing for HCV and HIV that is sufficient to provide final determinations on the status of individual patients as being positive, negative or indeterminate. This is achieved by using test kits designated as reference tests. Laboratories may provide both reference and non-reference level testing services and would be expected to be accredited by the independent accrediting body/bodies (e.g. NATA/RCPA). Where these Laboratories provide such tests for other Laboratories they are known as Reference Laboratories.

Appendix A (Normative)

Standards that apply to the Analytical phase testing (Section 6) equally apply to supplemental and confirmatory testing.

In line with test-kit manufacturer's directions, the Australian HIV and HCV Testing Policies and the recommendations of many regulatory agencies, a single reactive test for HIV or HCV should not be reported unless the result is confirmed. Suggested approaches for confirmatory testing are given in the Australian HIV and HCV Testing Policies. The principles of testing in the policies, in précis, include:

- Exposure to HIV or HCV is determined by testing for antibodies in serum or plasma
- A Specimen not reactive in the screening immunoassay can be generally regarded as negative and requires no further testing in the absence of specific risk behaviour
- A Specimen reactive in the screening immunoassay **must** be subject to a minimum of one alternative supplemental immunoassay to confirm the result in the case of HCV testing strategies and to western blot in an HIV testing strategy
- A Specimen reactive in two immunoassays with different antigen specificity can be reported as anti-HCV positive
- A Specimen fulfilling criteria for a positive western blot may be considered and reported as anti-HIV positive
- A Specimen positive on HIV immuno assay that fulfils the criteria for a positive western blot may be considered and reported as anti-HIV positive.

In general, assays for supplemental testing algorithms should be selected so that:

- Testing with a second immunoassay **must** be conducted with a test that uses antigen combinations that differ from those used in the first assay
- If second line antibody testing is equivocal or discordant, a qualitative test for presence of specific antigen or nucleic acid may be included
- Many assays now include HIV antibody and HIV antigen testing in procedure. In these tests the antibody and qualitative test presence for a specific antigen are performed simultaneously.

Western and other immuno-blots **must** be:

- Carried out according to Standards cited in Section 6
- Interpreted against validated interpretation criteria
- Conducted with sufficient frequency to maintain proficiency.

All the above assays **must** be conducted frequently and such proficiency evaluated by Australian assessment bodies ie. NATA and TGA.

Bibliography

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Further information

Other NPAAC documents are available from:

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