National Hepatitis C Testing Policy

Hepatitis C Subcommittee of the
Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis

and the

Blood Borne Virus and STIs Subcommittee of the
Australian Population Health Development Principal Committee

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Disclaimer

This Testing Policy has been developed as a concise source of standardised currently available information to assist government, health professionals, industry, people living with hepatitis C, and the community in general, about matters associated with hepatitis C testing. The diagnosis and treatment of medical conditions such as hepatitis C require the consideration of an individual's particular circumstances by a qualified medical practitioner. This Testing Policy is not a substitute for medical advice, and should not be used to diagnose or prescribe treatment for any condition.

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Contents

Executive Summary

In discussing hepatitis C testing in this policy a number of tests conducted at different times or together are described. These tests indicate whether an individual has come into contact with the hepatitis C virus (HCV), and if they have, whether they have cleared the virus (spontaneously or with previous interventions) or are chronically infected.

It is crucial, therefore that those people responsible for implementing the policy, particularly those performing pre-test and post-test discussions, have the skills and knowledge to fully communicate the significance of each of the tests available.

Principles of hepatitis C testing

The seven basic principles that guide hepatitis C testing in Australia are that:

- confidential, voluntary testing with informed consent and pre-test and post-discussion is fundamental to Australia's response to hepatitis C;
- testing is of the highest possible standard;
- testing is of benefit to the person being tested;
- testing is accessible to all those at risk of HCV infection;
- testing is critical to understanding the epidemiology of HCV infection in the community;
- testing can be critical to interruption of transmission and can support harm minimisation; and
- testing to monitor people with HCV before, during or after treatment is an integral part of their care.

Key points

Indications for hepatitis C testing

- Testing for hepatitis C provides considerable useful information for the individual, through engagement with the healthcare worker and at a population health level.
- There are benefits associated with testing which can outweigh the risks provided that the hepatitis C testing principles are followed.
- Testing is indicated for individuals with clinical or biochemical evidence of liver disease and/or the extrahepatic manifestations of HCV infection.
- Testing is indicated for individuals who have been exposed to risk factors associated with transmission of HCV most importantly injecting drug use and imprisonment.
- In the presence of other factors that confer a lesser risk of infection the indication for testing is decided on a case-by-case basis.

Transmission and infection control in healthcare settings

- Hepatitis C testing of health care workers should be conducted in accordance with the general principles set out in this document with regard to privacy, confidentiality and access to appropriate health care and support services.
- Hepatitis C testing of all health care workers is not recommended.
- Health care workers who perform exposure prone procedures (EPPs) must undergo hepatitis C testing so that they are aware of their HCV status.
- Health care workers who test positive for HCV RNA must not perform EPPs.
- Testing should be considered for health care workers following occupational exposure to blood or body substances, for example through needlestick injury.

Aboriginal and Torres Strait Islanders

- Strategies to improve access to testing need to be developed locally and reflect local HCV transmission routes, risk practices and patterns of health service use.
- Local pre-test and post-test discussion guidelines should take into account local issues of stigma and shame.
- Fear of breaches of patient confidentiality may be reduced through the development and publication of local confidentiality policies and the use of short-incubation tests as appropriate.
- Specific State and Territory and regional initiatives are needed to improve access to confidential testing and continuity of care for Aboriginal and Torres Strait Islander people moving through the corrections system.

Surveillance and research

- Systematic surveillance of newly diagnosed cases of HCV infection is a key component of the Australian response to the HCV epidemic.
- The results of anti-HCV antibody testing have been used to analyse hepatitis C prevalence and incidence, including the results of hepatitis C testing carried out at sentinel sites and for the annual Needle and Syringe Program (NSP) Survey.

Access to diagnostic testing

- Testing should be accessible to all who are or have been at risk of infection.
- A number of tests are required to determine the meaning of a positive antibody test as no single screening test is specific enough to inform clinical decisions.
- There are a range of barriers that may impact on access to hepatitis C testing by people who inject drugs, people from culturally and linguistically diverse backgrounds, Aboriginal and Torres Strait Islander peoples, people in custodial settings and people who live in rural and remote areas.

Pre-test and post-test discussions

- The terms ‘pre-test and post-test discussion’ are used in place of ‘hepatitis C test discussion and post-test counselling’.
- The healthcare worker delivering the test result should use their best judgement in establishing the most appropriate way to communicate the test result. Factors to

consider include the person's testing history, gender, cultural beliefs and practices, behaviour, ongoing risk, understanding of hepatitis C, language and literacy level.
- Pre-test and post-test discussions form an integral part of hepatitis C testing. Provision of information and support associated with testing is consistent with the goal of the second National Hepatitis C Strategy, which includes minimising the personal and social impacts of hepatitis C infection.
- Home based tests are not approved in Australia, and home-based testing is not supported.
- Test results should be given in person, wherever possible.

Diagnostic strategies for hepatitis C

- Past exposure to HCV is determined by testing for HCV antibodies (anti-HCV) in serum or plasma.
- A sample not reactive in the screening immunoassay can be generally regarded as anti-HCV negative.
- A sample reactive in the screening immunoassay should be subject to a minimum of one alternative supplemental immunoassay to confirm the result.
- A sample strongly reactive in two complementary immunoassays can be reported as positive.
- Current HCV infection is usually determined by qualitative testing for HCV RNA.
- Qualitative HCV RNA testing should be a standard component of the diagnostic work-up of all anti-HCV positive individuals.
- The major role of HCV genotype and viral load testing is in guiding treatment dose and duration.
- It is routine to perform a number of tests to determine the meaning of a positive antibody test as no single screening test provides enough information to inform clinical decisions

Quality assuring HCV testing

- The Therapeutic Goods Administration (TGA) has regulatory responsibility for in-vitro diagnostic devices (IVDs) ie pathology assays. The *Therapeutic Goods Act 1989* provides a national framework to ensure the safety, quality and performance of these therapeutic goods. Only assays that are registered by the TGA may be used for testing for HCV.
- In accordance with the conditions applied by the TGA to the registration of HCV assays, sponsors may only supply HCV IVDs to laboratories that participate in quality assurance programs prescribed by the TGA.
- Laboratories that perform hepatitis C testing must meet National Pathology Accreditation Advisory Council (NPAAC) standards, and have current National Association of Testing Authorities/Royal College of Pathologists Australasia (NATA/RCPA) Medical Testing accreditation that includes hepatitis C testing in the scope of the accreditation.

Funding of hepatitis C testing

- There is a Medicare Benefits Schedule (MBS) rebate for anti-HCV antibody testing.
- There is a MBS rebate for qualitative and quantitative nucleic acid testing and genotype testing.

- Some States and Territories provide free and de-identified hepatitis C testing when used to inform treatment or clinically indicated.

Introduction

Background and Context

Hepatitis C is a major public health problem in Australia. Since testing began in 1990, it is estimated that over 250,000 people have been exposed to hepatitis C virus (HCV) and that there are approximately 9,600 new infections each year. Infection persists in at least 65-85% of those infected. Cirrhosis develops within 20 years for 5-10% of this group and a further 10-15% after 40 years. Hepatocellular carcinoma will develop in 3-5% per anum of people who develop cirrhosis. Preventive and therapeutic interventions have proven effective in decreasing HCV transmission and improving quality of life and clinical outcomes for people with hepatitis C.

In 2003, the Commonwealth Department of Health and Ageing released the National Hepatitis C Testing Policy. The Hepatitis Sub-committee of the Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis (MACASHH) and the former Intergovernmental Committee on AIDS, Hepatitis and Related Diseases[1] (IGCAHRD) commissioned the development of this second Hepatitis C Testing Policy in 2006. The process was overseen by the National Hepatitis C Testing Policy Steering Committee. The members of the National Hepatitis C Testing Policy Steering Committee are listed in Appendix 1.

While the primary focus of this policy is diagnostic testing for hepatitis C, it also provides a framework for testing to monitor the clinical condition of people before, during and after treatment for hepatitis C and for screening the blood supply. This technical policy document is for the use of Commonwealth, State and Territory health authorities; members of professional bodies; members of the medical technology industry; health care professionals; members of community organisations; and people living with hepatitis C.

People who are most at risk of contracting hepatitis C due to certain behaviours, practices or settings are often the most marginalised groups within the community. General practitioners and other health care workers have an active and important role to play in reducing and responding to discrimination and isolation and have a primary responsibility to provide high quality and informed non-judgemental care and self-protection.

[1] The subcommittees of the Australian Health Ministers Advisory Committee were restructured in mid-2006 with the Intergovernmental Committee on AIDS, Hepatitis and Related Diseases being replaced by the Blood Borne Virus and STIs Subcommittee (BBVSS) of the Australian Population Health Development Principal Committee.

Steering Group – Terms of Reference

- To examine and provide recommendations to the relevant MACASHH subcommittees and BBVSS on elements of the current National Hepatitis C Testing Policy which require revision.

- Consult with key stakeholder groups on issues to be included in the review of the National Hepatitis C Testing Policy.

- To provide advice and input to the revised National Hepatitis C Testing Policy.

- To identify relevant issues which have emerged since the release of the National Hepatitis C Testing Policy in 2003 and provide advice on how best to incorporate these into the revised policy.

Consultation

This policy was sent to stakeholders (refer Appendix 2) for consultation. All comments received were considered by the Steering Group and drafts adjusted accordingly.

1 Guiding principles for hepatitis C testing

1.1 The guiding principles

The eight key principles that guide hepatitis C testing in Australia are:

- confidential, voluntary testing with informed consent and pre-test and post-test discussion is fundamental to Australia's response to hepatitis C;
- testing is of the highest possible standard;
- testing is of benefit to the person being tested;
- testing is accessible to all those at risk of HCV infection;
- testing is critical to understanding the epidemiology of HCV infection in the community;
- testing can be critical to interruption of transmission and can support harm minimisation; and
- testing to monitor people with hepatitis C before, during and after treatment is an integral part of their care.

1.2 Specific issues concerned with the application of the principles

There are consequences that follow from the development and implementation of a national testing policy. These are set out briefly below, further discussion of the guiding principles is found in Appendix 3.

Testing policy and consequent practices must comply with all relevant Australian Government and State and Territory anti-discrimination legislation, public health, and other relevant laws.

The testing policy is supported by congruent, local jurisdictional policies. These local policies foster the implementation of the national policy. For example, individual, community and professional education and support are fundamental to high quality and ethical testing for hepatitis C; this is provided at a State and Territory service level. Free and anonymous testing for hepatitis C, that does not require identification or a Medicare number, continues to be offered by some State and Territory funded health services.

Anonymous, de-linked testing occurs under circumstances that are scientifically justified and generate a positive public outcome. Such testing proposals should be assessed and agreed to by ethics committees constituted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research.

Testing does not diminish the need for standard precautions in handling blood, body fluids, tissues and organs in all health care settings. The Australian Government Department of Health and Ageing's *Infection Control Guidelines for the prevention of*

transmission of infectious diseases in the health care setting (2004)[2] sets out the key elements of standard precautions.

Mandatory or compulsory testing for hepatitis C is appropriate in certain rare circumstances (see Appendix 3). All testing whether it is voluntary, compulsory or mandatory, should all be accompanied by appropriate pre-test and post-test discussion.

[2] Department of Health and Ageing. *Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting.* Commonwealth of Australia, Department of Health and Ageing. Canberra 2004.

2 Indications for hepatitis C testing

Key points

- Testing for hepatitis C provides considerable useful information for the individual, through engagement with the healthcare worker and at a population health level.
- The benefits associated with testing outweigh the risks provided the hepatitis C testing principles are followed.
- Testing is indicated for individuals who have been exposed to risk factors associated with transmission of hepatitis C or for individuals with clinical or biochemical evidence of liver disease and/or the extrahepatic manifestations of hepatitis C.

2.1 The benefits and risks of diagnostic testing

Individuals are offered hepatitis C testing on the basis of their clinical condition or risk factors for exposure. There are advantages and disadvantages of testing at individual and population levels.

The benefits

- The testing process provides patients with information about hepatitis C, consequences of diagnosis and strategies to prevent transmission of HCV to or from others.

- Testing allows people to determine their hepatitis C status, whether positive or negative and, with the appropriate services and support, to be able to respond accordingly.

- A person given a diagnosis of hepatitis C can access information and support as well as treatments that offer improved health and an increasingly better chance of cure. People diagnosed with hepatitis C are also often able to cope better with the symptoms and illness of hepatitis C by improving their general physical health.

- Monitoring of testing, at the population level, provides the basis for an understanding of the changes in the rates of hepatitis C infection and distribution which, in turn, influences the planning of hepatitis C prevention and control programs (see Chapter 5: Surveillance and Research).

The risks

- As with any diagnostic test, there is a risk of false positive results; the chance of a false positive result may be higher than a true positive result in low risk groups such as pregnant women

- False negative results are rare but occur either due to technical problems, before seroconversion, or when samples are mishandled.

- People seeking testing for, or diagnosed with, hepatitis C may encounter discrimination from fears of transmission and/or assumptions of current or past drug use. This may place the person at risk of social isolation.

- A diagnosis of hepatitis C can be accompanied by feelings of fear, sadness, worry and regret, anger or disbelief.

- Access to appropriate treatment and support services may be difficult. Some people who have tested positive, feel anxious if they are unable to readily access treatment.

- In people who have tested positive, anxiety levels may be heightened by no, or inappropriate, pre-test and post-test discussion or inadequate support from healthcare services, family or friends.

Maximising the benefits and minimising the risks

Individuals who are well informed about hepatitis C and the consequences of testing are best able to assess the benefits and risks to themselves. Non-judgemental attitudes, harm reduction discussions, health promotion, pre-test and post-test discussion, provision of information and support, and ongoing health monitoring increase the likelihood of overall benefits from hepatitis C testing (see Chapter 7). In addition, taking account of the individual's social and cultural needs (eg using interpreters) will increase the benefits of hepatitis C testing, irrespective of the test result.

2.2 Risk assessment and indications for testing

Risk assessment involves an understanding of the relationship between (past or present) risk factors and hepatitis C transmission. Knowledge of the prevalence of risk factors and the epidemiology of hepatitis C in Australia and overseas is valuable in targeting individuals, who may have been exposed to the infection, for testing.

Testing should not be conducted without a full assessment of the relative risks and benefits. When routine testing is done as a matter of course to simply make a diagnosis - the benefits will be limited. However in some cases a person may request testing, but not wish to disclose the reason for seeking the test.

People who have ever injected drugs

In Australia, approximately 80% of current infections and 90% of new infections have been caused by sharing of injecting equipment contaminated with hepatitis C infected blood or other forms of infected blood exposure within the injecting environment. Therefore, any history of injecting, however long ago, is a very strong indication to offer testing. Individuals who have injected drugs only once, without taking precautions to prevent infection are at low but real risk of infection.

People who are or have ever been incarcerated

Imprisonment has been shown to be an independent risk factor for hepatitis C transmission. Hepatitis C prevalence for all prisoners is estimated at 30-40% and higher for women. While a history of incarceration is a very strong indication to offer testing, hepatitis C testing in prisons should be based on risk assessments

The document *Hepatitis C Prevention, Treatment and Care: Guidelines for Australian Custodial Settings* (which will be available on the Department of Health and Ageing Web Site once it is completed), provides further guidance on testing in prisons.

Recipients of organs, tissues, blood or blood products before February 1990 in Australia, or at any time overseas

Hepatitis C is very efficiently transmitted by transfused blood or blood products. Infections acquired in this way account for 5-10% of all cases. Recipients in Australia who were transfused before hepatitis C testing commenced in February 1990 are offered tests, as are individuals who received transfusions overseas. All organs and organ donors are screened for HCV at the time a donation is made to ensure that an appropriate donation is carried out which reduces the risk of infection or complications for the recipient.

People with tattoos or skin piercings

Skin penetration practices are not independent risk factors for hepatitis C transmission. The indications to test will include a consideration of other factors that may contribute to increased transmission such as population prevalence or poor infection control procedures, e.g. tattooing and skin piercings which were carried out in some overseas countries. The risks associated with high prevalence and poor infection control procedures are also much higher if the tattoo or piercing was carried out in a custodial setting.

People born in countries with high hepatitis C prevalence

The risk of hepatitis C infection may be greater for people born in countries where there is a high prevalence of hepatitis C infection than it is for people born in Australia. It is estimated that 11% of people in Australia who have been exposed to hepatitis C are immigrants from countries where there is a high prevalence of hepatitis C. In certain circumstances, country of birth is an indication to offer hepatitis C testing, particularly when dealing with people coming from countries in Asia, Africa and South America where hepatitis C transmission is not necessarily associated predominantly with injecting drug use.

Sexual partners of people with hepatitis C

The risk of sexual transmission of hepatitis C is very low unless blood is associated with sexual activity. There is emerging evidence of an increased risk of sexual transmission of hepatitis C for men who are also HIV positive.

2.3 Clinical indications and case detection

Indications for hepatitis C testing in primary care should be assessed on the basis of a history of potential exposure and/or specific signs and symptoms, or requests for testing.

Clinical features of hepatitis C infection are diverse. Patients may present with abnormal liver function tests or evidence of liver disease with no apparent cause. Other presentations include symptoms and signs of acute or chronic hepatitis, extra-hepatic manifestations or advanced disease such as liver cirrhosis or hepatocellular carcinoma.

The onset of acute hepatitis C is often difficult to substantiate because of the mild or nearly absent symptoms marking the acute phase of this disease. In chronic disease mild symptoms usually persist for two to three decades before complications occur. Hepatitis C has been labelled a "silent epidemic," and the natural course is slow but progressive. Because of its ability to activate the immune system yet avoid elimination, chronic infection results in prolonged antibody production and the formation of immune complexes, which can result in extrahepatic manifestations of the infection.

While the liver is the primary target of HCV, certain non-hepatic conditions (including certain dermatological and rheumatological presentations, haematological abnormalities, renal or neurological complications[3]) can be associated with hepatitis C infection.

When considering whether a test for hepatitis C is indicated for clinical reasons, epidemiological risk factors should also be investigated.

2.4 When diagnostic hepatitis C testing might be considered

Evidence suggests that hepatitis C testing should be offered to the following groups only if they have risk factors for infection or upon request:

Pregnant women and antenatal testing
The prevalence of hepatitis C in pregnant women without other risk factors is the same as the general population. The presence of known risk factors, rather than pregnancy itself, is a strong indicator for testing. Hepatitis C screening for pregnant women should be confined only to those women who provide a history of risk factors, or request screening when counselled about relevant risk factors.

The risk of mother-to-child transmission of hepatitis C is generally low.

Factors which increase the risk of transmission from mother to child during pregnancy include:
- HIV co-infection in the mother;

[3] These extrahepatic manifestations are described in more detail in the ASHM publication *HIV/Viral Hepatitis: a guide for primary care* (2004).

- A high viral load – although this is not exclusively predictive and no cut-off point at which transmission will occur has been identified;
- An increased duration between membrane rupture and delivery; and
- The use of invasive devices such as foetal monitors.

Nonetheless, any women identified as being at risk of hepatitis C infection should be offered testing. Testing should always be associated with specific informed consent, the provision of information about the meaning of the results (particularly in relation to the pregnancy) and post-test discussion.

Babies born to anti-HCV mothers may be anti-HCV positive at birth due to passive transfer of anti-HCV and should be retested at 18 months.

Pre-operative testing
There is no indication for routine pre-operative screening for hepatitis C. Pre-operative hepatitis C testing should be performed only if it will benefit the patient. Adherence to standard infection-control procedures offers the best protection against infection for both health care professional and patient.

Healthcare workers
Refer Chapter 3.

3 Transmission and infection control in the healthcare setting

Key Points:

- Hepatitis C testing of health care workers should be conducted in accordance with the general principles set out in this document with regard to privacy, confidentiality and access to appropriate health care and support services.
- Hepatitis C testing of all health care workers is not recommended.
- Health care workers who perform exposure prone procedures (EPPs) must undergo hepatitis C testing so that they are aware of their HCV status.
- Health care workers who test positive for HCV RNA must not perform EPPs.
- Testing should be considered for health care workers following occupational exposure to blood or body substances, for example through needlestick injury.

The HCV can be transmitted from an infected health care worker to a patient and from an infected patient to a health care worker. In general the risk of transmission of HCV in the health care setting is low (equivalent to social contact) provided standard infection control precautions are followed, and is most likely to occur in the context of the performance of exposure prone procedures (EPPs) by a HCV RNA positive health care worker[4].

The health care system must support health care workers to minimise the risk of transmission by creating safe work environments, including appropriate training in infection control techniques and personal protective equipment.

In view of the general low risk of transmission of HCV in health care settings, routine testing of all health care workers is not recommended, as testing cannot ensure that at any point in time health care workers or patients are not potentially infectious.

In view of the documented risk of transmission of the HCV from a HCV RNA positive health care worker to a patient during the performance of EPPs, health care workers who perform EPPs must undergo regular testing for HCV in accordance with the general principles for testing set out in this document with regard to privacy, confidentiality and access to appropriate information and health care. Health care workers who are found to be HCV antibody positive must also undergo HCV RNA testing, and where they are found to be HCV RNA positive they must not perform EPPs.

In order to ensure compliance with this recommendation it is essential that appropriate support is available to health care workers who test positive for HCV RNA given the potential psychological, social and economic costs to the individual.

[4] Australian Government Department of Health and Ageing. ***Australian Infection Control Guidelines for the Prevention of Transmission of Infectious Diseases in the Health Care Setting*** January 2004

In view of the risk, albeit low, of transmission of HCV from infected health care workers to patients during the performance of EPPs, health care workers who perform EPPs, or are about to commence performing EPPs, must know their HCV status by seeking serologic testing if untested. Serologic testing is also indicated for health care workers who perform EPPs, where:

- it is 12 months or longer since their last test;
- they have experienced a significant occupational exposure; or
- non-occupational exposure has been identified, including needle sharing with a person infected with or at increased risk of hepatitis C.

Guidance regarding the management and monitoring of health care workers who have cleared hepatitis C infection (with or without treatment) and are negative for HCV RNA should be sought from a medical practitioner with expertise in the management of hepatitis C.

In cases of either patient or healthcare worker exposure to blood or body fluids (for example, through needlestick injury) during the provision of health care, consent for testing of the source individual – either a patient or a health care worker - should be obtained in accordance with the guiding principles of this policy. Protocols for post-exposure management are included in ***Australian Infection Control Guidelines for the Prevention of Transmission of Infectious Diseases in the Health Care Setting*** January 2004 (http://www.icg.health.gov.au).

4 Aboriginal and Torres Strait Islander People

Key Points:

- Strategies to improve access to testing need to be developed locally and reflect local HCV transmission routes, risk practices and patterns of health service use.
- Local pre-test and post-test discussion guidelines should take into account local issues of stigma and shame.
- Fear of breaches of patient confidentiality may be reduced through the development and publication of local confidentiality policies and the use of short-incubation tests as appropriate.
- Specific State and Territory and regional initiatives are needed to improve access to confidential testing and continuity of care for Aboriginal and Torres Strait Islander people moving through the corrections system.

4.1 Background

For more information and background on hepatitis C testing for Aboriginal and Torres Strait Islander people, refer to Appendix 5.

The first objective of the *National Aboriginal and Torres Strait Islander Sexual Health and Blood Borne Virus Strategy 2005-2008*[8] (NATSISH and BBV Strategy) is to improve access to testing, diagnosis, treatment and care of hepatitis C, HIV/AIDS, STIs and other blood borne viruses for Aboriginal and Torres Strait Islander people. It is important to align the goals of this testing policy with current epidemiology around routes of transmission of HCV among Aboriginal and Torres Strait Islander people, including the higher rate of infection.

Improving access to testing requires an awareness of the differences among groups within the Aboriginal and Torres Strait Islander populations and the distinctive barriers that exist in their access. It may require local primary health services to develop locally adapted approaches for young people, prisoners, people who inject drugs and women.

These approaches will be best developed in the context of strong local partnerships between the Aboriginal community-controlled health sector and mainstream services that specialise in the provision of services to clients at higher risk for hepatitis C, HIV, STIs and other blood borne viruses (e.g. sexual health clinics, family planning services, AIDS Councils and services for injecting drug users). Coordination and leadership from State and Territory Aboriginal and/or Torres Strait Islander Sexual Health Committees may be needed to encourage partnerships that develop innovative and locally relevant approaches to service provision and raising awareness in the Aboriginal and Torres Strait Islander community about the need for testing, treatment and management of hepatitis C.

4.2 Pre-test and post test discussion

For many Aboriginal and Torres Strait Islander people, high levels of stigma are associated with hepatitis C. The stigma associated with the illness is compounded by its transmission through routes that are also highly stigmatised, such as drug use. Shame for some Aboriginal and Torres Strait Islander people may be incapacitating in the context of hepatitis C testing, particularly if there are differences between individual and practitioner in terms of race, age and gender. In some areas of the country ceremonial status, moiety and clan may also be important, particularly in contexts where blood has a ceremonial significance. Policies must be developed locally, so that health care workers are correctly advised and health services generate culturally appropriate policies and programs.

Local health service providers need to take these matters into account when developing a testing policy, and in the guidelines around provision of pre-test and post-test discussions. Some success has been achieved in clinics providing pre-test information on cassette or CD recorded in local language or plain English, so that the individual can listen to it privately through headphones without shame. The use of interpreters should also be considered.

4.3 Confidentiality

An added complication is that fear of a positive test may include fear of a breach of confidentiality, made worse when the provider is known to the person or when the test is provided in a local clinic that employs members of the person's family or community. Particularly in rural and remote clinics, the provision of any pathology test may routinely involve documentation passing through a number of hands, and results may be filed with relatively open access. Any variation to this routine may publicly signal that a "confidential" test is being done and unintentionally breach the person's right to privacy. There is no evidence that this fear is realistic, but it is likely to provide an additional barrier to someone seeking a test. Local health service providers should ensure that local guidelines regarding testing have agreed protocols on the handling of confidential information.

A publicised confidentiality policy may assist in reducing this barrier to testing. Such a policy should state that clients' privacy and confidentiality will be respected. It should refer to relevant State or Territory legislation that governs privacy and confidentiality and note that all staff have been trained in the confidentiality requirements of providing care in that service. The policy should also outline a grievance procedure if a client feels that their confidentiality has been breached. It may give examples of what will be done with a person's information, and what will not be done with it. It may also detail areas where the person's right to privacy cannot be respected, for example, where mandatory reporting is required under other State or Territory legislation.

4.4 Aboriginal and Torres Strait Islander Prisoners

Prison settings have been identified as a risk environment for transmission of hepatitis C, as well as for other STIs and blood borne viruses. Strategies to improve access to prevention measures, testing, treatment and care should include provision of continuity of care for those affected by HIV, STIs and hepatitis C. There is a disproportionate representation of Aboriginal and Torres Strait Islander people in prison settings and juvenile detention centres, and risk of transmission is increased with considerable movement of people in and out of the prison system.

Specific initiatives at the state and territory and regional levels should be developed in partnership between State and Territory Departments of Corrections, State and Territory Health Departments, prison service providers and the Aboriginal and Torres Strait Islander community-controlled health sector. Such initiatives could include improved access to testing in prisons including routine risk assessment conducted in a culturally safe manner, preventive approaches that consist of health promotion and prevention education, and re-entry to the community strategies for prisoners.

4.5 Pregnant Women

It is critical that antenatal testing for Aboriginal and Torres Strait Islander women is conducted in accordance with the guiding principles of this policy, especially regarding informed consent and pre-test and post-test discussions for Aboriginal and Torres Strait Islander women. The NATSISH and BBV Strategy strongly recommends the incorporation of HIV, STIs and HCV testing guidelines into antenatal clinical care guidelines. Antenatal hepatitis C testing for Aboriginal and Torres Strait Islander women should occur with appropriate consideration of culturally appropriate resources, and in a manner that is sensitive to the woman's safety and cultural security.

5 Surveillance and research

Key points:

- Systematic surveillance of newly diagnosed cases of HCV infection is recognised as a key component of the Australian response to the hepatitis C epidemic.
- The results of hepatitis C antibody testing have been used to analyse hepatitis C prevalence and incidence, including the results of HCV testing carried out at sentinel sites and the annual Needle and Syringe Program (NSP) Survey.

Background

The broad aims of hepatitis C surveillance are to:

- monitor trends and patterns in HCV transmission and the outcomes of HCV infection;
- guide and evaluate interventions; and
- provide early warning of changing patterns of HCV transmission and disease.

In Australia, surveillance for hepatitis C has been carried out under the framework of the Australian Hepatitis C Surveillance Strategy which was developed in 1999 by the Communicable Diseases Network (CDNA). It has been implemented through the National Centre in HIV Epidemiology and Clinical Research (NCHECR) in collaboration with State and Territory health departments and a range of other agencies and organisations.

The ability to track the incidence of hepatitis C through routine surveillance is limited by the lack of symptoms and of laboratory markers associated with acute infection.

5.1 Compilation and analysis of Hepatitis C diagnoses

HCV infection has been a notifiable condition (doctor and/or laboratory) in most Australian State and Territory Health jurisdictions since 1990, and all States and Territories since 1995. Cases of newly diagnosed hepatitis C infection are reported via State and Territory Health Departments to the National Notifiable Diseases Surveillance System. The extent to which there have been duplicate hepatitis C notifications is uncertain.

In each State/Territory, new hepatitis C diagnoses have been notified with case-identifying data, so that within each State/Territory duplicate notifications are likely to be limited. However, new hepatitis C diagnoses are forwarded by State/Territory Health Departments to the National Notifiable Diseases Surveillance System, maintained by the Australian Government Department of Health and Ageing, in anonymous aggregate format. This means that it is not possible to assess duplicate notifications between State/Territories.

While enhanced surveillance mechanisms to improve ascertainment of newly acquired hepatitis C cases were introduced in most State and Territory health jurisdictions, the vast majority of hepatitis C notifications have been prevalent hepatitis C diagnoses rather than newly acquired hepatitis C cases.

Newly acquired cases of HCV infection often cannot be separated from other reported cases because of limited capacity to verify previous negative results; and the relatively limited implementation of enhanced surveillance of notifications by States and Territories due to resource implications.

While HCV infection is a notifiable disease, it is unclear how prevalent hepatitis C is in Aboriginal and Torres Strait Islander people, due to the continued failure to identify Indigenous status. In order to ensure accurate data, it is critical that all people diagnosed with hepatitis C are requested to confirm their status.

5.2 Sentinel site surveillance for hepatitis C

Hepatitis C testing is routinely carried out at a number of sentinel sites such as sexual health clinics, Aboriginal Community Controlled Health Services, prisons, primary healthcare sites, drug user organisations and blood transfusion services. The numbers of people tested, and the proportion with diagnosed HCV infection are reported on a regular basis from these sites and provide estimates of hepatitis C prevalence and incidence in various population groups.

5.3 Special annual survey

The Australian Needle and Syringe Program Survey is co-ordinated by NCHECR and has been carried out over one week each year since 1995. During the designated survey week, NSP staff ask all clients who attend to complete a brief, self-administered questionnaire and provide a finger prick blood sample. The subjects are assured that the specimens are tested under code, so the results cannot be linked back to individuals.

This survey provides limited information on comparisons of hepatitis C infections between jurisdictions and over time.

5.4 Research

Considerable research effort towards combating and understanding hepatitis C is conducted in Australia. Much of this work is collaborative and may be carried out as part of international partnerships. This work may require the use of test kits not in use in Australia and those that have not been submitted for evaluation. These kits may be used by bone fide research institutes as well as the designated testing laboratories provided that the results are not used in diagnosis, screening or for patient related decisions. If a non-approved test kit is to be used therapeutically, for diagnosis or monitoring progression or therapy of hepatitis C, application must be made to the TGA for supply under one of the Special Access Schemes, and the use is subject to approval from an Institutional Ethics Committee in accordance with NHMRC guidelines.

6 Access to diagnostic testing

Key points

- One of the guiding principles is that testing should be accessible to all who are or have been at risk of infection.
- There are a range of barriers that may impact on access to hepatitis C testing by people who inject drugs, young people, people from culturally and linguistically diverse backgrounds, Aboriginal and Torres Strait Islander peoples, people in custodial settings and people who live in rural and remote areas.

The principle of equitable access to testing for hepatitis C involves many factors. Equitable access to testing requires services for testing, follow-up and support, prevention, treatment and care, education and workforce development. The *National Hepatitis C Strategy 2005-2008* identified various groups that potentially have a higher risk of hepatitis C infection and traditionally do not use hepatitis C related health services. These groups that generally are marginalised from healthcare, benefit from the provision of targeted and tailored services.

The groups for whom access to hepatitis C testing is a priority are:

- People who inject drugs or who have ever injected drugs
- People in custody or who have ever been in custody
- Aboriginal and Torres Strait Islander people with risk factors for hepatitis C infection
- People born in countries with high HCV prevalence.

Young people, people from culturally and linguistically diverse (CALD) backgrounds and people living in rural and remote areas are important members of all these diverse groups with particular service needs. Aboriginal and Torres Strait Islander people should also have choices in accessing diagnostic testing services and these services should be provided in a culturally sensitive manner. Under the *National Hepatitis C Strategy 2005-2008*, these priority populations will be accorded special attention to reduce transmission within the groups and improve their care and support.

7 Pre-test and post-test discussions

Key points

- Pre-test and post-test discussions form an integral part of hepatitis C testing and education about HCV and its prevention. Provision of information and support associated with testing is consistent with the goal of the second National Hepatitis C Strategy, which includes minimising the personal and social impacts of hepatitis C infection.
- The term 'pre-test and post-test discussion' are used in place of 'hepatitis C test discussion and post-test counselling'.
- Healthcare workers delivering the test result should use their best judgment in establishing the most appropriate way to communicate the test result. Factors to consider include the person's testing history, gender, cultural beliefs and practices, behaviour, ongoing risk, understanding of hepatitis C and language and literacy levels.
- Home based tests are not approved in Australia, and home-based testing is not supported.
- Test results should be given in person, wherever possible.

7.1 Informed consent

Gaining informed consent from the individual to be tested is a legal requirement and fundamental to an effective, best-practice testing process. Typically, informed consent should be obtained during pre-test discussion. Pre-test discussion should also incorporate an assessment of risk, an explanation of the testing process, as well as a discussion of the possible outcomes of the test, what these mean and support available to the person in the event of a positive result.

Risk assessments and testing should be conducted in a sensitive and culturally safe manner and additional consideration may be required for Aboriginal people such as time, skills and Aboriginal community specific resources. Strategies to gain informed consent from people from CALD backgrounds may include using health care interpreters (if available) or telephone interpreters who are available nationally for use by public and private health care professionals (see Appendix 7 for contact details).

Counselling is an appropriate term for the longer-term management of a person who has tested positive. Counselling may also be an option for a HCV negative person who requires support maintaining safer behaviours and/or support with changing personal behaviours that may be placing them at risk. In many cases, counselling needs to be delivered at a more specialised level of care than can be provided by generalist health care professionals.

The position of this policy is that the term "pre-test and post-test discussion" should be adopted in place of "HCV test discussion and post-test counselling".

Hepatitis C testing is a particularly sensitive health care issue for Aboriginal and Torres Strait Islander communities (Refer to Chapter 4).

7.2 Pre-test discussion

Pre-test information aims to prepare individuals for hepatitis C testing and to sufficiently equip the person requesting the test such that she/he can give informed consent. When a person requests or is offered a test, the practitioner should give appropriate information about risk, points of referral if necessary, assurances about confidentiality and privacy, and assessment of the person's preparedness to be tested. Written information in the person's first language (if available) should be provided when the pre-test discussion occurs (see Appendix 7 for details of relevant websites).

Specifically, the hepatitis C pre-test discussion should provide accurate information about safer practices that are appropriate to the person's gender, cultural beliefs and practices, behaviour, ongoing risk, understanding of hepatitis C and language and literacy level. The discussion should include:

- risk assessment and discussion of the reason for testing;
- how to reduce the risk of becoming infected or infecting others-for example information about safer injecting when this is relevant;
- possible desirability for other BBV testing and/or STI testing;
- information about confidentiality and privacy;
- information about the testing process including how results are to be provided, and the window period;
- information about what happens to test results (ie the notification process);
- seeking informed consent for the test to be conducted;
- assessment of the person's preparedness to be tested;
- information about what a negative or positive result means including basic printed information about hepatitis C; and
- assessment of support mechanisms while waiting for the test result and/or if the result is positive.

7.3 Post-test discussion

Test results should be delivered to the patient as soon as possible after results are received from the lab. It is strongly recommended that test results be given in person. Other methods of communication should only be used in exceptional circumstances. Post-test discussion provides the opportunity to discuss health issues, referrals and prevention issues.

The post-test discussion should include:

- giving the test result in person and in a manner that is confidential, sensitive and appropriate to gender, cultural beliefs and practices, behaviour, ongoing risk, understanding of hepatitis C and language and literacy level; and
- re-assessing support mechanisms and requirements of the person and making immediate referral to a support agency to be accessed at the person's discretion.

If the result is negative, the discussion should include reinforcing harm reduction strategies, education and information messages about safer behaviours, and examining any difficulties or issues that the person may have in practising safer behaviours. It should be emphasised that a negative test result following a risk event does not indicate that it is likely to be safe to repeat risky behaviour. The relief associated with a negative test result may also impede the processing of information and advice at that time.

If the result is positive, discussion should include at an appropriate time, issues such as:

- immediate needs and support including written referral information;
- safer behaviours – education, information and support including needle and syringe programs if appropriate;
- legal requirements for disclosure and how to disclose to family and friends;
- managing or understanding strong emotions, feelings, reactions and changes;
- options in drug treatments and medical management;
- ongoing counselling or therapy if required;
- complementary/alternative management options;
- ways to deal with loss and grief, depression, anger and anxiety;
- strategies for managing hepatitis C which are flexible and appropriate to the person's needs; and
- legislative requirements (notification, contact tracing, storage and coding).

Provision of information and support

In addition to post-test discussion, people diagnosed with hepatitis C infection may need continuing support, particularly in the period immediately after they learn their test result. The purpose is to provide reassurance, to help them work through any difficulties (such as telling others they are infected) and to help place the infection in context. This is also another opportunity to reinforce messages about the natural history of hepatitis C and to inform people of the available treatments, should treatment become necessary.

Community organisations such as hepatitis C councils and drug user organisations are well placed to provide information and support. People diagnosed with hepatitis C infection should be told how to contact these organisations. Contact details for these organisations and their peak bodies are listed in Appendix 7.

Ongoing health monitoring

For people infected with hepatitis C, the usefulness of testing will be maximised if their health status is regularly monitored.

Some groups of people infected with hepatitis C (such as people who inject illicit drugs) may have other, more pressing, health concerns. In this situation it is preferable that their overall primary health care needs, including their hepatitis C infection, be approached in a comprehensive way and in a setting that is non-discriminatory and sensitive to their situation. This will also assist in facilitating access to suitable health care, which is often limited for this group of people.

In population groups for which it is likely that infection with hepatitis C occurred a considerable time ago, there may be additional benefit in being tested: if infected, these people are more likely than those relatively recently infected to have progressed to the point where treatment might be indicated. This is most likely to apply to people infected in their country of birth, people who were infected through the receipt of blood or blood products in Australia before 1990, and people who previously injected illicit drugs.

7.4 Home based testing in Australia

Home-based testing refers to a process where hepatitis C testing is conducted outside a medical or clinical setting. The process is similar to conducting a home-based pregnancy test, in which the test is performed and interpreted by an individual in a non-medical setting. Home-based testing can also mean that an individual collects a sample at home and sends it to a centralised laboratory for formal testing and interpretation. For the purposes of this policy, the former will be referred to as 'home-testing' and the latter as 'home-collection'.

Hepatitis C testing in Australia should always be performed in a clinical context, where there is an appropriate level of interaction between the individual being tested and a suitably qualified health professional, including pre-test discussion. Introduction of home collection and home-testing for hepatitis C in Australia is not supported.

It is important to note that home-testing and home collection-kits have not been approved for use in Australia by the Therapeutic Goods Administration. As home-testing kits are available for purchase over the internet from overseas suppliers, it is important that access to and use of these tests is monitored through social research, anecdotal reports and observation. Health promotion interventions may be necessary if the practice of home-testing becomes prevalent.

8 Diagnostic strategies

Key points

- Exposure to HCV is determined by testing for HCV antibodies (anti-HCV) in serum or plasma.
- A sample not reactive in the screening immunoassay can be generally regarded as anti-HCV negative.
- A sample reactive in the screening immunoassay should be subject to a minimum of one alternative supplemental immunoassay to confirm the result.
- A sample reactive in two immunoassays with different antigen specificity can be reported as anti-HCV positive.
- Current HCV infection is usually determined by qualitative testing for HCV RNA.
- Qualitative HCV RNA testing should be a standard component of the diagnostic work-up of all anti-HCV positive individuals.
- The major role of HCV genotype and viral load testing is in guiding treatment dose and duration.

This chapter provides advice on minimum standards for laboratory diagnosis and investigation of hepatitis C. It should be noted that, because of their unique requirements, blood services have developed their own strategies for screening donations. This part of the National Hepatitis C Testing Policy does not apply to blood services.

Laboratory investigations are usually directed towards answering one or more of the following questions:

- Has the patient been infected with HCV? This is usually determined by testing for HCV antibodies (anti-HCV).
- Does the patient have current infection? This is usually determined by testing for HCV RNA.
- What is the current level of virus replication? Viral load prior to treatment can be a prognostic indicator of long-term response to interferon-based therapy and can also be used to monitor response while on therapy.
- What is the infecting virus genotype? Virus genotype is a key predictor of treatment response and can be used to guide treatment dose and duration of therapy.
- What testing should be performed for epidemiological surveillance?

While the significance of a test result is dependent on the patient's clinical condition and risk exposure history, that information is not always available to the testing laboratory. Therefore, testing protocols and interpretive comments need to be designed to encompass the likely clinical and exposure circumstances.

8.1 Anti-HCV testing. Has the patient been infected with HCV?

Exposure to HCV is usually assessed by performing an immunoassay for the detection of antibody to HCV (anti-HCV) in serum or plasma. The presence of true antibody shows that the patient has been infected with the virus but does not indicate whether the infection is acute, resolved or chronic. In a majority of cases (65–85%) an individual with genuine antibody to HCV will be chronically infected. The absence of anti-HCV usually means the patient has never been infected, although antibody may become undetectable years after the infection has been cleared. Furthermore, antibody may not be detectable very early in the course of infection (the so-called window period) or in people who are immunosuppressed, for example people with HIV infection and people undergoing therapies such as chemotherapy and dialysis.

Approaches to confirmatory testing

In Australia the practice for confirming the presence of true anti-HCV has been strongly influenced by the protocols set out in *A Strategy for the Detection and Management of Hepatitis C in Australia*.[5] This document stipulated that all samples initially reactive in one immunoassay should be retested with a second independent immunoassay to confirm specificity. A sample is not considered to be positive for anti-HCV until the supplemental immunoassay has been performed and found to be reactive. The algorithm has created interpretative difficulties with samples that are reactive in the initial immunoassay but not the secondary one. Furthermore, samples that have low reactivity for technical reasons may also show low reactivity in a second enzyme immunoassay because some combinations of immunoassays can share false reactivity[6]. Reasons for low or indeterminate activity include:

- Adventitious reactivity to the recombinant antigens
- Early period of seroconversion before antibody response has fully developed
- Immunosuppression by disease or therapy
- Waning antibody levels in resolved infection
- Maternal antibody passively transferred from an anti-HCV positive mother to her infant

In Australia there is no scientific consensus on the optimal way to confirm the presence of anti-HCV. There is continuing debate about whether it is preferable to repeat an initially reactive screening test (singly or in duplicate) before confirming with a second enzyme immunoassay and only confirm those samples that are repeatedly reactive in the initial screening procedure or whether it is better to proceed directly to confirmation. All manufacturers of test kits recommend the former

[5] National Health and Medical Research Council 1997, *A Strategy for the Detection and Management of Hepatitis C in Australia*, NHMRC, Canberra.
[6] Most low level activity in immunoassays is false reactivity but ***not*** always.

approach[7]. The choice will depend, at least in part, on the type of population being tested (and hence the positive predictive value of a reactive result), whether HCV-RNA testing has also been undertaken and on previous results for that patient, if known. In practice, most laboratories have used variations on one or both of the following approaches to confirm a true anti-HCV status:

- Testing with another immunoassay that uses antigen combinations that differ from those used in the first assay.
- Referral to a reference laboratory for advice or for further antibody testing or assessment by a qualitative test for HCV RNA.

Note: In the case of initially reactive results, it is important to follow the manufacturer's instructions on the package insert. These instructions are assessed by the Therapeutic Goods Administration as part of the evaluation of the test kit's performance. Responsibility for any deviation from the instructions rests with the user of the test kit. Non-compliance is considered a failure to perform the test as intended. Consequently, the in-vitro Diagnostic Device (IVD) will become an in-house IVD with the associated regulatory implications. For more information, refer to Chapter 9 Quality Assuring hepatitis C Testing.

Appropriate combinations of immunoassays

HCV recombinant antigens have been based predominantly on expression of clones from HCV genotype 1. As a result, the same or very similar antigens are used by a number of immunoassays designed with different test formats. The National Serology Reference Laboratory, Australia (NRL) has identified the immunoassays that share common false reactivity, that is, false positive results as defined in the NHMRC guidelines. The reliability of the results of these assays used in combination and their ability to yield specific confirmatory results should be assessed in an ongoing manner. Using this information, the NRL can advise which combinations of immunoassay kits are likely to provide the most reliable results. However, as new generation and modified assays for anti-HCV become available, they too will need to be evaluated as to their compatibility with other immunoassays.

Discordant results

Before results are reported pathologists and medical laboratory scientists should be confident that a discordant result is not due to non-specific reactivity because of technical limitations of the initial assay. Otherwise, further testing should be done, such as repeating the initial assay, using a third immunoassay or immunoblot (perhaps by referring to a reference laboratory) or performing a qualitative HCV RNA test.

Notifications

In Australia, it has been recognised that laboratory notifications of infectious diseases are a cornerstone of our disease surveillance system. Hepatitis C is a notifiable disease and it is important that notifications are reported to the respective State or Territory Health Department. Data is collated into the National Notifiable Diseases

[7] In the IVD Policy to be introduced in 2007, any changes in using commercial tests outside the manufacturer's instructions will render the test an "in-house test" which will require validation of the test to the level required by the IVD Policy Rules.

Surveillance System and then published in the Communicable Diseases Intelligence. (Refer to Chapter 5)

Determining anti-HCV positive samples

The following *minimum* practices should be adopted by all pathology services in determining whether a sample is anti-HCV positive:

- A sample non-reactive on a single immunoassay screen can be confidently reported as anti-HCV negative.
- Assays should be performed in accordance with the manufacturer's instructions. Samples testing positive by one method should be subject to a minimum of one alternative supplemental immunoassay to enhance the positive predictive power of the assigned result.
- A sample that is reactive on two separate immunoassays based on different antigens and different immunoassay formats has a very high probability of containing true hepatitis C antibodies and can be reported as positive.
- When seeking to confirm a result, laboratories should use only appropriate pairings of first and supplemental immunoassays, as recommended by the NRL or other reputable sources such as the scientific literature.
- Test results should not be reported until these minimum steps to confirm anti-HCV have been taken.

In the case of discordant antibody test results—the first test is reproducibly reactive and the supplemental enzyme immunoassay is negative—or where there is doubt about levels of reactivity, laboratories are advised to adopt *one or more* of the following strategies:

- If further information is not available from the requesting practitioner, then the interpretive comment should indicate that this result may be owing to non-specific reactivity or due to recent or distant past HCV infection. Testing a second, follow-up sample is recommended to exclude recent infection.
- Perform HCV-RNA testing. If HCV RNA is detected, then this may indicate a possible recent infection. Note that if the sample tested is not a dedicated aliquot (i.e. collected for the purpose of performing NAT), contamination during antibody testing may contribute to a false positive HCV RNA result. It is recommended that a second sample be collected in 4 weeks to confirm seroconversion and allow notification as new infection. If a discordant sample is negative by qualitative HCV RNA testing, a repeat sample should still be requested for anti-HCV and/or HCV RNA testing to determine the true HCV infection status.
- If none of the above procedures is possible in the testing laboratory or if none is appropriate, the sample should be referred to a reference laboratory for further investigation.

8.2 HCV RNA testing. Does the patient have current infection?

Between 15 and 35% of people infected with HCV will spontaneously resolve their infection within the first year of initial exposure to the virus. The predictors of this spontaneous resolution are not yet clear. This specific subpopulation may be anti-HCV reactive but HCV RNA negative. A single negative test for HCV RNA does not, however, definitively exclude the presence of infection. Some patients have levels of virus around the limit of detection of the test and may be intermittently negative, or their viraemia may be suppressed by antiviral therapy. Others may have a negative result owing to suboptimal specimen storage and transport conditions. A positive result from an appropriate sample in a qualitative HCV RNA test provides a high degree of certainty that the patient is currently infected but it does not confirm chronic infection unless the HCV RNA is shown to persist for at least 6 months.

Qualitative HCV RNA testing should be a standard component of the diagnostic work-up of all individuals who are anti-HCV reactive.

8.3 Viral load measurement. What is the current level of virus replication?

Measurement of the level of virus replication or viral load has become an important tool for clinical management of patients with HCV infection. The initial level of virus is a predictor of response to antiviral therapy and long-term response to therapy can be predicted by viral dynamics on therapy. In particular, for patients infected with HCV genotype 1, non-response can be predicted by viral load measurement at week 12 of therapy.

A number of commercial HCV RNA quantification assays are registered on the Australian Register of Therapeutic Goods (ARTG). These may be used for measuring levels of HCV RNA. They include target amplification assays, predominantly PCR based and signal amplification assays which rely on hybridisation of HCV RNA.

8.4 Virus characterisation. What is the infecting virus genotype?

Based largely on sequence divergence, HCV can be divided into six genotypes (HCV 1-6). In Australia, the predominant genotypes are 1 (around 55%) and 3 (around 35%). It has been shown that genotype is a major predictor of response to interferon-based therapy. A number of methods have been described to determine genotype and most are based on sequence variation in the conserved 5’ untranslated region (5’ UTR) and include direct sequencing after PCR amplification and a reverse phase hybridisation assay. Genotyping should only be carried out using test kits registered by the TGA.

8.5 Epidemiological surveillance

Data from the assays discussed, in particular immunoassay data, are regularly analysed to assess the extent and distribution of HCV infection in the community. For this purpose, it is critical that each confirmed positive result is classified as:

- A repeat sample from a known infected individual who has already been entered on the appropriate database.

or

- The first test on an individual who has not previously been tested, that is, a newly notified individual for whom the date of acquisition of infection is not necessarily known.

or

- A repeat test on an individual who previously tested negative, that is, a new infection or seroconversion where the time boundaries of the transmission event may be estimated. The Communicable Diseases Network of Australia defines a new infection as being a positive anti-HCV test in a patient known to have had a negative test within the preceding 24 months.

9 Quality assuring hepatitis C testing

Key Points:

- The Therapeutic Goods Administration (TGA) has regulatory responsibility for in-vitro diagnostic devices (IVDs) ie pathology assays. The *Therapeutic Goods Act 1989* provides a national framework to ensure the safety, quality and performance of these therapeutic goods. Only assays that are registered by the TGA may be used for testing for HCV.
- In accordance with the conditions applied by the TGA to the registration of HCV assays, sponsors may only supply HCV IVDs to laboratories that participate in quality assurance programs prescribed by the TGA.
- Laboratories that perform hepatitis C testing must meet National Pathology Accreditation Advisory Council (NPAAC) standards, and have current National Association of Testing Authorities/Royal College of Pathologists Australia (NATA/RCPA) Medical Testing accreditation that includes hepatitis C testing in the scope of the accreditation.

This chapter describes the mechanisms in place to assure that hepatitis C testing is of the highest quality. It describes the policy framework[8] for evaluating the performance of hepatitis C test kits, post-marketing quality assurance of the kit via participation in a uniform national quality assurance program, the categorisation of test kits for regulatory purposes and restrictions on the use of certain test kits. It also reviews the means by which the quality of the laboratory testing process is assured.

Background

For more information and background on the quality assurance of hepatitis C testing, including categorisation systems and quality assurance programs, refer to Appendix 6.

9.1 Performance evaluation of hepatitis C test kits

The Therapeutic Goods Administration (TGA) has regulatory responsibility for in-vitro diagnostic (IVD) test kits through the *Therapeutic Goods Act 1989* and its associated regulations. The TGA conducts a full pre-market evaluation on test kits for the hepatitis C virus and HIV to demonstrate that they meet the quality, safety and efficacy standards required for registration in Australia. The TGA currently contracts the performance evaluation of assays to the NRL.

The TGA is developing a new regulatory framework for IVDs. It is proposed that the framework will be implemented during 2007-2008. Pre-market performance evaluation of all new HCV assays will remain a requirement.

[8] This Chapter represents the assurance mechanisms currently in place. Should this situation change in the future, this Chapter will need to be updated accordingly.

Post-market quality assurance of HCV IVDs

The TGA also has responsibility for post-market surveillance of IVD performance. The TGA has the power to remove from the market any IVD that is not performing to the expected standard or that is known or demonstrated to be defective.

A condition of TGA registration of HCV and HIV test kits is that tests may only be used in laboratories participating in the Quality Assurance Program coordinated by the NRL. This program includes:

- the external quality assessment scheme (EQAS);
- the quality control program (QC); and
- specificity monitoring.

These components are described in detail in Appendix 6. The QC and specificity monitoring programs are intended to monitor in-field assay performance, and thus supplement the information obtained for quality of overall performance between laboratories gained from the EQAS program. Participation in the NRL EQAS does not preclude participation in other quality assessment programs.

It is proposed that a quality control program will be utilised as the TGA's major post-market monitoring tool.

9.2 Categorisation of HCV IVDs for regulatory purposes

The TGA has the authority to impose conditions on the registration of products including the category describing the approved intended use of a HCV assay. Tests are categorized as being suitable either for routine screening (those with a performance that is suitable for blood donor screening and determining the HCV antibody status of a sample) or for reference (or supplemental) tests (those that are used to clarify the nature of the reactivity of a sample following initial standard tests). Tests are further categorised as Level 1 to 4, as outlined in Appendix 6.

This additional level of categorisation enables the TGA to recognise a wide range of test functions. Technological advances have led to the production of test kits that are suitable for purposes other than screening and confirmation of diagnosis, such as surveillance and monitoring, and possibly for use in emergency situations.

The advantages of the hepatitis C testing categorisation system (outlined at Appendix 6) is that it provides:

- a wider choice of testing protocols;
- indications of current usage;
- possible models for accommodating new technologies;
- a framework for establishing the extent of evaluation for each type of test kit; and
- a categorisation that can be generalised to other areas of serology.

9.3 Quality assurance of hepatitis C testing

To assure high quality testing, the performance of the laboratory must also be monitored. Laboratories that perform HCV testing must comply with National Pathology Accreditation Advisory Council (NPAAC) standards. Failure to meet these standards poses a perceived risk to public health and patient safety.[9] Evidence of continued compliance with these standards can be demonstrated by ongoing accreditation by National Association of Testing Authorities/Royal College of Pathologists of Australasia (NATA/RCPA) Medical Testing.

The NPAAC standard "Standards and Guidelines for Laboratory Testing of Antibodies to the Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) 2006" describes the minimal standards expected when testing for HCV antibodies. The NPAAC document "Laboratory Accreditation Standards and Guidelines for Nucleic Acid Detection and Analysis 2006" describes minimal practice to be followed when testing for HCV nucleic acid.

Good laboratory practice also prescribes the regular use of quality control testing and enrolment in relevant External Quality Assessment Schemes. These are mandatory requirements of the laboratory based quality management standard ISO 15189. These quality assurance tools provide the laboratory with both internal and external assessment of the testing process. In Australia, the major providers of these quality assurance programs are the NRL and the RCPA QAP P/L SQAP.

HCV testing should only be performed in laboratories holding current NATA/RCPA medical testing accreditation that includes hepatitis C testing in the scope of the accreditation.

[9] NPAAC Standard "Standards and Guidelines for Laboratory Testing of Antibodies to the Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV)" 2006

10 Funding

Key Points

- There is a Medicare Benefits Schedule (MBS) rebate for HCV antibody testing.
- There is a MBS rebate for qualitative and quantitative nucleic acid testing and genotype testing.
- Some States and Territories provide free and de-identified hepatitis C testing.

10.1 Hepatitis C testing in Australia

By 2005, over 1 million hepatitis C antibody tests for diagnostic testing had been performed in Australia by standard and reference laboratories (excluding blood bank testing and supplemental testing).

10.2 Funding arrangements for hepatitis C diagnostic and monitoring tests

The Medicare Benefits Schedule (May 2006) funds the following hepatitis C treatment assessment and monitoring tests:

• Testing for hepatitis C using hepatitis C antibody test
• Supplementary testing for hepatitis C antibodies using different hepatitis C antibody assay on the specimen which has a reactive result on the initial hepatitis antibody test
• Quantitation[10] of HCV RNA load in plasma or serum in the pre-treatment evaluation or the assessment of efficacy of antiviral therapy of a patient with chronic HCV hepatitis - where any request for the test is made by or on the advice of the specialist or consultant physician who manages the treatment of the patient with chronic HCV hepatitis – (to a maximum of 2 of this item in a 12 month period).
• Nucleic Acid amplification and determination of hepatitis C genotype (subject to certain conditions)
• Detection of Hepatitis C viral RNA (subject to certain criteria being met)
• Detection of hepatitis C RNA in a patient undergoing antiviral therapy for chronic HCV hepatitis (not exceeding 4 episodes in a 12 month period).

More detailed information on hepatitis C funding under the MBS is available at: **http://www.health.gov.au/internet/wcms/publishing.nsf/Content/mbsonline-downloads** (Category 6 – Pathology items and descriptions)

[10] While the term “quantitation” is used in the MBS, “quantification” is used elsewhere in this document.

Appendix 1 Membership of the National Hepatitis C Testing Policy Steering Committee

Professor Robert Batey (co-Chair)	Hepatitis C Subcommittee of the Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis (MACASHH)
Ms Kim Stewart (co-Chair)	Blood Borne Virus and Sexually Transmissible Infections Subcommittee of the Australian Population Health Development Principal Committee (APHDPC)
Dr Scott Bowden	Victorian Infectious Diseases Reference Laboratory (VIDRL)
Mr Daniel Coase	Blood Borne Virus and Sexually Transmissible Infections Subcommittee of the Australian Population Health Development Principal Committee (APHDPC)
Dr Darrell Crawford	Australian Liver Association (ALA)
Associate Professor Elizabeth Dax	National Serology Reference Laboratory, Australia (NRL)
Dr Erol DiGuisto	National Centre in HIV Social Research (NCHSR)
Dr Greg Dore	National Centre in HIV Epidemiology and Clinical Research (NCHECR)
Dr Gary Lum	Public Health Laboratory Network (PHLN)
Professor Stephen Locarnini	Victorian Infectious Diseases Reference Laboratory (VIDRL)
Ms Annie Madden	Australian Injecting & Illicit Drug Users League (AIVL)
Ms Shelley Tang	Therapeutic Goods Administration (TGA)
Ms Skye Wisbey	Australian Hepatitis Council (AHC)

Observers

Ms Levinia Crooks	Australasian Society for HIV Medicine
Dr Jan Savage	Australasian Society for HIV Medicine

Australian Government Department of Health and Ageing

Dr Bronwen Harvey	Population Health Division
Mr Andrew McCormack	Office for Aboriginal and Torres Strait Islander Health
Ms Sharyn McGregor	Population Health Division

Appendix 2 Stakeholder consultation

The following stakeholders were provided with a consultation draft of this document for comment:

Australia:
Aboriginal Health and Medical Council (NSW)
Australasian Professional Society on Alcohol and Other Drugs
Australasian Society for HIV Medicine
Australian Association of Pathology Practices
Australian Centre in Hepatitis and HIV Virology Research
Australian Divisions of General Practice
Australian Injecting and Illicit Drug Users' League
Australian Liver Association
Australian Red Cross Blood Service
Australian Society for Infectious Diseases
Blood Borne Virus and Sexually Transmissible Infections Subcommittee (BBVSS) of the Australian Population Health Development Principle Committee (APHDPC)
Communicable Diseases Network Australia
Gastroenterological Society of Australia
Haemophilia Foundation Australia
HIV/AIDS and STIs Subcommittee of MACASHH
Indigenous Australians' Sexual Health Committee of MACASHH
Medical Industry Association of Australia
National Association of Testing Authorities, Australia
National Coalition of Public Pathology
National Pathology Accreditation Advisory Council
National Serology Reference Laboratory, Australia
Public Health Association
Public Health Laboratory Network
Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Royal Australian College of General Practitioners
Royal Australasian College of Physicians
Royal Australian College of Surgeons
Royal College of Pathologists of Australasia
RCPA QAP Pty Ltd (Serology QAP)
Turning Point Alcohol and Drug Centre
Transplantation Society of Australia and New Zealand
Therapeutic Goods Administration

New Zealand:

Ministry of Health
New Zealand Hepatitis Foundation

Appendix 3 Guiding Principles

The following points expand on the guiding principles:

Test discussion and post-test discussion. Appropriate test discussion and post-test discussion should be an integral part of all voluntary, mandatory and compulsory testing. People with antibody-positive results will need continuing support and information, which may involve referral to community agencies such as hepatitis C councils and drug user organisations. Home-based testing does not provide for appropriate test discussion and is not supported.

Informed consent. While informed consent should be obtained for all people seeking testing, particular care should be taken to obtain specific informed consent from marginalised groups. The process of obtaining that consent may need to take account of cultural and language barriers and matters associated with discrimination.

Confidentiality. If people who have been tested or are contemplating testing are to have confidence in the health system it is essential that adequate mechanisms exist to ensure the confidentiality of test results at all levels—clinical, data management, and the notification process. People who are considering testing are entitled to be told about how notification to health authorities of confirmed positive tests results occurs and the confidentiality safeguards that apply.

Access. People who have been at risk of exposure to hepatitis C infection should have ready access to testing. Where barriers to testing exist, especially for marginalised groups, special provisions may need to be made to facilitate access. Funding arrangements should be such that the cost of testing does not discourage people at risk of infection from being tested.

Anonymous testing. To facilitate access for people who might be reluctant to seek hepatitis C testing, free de-identified testing should be available from a number of health care settings in each jurisdiction.

Health promotion. The benefits of testing should be maximised by using the opportunity to deliver health promotion messages aimed at minimising transmission and encouraging lifestyle modifications that may limit the adverse consequences of infection.

The primary health care context. The benefits of hepatitis C testing will be maximised when a patient's other primary health care needs are taken into account. This applies particularly to people who inject illicit drugs, who may have complex health care needs and often experience discrimination by health care providers.

Monitoring and treatment. Continuous monitoring of their health status should be available to all people infected with hepatitis C, with assessment for treatment occurring in accordance with eligibility guidelines.

Regulation and quality assurance. Requirements for the registration and supply of hepatitis C test kits by the Therapeutic Goods Administration and for their use

(this is discussed in Chapters 8 and 9) should be adhered to. Only TGA registered assays are to be used.

Cost-effectiveness. Testing should be carried out in a cost-effective manner.

Human rights. Testing practices must comply with federal and State or Territory anti-discrimination legislation and other relevant laws. This could mean that it is unlawful to require a person, on the basis of actual or imputed hepatitis C infection, to undergo a hepatitis C test as a pre-condition of any medical treatment or that it is unlawful to refuse, delay or defer treatment if the patient refuses the test.

Harm Reduction. Whilst this policy does not condone drug use it refers to policies and programs aimed at reducing drug related harm. Harm reduction interventions aim to improve health, social and economic outcomes for the community and the individual, and encompass a wide range of approaches, including Needle and Syringe Programs and assisting people with drug dependencies to seek treatment.

Remedies. Effective, practical and accessible redress (apart from recourse to the law) should be available for unauthorised hepatitis C testing - for example, a health care complaints mechanism.

Mandatory and compulsory testing. Mandatory or compulsory testing is appropriate only in specific circumstances:

- Compulsory testing is appropriate in some rare situations (as provided for in public health legislation) where the welfare of others in the community depends on the testing of an individual - for example, if a person suspected on reasonable grounds of being hepatitis C positive persistently behaves in a way that places others at risk of infection. Adequate safeguards should exist to ensure that compulsory testing is used only when there are no alternatives. The right of appeal against a decision or order to be tested should always exist.

- Mandatory testing, where a person may be prohibited from participation in certain activities unless they undergo testing and are found to be hepatitis C negative, is appropriate in some circumstances - for example, homologous blood donation. Any mandatory testing must be firmly based on scientific knowledge of how the virus is transmitted and on ethical considerations. To protect against potential abuse, any requirements for mandatory testing should be fully documented in guidelines that describe the justification, the procedure to be followed, and safeguards to ensure protection against abuse and compliance with ethical standards.

Mandatory and compulsory testing should always be accompanied by pre-test and post-test discussion.[11]

[11] Test discussion, as outlined in this policy, is not required for blood donors. Post-test counselling is not required for blood donors who test negative for hepatitis C. Blood services should either provide post-test counselling for donors who test positive or refer these people to appropriate services.

Surveillance. Information from hepatitis C testing contributes to an improved understanding of epidemiology and allows for targeting of health promotion interventions and planning of care and treatment services.

Anonymous de-identified testing. For surveillance purposes anonymous de-identified testing may be considered in special circumstances. It must, however, comply with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Research Involving Humans*[12], include full scientific justification (as for all research), and be consistent with the Australian Hepatitis C Surveillance Strategy.

Infection control. Testing does not diminish the need for standard precautions in handling blood and body fluids in any health care setting.

[12] National Health and Medical Research Council 1999, *National Statement on Ethical Conduct in Research Involving Humans*, NHMRC, Canberra.

Appendix 4 Antenatal testing

Factors not associated with a higher risk of transmission are the mode of delivery, hepatitis B co-infection and breastfeeding. At present no drug therapies can be recommended to reduce the risk of mother-to-child transmission. No specific intervention at the time of delivery has been shown to reduce the risk of transmission and breastfeeding has not been shown to increase the risk of HCV transmission to the baby.

There is no evidence that the prevalence of hepatitis C among pregnant women is significantly higher than for the general population. Routine screening of pregnant women is not a cost effective or clinically justifiable approach.

Any woman identified as being at risk of, or personally concerned about, HCV infection should be offered testing, including prior to undergoing any invasive medical procedures. The process of testing should follow the processes detailed in this policy.

Transmission from mother-to-child will not occur if the mother has spontaneously cleared the viral infection, so all pregnant women who test positive for anti-HCV antibodies should be offered qualitative HCV RNA testing to determine if they are still infectious. This indication for qualitative HCV RNA testing is covered under the Medicare Benefits Schedule (see Chapter 10).

Infants born to anti-HCV positive mothers will have passively acquired antibodies. In uninfected infants, seroreversion or loss of maternal antibodies will be seen within 18 months. Antibody testing should therefore only be carried out after the child reaches 18 months of age.

This section of the National Hepatitis C Testing Policy will be regularly reviewed, to take account of any therapeutic advances that could minimise the risk of transmission and other new information, including information on hepatitis C sero-prevalence.

APPENDIX 5 Aboriginal and Torres Strait Islander People

Increasing testing in Aboriginal and Torres Strait Islander Communities

The NATSISH and BBV Strategy recommends several initiatives to increase hepatitis C testing in Aboriginal and Torres Strait Islander communities.

Techniques to improve access to testing should include:

- staff development for workers in primary health care services through dissemination of information and facilitating access to new testing and treatment regimes;
- improved linkages between service providers, including linkages between ACCHSs and mainstream services, as well as those between primary health care and specialist and tertiary services; and
- ensuring access for Aboriginal and Torres Strait Islander communities to technological advances and their application in clinical care.

Implement population based screening programs where indicated through:

- national surveillance data used to inform priority groups to be targeted for screening programs;
- continual expansion of comprehensive primary health care services to Aboriginal and Torres Strait Islander people ;
- increased collaboration and partnership between Aboriginal and Torres Strait Islander community controlled health services to increase capacity to priority groups; and
- ensuring community education and consultation is undertaken, and appropriate consent is given by Aboriginal and Torres Strait Islander peoples prior to conducting population based screening.

Facilitate access to new testing and treatment regimens by:

- dissemination of information on new testing and treatment regimens to Aboriginal community controlled health organisations, mainstream health services and community based organisations;
- support for research into the development of sensitive and specific diagnostic tests suitable for use in remote locations; and
- investigation of the use of new point of care testing technologies in different settings.

Epidemiology and testing research

Both the NATSISH and BBV Strategy and the National Hepatitis C Strategy recommend improvements to the collection, analysis and use of surveillance data, particularly increased use of Indigenous identifiers, for nationally notifiable diseases. The Department of Health and Ageing should work with the Communicable Diseases

Network of Australia to improve surveillance data by building on recent analysis and recommendations for improving Indigenous identification in communicable diseases reporting systems. In line with this, State and Territory jurisdictions should review notification forms and procedures, and implement measures to increase use of Indigenous identifiers.

Appendix 6 The Regulation of hepatitis C Testing and Mechanisms for Quality Assurance

1. Assuring the Quality of the HCV Test

The TGA has the regulatory responsibility for ensuring the quality, performance and safety of hepatitis C test kits and other IVDs through the *Therapeutic Goods Act 1989* and its associated regulations. The objective of the TGA is to assure the safety, quality, performance and timely availability of all test kits available in Australia at a standard at least equal to that of comparable countries. The TGA has the authority to remove from the market any test that does not perform to the expected standard or that is known or demonstrated to be defective.

The TGA is responsible for the pre-market evaluation and post-market monitoring of HCV assays. Under the regulatory framework, pre-market assessment includes a review of evidence of the manufacturer's quality management system, kit performance, kit presentation, labelling and promotional material and reagent safety and stability.

The TGA currently contracts evaluation of an assay's performance to the NRL, to ensure it will be suitable for the Australian population. The level and depth of an evaluation is governed by, and commensurate with the risks associated with failure in their use. The evaluation is designed to ensure that the performance is acceptable for the intended use or category of the IVD.

If the performance and other regulatory issues are deemed acceptable, the test kits are included on the Australian Register of Therapeutic Goods (ARTG) as 'registered' goods.

The NRL is subcontracted by the TGA to monitor HCV assays in the post-market setting. Participants' HCV results in external quality assessment schemes provide information about an assay's ongoing performance during use. Any observed deficiencies are reported to the TGA.

The TGA has mechanisms for the investigation and recall of faulty IVDs. This includes the Incident Report Investigation Scheme (IRIS) for the investigation of all reports submitted to the TGA on adverse events or problems associated with the use of medical devices, including HCV tests. IRIS can be utilised by the laboratories noting performance and safety issues with an assay.

The TGA Recalls Coordinator has the power to withdraw faulty HCV assays, and in the extreme case, to cancel product registration.

2. Assuring the Quality of hepatitis C Testing

Ongoing quality of testing is best achieved when quality management systems are implemented to ensure good laboratory practice is enforced. Good laboratory practice is supported and defined by relevant industry standards. For Australian medical laboratories, these standards are identified or authored by the National Pathology Accreditation Advisory Council (NPAAC).

ISO 15189 is recognized as the quality management system to be used by medical laboratories. The standard describes, amongst other aspects, the requirement for ongoing monitoring of the laboratory's performance. Use of quality control (QC) testing and enrolment in External Quality Assessment Schemes are mandated. These tools provide internal and external comparative data to monitor performance. Each is discussed in more detail below.

NPAAC has developed many standards that describe a minimal requirement for good laboratory practice, covering general issues such as laboratory supervision, retention times for records and samples, as well as specific discipline standards. Two standards of this latter group are highly relevant for laboratories testing for hepatitis C. They are "Standards and Guidelines for Laboratory Testing of Antibodies to the Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV)" 2006 and "Laboratory Accreditation Standards and Guidelines for Nucleic Acid Detection and Analysis" 2006.

Evidence of ongoing compliance with these standards can be demonstrated by successful NATA/RCPA Medical Accreditation. Hepatitis C testing should only be performed in laboratories that hold this accreditation as evidence that laboratory practice is of a high standard.

Quality Assurance Programs

Quality Assurance programs (QAPs) provide a means of assessing the successful implementation of effective laboratory management, and in the case of hepatitis C testing, a means of demonstrating ongoing quality of the test and the testing process. Evaluations of HCV tests are conducted before registration and provide base-line information on how a test kit should perform. In Australia, QAPs are used by the NRL to monitor both post-market kit performance and competence of laboratory process using the kits. Providers of QAPs for HCV testing in Australia include the NRL and the RCPA QAP P/L SQAP. The role of different types of QA monitoring tools are described below.

External Quality Assessment Schemes (EQAS)

EQAS are designed to assess the accuracy of the laboratory testing process, from receipt of the specimen to release of the analysed test result. EQAS usually consists of a panel of specimens sent to participating laboratories for testing at regular intervals. The panels are constructed so that aspects of the testing process and the kit in use can be assessed. The laboratories are able to compare their results with reference results and with the results of similar laboratories. This allows problems to be identified and follow-up provides for resolution of the problems, particularly those that are kit-based. It also creates a networking ability across laboratories so

performance evaluation is enhanced. Both Australian QAP providers offer this form of QAP.

Quality Control Samples

Laboratories use quality control samples to continuously monitor the accuracy of HCV antibody and nucleic acid tests. When used in every assay run, the samples allow for confirmation that the test results are reproducible and reliable. Monitoring the reactivity of a quality control sample, which should deliver consistent results across runs and batches, means that intra-laboratory and batch-to-batch variability can be tracked and abnormalities in performance can be assessed as laboratory or test based.

Specificity Monitoring

Ongoing performance of testing can be reviewed through specificity monitoring. If the level of false reactivity in tests in large numbers of samples is monitored, both assay and laboratory problems can be detected. There is usually a low rate of false reactivity, therefore a sudden increase in the false reactivity rate could suggest that the assay's performance is unsuitable.

Reference Testing

Reference testing serves as a reference point for HCV samples whose status cannot be resolved at the standard or reference laboratory level. Specialised testing strategies are used, among them selected tests not used by other laboratories. This provides an extra layer of testing for samples that are difficult to diagnose using screening laboratories' usual methods. It is also a base for testing the integrity of samples to be used in quality programs to assure their sameness and stability.

3. Categorisation

As discussed in Chapter 9, HCV test kits are categorised according to the manufacturer's assigned intended use. These categories are described in the following table (Table 1).

Table 1: Categorisation of HCV test kits for regulatory evaluation and use

<table>
<tr><td></td><td colspan="2">Test categories[A]</td></tr>
<tr><td>Purpose or uses of kits</td><td>Standard[B]</td><td>Reference[C]</td></tr>
<tr><td>Donor Testing – screening of blood and tissue donations.</td><td>Enzyme immunoassay
Particle agglutination assay
Machine-based immunoassay
NAT screening tests
Level 1*</td><td rowspan="2">Enzyme immunoassay
Western blot
Line assay
Rapid assays
Antigen enzyme immunoassay
Discriminatory NAT assay
Qualitative amplification assay
Quantitative amplification assay
Level 3 *</td></tr>
<tr><td>Diagnostic Testing – to determine the infection status of a sample for clinical purposes e.g. diagnosis, antenatal screening, pre-operative, visa, insurance, emergency, testing and supplemental and confirmatory purposes.</td><td>Enzyme immunoassay
Particle agglutination assay
Machine-based immunoassay
Rapid test
Alternative sample assay
Level 2*</td></tr>
<tr><td>Unlinked epidemiological surveillance – or definition of infection status of a population where no results are conveyed to individuals from whom samples are taken.</td><td>Rapid test
Alternative sample assay
Level 3*</td><td></td></tr>
<tr><td>Monitoring and management – quantifies or characterises the virus for clinical management.</td><td></td><td>Amplification assay
Antigen enzyme immunoassay
Typing assays
Assay for the detection of drug-resistant types of virus
Level 4*</td></tr>
</table>

* Denotes the minimum level of evaluation (see below). The levels do not relate to the Classes of kits defined in the IVD regulations to be implemented in 2007.

(A) **Test categories:** Laboratories perform standard and/or reference testing.

(B) **Standard tests**: Standard tests may be used by laboratories performing diagnostic or screening testing to identify the HCV negative antibody status of samples using screening or standard assays. Any test may be used for screening purposes provided it is evaluated to the appropriate level and shown to be appropriately sensitive and specific and approved by the TGA for that use. Those samples yielding non-reactive results do not need to be further tested unless clinical considerations demand it. Reactive samples must be subjected to supplemental testing to distinguish true reactivity from false reactivity. The reference testing must confirm the presence of specific antibody or virus before the result is accepted as a true positive.

(C) **Reference tests:** Reference tests are used by laboratories to conduct confirmatory or additional special testing. This testing is conducted to confirm true positive status by distinguishing true from false reactivity. Usually this testing is conducted within a diagnostic strategy and an immunoblot is often used; but other reference testing situations occur (e.g. in a setting of possible seroconversion illness) when the first-used reference tests may include a nucleic acid test. Other reference tests may be used once the HCV status is confirmed to quantify viral load, characterise the virus or predict treatment response. These tests may be conducted outside reference laboratories as long as any TGA conditions for the kit registration are met.

Test kit performance evaluations (indicated by Levels 1, 2, 3, 4 in Table 1)

The level of evaluation for any test is commensurate with the risk of delivering a false result associated with its use:

Level 1 Number of samples selected to fully determine all characteristics of the assay in a statistically valid manner and within narrow confidence limits. A full scale Level 1 evaluation involves estimation of sensitivity and specificity in sufficient samples to yield statistically valid assay comparison. Samples for estimation of sensitivity include samples from infected people through the entire course of infection including seroconversion.

Level 2 Full evaluation of sensitivity often within a multi-site protocol and with more limited determination of specificity (i.e. in fewer samples and therefore with a wider confidence interval around the estimation).

Level 3 Evaluation only in a characterised sensitivity panel, with testing in a limited number of negative samples which have potential for or established false reactivity. Rapid test or alternative sample assays, if used for screening, should be evaluated as screening tests (i.e. at Level 1 or 2).

Level 4 Evaluation protocol designed on submission of the assay. Post-market monitoring or collection of data that indicate how the test is performing as it is used will be required as a condition of supply of the kits. The conditions will be indicated on the TGA registration certificate.

Appendix 7 Resources and referral details for consumers and providers

GENERAL INFORMATION

Hep C: What You Need To Know - a comprehensive overview of hepatitis C.
http://www.hepatitisc.org.au/resources/documents/WYNTKed4.pdf

I Have Hep C: what could happen to me
http://www.hepatitisc.org.au/resources/documents/IHHC0608.pdf

Hepatitis information and support line 1300 HEP ABC

National Hepatitis C Resource Manual (2001)
http://www.health.gov.au/internet/wcms/publishing.nsf/content/health-pubhlthstrateg-hiv_hepc-hepc-manual.htm

Aboriginal Health and Medical Research Council of NSW 2006 'STI & BBI Manual'. A manual for improving access to early detection and treatment programs for Aboriginal people and Communities in NSW

ASHM directory is a compendium of contact details that is updated each year and available in print at no charge. It includes detailed listing of practitioners, organisations, locations, languages and specialities. http://www.ashm.org.au/ashm-directory/

FACTSHEETS

Antibody Testing
http://www.hepatitisc.org.au/quickref/documents/Antibody_testing.pdf

Genotypes
http://www.hepatitisc.org.au/quickref/documents/Gentypes.pdf

Liver Biopsy
http://www.hepatitisc.org.au/quickref/documents/Liver-biopsy_000.pdf

Liver Function
http://www.hepatitisc.org.au/quickref/documents/Liverfunction.pdf

PCR Availability
http://www.hepatitisc.org.au/quickref/documents/PCR_availability.pdf

PCR & Hep C Transmission
http://www.hepatitisc.org.au/quickref/documents/PCR_transmission.pdf

Pre-Test Discussion
http://www.hepatitisc.org.au/quickref/documents/Test_counselling.pdf

Australian Hepatitis Council (2006), 'Contact: Post-test information for Hepatitis C'
http://www.hepatitisaustralia.com/pages/Publications___Resources.htm

Australian Hepatitis Council (2006), 'Preparing for testing'
http://www.hepatitisaustralia.com/pages/Publications___Resources.htm

Australian Hepatitis Council (2006), 'Women and Hepatitis C: a resource for women with hepatitis C'
http://www.hepatitisaustralia.com/pages/Publications___Resources.htm
Factsheets on hepatitis C in a range of community languages and Plain English are available at:
Multicultural HIV/AIDS and Hepatitis C Service (www.multiculturalhivhepc.net.au)
Australasian Society for HIV Medicine (www.ashm.org.au)

ASHM 2002 (to be revised 2007) 'Ambulance Officers and Hepatitis C
ASHM 2006 'Dental Health and Hepatitis C'
ASHM 2006 'General Practitioners and Hepatitis C'
ASHM 2006 'Nurses and Hepatitis C'

ASHM 2006 'Hepatitis C in Brief '- patient fact sheet is a resource designed for people who have received a positive hepatitis C antibody test result and for people wanting to know more about hepatitis C. Two versions of the hard copy pads in English are available: National and NSW/ACT/VIC (HCV S100 Pilot States/Territory).
'Hepatitis C in Brief' is also available in and eight (8) community languages: Arabic, Chinese, Greek, Indonesian, Italian, Khmer, Spanish and Vietnamese.

MONOGRAPHS
Monographs which can be downloaded, or ordered from ASHM at http://www.ashm.org.au/publications/, include:

ASHM 2006 'HIV/Viral hepatitis – a guide for primary care' is designed to meet the needs of general practitioners and other health care providers. It provides up to date information and guidelines on risk assessment, diagnosis, management and professional issues.

ASHM 2006 'Coinfection - HIV and viral hepatitis: a guide for clinical management' reflects best practice in Australia today for the management of HIV and viral hepatitis in the primary care setting.

ASHM Edition 3 2006'Australasian Contact Tracing Manual' is a practical handbook for health Care providers managing people with HIV, viral hepatitis, other sexually transmitted infections and HIV related tuberculosis.

ASHM 2005 'HIV and hepatitis C: policy, discrimination, legal and ethical issues' is a collection of essays describing the legal, ethical and discrimination issues presented by two important challenges to global public health: HIV and hepatitis C.

ASHM 2005 'Talking together' is a distance learning package for those working in Indigenous Health includes slides, HIV/Viral Hepatitis monograph and training materials.

OTHER RESOURCES

Crofts, Dore, Locarnini et al 2001 'Hepatitis C An Australian Perspective'.

Geoffrey C Farrell 2002 'Hepatitis C, other liver disorders and liver health'.

INTERPRETERS

Telephone Interpreter Service 131 450 (available nationally)

Private medical practitioners can access telephone interpreters (at no cost) through the Doctors' Priority Line 1300 131 450

In addition some jurisdictions have healthcare interpreters which are generally available at public health facilities

ALCOHOL AND DRUG INFORMATION SERVICES

Australian Drug Information Network (ADIN)
(03) 9278 8100
www.adin.com.au

ACT
(02) 6207 9977

NSW
(02) 9361 8000 or 1800 422 599 (rural)

NT
1800 131 350

QLD
(07) 3236 2414 or 1800 177 833 (rural)

SA
1300 13 13 40

TAS
1800 811 994

VIC
DirectLine 1800 888 236
DrugInfo 1300 85 85 84
Youth Substance Abuse Service
(03) 9418 1020 or 1800 014 446 (rural)

WA
(08) 9442 5000 or 1800 198 024 (rural)

DRUG USER ORGANISATIONS

AIVL
Australian Injecting and Illicit Drug Users League
(02) 6279 1600
www.aivl.org.au

ACT
CAHMA
(02) 6279 1600

NSW
NUAA
(02) 8354 7300
1800 644 413

NT
NAP
(08) 8941 9921

QLD
QUiHN
(07) 3620 8111

SA
SAVIVE
(08) 8334 1699

VIC
VIVAIDS
(03) 9329 1500

WA
WASUA
(08) 9321 2877

HEPATITIS COUNCILS

Hepatitis Australia
(02) 6232 4257
www.hepatitisaustralia.com

ACT
Helpline 1300 301 383

SA
(08) 8362 8443 (Adelaide callers)
1800 021 133 (SA Regional callers)

NSW
Hep C Helpline 9332 1599 (Sydney callers)
1800 803 990 (NSW regional callers)

TAS
Information and Support Line
1800 005 900

NT
(08) 8941 1711 (Darwin callers)
1800 880 899 (NT regional callers)

VIC
(03) 9380 4644 (Melbourne callers)
1800 703 003 (VIC regional callers)

QLD
Information Line (07) 3236 0612
(Brisbane Callers)
1800 648 491 (Qld regional callers)

WA
information & Support Line
(08) 9227 8538 (Perth callers)
1800 800 070 (WA regional callers)

Glossary

Anonymous de-linked test	Testing of samples that have been irreversibly de-identified.
Compulsory testing	Testing when a person has no choice about being tested.
Confirmatory testing	Testing that leads to a diagnosis being confirmed. A confirmatory test is the test that gives the diagnosis.
Custodial settings	Includes the various settings in which adults and juveniles can be detained or imprisoned—prisons, juvenile justice centres, and remand and other detention centres.
Discriminatory NAT	Used in the ARCBS to discriminate activity which could be either HIV or HCV related.
Exposure prone procedure	Exposure prone procedures (EPPs) are a subset of invasive procedures characterised by the potential for contact between the skin (usually finger or thumb) of the health care worker (HCW) and sharp surgical instruments, needles or sharp tissues (spicules of bone or teeth) in body cavities or in poorly visualised or confined body sites (including the mouth). In the broader sense an EPP is considered to be any situation where there is a potentially high risk of transmission of bloodborne disease from HCW to patient during medical or dental procedures.
Gold-standard test	A test that unequivocally identifies the presence of an infection.
Heteroduplex mobility analysis	Method by which nucleic acid species of similar composition are separated in a gel on the basis of mass or charge, or both, to demonstrate differences in sequence or structure.
Home collection	Taking blood or another type of sample in a non–health care environment without the supervision of trained personnel and then forwarding the sample to a laboratory for analysis.
Home-based testing	Testing conducted in a non-laboratory or non–health care environment without the supervision of trained personnel.
Home-use IVD	Devices used for testing in the home, as distinct from point-of-care testing. Two common reasons for using home-use in-vitro diagnostic devices in Australia are for home collection, self-diagnosis and management and for home collection of a sample to be tested elsewhere and/or interpreted without the involvement of a health care practitioner.
Indeterminate test result	A result that is neither clearly negative nor clearly positive.

In-house tests	A test that is developed or modified from another source within the confines of a laboratory, validated for use within that laboratory only, and not supplied for use outside that laboratory. For the purposes of this document, 'laboratory' means an Approved Pathology Laboratory, as defined in section 23D of the Commonwealth's *Health Insurance Act 1973*; the term 'supplied' is used with reference to the definition of the term 'supply' in the *Therapeutic Goods Act 1989*—that is, 'supply' includes (a) supply by way of sale, exchange, gift, lease, loan, hire or hire-purchase; and (b) supply, whether free of charge of otherwise, by way of sample or advertisement; and (c) supply, whether free of charge or otherwise, in the course of testing the safety or efficacy of therapeutic goods in persons or animals; and (d) supply, by way of administration to, or application in the treatment of, a person or animal.
IVD	Any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination (with other diagnostic goods for in-vitro use), intended by the manufacturer to be used in-vitro for the examination of specimens derived from the human body, solely or principally for the purpose of giving information about a physiological or pathological state, a congenital abnormality or to determine safety and compatibility with a potential recipient or to monitor therapeutic measures.
Mandatory testing	Where testing is pre-condition of obtaining a service or benefit.
PCR testing	A technique whereby nucleic acid (cell genetic material) is amplified in order to detect the presence of particular and specific nucleic acid sequences.
Predictive values	Parameters that define the chance of a reactive test being truly positive (the positive predictive value) or a non-reactive test being truly negative (the negative predictive value) for the substance that a test is designed to detect.
Quality assurance	The methods by which the integrity of tests and testing is assured.
Qualitative test	A test that detects the presence or absence of an agent or substance without measuring the level or quantity of that agent or substance.
Quantitative test	A test that not only detects the presence of an agent or substance but also gives the level or amount of the agent or substance.
Reference testing	Testing conducted to clarify the nature of samples' reactivity or status following initial tests conducted with standard tests in the same or another laboratory.

Sensitivity	The proportion of reactive results found by a given test in a known positive population. Indicates the potential false negative rate of a test.
Serology	Scientific testing to determine the presence, evidence or quantity of antibodies specific for infectious or other agents, chemicals or substances in blood.
Specificity	The proportion of non-reactive results found by a given test in a known population of negative samples. Indicates the potential false positive rate for a test.
Supplemental test	A test performed after initial, standard or screening testing, usually to clarify the sero-status of a reactive sample.
Test Kit	An IVD assay, where an assay is an analysis done in-vitro to determine the presence of a substance and the amount of that substance in a specimen taken from the human body.
Window period	The time between when a person has been exposed to hepatitis C and the time that detectable level of hepatitis C antibodies are present in the blood

Abbreviations

ALT	alanine aminotransferase
APHDPC	Australian Population Health Development Principal Committee
BBVSS	Blood Borne Virus and Sexually Transmissible Infections Subcommittee of the APHDPC.
CALD	Culturally and Linguistically Diverse
CDNA	Communicable Diseases Network of Australia
EIA	enzyme immuno-assay
EPP	Exposure Prone Procedure
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IDU	injecting drug use
IGCAHRD	Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases
IVD	in-vitro diagnostic device
LFT	liver function test
MBS	Medicare Benefits Schedule
MSAC	Medicare Services Advisory Committee
NAT	nucleic acid test/testing
NATA	National Association of Testing Authorities
NHMRC	National Health and Medical Research Council
NPAAC	National Pathology Accreditation Advisory Committee
NRL	National Serology Reference Laboratory, Australia
PCR	polymerase chain reaction
PHLN	Public Health Laboratory Network
RCPA	Royal College of Pathologists of Australasia
RNA	ribonucleic acid
TGA	Therapeutic Goods Administration