Introduction

What is point-of-care testing? For the purpose of this guideline document, point-of-care (POC) testing is defined as ‘pathology testing which is performed on behalf of the treating medical practitioner by a trained operator in an on-site clinical setting while the patient is in attendance, allowing the test result to be generated and used to make an immediate informed decision that contributes to an improved health outcome for the patient’. POC testing for clinical chemistry and haematology has come of age in Australia over the past decade, as the scope and application of this rapidly evolving field of medical science has diversified from hospital laboratories, wards and clinics to a range of community-based clinical settings (Shephard 2010). However there are many issues, considerations and barriers around the introduction of POC testing for infectious diseases and drugs of abuse in Australia.

The aim of this guideline document is to provide a practical framework for the quality-assured and safe conduct of POC testing for infectious diseases and drugs of abuse that is relevant to, and can be applied in, both laboratory settings and clinical settings outside the laboratory.

Standards and guidelines for POC testing (general)

The International Organisation for Standardisation (ISO), a worldwide federation of national standards bodies, recently published a standards document (ISO 22287-0), detailing requirements for quality and competence for POC testing (International Organisation for Standardisation 2005). In Australia, national standards for the conduct of POC testing are not currently available. A set of interim standards was developed for use in
the Point of Care Testing in General Practice Trial by a subcommittee of the Australian Government Department of Health and Ageing’s Quality Use of Pathology Committee (Australian Government 2004). This randomised controlled trial involved just under 5000 patients and focused on the use of clinical biochemistry and haematology markers for chronic disease management (Laurence et al 2008).

Multiple guidelines on how to establish and manage a POC testing service (both generally and for specific tests) have been published by professional societies and expert panels representing many countries and/or regions of the world. The Clinical and Laboratory Standards Institute (CLSI) has been particularly active in producing a range of guideline documents related to POC testing over the past five years (CLSI website). In 2006, the National Academy of Clinical Biochemistry (NACB) also published guidelines for the evidence-based practice of point-of-care testing, which covered all the major pathology disciplines (Nichols 2006). The Medicines and Healthcare products Regulatory Agency (MHRA), a UK Department of Health government entity, recently published comprehensive guidelines on the management and use of POC testing devices (MHRA 2010).

In Australia, the Australasian Association of Clinical Biochemistry (AACB) produced an implementation guide for POC testing, which was particularly relevant for clinical biochemistry and haematology POC tests (AACB 2008). Most guideline documents embrace similar underlying principles for the conduct of POC testing, whether it be within or outside the laboratory, which include clinical need, selection of device, cost benefit analysis, governance, documentation of standard operating procedures, training and competency assessment, quality management for routine implementation, and continuing audit and accreditation.

Standards and guidelines for POC testing (for infectious diseases and drugs of abuse)

Limited published information is available with specific reference to POC testing for infectious diseases and drugs of abuse. The World Health Organisation (WHO) has produced excellent guideline documents for training and applying quality systems for POC or ‘rapid’ testing for HIV and malaria in developing countries (WHO 2005, 2006, 2009). The recently published 2011 National (Australian) HIV Testing Policy contains a section on POC testing for HIV in community settings and discusses which health professionals can perform such testing, accreditation requirements for prospective POC testing sites wishing to claim Medicare rebate, restrictions on where and how community testing can occur, the need for quality assurance systems to be in place, and to whom community POC testing can be offered (ASHM website; HIV guidelines and policy). The draft 2012 National HBV Testing Policy makes the following reference to the use of rapid tests at the point-of-care “HBsAg PoC tests are available and may be useful in some settings, e.g. testing in remote communities and where there are barriers to accessing traditional healthcare. However, HBsAg PoC tests are known to have a lower analytical sensitivity compared to standard laboratory EIAs and may be unable to detect low levels of HBsAg. PoC tests must comply with TGA regulatory framework for IVDs and be included on the ARTG” (ASHM website; Hepatitis B guidelines and policy).

In relation to testing for drugs of abuse, in 2008 Standards Australia/Standards New Zealand (AS/NZS) released the document Procedures for Specimen Collection and the Detection and Quantitation of Drugs of Abuse in Urine (AS/NZS 4308). The objective of this standard was to ensure that the detection of drugs in urine meets the expectations for testing of specimens for medico-legal, workplace or court-directed purposes. While focused principally on the requirements of laboratories, the document contained an appendix which provided general information for the on-site screening of drugs of abuse in human urine using POC devices. It contained limited information on requirements for training and competency of POC device operators but detailed very stringent requirements for the conduct of quality testing processes.

This guideline document is designed to complement information contained in the disease-specific guidelines mentioned previously, and it has a deliberate emphasis on recommendations for device selection and training and quality systems to support POC testing for infectious diseases and drugs of abuse as information on these aspects of testing are generally lacking in the published literature.

Regulatory requirements of POC testing for infectious diseases and drugs of abuse in Australia

Whereas all clinical pathology laboratories in Australia claiming Medicare rebates are required to be accredited to ISO/IEC standard 15189: 2009, this may not be the case for POC testing facilities that do not claim Medicare rebates. The 2011 HIV Testing Policy and 2012 HCV Testing Policy state that facilities performing POC testing for HIV and HCV and claiming Medicare rebates must either have attained National Association of Testing Authorities (NATA) accreditation and comply with the National Pathology Accreditation Advisory Council (NPAAAC) standards for HIV and HCV testing, or have established a formal supervisory relationship with a laboratory that does (ASHM website; HIV guidelines and policy, and Hepatitis B guidelines and policy).

Currently, any In-vitro Diagnostic Device (IVD) that is already available for distribution in Australia can be sold prior to June 2014. However any new IVD, including POC testing assays, will need to be listed on the Australian Registry of Therapeutic Goods (ARTG) by
June 2014 (TGA website; ATRG). The level of scrutiny by the Therapeutic Goods Administration (TGA) for each assay will be dependent on the Class of the IVD. All assays used to test for HIV, Hepatitis B and C will be classified at the highest level (Class IV). Most other tests for infectious diseases will be classified as Class III (TGA website; IVD classification). The cost of registration is high and depends upon the intended use of the IVD. It is the sponsor’s responsibility to submit the IVD for registration prior to selling the product in Australia, and therefore the sponsor must determine the cost/benefit of the IVD in the marketplace. POC products for drugs of abuse that are not used for a therapeutic purpose are outside the scope of TGA regulations and therefore do not need to be included on the ARTG.

Scope of POC testing for infectious diseases and drugs of abuse

The potential scope for using POC testing for infectious diseases and drugs of abuse is extensive. Examples of clinical settings outside the laboratory where POC testing for infectious disease has been applied globally includes (but is by no means limited to) hospital emergency departments, sexual health clinics, indigenous and non-indigenous community health services, bars, public parks, homeless shelters, drug treatment facilities and syringe-exchange programs, sex-on-premise venues, mobile vans and the aftermath of disaster events. POC testing for drugs of abuse is widely used in industries such as mining, transport and sporting, particularly as part of pre- and post-employment schemes. In these settings, POC testing is primarily used for screening rather than management purposes. In Australia, the laboratory continues to remain the principal site for infectious disease and drugs of abuse pathology testing. However, large clinical trials of community-based POC testing for HIV (in urban settings in Melbourne, Sydney and Brisbane) and chlamydia and gonorrhea (in remote indigenous settings) are currently being undertaken. As stated POC testing for drugs of abuse is becoming increasingly common in the Australian mining sector, primarily due to the geographic isolation of these locations, and logistical challenges associated with laboratory testing such as frequency of transport and maintenance of required environmental conditions in transit. The clinical and operational value of POC testing for infectious diseases and drugs of abuse lies in the immediacy of result, the ability to rule out the presence of infectious agent or drug which reduces stress and anxiety for patients facing a long waiting period for turnaround of laboratory results, and the rapid administration of targeted treatment.

Globally, the range of infectious agents/diseases that can be detected by POC testing is increasing rapidly and now includes (but is not limited to) *Clostridium difficile*, *Chlamydia trachomatis* (chlamydia), Dengue fever virus, *Helicobacter pylori*, Hepatitis B and C, HIV-1 or 2, Influenza A and B, *Mycobacterium tuberculosis* (tuberculosis), *Neisseria gonorrhoeae* (gonorrhea), *Plasmodium spp* (malaria), Respiratory Syncytial Virus (RSV), *Streptococcus pneumoniae*, *Treponema pallidum* (syphilis), and *Vibrio cholera* (cholera) (Tran and Kost 2006, Campbell et al 2006, Motta et al 2012). In Australia and New Zealand, the most common drugs (or drug classes) measured by POC testing are cocaine, amphetamine, methamphetamine, cannabis (tetrahydrocannabinol or THC), opiates and benzodiazepines.

There are many fundamental differences between POC testing for infectious diseases and drugs of abuse and POC testing for most clinical chemistry and haematology markers (Table 1). The vast majority of POC infectious disease and drugs of abuse testing is targeted towards screening for the presence of specific infectious agents or (groups of) drugs, with all initially reactive results requiring laboratory confirmation as a true positive result. Clinical chemistry and haematology POC tests are generally used more for diagnosis and management purposes. Most POC testing for infectious disease or drugs of abuse generate a qualitative result (for example whether the infectious agent or drug is present or absent in the sample), while clinical chemistry and haematology tests usually produce a quantitative result (the absolute level or concentration of analyte). The key measures of analytical performance for infectious diseases and drugs of abuse tests are their sensitivity, specificity, positive and negative predictive values, whereas for clinical chemistry and most haematology tests, measures of accuracy and precision are more commonly used to assess performance. While blood and urine are the principal matrices for measurement of most POC clinical chemistry and haematology tests, there are many different fluid types used as the preferred sample for infectious disease and drugs of abuse testing; for example genital nasal or throat swabs, and faeces for infectious diseases, and sweat, saliva, and breath for DOA (Rowland 2004). Compared with clinical chemistry and haematology testing, infectious disease or drugs of abuse POC testing generally has a requirement for pre and/or post-test counseling, with particular emphasis on the patient understanding of the ramifications of an initially reactive result.

Table 1. General differences between POC testing across medical science disciplines

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Infectious disease and drugs of abuse POC testing</th>
<th>Clinical chemistry and haematology POC testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical use</td>
<td>Screening</td>
<td>Management</td>
</tr>
<tr>
<td>Result</td>
<td>Qualitative</td>
<td>Quantitative</td>
</tr>
<tr>
<td>Analytical performance indicators</td>
<td>Sensitivity, specificity, positive and negative predictive value</td>
<td>Accuracy and precision</td>
</tr>
<tr>
<td>Testing matrices</td>
<td>Multiple fluid types</td>
<td>Mainly blood</td>
</tr>
</tbody>
</table>
Range of devices, method principles and other aspects of technology

For many years, most POC tests for infectious diseases and drugs of abuse have been based on lateral flow technology which generally involves the detection of an antibody response (often the immunoglobulins IgM, IgG or IgA) or the detection of antigens (such as surface antigens, proteins and enzymes that are secreted by the host, the infectious agent or released during cell lysis) (Rowland 2004). Underlying method principles have become increasingly sophisticated and may now use, for example, agglutination reactions, chromogenic antibodies or fluorogenic or chromogenic drug-conjugates (Watson et al 2006).

A fundamental difference between lateral flow POC testing for infectious diseases and drugs of abuse lies in the interpretation of the test result. For infectious disease POC testing, the presence of a line in the test result region indicates a positive result for that test. However, for drugs of abuse POC testing devices, the presence of a line generally means the drug of interest is below the threshold of detection while the absence of a line indicates the drug is present; that is, the test is often referred to as a ‘negative read’.

Recently, POC testing for infectious diseases has entered a new phase where devices are now being developed that utilise nucleic acid amplification technology (NAAT) as their underlying method principle. Here nucleic acid from the infectious agent is extracted, amplified and then detected using either coloured or fluorescent dyes. Refinements to this technology are rapidly occurring such as the use of loop-mediated isothermal amplification (LAMP) for the detection of *Plasmodium vivax* and many kinds of pathogens for detecting food-borne diseases (Parida et al 2008, Mori and Notomi 2009, Tao et al 2011). LAMP amplifies the target DNA sequences at a constant temperature (63°C) rather than employing thermal cycling. Devices based on NAAT technology have markedly improved diagnostic sensitivity and specificity, but at present their field application is limited by the high cost of these devices as well as their longer time for result generation.

Recommendations for device selection

The performance characteristics of IVDs that test for the same analyte are not necessarily the same. For example, POC tests for syphilis may detect specific or non-specific analytes, have different analytical sensitivity (i.e. detect different levels of antibody), and have different levels of clinical sensitivity and specificity (i.e. levels of false negativity and reactivity). When selecting a POC test each facility may have a different intended use. For example, some facilities may use the test to screen women for chlamydia in an antenatal setting where the prevalence of disease is low, whereas other users of the POC test may be testing high-risk individuals at a dance party or bar. Knowledge of the population to be tested is critical prior to choosing a POC test. The performance characteristics provided by the manufacturer and published in the literature should be reviewed carefully in this light.

Analyte being detected

Different POC tests may detect different analytes to confirm the presence of disease or drug of abuse. For example, a HIV assay may detect a specific anti-HIV-1 antibody, an anti-HIV-1/2 antibody, a HIV p24 antigen or a combination of anti-HIV-1/2 and p24 antigen. Syphilis POC tests may detect antibodies to non-specific reagin antigen or specific anti-treponemal antibodies. The specific treponemal antibody tests will remain reactive for life, even after effective treatment, whereas the reagin test will become non-reactive after treatment, and therefore different information will be derived from each test. The majority of DOA POC tests work by utilising antibodies to various drugs or drug groups, in a competitive binding (or ‘sandwich’) immunoassay procedure. Many of these antibodies will have a broad range of cross reaction between very similar drugs in the same class (codeine and morphine for example) but also possibly between entirely unrelated drugs pharmacologically that may share some common structural feature recognised by a particular antibody. Different drugs (or their metabolites) may also only be present in a specific matrix; for example, the target analyte for THC is the carboxy metabolite in urine, whereas it is the parent drug itself in oral fluid. Therefore, before selecting an assay, the user should be aware of principles of each assay.

Analytical sensitivity

Each assay will be reactive at differing levels of the analyte being tested. Some assays will detect low levels of the specific analyte while others require higher concentrations of the analyte before it will be reactive. A level of understanding of the analytical sensitivity of the chosen assay, and the consequences on performance, is essential. For example, POC tests for hepatitis B surface antigen (HBsAg) are generally less analytically sensitive than laboratory-based tests. Therefore false negative test results will ensue if a patient has low levels of circulating HBsAg. For this reason POC tests are generally not recommended for screening of blood donations for HBsAg prior to transfusion. For DOA POC testing, the cut-off for the target analytes can and does vary between different devices, even if they are targeting the same drug classes. This can be due either to a different clinical requirement or because of the variation in respective standards for DOA testing across the world. For example, under the Australian and New Zealand Standard (AS/NZS 4308), the cut-off for a positive amphetamine result is 300 ng/mL while under the US Substance Abuse Mental Health Services Administration (SAMHSA) legal requirement, it is 500 ng/mL. Additionally, devices which are compliant with the existing Australian and New Zealand Standard for drugs
of abuse screening are not intended to detect the presence of any amount of drug, only concentrations greater than those listed in the Standard. Therefore it is not correct to say that a negative test indicates that the sample is “drug free” but rather that the levels present are below those set out in the Standard.

Clinical sensitivity

Clinical sensitivity is defined as the proportion of those with the disease/drug who test positive (i.e. the number of true positive results divided by the number of true positive results plus the number of false negative results, expressed as a percentage) (see Appendix 1). All assays will report some false positive and some false negative test results. Generally, as the percentage of false positive results increases, the percentage of false negative results decreases. Therefore, it is important to understand these assay characteristics when choosing a POC test appropriate for the population being screened.

Clinical specificity

Clinical specificity is the proportion of those without the disease/drug who test negative (i.e. number of true negative results divided by the number of true negative results plus the number of false positive results, expressed as a percentage) (see Appendix 1).

Testing strategy

The use of POC testing for clinical screening requires a testing strategy that takes into consideration (i) the clinical sensitivity and specificity of the test, (ii) the prevalence of the disease or drug of abuse in the clinical setting in which screening is undertaken and (iii) a protocol for the confirmatory (or supplemental) testing of initially reactive POC screening tests.

Usually a POC test with high sensitivity is selected to screen a population for the presence of an infectious disease or drug of abuse, as this will limit the number of false negative results being reported.

The prevalence of disease or drugs of abuse will significantly affect the likelihood of a positive test result being a false positive. As a general rule, in a population where the prevalence is high, the possibility of initially reactive POC test results being falsely reactive is low. However, in a population where the same POC screening test is used but where the prevalence is lower, the possibility of reactive test results being falsely reactive is higher (Appendix 1). Issuing a falsely reactive test result can cause serious consequences when testing for drugs of abuse or infectious diseases, especially with blood-borne or sexually transmitted infections. It is therefore important that all initially reactive POC test results are confirmed. Confirmatory testing is most commonly undertaken by referring the sample with a reactive POC test for a laboratory-based test or by not reporting reactive test results and referring the individual on for repeat screening in a laboratory-based testing facility.

In countries where confirmatory testing of initially reactive samples in a laboratory is unavailable or not feasible, testing algorithms may be used. These algorithms involve the use of a combination of POC tests, either serially or in parallel, to achieve predictive values close to 100% (Motta et al 2012). Such an algorithm for HIV testing is currently being implemented in the Pacific Islands (Dick et al 2010).

In summary, as the selection of assays for screening and confirmatory testing is dependent upon the prevalence of disease or drugs of abuse in the population, the clinical sensitivity and specificity of the assay and the level of common false reactive results shared between the screening and confirmatory assays, a testing protocol suitable for one clinical environment may not be suitable for another. Therefore an assessment of the suitability of each assay must be undertaken for each new environment in which the testing will be implemented (CDC 2001). Help from external organisations, such as laboratories, that are familiar with establishing these studies is recommended.

In addition, as POC devices for drugs of abuse will deliberately and inadvertently (through cross reaction of the antibodies used in the device) detect a range of prescription medications, an appropriate strategy must be in place to deal with issues arising from any declared or non-declared prescription drug use prior to implementation of any testing regime.

Recommendations for sample collection

In preparing these recommendations, it is acknowledged that POC testing for infectious diseases and drugs of abuse, and associated sample collection, is often carried out in geographically remote locations, and/or performed by health professional staff other than trained laboratory personnel.

The recommendations below therefore provide a general guide only to selected criteria that should be considered when developing a local standard operating procedure (SOP) for a POC testing protocol, including sample collection. The exact requirements will vary depending on the sample type, the manufacturer’s instructions, the type of test or collection being performed and any possible legislative (e.g. OH&S laws) or regulatory requirements (e.g. from the Therapeutic Goods Administration).

Staff performing POC testing must be aware of the microbiological hazards of collecting sample from patients and of handling and disposing of body fluids and sharps.
Appropriate specimens for POC testing should be collected according to the manufacturer’s instructions or other endorsed collection procedures, e.g. hospital policy for specimen collection.

Staff should consistently treat all patient samples as potentially infectious and wear gloves and ideally other appropriate personal protective equipment (PPE) including a gown or plastic apron, and safety glasses. Gloves must be worn when handling or touching any blood and body substances, mucous membranes or non-intact skin, and for handling items or surfaces contaminated with blood or body fluids. Gloves must be changed after contact with each patient and hands must be washed on removal of gloves. Safety glasses should ideally be worn for phlebotomy procedures or when handling body fluids.

All sharps (needles, lancets, slides, broken tubes) should always be placed in a puncture resistant container for disposal.

The specimen collection area should be as secure and private as facilities allow, as the patient may be required to answer questions on their medical history relevant to the specific type of POC test to be performed. This may require a separate room for confidentiality or sample collection purposes.

Consideration for unequivocally establishing the identity of the patient must also be considered in non-clinical environments. As a minimum two unique identifiers (full name and date of birth as examples) are required.

A permanent record system should be kept of the date and time of collection and any subsequent POC testing to allow a record of the time and result (if any) as some sample types may be required to be tested within certain set parameters (for example, time or temperature) or the result of the POC test may only be valid on the device for a set period of time (for example, a manufacturer may state “read result after 5 minutes. Do not interpret results greater than 1 hour after sample application”). The permanent record system should allow for enough information capture to state with confidence that this has occurred.

Transport of samples for confirmatory testing needs to take place in accordance with the instructions supplied by the device manufacturer, in consultation with the appropriate laboratory receiving the samples and in accordance with the relevant regulatory bodies (such as the International Air Transport Association [IATA]) involved in sample shipment and transport.

Specific sample types will require specific detailed collection and/or testing guidelines. An example of a urine drug screen collection protocol is provided in Appendix 2.

**Recommendations for training**

A wide variety of health professionals now perform routine POC testing for infectious diseases and drugs of abuse. These include medical scientists in the hospital environment, nurses in both hospital and a range of specialised primary care environments (such as sexual health clinics and mining sites), Aboriginal health practitioners in the Aboriginal and Torres Strait Islander medical services and, in some cases, administrative or security staff.

Only staff who have undergone training from a recognised training organisation, received a competency certificate as a qualified POC device operator, undertaken continuing education to maintain their competency and consistently perform quality testing procedures to monitor analytical performance, should be conducting routine patient POC testing for infectious diseases and drugs of abuse. A recognised training organisation may include an accredited laboratory, a professional organisation or a specialist POC provider from a tertiary institution.

A training program targeted to a specific clinical need and setting where POC testing is undertaken should be developed and delivered by a POC coordinator from the recognised training organisation. A POC coordinator should be a qualified medical scientist, nurse or Aboriginal health practitioner skilled and experienced in both the practice of POC testing and in the delivery of training. Health settings undertaking POC testing should consider establishing a formal supervisory link with a laboratory that is accredited by the NATA to support both training of staff and the governance of POC testing.

Currently in Australia there are a very limited number of training providers and this is an area which requires considerable future development. The AS/NZS 4308 Standards document for drugs of abuse testing states that, in relation to POC testing, ‘the collecting agency should be able to demonstrate that the collectors are proficient in the use of device’, but there is no directive on how proficiency should be formally assessed.

As part of delivering training, the POC coordinator should provide a training manual in hard copy or electronic form which systematically guides the trainer POC device operators through the principles and practice of POC testing. This manual should be comprehensive, intuitive, and not require specialised technical knowledge. The content of the training manual should be tailored to the specific POC application and the environment in which it will be used, but should include the following core elements:

- setting the clinical scene (disease process, pathophysiology and prevalence)
- a description of the clinical significance of the test
• performance characteristics of the POC testing device (including analytical and clinical sensitivity and specificity, as well as positive and negative predictive values)
• technical limitations of the POC device
• validated sample types
• patient preparation, pre-test counseling and specimen collection requirements
• conditions for reagent preparation and storage, including expiry dating
• how to perform the test on the POC device
• interpretation, documentation, reporting and traceability of results
• action required on POC test results (with particular reference to initially reactive POC test results)
• the principles and practice of quality management (including quality control and external quality assessment testing, where appropriate)
• maintenance and troubleshooting (if appropriate)
• occupational health and safety issues including infection control practices and,
• statement of compliance with national standards (for drugs of abuse), policy documents (for HIV and HCV for example) or accreditation requirements (when available).

Face-to-face training in small group settings is the preferred mode of delivery; where this is not possible, online or self-directed training present further training options. Training should include both a theoretical and practical component where trainees can practice performing POC testing under the supervision of the POC coordinator and gain confidence in performing the test. At the completion of training, competency should be formally assessed in a structured manner that includes completion of a written and practical assessment. All trainees who successfully complete training should be issued with a competency certificate that includes an expiry date, after which competency should be renewed. Most programs recommend that competency should be reassessed after a period not shorter than 12 months and not longer than 2 years. A register of all qualified operators should be maintained. Recently photographs of rapid test results, either on paper or via the internet, have been used to assess the trainee’s ability to read and interpret results of HIV POC assays (Chang et al 2006, Learmouth et al 2007, Chui et al 2011). This practice has potential to complement operator training programs, but should not substitute for need and requirement for operators to undertake practical training.

Recommendations for quality

For the purposes of this document, and to reduce mis-interpretation, the following definitions are provided as follows:

Quality Assurance (QA) – an overarching term to describe all activities to improve or maintain quality of tests and testing.

Quality Management Systems (QMS) – a systematic approach to document the quality principles used by the testing facility.

Quality Control (QC) – the routine testing of sample(s) with known reactivity to ensure the POC test device is performing to analytical expectations.

External Quality Assessment Schemes (EQAS) (also known as proficiency testing [PT]) or external quality assurance [EQA] by some providers in Australia) – periodic testing of a panel of samples containing a range of reactivities. The test results of the samples are unknown to the tester and the results obtained are submitted to the EQAS provider for peer assessment.

Table 2 provides a brief summary of the differences between QC and EQAS.

Laboratories conducting POC tests are recommended to implement QA programs to ensure the quality of performance of the tests and the testing procedures (CDC 2007). QA involves a range of activities including the implementation of QMS and the participation in EQAS and QC. POC testing conducted in remote or primary care settings by personnel without formal laboratory training should follow these same principles, which need to reflect the testing environment but remain effective and efficient. Developing QA processes to accommodate POC testing in different environments raises certain challenges, particularly in relation to staff time and difficult working conditions (Handorf 1997).

Quality management systems

As all POC test facilities wishing to claim Medicare rebates will be associated with a NATA accredited laboratory, established QMS will already be in place. For facilities that conduct POC testing but do not wish to claim Medicare rebates, it is highly recommended that they establish a QMS with the following elements.

Staff training and competency

As mentioned above, all staff performing POC testing should be trained to prepare, use and interpret the result of the test(s) employed in their facility. Training should be conducted in a formal setting by organisations recognised and competent in the delivery of training.
Pre-analytical procedures

A process for preparing the patient for specimen collection, ensuring the test is appropriate for use (for example, within expiry date and at the appropriate temperature) should be documented and followed. A check-list of materials required and instructions for testing should be available. Pre-test counseling of the patient should be conducted in a space that maintains confidentiality and privacy.

Reagent storage and management

All POC tests used in a facility must be validated for fitness-for-purpose prior to use. When an assay is changed, re-validation is required. A process for ordering, receiving, storing and discarding expired reagents should be documented and available. No reagents should be used after expiry and so, to reduce the risk of wastage, a long expiry dating of reagents at the time of purchase and delivery is preferable. Where possible, use of the same reagent batch over a long period of time is recommended. Facilities should perform some batch release testing on each new batch and each new shipment of reagents prior to using tests from that batch/delivery for routine patient testing. At a minimum, a QC sample of known reactivity should be tested prior to use of a new batch/delivery. All reagents should be stored as per the manufacturer’s instructions, with particular regard to temperature and humidity, especially in remote and rural settings or if refrigeration is unavailable.

Record keeping

A record of all patient and QA testing should be kept in a secure, confidential and pest-free environment. The results must be traceable and, when transcribed, be ideally checked by a second person. Retention of patients’ records should comply with NATA requirements.

Governance/supervision

Oversight of staff performing POC testing should be performed by a trained health professional, ideally the POC coordinator or an on-site POC Supervisor. Responsibility for the issuing of test results ultimately lies with the medical director (in a laboratory), the most senior medical practitioner within the facility (outside the laboratory) or, if the latter is not available, the practice or primary care facility manager.

Accommodation

The facility in which the POC test is performed should comply with local building and safety regulations. In addition, the facility should maintain temperature and humidity levels conducive to the test’s storage and routine use. Patient testing should be performed in an area that is removed from other areas to provide privacy to the patient and the POC operator. The facility should have suitable equipment and fittings (e.g. chairs, table, and lighting) and have an area for private pre- and post-test counseling.

Health and safety

Each testing facility must comply with fire safety regulations and have access to general safety equipment including running reticulated water source, disposable gloves, protective garments, disinfectants, eye-wash facilities, sharps containers and bio-hazard waste bins. Collection tables and the floor should ideally be constructed from non-porous materials. Additional safety equipment such as eye protection and laboratory bench covers are recommended. Further information on health and safety is provided later in this document.

Documentation

At a minimum, written procedure (or Policy Manual) for the preparation and performance of the POC test and the interpretation and reporting of the test result should be available. The document should detail the referral system used for reactive test results. Documents should be reviewed and updated periodically consistent with NATA requirements. Testing instructions should be simple, easy to follow and preferably have images that support the text, especially when non-technical staff are performing POC testing. Any equipment maintenance should be performed at the frequency and manner described by the manufacturer and the results recorded, dated and signed. All documentation should have a name or identity and version number and a known number of copies issued. A list of documents should be maintained to ensure all circulating copies are in date.

Referral and reporting of reactive samples

Each facility must have a referral system for samples with indeterminate or reactive test results, unless confirmatory testing is performed in-house. A record of all samples sent to the reference laboratory should be maintained and include the patient identification (minimum three identifiers e.g name, date of birth and laboratory number), the date of testing, the screening test result and the result issued by the reference laboratory.

EQAS

Participation in an EQAS is required for facilities accredited to ISO 15189 under most circumstances (NATA 2012). The National HIV and HCV Testing Policies specify that all laboratories testing for HIV and HCV and claiming Medicare rebate must participate in a nationally coordinated EQAS and comply with NPAAC guidelines. The requirements for facilities not claiming Medicare rebates are less well defined. However, good practice dictates that the same level of QA is required for these facilities and therefore participation in EQAS is highly recommended.

The EQAS should ideally have sufficient samples to monitor the performance of each operator and each device. Ideally, each operator should undergo at least one testing challenge per 12 month period, preferably with multiple
(>5) samples. Where possible, the samples in the EQAS should be of the same matrix as patient samples (e.g whole blood rather than spiked human plasma) and undergo minimal or no manufacturing processes. The samples must be homogeneous and stable over the period of testing. EQAS results are submitted to the scheme’s provider, who issues a delayed, peer-reviewed assessment of the quality of these results.

QC

Participating in EQAS provides the facility with a snapshot of the performance of the test and testing at a point in time. The frequent use of QC provides evidence of testing quality over time. At a minimum, a QC sample should be tested before each new batch of reagent is put into use. Ideally, QC samples should be tested with each group of patient tests performed; however it is up to the facility to determine the frequency of QC testing required, which will in part be determined by the volume of patient testing undertaken.

The QC samples should ideally be of the same matrix as the patient’s samples. Unfortunately, many POC tests for infectious diseases use capillary whole blood (via finger prick) as well as having different procedures for whole blood and serum/plasma. Many POC test procedures for finger prick samples differ from serum/plasma testing because only approximately half the volume of whole blood is serum/plasma. Therefore consideration of the QC sample matrix and the type of patient sample being routinely tested is required when choosing an appropriate QC sample.

The QC sample should be available in sufficient quantities enabling testing of the same batch of QC sample over a long period of time (for example 6 months). The QC sample should be homogeneous and stable over that time and should contain a level of the analyte being tested that is high enough to always produce a reactive result in the particular assay, but at a level low enough to be sensitive to changes in the assay’s performance. The QC sample should be stored under the conditions recommended by the manufacturer. Some QC samples can be stored frozen at -20 °C. In these cases, repeat freeze-thawing should be avoided, preferably limited to three times before discarding. Other commercial QC samples are provided in lyophilized form. Care should be taken when reconstituting lyophilised samples, especially in a non-laboratory setting. The diluent used for reconstitution must be that recommended by the manufacturer and be measured accurately. The QC sample must be dissolved and mixed according to manufacturer’s instructions. On reconstitution, the date should be recorded on the sample. No QC sample should be used past its expiry date.

The QC sample can be obtained from a commercial source or be manufactured in-house. Note that all QC samples, whether commercial or in-house, are an IVD and must be registered on the ARTG by July 2014. The decision as to what QC sample is best will be dependent upon several variables such as cost, access to reactive samples, storage facilities and matrices.

The QC test results should be recorded routinely in a manner which is traceable. Each QC test result should also record the operator identity, the reagent batch number and the test result. As many POC test results are qualitative in nature, a system of recording ordinal values (-, +/-, +, ++, ++++) should be introduced. A documented system of acceptance and rejection of QC test results should be established, including what actions is undertaken in the case of a rejection.

Table 2. General differences between QC and EQAS testing for infectious disease and drugs of abuse

<table>
<thead>
<tr>
<th>Parameter</th>
<th>QC testing</th>
<th>EQAS testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range of test results</td>
<td>Generally Positive</td>
<td>Negative and a Range of Positivity</td>
</tr>
<tr>
<td>Testing frequency</td>
<td>Frequently (ideally daily)</td>
<td>Periodic Quality at a set point in time</td>
</tr>
<tr>
<td>Supplier</td>
<td>Commercial or third party QC provider</td>
<td>Accredited EQAS (PT) provider</td>
</tr>
<tr>
<td>Reporting</td>
<td>Internal, immediate</td>
<td>External, delayed, peer reviewed</td>
</tr>
</tbody>
</table>

Health and safety issues for POC testing for ID and DOA

The testing of all clinical specimens should be performed in such a manner as to minimise occupational risk. Guidelines for good POC testing practice should be developed by the POC testing facility that will ensure safety and keep accidents to a minimum.

The provider of a POC service must ensure compliance with current workplace health and safety legislation and staff should understand the medico-legal implications of the transmission of infection due to lack of safe specimen handling or spillage.

Staff performing POC testing must be aware of the microbiological hazards of samples from patients, the chemical hazards of reagents and the physical or electrical hazards of equipment (IBMS 2004). The hazards of handling and disposing of body fluids and sharps outside a laboratory setting must be recognised. Suitable and sufficient risk assessments must be carried out before equipment is commissioned.

As part of training provided, all POC users should be aware of the importance of:

• standard (universal) infection control precautions
• the prevention of occupational exposure to blood-borne viruses, the wearing of gloves and other protective clothing, and the prevention of sharps injuries
• prevention of cross infection with blood-borne viruses, including selection of appropriate lancing devices
• safe handling and disposal of healthcare waste, including sharps
• safe medical device use, including decontamination of reusable devices (MRHA 2010).

Staff potentially exposed to microorganisms in the course of their work should be offered vaccination (where available) in order to reduce the risk of possible illness.

To minimise the risk of an acquired infection, it is recommended that staff know their hepatitis B (HBV) antibody status. If non-immune, HBV vaccination should be offered. Other vaccinations to consider are rubella, measles, mumps and influenza. An adverse incident is an event that causes, or has the potential to cause, unexpected or unwanted effects involving the safety of device users including patients or other persons. An essential part of the management of a POC testing service is a system for reporting adverse incidents to the appropriate authorities.

References
Australasian Association of Clinical Biochemists. Point of care testing implementation guide. Mt Lawley: AACB; 2008


Therapeutic Goods Administration (TGA) website: Australian Registry of Therapeutic Goods (ARTG); https://www.ebs.tga.gov.au/ebs/
Useful websites & reading


Appendix 1

Calculation of clinical sensitivity, specificity, positive predictive values (PPV) and negative predictive value (NPV) for an infectious disease or drug of abuse.

<table>
<thead>
<tr>
<th>Disease state or DOA*</th>
<th>Disease state or DOA Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>False Positive (FP)</td>
</tr>
<tr>
<td>False Negative (FN)</td>
<td>True Negative (TN)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>POC Test Positive</th>
<th>True Positive (TP)</th>
<th>False Positive (FP)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>POC Test Negative</td>
<td>False Negative (FN)</td>
<td>True Negative (TN)</td>
<td>NPV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
</tr>
</thead>
</table>

*DOA: Drugs of abuse

Sensitivity = the proportion of those with disease who test positive = TP / (TP + FN)
Specificity = the proportion of those without disease who test negative = TN / (TN + FP)
PPV = the proportion of positive test results that are true positives = TP / (TP + FP)
NPV = the proportion of negative test results that are true negatives = TN / (TN + FN)
Prevalence = the proportion of individuals in a population who have the disease = TP + FN / (TP + FN + FP + TN)

The effect of prevalence on proportion of false positive results is illustrated in the accompanying two examples.

**Example 1**

If the prevalence of the disease in a population was 0.01%, then it would be expected that if 100,000 individuals are tested, only 10 individuals will be truly positive for the disease.

If the POC screening assay used to test each individual has a specificity of 98% then, from the 100,000 individuals tested, the number of false reactive test results would be 2,000.

Therefore, in total, when screening these 100,000 individuals, there would be 2,010 reactive tests, of which only ~0.5% were truly positive.

**Example 2**

If, however the prevalence of disease in a population is much higher at 5%, then it would be expected that when testing the 100,000 individuals, 5,000 will be truly positive for the disease.

Using the same POC screening test with 98% specificity and testing the same 100,000 individuals, 2,000 test results would again be falsely reactive.

Therefore, in this case, there would be a total of 2,500 individuals with reactive tests, of which 20% would be truly reactive.
Appendix 2
Example of urine drug screen collection protocol

- Collection and testing area should be prepared with consideration given to the potential for human urine to be a possible infectious agent.
- Collection container needs to be in a chemically clean container that has been protected from possible environmental contamination (e.g. dust, laboratory chemicals).
- The specimen temperature should be determined at the time of collection (within 4 mins of collection) to ensure specimen validity. The acceptable temperature range is 33-38 °C.
- The specimen collection area should be as secure (ie only the donor and authorised staff should be able to enter) and private as facilities allow. This is especially important for point-of-care testing for non-clinical uses (e.g. pre-employment testing, post-accident investigation).
- Reasonable steps should be taken to ensure sample validity
  - no other source of water should be available in the collection area,
  - where this is not possible (e.g. toilet water), any open water sources should be coloured to display evidence of dilution attempts
  - access to the area should be as restricted as is reasonable, and no unauthorised access should be allowed for any reason.
  - full witnessing of the actual collection is not required.
- In addition to the minimum of two separate unique identifiers, the actual identity of the donor needs to be establish unequivocally (e.g. photo ID) for workplace samples
- A permanent record form must include as minimum
  - The time and date of collection
  - A minimum of 2 unique identifiers as described above
  - The presence or absence of photo ID for non-clinical samples
  - The printed name and signature of the collector
  - The result of the point-of-care test
  - Details on subsequent further testing (e.g. lab number of confirmation sample if required)
  - The signature the donor accepting the above information as correct.
- Donors should be asked to declare any prescription or over-the-counter medication prior to any testing taking place.
- All collection, testing and packaging for transport to the laboratory (if required) should take place in full view of both the donor and the tester at all times (with the exception noted above for full witnessing of the provision of the sample)
- If the sample needs to be sent to a laboratory or other facility for further testing, all transport should occur under appropriate chain of custody provisions. This requires
  - Tamper evident seals to be signed by donor and collector to be placed over any containers to be sent
  - A copy of the above permanent record to be provided to the donor with all details (e.g. such as laboratory bar code number)
  - Samples to be stored in a secure location prior to transport, with consideration given to environmental conditions (i.e. this may require storage in a secure refrigerator)
  - Transport to be in a tamper evident packaging
  - An ability for the laboratory to acknowledge the individual samples have arrived intact and not shown any evidence of access or tampering