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Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

Removal of TGA regulations precluding IVDs for HIV being placed on the ARTG

The Therapeutic Good Administration (TGA) has approach ASHM for advice on the removal of the regulation which prevents listing of devices for HIV self-testing and other matters relating to HIV self-testing. While we recognize that the excluded purposes regulations may be relevant for other conditions, ASHM strongly supports the removal of the Excluded Purpose regulations which currently restrict self-testing for HIV, viral hepatitis and sexually transmitted infections. ASHM further encourages the TGA to consider a number of conditions to be attached to any successful application of a self-testing device to ensure optimal public health and individual outcomes.

Key recommendations:

- The regulation should be repealed or amended so as to remove the exclusion of self-testing for HIV, HCV, HBV and STIs. ASHM is happy to comment on any proposed wording to achieve this change.
- The TGA should be able to assess these technologies in accordance with their fit-for-purpose evaluation approach and with reference to the specific Instructions for Use (IFU).
- The TGA should recognize that any home test will only be a screening test, not a diagnostic test, and any reactive result on a home test would need to be followed up by conventional laboratory testing.
- The TGA should stipulate appropriate manufacturer and supplier conditions on supply so as to ensure;
    - Clear messaging for the consumer around the appropriate use and interpretation of self-tests including the need to confirm reactive tests via conventional laboratory testing
    - Clear instructions for the consumer on how to use and interpret results
    - Clear information around window periods and limitations of self-testing
    - Local information for the consumer on linkages to care and the provision of a 24/7 information and referral service
    - Clear guidance around appropriate frameworks for distribution of self-tests
    - Mechanisms for the collection of denominator data to ensure surveillance of numbers testing via self-tests

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    - Appropriate training and information provided to suppliers of self-tests both in physical and online retail locations
- The recommendation of the Advisory Committee on Medical Devices (ACMD), 2013/1 should be reviewed and consideration be given to the role of the trained operator in assisting the individual undergoing HIV and HCV Point of Care Testing (PoCT), and the public health benefit conferred by these tests.
- Should the regulations be repealed or amended, the risks associated with self-testing could be overcome with a number of strategies including;
    - A clear framework for distribution and recommended use
    - An appropriate and locally relevant package insert provided at the point of sale by both physical and online retailers
    - Trial of the self-test by an experienced operator as part of the TGA's evaluation process before a test's registration to confirm that results are easily read[1]
    - An instructional video on use and interpretation of results which could be made available through a range of social media and other mechanisms,
    - Links into 24/7 national health and crisis hotlines for individuals who might become distressed at a reactive result
    - Training for suppliers of self-tests
    - Training for people who will be likely to be dealing with individuals who have had a true or false positive result (general practitioners, counsellors, etc)).

[1] It is vitally important that a home test or point of care test is easily interpreted and gives clear reactive or non-reactive result. This can only be determined by reviewing the literature or by performing trial testing. The TGA cannot currently trial a device, but we understand is currently seeking to reverse this situation. It would be advantageous for the TGA to have the capacity to trial the performance of home tests and point of care tests

Relevant Background documents:

Statement from the Draft HIV Testing Policy[2]:
The most recent draft of the HIV Testing Policy is currently with the Commonwealth for considered endorsement. This Policy was developed with a wide range of stakeholders including representatives from TGA, Commonwealth and jurisdictional Health Departments and provides support for the introduction of a quality framework for testing which supports the National Strategies and identifies barriers which need to be removed to facilitate appropriate testing. Significant differences between the current draft Policy and its predecessor include:

- Simplification of arrangements for non-laboratory based testing
- Support for all current and new testing technologies, including tests designed for self-testing, to be evaluated and regulated by the TGA using its fit-for-purpose criteria.
- Support for the removal of any overarching legislative barriers to self-testing for HIV with TGA approved tests
- Removal of sections which are covered under other existing arrangements, requirements, operational guidelines and/or standards.

Therapeutic Goods (Excluded purposes) Specification 2010:

4 Excluded purposes:

1. This section applies to a kind of IVD medical device for self-testing.
2. For section 41BEA of the Act, each of the following purposes mentioned for a device is specified for paragraph 41FD (ia) and subsection 41FF (1A) of the Act, unless the device is also to be used for another purpose, including a purpose mentioned in subsection (3):
    a. to test specimens from the human body for the presence of, or exposure to, pathogenic organisms or transmissible agents, including agents that cause notifiable infectious diseases;

Advisory Committee on Medical Devices
Ratified Minutes, 2013/1 (12th) Meeting – Teleconference, 15 March 2013

1. In relation to point of care testing devices used in the diagnosis of HIV infection:
The ACMD recommends that, when compared to Western Blot testing of known HIV positive specimens (not including seroconversion specimens), the overall sensitivity of point of care testing devices should be 100% and the specificity at least 99%.

2. In relation to point of care testing devices used in the diagnosis of Hepatitis C infection:
The ACMD recommends that the sensitivity of point of care testing devices should be at least 99.5%, and the specificity at least 99%.

[2] Draft National HIV Testing Policy, with the DoH for consideration by SCoH along with the National HIV Strategy, p 4

Background:
In the most recent review of the National HIV Testing Policy, the Expert Reference Group identified the barrier to the TGA considering class 4 IVDs for self-testing purposes, imposed by the Therapeutic Goods (Excluded purposes) Regulation, 2010 and has sought advice from the TGA and the Department of Health (DoH) as to how to progress a review and repeal of this regulation.

In 2013 The Co-Chair of the HIV Testing Policy ERG brought this to the attention of the Ministerial Advisory Committee on BBV & STI and to a joint meeting of DoH representatives from NPAAC, Health Protection Policy Branch and the RCPA, ASHM and BBVSS. We understand this has also been taken up at the Australian Therapeutic Goods Advisory Council.

ASHM welcomes this review and supports the removal of the regulatory barrier so that class 4 IVDs can be evaluated for self-testing purposes. We note that the Excluded purposes regulation covers other conditions and we strongly recommend that along with self-testing for HIV, hepatitis B, hepatitis C and sexually transmissible infections also be removed from the exclusion. We offer the following in response to the specific questions raised in your correspondence.

TGA point 1: The risks and benefits of home-testing as a means to enable and promote timely HIV detection and increase testing rates overall, particularly amongst hard-to-reach population groups;

Current National and Jurisdictional strategies all identify a desire to increase testing amongst high risk populations. There is considerable evidence that these high risk populations would like access to home testing and indeed, are already accessing self-testing via overseas internet sales. ASHM accepts that there are risks associated with self-testing, however, given the current availability of these devices via international markets, it is necessary to allow their listing to ensure appropriate regulation and mitigation of these risks.

ASHM supports a variety of testing options being made available to destigmatize and normalize testing for novel or hesitant testers and to allow those already testing to test more regularly and at their convenience. When taking the international experience into account, it is clear that the risk/benefit balance has been carefully considered and that the likely increase in overall numbers and frequency of testing have been seen as well worth the potential risks. Those risks have, in summary, been identified as issues with the sensitivity and specificity of the test when compared to laboratory tests, issues around the costs and question of who should pay, individuals testing outside of the window period, possibility of misinterpreting results, possibility of using the test incorrectly, failure to link into care and general loss to follow up.

On Balance, USA regulators decided that the benefits of increasing the number of testing options was of benefit, but reservations remain about the performance of the OraQuick device which has a one in twelve false negative rate[i] [ii].

A home sample collection kit is also available in the USA[iii] this requires the user to take a dry bloodspot sample and mail it to a laboratory for testing and results are returned via a sexual health service and home sampling using dry blood spot has been trailed in the UK[iv], with three studies reporting at the BHIVA and BASHH conference in April 2014. Home sampling was found to be acceptable and being used by a high proportion of people who had not previously tested. The positivity rate was 1.7% in the THT pilot 3.6% among Africans and 1.8% among MSM, with similar results in the other studies. The men who used home sampling also said they would use or prefer home testing.[v]

The cost of OraQuick is thought to be a deterrent to HIV testing in the USA. But the undiagnosed HIV positive population in the USA is thought to be poor and indigent. This is not necessarily true in Australia, so cost of over the counter tests may not be as large a barrier, though it is likely to be raised as an issue.

Risks and benefits associated with timeliness of HIV testing:

Home testing will not identify HIV earlier than conventional laboratory testing. But it may improve frequency of testing and even with the risk of false negatives increase the identification of people with HIV who have not tested recently. The fundamental risk associated with the timeliness of HIV self-testing has to do with the window period. Tests which could be used for self-testing do not have the same sensitivity as laboratory testing and will detect HIV in the vicinity of one month later than 4th generation laboratory tests. In order to mitigate this risk, it is vital that any approved device have clear messaging around the limitations of the test in detecting a reactive result.

The issue of timeliness is important as the person testing needs to be cognisant of this limitation. As was evidenced in the Australian study[vi] [vii]5 of the 39 people found to be HIV positive in sample of 3190 were wrongly identified as HIV negative by the test. In the USA the reported false negative rate in the test being sold over the counter is 1 in 12[viii]. One study[ix] looking at the performance of the OraQuick test found that false negatives also occurred in people with a fully developed antibody response, and there was no common, identifiable cause for this. Some errors were thought to be attributable to proficiency of the sample collection technique which is critical to the optimum performance of rapid HIV testing. This is why many of the blood tests are unlikely to ever be submitted for self-testing.

These limitations can be addressed with appropriate packet labelling and instructions for use (IFU). But this will require complex messaging to target different populations from different linguistic and educational backgrounds.

Increase testing rates overall, particularly amongst hard-to-reach population groups

The availability of PoCT has not greatly increased the number of tests performed in Australia, but the test is relatively new and resistance from some quarters to having simple accreditation for test users outside of public health settings has further limited the uptake of HIV PoCT. It is believed that the introduction of self-testing might generate a larger number of new testers than has PoCT due to the extra levels of convenience and anonymity associated with self-testing.

Limited data is coming in from community sites that testers had not tested recently or found the access more convenient. These activities have not been occurring long enough to see if people are returning to test more frequently. But the initial data from the - a-test community based testing service run by the NSW AIDS Council at their premises in Sydney reveal a significant number (approximately one third) of men attending have not tested previously or not tested within the last year, which is evidence that they are reaching the target audience.

There is a strong feeling that over the counter (or more likely over the internet) tests will be an option for people concerned about HIV and concerned about disclosure. This was true in the home collection studies from the UK.[x] But this has not been studied in Australia. We are aware there is a significant increase in HIV non-MSM across Australia. This group is characterised as being from or having travelled to high prevalence countries and/or having partners from high prevalence settings. Over the counter (or over the internet) home tests may be a favourable option for this group. Any efforts to restrict access to the test, through prescription or needing to get it from a doctor or clinic will defeat the main anticipated benefit of getting a test to people who are not accessing conventional services.

Linkage to care will be an issue for all individuals using home HIV testing as will decoupling from STI screening, but this will be able to be dealt with in the IFU which will need to stress the importance of regular STI screening. It will be a particular issue for geographically isolated individuals and people who are reticent to seek care or divulge risk. Patiel[xi]identified this risk along with the need for more detailed management of these people after they have received a positive result. Again the package insert and company as well as other service provided phone hot-lines and on line support may help to ameliorate this. While there are certainly concerns around loss to follow up for reactive results, it is important to note that self-testing individuals are engaging in health seeking behaviour and any test which needs to be sought-out and purchased demonstrates motivation and resource commitment on the part of the person being tested towards engaging in their health.

TGA Point 2: The risks and benefits of allowing TGA to approve such devices for HIV self-testing that are of acceptable safety and quality and perform as intended to increase HIV detection rates in Australia;

The performance of all potential home tests is lesser than that of laboratory tests. We know that some people with HIV are not testing using conventional methods. The availability of these tests would be taken up by some of these individuals.

The performance of the tests is largely a function of the prevalence. In a low risk setting the majority of reactive results will be false positives. This introduces a level of concern into a population which is far less familiar with HIV than MSM, frequent sexual health clinic attendees or sex workers for example. This could mean that the response to a reactive HIV test result may be more shocking for this group. While suicide was

considered as a possible response to a positive result, none have been described following the introduction of over the counter tests in the USA.

The HIV Testing Policy which recommended that PoCT be introduced into Australia in 2012, stipulated that is use should be restricted to high prevalence settings and should not be used generally in remote indigenous setting, because of particularly low prevalence.

The draft HIV Testing Policy 2014 recommends evaluation by the TGA of tests for home use. It also discusses that such listing would remove the capacity to restrict use of the test to high prevalence setting or people considered to be at elevated risk.

The package insert (IFU), and any promotion of the tests availability over the counter including education to pharmacists and pharmacists' assistants will need to reflect the performance of the test in a very low prevalence population. This is possible and a good example is the package information included with the bowel cancer screening test and the correspondence sent to individuals with reactive samples. It effectively says, most people who have a trace of blood in their sample will not have bowel cancer, microscopic haemorrhoids, chaffing, minor tears and many other common conditions which you may not be aware of can cause this. But, traces of blood are also a symptom of bowel cancer. This screening test identifies/has identified some blood so you should have this checked out, please contact your doctor.

Text to that effect could be developed for HIV test package insert (IFU):

> This is a screening test. It does not detect the virus (HIV), but your immune response (antibodies) to it and may indicate exposure to HIV. It can only identify established HIV infection. The test will not identify a recent infection it will only detect infections that occurred more than six weeks ago. So if you have had unsafe sex or shared injecting equipment in the last six weeks you will need to test again. The false negative rate of the chosen test should be stressed. Any reactive result is only a screen and must be confirmed by a pathology laboratory test. So you must go to your doctor. Many people who get a reactive result will not have HIV.
>
> If you have had an exposure to HIV in the past 3 days you should attend your local emergency department and be assessed for post exposure prophylaxis.

Simple comparisons should be included in the package insert (IFU):
Screening tests identify false positives at a rate of 10 in 1000
HIV in the general population is 2 in 1000
HIV in men who have sex with men is 100 in 1000

> If you are not a man who has sex with men or other individual who knows or suspects that you are at increased risk of having acquired HIV, then use of this test is not recommended. Based on the rate of HIV in the Australian population for every true HIV positive identified by this test there will be 8 false positive results identified with a self-administered test. If you just want to be assured

that you don't have HIV ask your doctor for a test next-time you visit and ask for a sexual health screen at the same time.

It should also be apparent in all promotional material that the test (which ever test is chosen) has a false negative rate of, whatever. This is dominant on all material about the test in the USA[xii].

The package inserts in the USA have go-through rigorous focus testing but these may need to be adapted to the Australian data. It should be noted that prevalence in the USA is roughly three times higher than Australia. So the claims and data may not be transferable.

The TGA has set an unacceptably high bar[3] for PoCT which fails to recognise their contribution to public health. The restriction on these tests when used as PoCT, where there is a trained and experienced test counsellor or clinician present to expedite confirmatory testing does not appear to be taken into consideration. This needs to be redressed and the ACMD recommendations changed. We not that there are no public health or prevention experts on the ACMD, no infectious diseases expert and no-one involved in point of care testing. The ACMD appears heavily reliant on experts from the device area, rather than the testing area. No advice was sought by the ACMD from the Australasian Society of HIV. Nor was advice sought either from the National HIV Testing Policy Expert Reference Committee or Hepatitis C Test Policy Expert Reference Committee. We are corresponding with them separately about this decision, with the view to it being reviewed.

TGA Point 3: Any limitations or conditions that should be placed on the supply of HIV self-testing devices.

Training

Training[xiii] [xiv]and clear instructions[xv] have been identified as important factors influencing HIV test performance. Uptake of the devices for sale in the USA has not been high and only about one in four pharmacies is stocking the tests one year after their approval[xvi]. The pharmacy assistants training package should be updated to include information about point of care testing and there should be discussion about whether or not the supply should be restricted to supply by the pharmacist or through a health focused community agency. If possible post market research on two different approaches could be useful. Training for test distributors should also be developed in conjunction with and promulgated through the Pharmacy Guild as part of their ongoing professional education.

A training video should be developed in multiple languages which explains to the person who is going to use the test, how to use it, how to interpret it and how to access follow-up.

[3] ACMD meeting minutes 15 March 2013 – 1 Require HIV PoCT to have 100% Specificity and 99% Sensitivity

Package insert

An appropriate package insert should be adapted to the Australian market in consultation with the Australasian Society for HIV Medicine, the HIV Testing Policy Expert Reference Committee, researchers who have been involved in the Australian research on home testing and relevant international colleagues from the CDC, who have experience in the use of the tests in home setting.

The package insert should be referred to in the video. Both the package insert and video should have detailed Australian information on contacts for follow-up and referral.

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References

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[ii] Myers,et. al. Availability, Accessibility, Price of Rapid HIV Self-Tests, New York City Pharmacies, Summer 2013 http://croiconference.org/sites/all/abstracts/970.pdf

[iii] http://www.cdc.gov/hiv/testing/lab/hometests.html

[iv] http://www.bhiva.org/News.aspx?NewsID=3945d64a-df7e-41ac-b2ac-d7fc171e98bb#.U03sHJIrMjE.mailto

[v] Ib id

[vi] Conway et.al, Plos One 0094062

[vii] Cunningham, P. Sensitivity evaluation of six rapid tests for detection of human immunodeficiency virus infection, Australasian HIV AIDS Conference ASHM 2013

[viii] http://www.cdc.gov/hiv/testing/lab/hometests.html

[ix] Medcsape interview, soon after the test was licensed in the USA reference is being sought and will be available on request.

[x] http://www.bhiva.org/News.aspx?NewsID=3945d64a-df7e-41ac-b2ac-d7fc171e98bb#.U03sHJIrMjE.mailto

[xi] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3661188/

[xii] http://www.cdc.gov/hiv/testing/lab/hometests.html

[xiii] http://www.rcpa.edu.au/getattachment/75f01469-00a2-4dd7-ae6d-51f880e3ffe9/Philip-Cunningham-Point-of-Care-tests-for-HIV-in-A.aspx

[xiv] Chiu C, Ong J, Walker S, Mayana M, Kumalawati J, Dax E. Using Photographed HIV rapid tests in a pilot EQAS National Serology Reference Laboratory Workshop on Serology 2006

[xv] Rick Galli, K. Green, A. La Marca, L. Waldman and R. Powers Evaluation of the Accuracy and Ease of Use of a Rapid, 60 Second HIV Test Performed by Untrained Operators in POC Test Centers in the U.S. https://custom.cvent.com/ADE0EB81B3184D618E2FB8340F1EC28E/files/29f3717707a44f91859f65feb4cefec6.pdf

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