30 January 2015

Dr Anthony Hobbs
Principal Medical Adviser
TGA Executive
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Sent via email: devicereforms@tga.gov.au

Dear Dr Hobbs,

Thank you for the opportunity to provide comment on the TGA's proposed performance requirements for tests to detect the presence of human immunodeficiency virus (HIV).

We support the development of performance requirements for laboratory, point of care (PoCT) and home HIV tests (self-tests) that ensure high quality tests are licensed for use in the Australian market.

While HIV PoCT devices and home tests (self-tests) will not perform to the same standards as conventional laboratory HIV tests, they offer other advantages, such as providing results at a single visit, and increasing access to HIV testing. They are therefore an important tool to have available in Australia order to increase HIV testing in populations most at risk for HIV infection, such as gay and bisexual men , which is recognised in the 2013 National HIV Strategy and National HIV testing policy.[1]

HIV testing is a key public health strategy to control the HIV epidemic, however in Australia, HIV testing rates are less than ideal. For example:

- The proportion of gay and bisexual men who report ever having tested for HIV has fallen slightly in recent years. In 2013, 87% of men surveyed in the Gay Community Periodic Surveys reported that they have had at least one test,[2]
- The proportion of gay and bisexual men who report having tested for HIV in the last 12 months has been stable in recent years at around 60% among all men, but there has recently been a significant decrease among men aged under 25 years (from 60% in 2004 to 57% in 2013),[2]
- Less than a quarter of high risk gay and bisexual men (men who have high numbers of casual partners and/or unprotected anal intercourse) re-test for HIV at the frequency recommended in HIV testing guidelines,[3, 4]
- In surveys of gay and bisexual men where recruitment is conducted online, leading to a higher proportion of non community-attached gay and bisexual men, a higher proportion of men report never having tested for HIV. In the 2008 E-male survey, 23.8% of men reported never having tested for HIV,[5] and

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- Among Australian people from countries in Sub-Saharan Africa and Asia with high HIV prevalence, only 50.3% report having ever tested for HIV[6]

PoCT and home tests that increase the convenience of HIV testing would help improve access to HIV testing. Increased HIV testing should lead to earlier detection of HIV infections. This allows a reduction of transmission to others by the person being aware of their HIV status and modifying risk practices, or by initiating treatment which can suppress viral replication and thereby reduce infectiousness.

From October 2011 to December 2014, the Kirby Institute conducted a study of rapid HIV testing at publicly funded sexual health clinics, private general practice clinics, and community-based HIV testing services in NSW and WA. Key benefits that we observed from making rapid HIV testing available to gay and bisexual men were:

- Men no longer needed to return to clinics to collect test results (reducing clinic visits),
- 79% of men prefer rapid HIV testing over conventional laboratory testing,
- Rapid HIV testing offered at outreach and community sites reached over 2,500 men in NSW and nearly a third had never previously tested for HIV before.
- Rapid testing combined with health promotion increased demand for HIV testing, by 19% in some settings

To maximise the benefits of using PoCT and home tests, we also support the development of clear risk mitigation strategies.

We provide our comments on each section of the consultation paper below.

**Performance Requirements** (*whether we support the proposed requirements, and, if not, suggestions for alternative requirements, with supporting reasons*).

**Laboratory testing**

The proposed requirements are supported.

**PoCTs for HIV**

We support the licensing of high quality HIV tests for use at the point of care.

We support the minimal sensitivity of 99.5% for whole blood, and 99% for oral fluid, and specificity of 99.0%

However regarding the proposed minimum performance requirements for HIV PoCTs, we suggest that the definition used in the TGA discussion paper for comparison tests for assessing the sensitivity and specificity of HIV PoCTs needs clarification. For example, the paper refers to '…the expected performance of the test for 'confirmed HIV positive samples' based on a direct comparison with a currently accepted state-of-the-art device (e.g. third or fourth generation EIA)…'

A key issue with this definition is that an EIA test alone cannot be used to determine if a case has 'confirmed HIV' instead, as specified in the Australian national case definition, this requires the following information:

1) Repeatedly reactive result on a screening test for HIV antibody followed by a positive result on a western blot. A positive result on a western blot is defined by the presence of a glycoprotein band (gp41, gp120 or gp160) and at least three other HIV-specific bands.

   Or

2) Detection of HIV by at least two virologic assays (nucleic acid testing for proviral DNA; HIV p24 antigen, with neutralisation; virus isolation) performed on at least two separate blood samples.[7]

We recommend the comparison tests for assessing minimum performance for PoCTs be modified to be consistent with option 1 of the case definitions above.

The second issue is that both third and fourth generation EIAs are mentioned as appropriate comparison tests, however these have different eclipse (window) periods in samples from people with very recent HIV infections (seroconverters). Thus, comparisons of the performance of PoCTs to EIAs are likely to produce different results depending on which EIA is chosen.

Finally, we recommend performance data (sensitivity and specificity) data provided to the TGA be based on an adequate sample size of at least 300 western blot positive samples and 300 negative samples to ensure a narrow confidence interval (+/-2%) around the point estimate of 99.5%. We provide some scenarios in Appendix 1 to demonstrate how the confidence interval becomes much wider with lower sample sizes, and thus reduces the confidence that the point estimate is actually 99.5%.

**HIV Self-tests**

Based on studies in the United States it is expected that there will be a reduction in sensitivity in the hands of inexperienced users[8]. However the introduction of HIV self-tests in Australia may result in a public health benefit if their availability encouraged uptake of HIV testing among members of at-risk populations who have either never previously tested for HIV or do not test regularly. [redacted]

We are also 1-year into a randomised controlled trial, which will determine the effectiveness of self-testing in GBM. We will measure the *actual* frequency of HIV testing in high risk men when they have access to home HIV tests.

Thus consistent with the calculations in Australia and the US we support the licensing of HIV self-tests (even with sensitivity in the hands of users) if there is evidence which supports that there

would be an increase in HIV testing frequency sufficient to overcome the reduced sensitivity of tests in the hands of inexperienced users.

The specificity of HIV self-tests should be as high as possible in order to avoid a high rate of false positive results if tests are used by people from populations with low HIV prevalence in Australia (i.e. people other than gay and bisexual men). We believe that a minimum specificity of 99% should be required for self-tests, and that specificity above 99.5% would be desirable.

**Risk mitigation strategies** (*suitability and likely effectiveness of proposed risk mitigation strategies to be employed by manufacturers to allow a risk/benefit assessment of a device. Suggestions for amendments to strategies can be made or suggestions for additional risk mitigation measures*)

**Laboratory testing**

The standard practices used by Australian laboratories described in the TGA discussion paper are acceptable, and no additional risk mitigation strategies are suggested.

**PoCTs for HIV**

Due to the lower sensitivity of HIV PoCTs in seroconverters, we recommend that people presenting for HIV testing within twelve weeks following a high risk event should be offered laboratory HIV testing in addition to, or as an alternative to a HIV PoCT.

We support the administration of HIV PoCTs by properly trained and supervised personnel. We recommend that the definition of 'health professional' used in the TGA discussion paper be broadened to include doctors, nurses, counsellors and other appropriately trained personnel. We note that studies have shown that, following specific training in HIV PoCT procedures, personnel without previous clinical or laboratory experience achieve equivalent accuracy in the interpretation of HIV PoCTs to personnel with clinical or laboratory training.[10] We support the comments made in the submissions by the Australian Federation of AIDS Organisations and ACON regarding appropriate supervision arrangements for non-clinical staff who administer HIV PoCTs.

We suggest that the references to pre-test and post-test counselling be removed and that terminology used should be in line with that of the 2013 Australian National HIV Testing Policy[1], which refers to 'gaining informed consent' (instead of 'pre-test counselling'), and 'conveying HIV test results (instead of 'post-test counselling').

Associate Professor Rebecca Guy

1. Australian Commonwealth Government, *National HIV Testing Policy*, 2013.
2. De Wit, J., Mao, L., Adam, P., & Treloar, C. (Eds.) *HIV/AIDS, hepatitis and sexually transmissible infection sin Australia: Annual report of trends in behaviour 2014 (Monograph 6/2014).* 2014, Centre for Social Research in Health: Sydney.
3. Guy, R., et al., *Does the frequency of HIV and STI testing among MSM in primary care adhere with Australian guidelines?* Sexually transmitted infections, 2010.
4. Holt, M.L., T. , *GCPS Sydney and Melbourne: selected HIV testing indicators.*, 2013, Centre for Social Research in Health: Sydney.
5. Rawstorne, P., *E-male survey 2008: key findings from a national online survey of men who have sex with men in Australia (Monograph 3/2009).* 2009.
6. Asante, A., Korner, H., McMahon, T., Sabri, W., & Kippax, S., *Periodic Survey of HIV knowledge and use of health services among people from culturally and linguistically diverse backgrounds, 2006-2008 (monograpgh 2/2009).* 2009, National Centre in HIV Social Research: Sydney.
7. Australian Commonwealth Government, *Australian national notifiable diseases case definitions - Human immunodeficiency virus (HIV) - unspecified*, 2004.
8. OraSure Technologies, *OraQuick In-Home HIV Test: US FDA Blood Products Advisory Committee Briefing Document*, 2012.
9. [redacted]
10. Yu-Ho C, C., Ong, J., Walker, S., Kumalawait, J., Gartinah, T., McPhee, D. A., Dax, E.M., *Photographed rapid HIV test results pilot novel quality assessment and training schemes.* PLOS One. **6**((3)).

**Appendix 1. Confidence intervals for different sample sizes used to determine the performance (sensitivity or specificity) of a HIV PoCT test**

| Observations | Sensitivity | 95% Confidence Interval |
|---|---|---|
| 50 | 99.5% | 92.9-100% |
| 100 | 99.5% | 96.4-100% |
| 200 | 99.5% | 97.2-99.99% |
| 300 | 99.5% | 98.2-99.99% |

*Calculated using STATA 12.1 Statistical software