IVD AUSTRALIA

Response to the Proposal:

"Self Testing for Human Immunodeficiency Virus (HIV) in Australia "

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Executive Summary

IVD Australia is pleased to be asked to comment on the proposal from the Department of Health (DoH) to allow for self testing (aka: home testing) for human immunodeficiency virus (HIV) in Australia.

As the peak body responsible for manufacturers and sponsors of *in vitro* diagnostic (IVD) products in Australia, IVD Australia is supportive of this proposal; albeit with a number of important caveats.

IVD Australia believes that the availability of self test HIV IVDs may potentially assist in the identification of some of the estimated 30% of HIV affected individuals who remain undiagnosed These people are at risk of not being optimally treated for their infection, and also are at significant risk of passing the infection to sexual or IV drug using contacts. These individuals are often less likely to present at a healthcare facility and to be tested using professional use IVD products that can provide a definitive result, and thus self test HIV IVDs may provide an alternative means of identifying them.

However, IVD Australia believes that there are a number of risks with this approach, and has concerns about its implementation.

Firstly, self test HIV IVDs will be used infrequently by inexperienced users. This means that the devices must be easy to use, and the instructions for use clear and unambiguous. The TGA must ensure that any devices included on the Australian Register of Therapeutic Goods have instructions for use that are appropriate for the Australian market. IVD Australia recommends that TGA's pre-market review must include extensive assessment of the usability of the IVDs by lay users.

Secondly there must be a Help Line service available to assist users with the performance of the test, reading and interpretation of the test and provide follow-up counseling. IVD Australia recommends that this should be the responsibility of the Department of Health. HIV is a notifiable disease in Australia and thus the responsibility must lie with the Department of Health.

Thirdly, adequate post market surveillance programs need to be established to assist with the ongoing review of approved tests. Given that it will not be possible to set up an external quality assurance program for self test IVDs, an effective mechanism needs to be established to educate healthcare professionals and users about the importance of reporting issues with these products.

IVD Australia recommends that the TGA also approve the inclusion of sampling devices specific for HIV testing that can be posted back to Australian pathology laboratories. These could be supplied via pharmacies at lower cost than the self test HIV IVDs. This would provide an alternative method for at-risk patients to have their HIV (and or other STI) status determined and appropriate follow up provided.

Finally, IVD Australia believes that, should the change of policy be adopted, careful timing of announcements, and legislative amendment, is required to ensure that self test HIV IVDs are immediately available in the market. Experience has shown that unless the devices are available soon after the announcement of the change, confusion will ensure, and the possibility of exploitation by suppliers may exist.

In conclusion, IVD Australia thanks the Government, the Department of Health, and the Therapeutic Goods Administration for the opportunity to comment on the Proposal.

IVD Australia will continue working with the Government, the Department and the Therapeutic Goods Administration to foster a regulatory framework for *in vitro* diagnostics that, while providing the level of safety and reassurance required by the Australian community, imposes as far as possible "*light touch"* regulation on manufacturers and sponsors of *in vitro* diagnostic medical devices, especially in sensitive areas such as self testing for serious diseases.

About IVD Australia

IVD Australia is the peak body representing sponsors and manufacturers of *in vitro* diagnostics based in Australia.

In vitro, literally "*in glass*", diagnostics (IVDs) comprise the instruments, reagents and consumables that are used to perform laboratory based pathology tests requested by General Practitioners, specialist Physicians or other healthcare professionals.

These pathology tests are generally performed in accredited Public and Private pathology laboratories across Australia, but IVDs also include over-the-counter tests such as blood glucose meters for diabetes testing, home pregnancy tests and point-of-care (PoC) IVDs used in general practice and healthcare clinics to measure parameters such as INR or HbA1c.

Supply of all IVD products in Australia is regulated for the Government by the Therapeutic Goods Administration (TGA).

IVD Australia was formed in July 2009 and currently represents Australian manufacturers, multi-national and local distributors of IVDs, as well as regulatory consultants working in the IVD sector. Our 55 members supply *in vitro* diagnostic products in Australia valued at over $750,000,000 per annum and they employ around 2000 people across Australia.

Currently, most of the companies that are supplying products for professional laboratory testing for HIV are IVD Australia members. Recently the TGA has approved, with stringent conditions, one IVD product for near patient testing for HIV in sexual health clinics and other facilities. IVD Australia understands that a number of additional rapid HIV IVD devices are currently undergoing assessment by TGA for this intended purpose.

General Comments on the Proposal

IVD Australia thanks the Department of Health and the Therapeutic Goods Administration (TGA) for the opportunity to comment on the Proposal to allow for self testing of Human Immunodeficiency virus (HIV) in Australia

IVD Australia will make some general comments on the proposal along with some specific comments that relate to the regulation and evaluation of self testing HIV IVDs.

Firstly, in reviewing the Proposal, IVD Australia acknowledges that the incidence of HIV in the Australia community is currently increasing slowly and that there are apparently a number of people who are living with undiagnosed HIV infection. Many of these people are not under the care of a healthcare professional and hence are at risk of progressing to more severe disease and/or of passing the infection to others, including their sexual partners or other intravenous drug users.

IVD Australia also notes that the technology for testing for and monitoring of HIV infection has improved significantly over the past 5 -10 years. The professional laboratory assays used to diagnose HIV can now detect infection within 10 days. There are also a number of rapid HIV assays available, including rapid finger prick blood assays and oral fluid based assays, that can be used in a near patient setting to provide point-of-care testing in sexual health clinics and in other facilities.

These tests have been adopted in a number of jurisdictions including USA where the FDA has approved the use of an oral fluid self test HIV IVD, and, as indicated above, also in Australia where the TGA has approved the use of a finger prick whole blood assay for use in near patient testing. Self testing for HIV has also been recently been permitted in the UK, although no tests have yet been approved for this indication. In Canada, the opportunity exists for Health Canada to approve self test HIV IVDs i.e., they are not banned as they are currently in Australia. However no sponsors have yet taken up the opportunity to apply.

It is also clear that the Australian at-risk population is undertaking self testing already; either through purchasing tests kits (both approved and otherwise) on the internet and via under-the -counter illegal supply.

Hence IVD Australia believes that if such testing is already happening, either legally or illegally, it makes sense to ensure that, as far as possible, it is conducted using self test HIV IVDs that have been assessed for safety and efficacy by the Therapeutic Goods Administration. Hence IVD Australia supports the proposal in principle.

However IVD Australia is also concerned to ensure that the larger population of at-risk individuals who actually do consult a healthcare professional regarding the possibility that they may have acquired HIV are also not forgotten.

The currently approved test for near patient testing (Alere HIV 1/2 Combo) has only been available on the Australian market for just over 15 months and, given the strict conditions attached to its approval, has not yet had sufficient time to demonstrate its effectiveness for this purpose. In addition there are several other rapid HIV IVDs awaiting approval by the TGA for the same indication.

IVD Australia recommends therefore, along with approval of the use of self test HIV IVDs, that an education campaign around the use of these near patient tests be conducted by the Department to raise awareness of the availability of testing at sexual health clinics and other facilities. Irrespective of the availability of self test HIV IVDs such a awareness campaign may assist in further improving the detection rate for HIV infection.

IVD Australia also recommends, as well as approval of self test HIV IVDs, that self test sample IVDs for HIV and other sexually transmitted infections also be approved by the TGA for use in Australia. These would enable users to collect a sample of either blood or oral fluid and then mail the specimen to a professional pathology testing laboratory in Australia for testing. This process would overcome concerns regarding the satisfactory performance of the test as well as provide the opportunity for counseling on a positive result, as supply of contact details, including a mobile phone number, could be made compulsory when submitting a specimen for testing. These sample collection devices would be considerably cheaper than self test HIV IVDs and would possibly be more attractive from an at-risk patient perspective, resulting in a greater uptake of testing than just with self test HIV IVDs alone. Arrangements would be required to reimburse the laboratory for the cost of the test, but the Department could possibly tender out the service to a laboratory or laboratories in the same way as the National Bowel Screening program.

Specific Issues to be addressed

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.

Over the last 10 years there has been significant progress in the detection and monitoring of HIV and similar infectious agents. This has not only occurred for the professional laboratory tests, where the window of detection for HIV has been significantly reduced, and the sensitivity and specificity of the assays improved, but also in the area of rapid HIV IVDs, where a number of devices have recently been approved for use in jurisdictions such as USA. These rapid test HIV IVDs, which use either finger prick whole blood or oral fluid, have been approved not only for use by healthcare professionals in a near patient setting but also for self testing use.

It is clear that in Australia that there is still a need to improve testing rates and to ensure that affected individuals are detected early so that they receive appropriate care and advice as soon as possible. Hence the use of self test IVDs to detect HIV in at-risk populations is one approach that can be used to improve the control of HIV infection within the Australian community.

The benefits of the ready availability of such IVD devices include;

Benefit Of Earlier Detection - the availability of over-the-counter (OTC) HIV tests is likely to result in earlier detection of HIV in a subset of at-risk individuals who do not currently get tested. Availability of OTC HIV tests or OTC sample collection devices may encourage these people to undertake a home test or home sample collection, and hence assist in identifying a population cohort who may never have been identified through the current methodology.

Benefit Of Less Transmission - the identification of infected patients early in the infective window may assist in reducing the transmission of HIV among affected populations. Availability of self test HIV IVDs will encourage the notion of testing among affected groups and will lift the acceptance of testing generally within the community.

The risks of allowing the supply of self test HIV IVD devices include;

Risk Of Incorrect Performance Of Tests - many Australians currently perform self testing of their blood glucose, or their INR level, at home and effectively monitor and control their disease status. However these are tests for chronic disease and affected patients get very experienced at performing these tests. With OTC rapid HIV tests however many patients will only use these devices on a once off or infrequent basis. Due to the lack of expertise issues can occur with specimen collection (either whole blood or oral fluid swab), performance of the test and reading and interpretation of the result. This can result in false negatives providing a sense of security that may not exist. In addition it must be made clear to users that the tests have a “window of validity” and testing outside this may invalidate the result obtained.

Risk Of Lack Of Counseling - With self testing HIV IVDs, pre or post-test counseling would not necessarily occur.

Patients with a positive result from HIV self testing must be advised to go to their GP, who will either request further confirmatory testing via a reference method e.g. Serology or PCR, or organize a referral to a HIV/STI specialist, who would request further confirmatory testing via a reference laboratory. Based on the confirmatory test result, patient counseling should occur via specialised counseling services already established. Therapy choices will then be made by a HCP rather than by the patient.

The risk however is that self testing patients who have "positive results", either "true" or "false positive" do not seek professional advice. This may mean, for example, the patient could "self-harm" in panic on testing positive. Alternatively, patients who test "Negative" either through a "false negative" result or through an poorly performed test may incorrectly assume that they are not infected and hence may then transmit the infection to others. To overcome this IVD Australia recommends that there be a 24 / 7 counseling service available to assist users of self test HIV IVDs to perform testing, read the test result and interpret the result.

IVD Australia believes that the cost of providing a 24/7 counseling service would be prohibitive for any individual Australian sponsor and, as HIV is a notifiable disease, that, if the Government really wants to encourage self testing for HIV, then it should be prepared to fund the service.

Risk To Patient Wellbeing - Lack of counseling could lead to confusion by the patient about what to do with the positive result. Quick action is needed for immediate follow-up medical consultation, confirmatory testing and early treatment if required. This advice is currently mandatory and available for all patients who undergo HIV testing either in a traditional medical setting or in the outpatient Sexual Health settings which are in use in some states.

Risk of Incorrect Result Interpretation - in general, patients have little understanding of how to interpret the results of POCT devices. Timing is critical as the test must be read at a specified time, not before, not later, as the results in the read-window can change over time, leading to incorrect interpretation. This may lead patients who self test to assume they are falsely negative or alternatively may get a false positive result.

Risk Of False Sense Of Security for Patients - the somewhat lesser sensitivity of OTC HIV tests may give a "delayed picture" of the patient's actual HIV status for up to 3 months. Lab-based tests are more sensitive and can detect HIV infection as early as 10 days post-infection with HIV. A patient may be HIV Positive yet still test negative on the self test HIV IVDs for some period of time, and may continue to spread HIV to partners.

Risk To Quality: How can QA be monitored and managed in OTC POCT HIV devices? Quality Assurance is mandated by the TGA for all laboratory-based HIV testing and the limited community-based HIV testing programs. However in a self test situation it is not possible to undertake external quality assurance, and there has to then be reliance on users reporting poor performance of the test to the TGA. This is not done at present with existing self testing IVDs such as blood glucose meters and home pregnancy test kits so it is difficult to see how it would be any better with self test HIV IVDs. In fact the situation is likely to be worse for self test HIV IVDs due to the infrequency of use and the population demographic.

Risk Of Incomplete Medical Records - Home HIV testing does not guarantee the patient will report or act on positive results. It is not clear that there will be any recording of the results of OTC HIV tests. Depending on the distribution channels, only the number of total tests sold can be recorded. Will customer details be recorded when they purchase their OTC HIV test? What will the patient do with the results when they have them? They may do nothing, they may (appropriately) go to their doctor or HCP for confirmatory testing, they may continue to practice unsafe sex because they think (rightly or wrongly) that they are uninfected, or indeed even if they think they are infected. In many cases there will be no record of the test created in the patient's medical record.

Risk of Test Performance due to Incorrect Handling and Storage: Due to the nature of the likely distribution channels for self test HIV IVDs, there is a risk that the test devices could be stored or handled incorrectly between delivery to the point of sale and use by the patient. This could result in an incorrect result being generated.

Risk Of Transmission Of STI's In Addition To HIV: The NSW HIV Strategy 2012-2015 recommends (p19) that other STI testing should be included when testing for HIV as concomitant STI's can greatly increase the risk of transmission of HIV. Separation of HIV testing from other STI testing is therefore not generally desirable. Home HIV testing could increase the risk of transmission of other important STI's as well as HIV if patients are deterred from seeking professional advice and laboratory based testing through reliance on OTC HIV IVDs.

Risk of Patients undertaking self testing rather than near patient testing - one of the concerns that IVD Australia has is that the introduction of self testing HIV IVDs will take away from the recent introduction of near patient testing for HIV. There is a concern that at-risk individuals may chose to use self testing, with all its inherent issues (above) rather than attending a sexual health clinic or other healthcare facility where the near patient test can be performed in a more controlled and regulated environment and where appropriate counseling can be provided.

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.

As present in Australia it is possible to purchase self test HIV IVDs via the internet from a number of websites, including eBay. Most of these websites are located in USA where the Orasure™ oral fluid HIV tests can be legally supplied. However there are also a number of websites which purport to offer other products of doubtful manufacture, including Singapore and Poland, or indeed some that appear to offer rapid professional use HIV IVDs. Use of these pathways by individuals purchasing and importing for their own use is permitted currently under the Therapeutic Goods Act.

However it is also possible to purchase self test HIV IVDs in a number of locations in Australia, including Oxford St in Sydney and Fitzroy St in St Kilda in Melbourne. These products are being imported and then clearly sold illegally as they have not been approved for supply under the TGA IVD regulations.

As indicated, IVD Australia believes there are benefits in changing the Excluded Purposes (2010) Regulation and allowing the TGA to approve devices for self testing for HIV. This would mean that the TGA would have evaluated these products for their safety and efficacy, and determined that they have sufficient sensitivity and specificity, and that the packaging and labeling is appropriate for Australia. Given that these TGA evaluated products may then be legally supplied through distribution channels in Australia such as pharmacies and sexual health clinics, this may reduce the illegal importation of products as well as the level of importation for personal use that is currently occurring.

Classification Of Self Test HIV IVDs - IVD Australia's current understanding is that HIV self testing devices would be classified as Class 4 IVDs under Classification Rule 1.1b

> ***From Therapeutic Goods (Medical Devices) Regulations 2002 - Schedule 2A***
>
> ***1.1 Detection of transmissible agents posing a high public health risk***
>
> *An IVD medical device intended to be used for any of the following purposes is classified as a Class 4 IVD medical device or a Class 4 in-house IVD:*
>
> a. *to detect the presence of, or exposure to, transmissible agents in blood, blood components, blood products, cells, tissues or organs or any derivatives of these products of human or animal origin, in order to assess their suitability for transfusion or transplantation;*
> b. *to detect the presence of, or exposure to, a transmissible agent that causes a serious disease with a high risk of propagation in Australia.*

This classification means that IVDs for self testing for HIV would be subject to the same conformity assessment procedures as other Class 4 IVDs;

- Application for TGA Conformity Assessment Certificate
- Assessment of Performance by TGA (performed by accredited laboratories such as NRL or SYDPath)
- Design Examination Certificate
- Application for and then entry onto the ARTG as a Class 4 IVD

IVD Australia however has a number of concerns regarding TGA approval and ARTG inclusion of self test HIV IVDs. These include;

Concerns with Delays in Assessment - it is currently taking over 15 months to approve high risk IVDs that require TGA Conformity Assessment and Design Examination. Such a delay for new products that have such a high public profile as self test HIV IVDs will create expectations in the community. It is clear from the situation in the UK that announcing a change to the policy regarding availability of self tests for HIV without products being immediately available for sale has led to considerable confusion within the community and the possibility of exploitation of that by suppliers of non approved products. Given that the policy will require a change to a disallowable instrument, announcement of the change of policy should only be made once there are products that will be approved within a short timeframe. This may require discussion with possible sponsors to ensure that the appropriate documentation has been prepared and the physical testing, if required, has been undertaken.

Concerns with Performance Examination - currently new HIV and HCV tests are required to undergo physical performance testing by the TGA sub-contracted laboratories (SYDPath and NRL). These tests take a considerable time to arrange and perform and will add to the delay in approval of the self test HIV IVDs.

In addition, these laboratories presently have a series of test panels that they use to assess HIV assays. However these panels are designed to be used on laboratory based tests, not on whole blood, or on oral fluid samples. If the TGA is to approve self testing HIV IVDs then the subcontracted laboratories will have to create assessment panels that are suitable for self test HIV IVDs.

Concerns with Instructions for Use / Labelling - one of the major issues for self testing IVDs that they are required to have very specific and clear instructions for use. At present all self test IVDs such as blood glucose meters and home pregnancy tests are imported into Australia but in general they do not have “Australian specific” Instructions for Use (IFU). If self test HIV IVD products are required to have additional or replacement IFUs, and the sponsor name and address on the packaging, then this may make some products non viable in the Australian market.

In addition, while many of these devices are packaged individually, they are not presently packaged as a ready-for-sale products and may require repackaging to make them appropriate for sale in Australia.

Concerns with Distribution Channels and Recalls - At present there are no distribution channels established for self test HIV IVDs. The currently approved near patient HIV IVD is distributed directly by the sponsor under strict conditions imposed by TGA.

IVD Australia is concerned that the distribution channels used for self test HIV IVDs will be different to most other IVDs and may involve pharmacies, sexual health clinics, rural and remote clinics and GP surgeries. This will create a series of issues that will need to be addressed including distribution, shelf life, storage conditions and recalls.

Currently the UK Government has allowed for the sale of self test HIV IVDs within the UK. However since the announcement in January 2014 the UK regulatory agency (MHRA) has not approved any devices and it is expected that it will take some time for appropriate devices to attain CE mark status. This has caused considerable consternation within the UK at-risk community.

Concerns regarding Training on Devices - The currently approved near patient HIV IVD is subject to strict conditions imposed by TGA on the training of healthcare professionals (HCP) who use the product. These require the sponsor to train each individual HCP who is undertaking testing, and to keep records of that training.

Clearly it is impractical for sponsors of self test HIV IVDs to train individual home users, given that this would necessitate the use of a number of devices for only one or two test results, and training would need to be phone and / or internet based.

The Government could possibly address the training issue in a number of ways;

- Set up a 24 / 7 Call Centre to assist users with performance of the test and interpretation of the result; and /or

- Establish a website / smartphone app with instructions / animations showing how to perform a valid test and with information on counseling.

The Government could contract this out to organisations that are experienced in training on point-of-care devices such as Australian Point of Care Practitioners Network (APPN).

Concerns with the Supply of Illegal IVDs - at present it is clear that self testing HIVs are being supplied illegally in Australia, as it is possible to buy these products at shops in both Sydney and Melbourne and other locations.

Should the Government approve the proposal, IVD Australia would be insisting that these illegal products be removed from the marketplace and the TGA use its legislated powers to prosecute those who are illegally importing and selling the products.

In addition IVD Australia would recommend that a campaign be undertaken by the Department and TGA in conjunction with other stakeholders to educate at-risk populations regarding the availability of TGA approved self test HIV IVDs and the risks of using products obtained illegally or from internet sources that have not been assessed for safety and efficacy by the TGA.

3 - any limitations or conditions that should be placed on the supply of HIV self testing devices.

IVD Australia believes that there should be several conditions placed on the supply of self test HIV IVDs .

While the conditions placed on the current near patient rapid test HIV IVD are appropriate for a device that is used specifically by HCPs, a device that is to be used in a self test setting requires other conditions;

Labelling - the labels for self test HIV IVDs must include a sponsor name and contact details to enable users and others to directly contact the sponsor in case of confusion / misunderstand of instructions.

Counseling Service - approval of self test HIV IVDs in other jurisdictions (US / UK) have required the manufacturer (or sponsor) to provide a 24 / 7 counseling service to enable user to gain instructions on how to use the device, how to read the result, and how to interpret the result.

IVD Australia believes that in Australia the appropriate course is for the Department of Health to be responsible for providing a 24/7 service covering the use and result interpretation of the (limited number of) approved devices, and more importantly, the counseling required in the event of a positive result. It is also important that counseling also deals with the possibility of a false negative result and the need to test within the appropriate window for the device.

In addition however sponsors could be required to develop a specific website dealing with their device that would provide similar information to the information service recommended above.

Post-market Surveillance - IVD Australia believes that there needs to be adequate post-market surveillance systems developed to deal with product issues and recalls. Given that self test HIV IVDs will probably be distributed through retail environments (e.g. pharmacies) and through clinic environments (sexual health, rural and remote, indigenous and GP) emphasis need to be put on reporting of any issues with performance of tests.

List of Abbreviations and Acronyms

APPN	Australian Point of Care Practitioners Network
ARTG	Australian Register of Therapeutic Goods
DoH	Australian Department of Health
HIV	Human immunodeficiency virus
IFU	Instructions for Use; package insert
IVD	*In vitro* diagnostic
NRL	National Serology Reference Laboratory
OTC	Over-the-counter; retail supply
PoC	Point-of-Care
TGA	Therapeutic Goods Administration