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Horizon Scanning Technology Prioritising Summary

OraSure HIV point-of-care testing

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PRIORITISING SUMMARY

REGISTER ID: **000325**

NAME OF TECHNOLOGY: **ORASURE HIV POINT OF CARE TESTING**

PURPOSE AND TARGET GROUP: **POINT OF CARE HIV TESTS ALLOW RAPID REPORTING OF RESULTS TO PATIENTS IN SETTINGS SUCH AS CLINICS.**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL:

☐	Yes	ARTG number
☒	No	
☐	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
USA			✓

IMPACT SUMMARY

OraSure Technologies Inc. markets two rapid, point-of-care HIV-1 antibody detection devices: the OraQuick® Rapid HIV-1 Antibody Test and the Oraquick® Advance™ Rapid HIV-1/2 Antibody Test. Both kits are the subject of FDA CLIA[1] waivers allowing their application to settings other than certified testing laboratories. Both provide results in 20 minutes, from whole blood sourced from finger-stick or venepuncture and, additionally, the Advance kit may also be used to test oral fluid samples. Both test devices are currently not available in Australia.

[1] Clinical Laboratory Improvement Amendments of 1988 (CLIA) waiver. This allows them to be used in settings which are not clinical laboratories. Specifically, waivers are able to be given to "simple laboratory examinations and procedures that are cleared by the Food and Drug Administration (FDA) for home use; employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible; or pose no reasonable risk of harm to the patient if the test is performed incorrectly." FDA (2001). *Information on CLIA Waivers* [Internet]. Available from: http://www.fda.gov/cdrh/clia/cliawaived.html [Accessed 4th July]..

BACKGROUND

Currently, Human Immunodeficiency Virus type 1 (HIV-1) home sampling or home testing is not supported by Australian national policy. The National Policy is based on several principles: confidential voluntary testing, testing of the highest possible standard, the person tested must benefit from the test, testing is critical for the epidemiology of HIV-1, testing is critical to prevention of transmission (MACASHH & DHA 2006).

The OraQuick® Rapid HIV-1 and Advance HIV-1/2 Antibody Tests (OraQuick) are test kits designed to give quick (20 minute) results regarding the HIV-1 status of the subject. The point of care test kits can be used in either a clinic or at home and require no specialist knowledge or skills. Blood from either a finger-stick or standard phlebotomy can be used for these tests. The Advance test can also be used on saliva samples. The kits, which are based on lateral flow immunochromatography, detect HIV-1 antibodies in the subject's sample. The contents of the kits consist of: a test stand, a vial of developer solution, specimen collection loop, and the test device which holds the test strip. The specimen collection loop is used to transfer blood from either the finger-stick blood sample or the tube of blood collected by phlebotomy into the developer solution. For saliva samples, an absorbent pad attached to the device is wiped across the upper and lower gums, collecting saliva, the device is then placed in the supplied developer solution and left for 20 minutes. For blood samples, the specimen collecting loop is used to mix the sample with the developer solution, a plastic device holding the assay test strip is then inserted into the developer solution and left for 20 minutes. The assay strip can then be read and the results interpreted. The test strip provides three possible states: two lines visible, indicating a positive result for HIV-1 antibodies; one line visible, corresponding to the control line and indicating a negative HIV-1 result; or no lines visible indicating an invalid test result. The test, if positive, must be confirmed by a second independent test (Orasure Technologies Inc. 2007).

CLINICAL NEED AND BURDEN OF DISEASE

HIV-1 is a blood borne virus that causes chronic, lifelong infection. HIV-1 infection can proceed to acquired immunodeficiency syndrome (AIDS), in which many normally benign infections and asymptomatic diseases can opportunistically manifest, given the lack of an effective immune response, into life threatening disease. HIV-1 incidence in Australia has fallen from peak levels of around 1,700 in 1984 to 718 in 1999 and then has increased to 998 diagnoses in 2006 (Guy et al 2007, MACASHH 2005). Due to the widespread effective use of anti-retroviral drugs, AIDS diagnoses and deaths are decreasing, with diagnoses declining by 80% in the period 1994 to 1999. There have been a cumulative total of 25,981 HIV-1 infections, 9,940 AIDS diagnoses, and 6,658 deaths due to HIV-1 infection in Australia up until September 2006 (NCHECR 2007). In Australia the predominant mode of transmission is via

homosexual sexual contact (76.5% of transmissions), with heterosexual sexual contact being the second largest route of transmission (12.2% of transmissions). Unlike other comparable developed countries, Australia has a relatively low rate of transmission and prevalence within the injecting drug user population. Late presentation with HIV-1 is a serious problem in Australia, with approximately 50% of AIDS cases occurring within three months of initial diagnosis of HIV-1 positive status (McDonald et al 2003). The diagnosis of HIV-1 positive people at such a late stage is problematic for the patient as they generally have a poorer prognosis and, from a public health perspective, an HIV positive person that is unaware of their status has an increased likelihood of transmitting HIV to others because behaviour modification is not an imperative. Wider access to, and earlier testing for, HIV is essential to facilitate the early diagnosis of the many unaware HIV positive individuals in the Australian population.

DIFFUSION

Both the OraQuick® Rapid HIV-1 Antibody Test and the OraQuick® Advance™ Rapid HIV-1/2 Antibody Test have not been submitted for approval by the TGA and thus are not in use in Australia. The FDA has given both the OraQuick Rapid HIV-1 Antibody Test and the OraQuick® Advance™ Rapid HIV-1/2 Antibody Test a Clinical Laboratory Improvement Amendments of 1988 (CLIA) waiver. This allows them to be used in settings which are not clinical laboratories. Specifically, waivers are able to be given to "simple laboratory examinations and procedures that are cleared by the Food and Drug Administration (FDA) for home use; employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible; or pose no reasonable risk of harm to the patient if the test is performed incorrectly." (FDA 2001). Sites offering either the OraQuick® Rapid HIV-1 Antibody Test or the Oraquick® Advance™ Rapid HIV-1/2 Antibody Test must apply to the FDA to be legally able to do so and must adhere to specific rules about the usage of the kit and performance of the site with regard to the training and practices followed.

COMPARATORS

People wishing to be HIV-1 tested in Australia generally have their blood sampled by a general practitioner or other qualified medical worker. The blood sample is sent to a certified laboratory for HIV-1 testing. The gold standard for HIV-1 testing is a repeatedly reactive enzyme immunoassay (EIA) confirmed by western blot.
Both tests qualitatively assess whether the patient blood sample contains antibodies to HIV-1.

SAFETY AND EFFECTIVENESS ISSUES

No safety issues associated with the tests were found while compiling this summary.

In a high risk population, 450 participants at a hospital were tested with the OraQuick® Rapid HIV-1 Antibody Test. The OraQuick® Rapid HIV-1/2 Antibody Test was used in both the blood testing and saliva testing modalities[2]. The results were compared to the reference standard of EIA and western blot (WB). Interviews were performed to assess participant preference for a particular test or test modality. 146 from 450 (32%, 95% CI [28, 37]) subjects were found to be positive for HIV antibodies using the reference standard. The blood testing performance of the OraQuick® Rapid HIV-1/2 Antibody Test was slightly less accurate compared to the reference standard, having a sensitivity of 100% (95% CI [98, 100]) and a specificity of 99.7% (95% CI [98.4, 99.9). The OraQuick® Rapid HIV-1/2 Antibody Test performed slightly better on saliva samples, showing absolute concurrence with the reference standard test for sensitivity (100%, 95% CI [98,100]) and specificity (100%, 95% CI [99, 100]). Sixty per cent of participants were found to prefer the oral testing modality for repeat tests. The authors noted that the kit performed well in settings with resource scarcity (Pant Pai et al 2007) (Level III-2 diagnostic evidence).

A large, U.S. based study across 368 sites collected data from a total of 161,790 OraQuick® Advance Rapid HIV-1/2 Antibody Tests, of which, 135,724 were performed on whole blood and 26,066 were performed on oral fluid. This data collection was part of the post-marketing surveillance required by the FDA. The outcomes were very similar to those expected of the standard EIA used for routine HIV detection (Level III-2 diagnostic evidence). The results are presented in Table 1 (Wesolowski et al 2006).

Table 1 OraQuick test kit performance determined by comparison to WB or Immunofluorescence

	Specificity (%) [95%CI]	Positive Predictive Value (%) [95%CI]	Not confirmed by WB or Immunofluorescence
OraQuick (Blood) n= 135,724	99.98%, 95%CI [99.7, 100]	99.24%, 95%CI [66.7,100]	68 ± 0.05%
OraQuick (Oral fluid) n= 26,066	99.89%, 95%CI[99.4,100%]	90.00%, 95%CI [50.0,100]	56 ± 0.22%

WB = western blot

COST IMPACT

It was reported in a 2006 journal article that the OraQuick® test kit is sold to laboratories for $US12 to $US17. It was unclear which kit this was referring to, but as they have very similar components it may well be applicable to either kit. It is predicted that this price will rise if marketed to consumers directly, due to loss of bulk discounts. It has been shown that prospective buyers would only pay $US15 for a kit to self-test for HIV-1 (Wright & Katz 2006).

[2] the study stated the OraQuick® Rapid HIV1/2 test was used, but it is not clear if this was the Advance kit which is normally used for saliva testing

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

Some individuals, for various reasons, choose not to engage with the mainstream health care establishment.

A San Francisco cross-sectional study, involving homeless and marginally housed individuals, investigated the hypothesis that a rapid test result would allow a larger than normal subset of tested subjects to know their HIV status. This is compared to normal testing regimens in which many tested subjects do not return for their results, and thus do not learn their HIV-1 status. Of the 1,614 individuals asked to participate, 1,213 (75.2%) consented to testing. 187 of those tested (15.4%) were positive for HIV-1 using the OraQuick® Rapid HIV-1 Antibody Test. All tested participants received their HIV-1 status. 26 of 30 HIV-1 positive subjects confirmed by EIA or WB went on to receive further primary care within six months after the initial diagnosis (Bucher et al 2007).

A cross-sectional study of 7,770 Tanzanian students from rural and urban settings demonstrated the use of HIV testing using the Oraquick® Advance™ Rapid HIV-1/2 Antibody Test under 'real world' conditions. The test was performed using the saliva testing modality. The study did not compare or confirm the test with a standard HIV-1 detection method but found that with the saliva testing method, the potential for fast results and the ability to perform the test *in situ* were important factors for the students to comply with testing. There was a difference in the incidence of HIV-1 infection between the rural and urban settings, with 41 of 3945 (1.0%) rural and 211 of 3825 (5.5%) urban students testing positive for HIV-1 (Holm-Hansen et al 2007).

If an effective and safe test exists and yet is not allowed to be legally used in Australia, particularly in high risk population subgroups, such a decision may be deemed unethical given the advantages that early diagnoses afford both the HIV positive individual and the community at large.

OTHER ISSUES

Other issues have been raised by those involved in the debate over the introduction of these kits in the USA including the following factors favouring introduction: increased awareness of HIV status, treatment can begin earlier, behaviour modification can begin earlier to prevent HIV transmission, potential to de-stigmatise HIV testing, testing could become more widespread and frequent, more young people would likely use the kits versus their lower involvement rates in conventional testing. Factors against introduction include: improper usage within infection window period, effect of untrained users with regard to usage and interpretation, negative psychological outcomes without appropriate counselling, lack of confirmatory tests, coercive testing, lower participation in screening programs, cost and availability to poorer at need populations, inappropriate use in low risk populations, and lack of reporting to health authorities (Campbell & Klein 2006).

SUMMARY OF FINDINGS:

The OraSure® HIV test kits are at least as safe and effective as the current generation of EIA tests, and also deliver results more quickly. The kits have not been submitted for TGA approval, but are available for purchase over the internet and hence may currently be in use in Australia. The main issues surrounding the introduction of these kits into Australia are ethical and political. In addition there is a lack of published cost effectiveness data. If used appropriately, these kits could facilitate the earlier diagnosis of the many HIV infected people who are unaware of their status.

HEALTHPACT ACTION:

The OraSure® HIV appears to be effective for the rapid diagnosis of HIV. The ethical issues involved in the use of this test are of critical importance, highlighted by the fact that the United Kingdom's HIV guidelines did not endorse the use of this test due to ethical issues. Although HealthPACT has recommended that further assessment of this technology is no longer warranted, the contents of this summary should be forwarded to the relevant HIV agencies.

NUMBER OF INCLUDED STUDIES

Total number of studies	
Level III-2 diagnostic evidence	2
Cross-sectional studies	2

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SOURCES OF FURTHER INFORMATION

No other sources were identified.

SEARCH CRITERIA TO BE USED:

HIV Infections/ diagnosis/drug therapy
Health Policy
Humans
AIDS Serodiagnosis/ utilization
HIV Antibodies/ analysis
HIV Infections/ diagnosis/epidemiology/immunology
Reagent Kits, Diagnostic/virology
Saliva/ immunology