TGA Consultation: Review of the regulation of certain self-testing IVDs in Australia

Cancer Council is Australia's peak national non-government cancer control organisation and advises the Australian Government and other bodies on evidence-based practices and policies to help prevent, detect and treat cancer.

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In preparing this submission, Cancer Council has reviewed the information relevant to the questions raised in the discussion paper, *Review of the regulation of certain self-testing in vitro diagnostic medical devices (IVDs) in Australia*.

Responses to each question are provided below:

1. **Following evaluation by TGA to determine their safety and performance, and considering the experience with HIV self-testing, should:**
    a. self-tests for other infectious diseases;
    b. genetic self-tests (i.e. direct to consumer genetic testing);
    c. self-tests for determining the presence of other serious diseases (e.g. cancer, diabetes)

    be able to be legally supplied in Australia subject to evaluation and approval by the TGA with appropriate risk mitigation strategies?

The Excluded Purposes Specification should be remade to prohibit the supply of certain self-testing in vitro-diagnostic medical devices with implications for the detection, diagnosis and treatment of cancer. However, each product and indication should be assessed on an individual basis for self-testing appropriateness. The national screening programs for bowel and cervical cancer in Australia demonstrate that appropriate risk mitigation strategies can be used successfully to enable people to use self-tests with higher benefit than risk. This may not be the case with all self-tests.

b. genetic self-tests (i.e. direct-to-consumer genetic testing);

It is the position of the Human Genetics Society of Australasia that *both individuals/consumers and health care professionals/providers should be supported to make informed choices about online DNA testing. This means adequate and ongoing education and resources should be available for individuals/consumers and health care professionals/providers before, during and after testing. Health care professionals/providers should be appropriately trained, have relevant experience and should be able to demonstrate (or provide evidence of) a current certification in their field of practice*[1].

Genetic self-tests to detect familial risk of cancer

Predictive genetic tests to identify inherited risk of cancer pose a risk to family members, and the individual. Therefore, significant consideration is required to determine the need for genetic testing.

People at increased risk of inherited cancer should be referred to a family cancer clinic, have access to a genetic counsellor, in addition to their general practitioner or doctor to consider the risks and benefits of genetic testing. The results should be interpreted accurately by a qualified health professional and a plan of action developed between the person and their doctor.

Two examples of this recommendation are:

- *Optimal Care Pathways for breast cancer* recommend that women at moderate or high risk should be referred to a family cancer clinic to have their risk further clarified and for possible genetic testing. They should have access to a range of health professional including a genetic counsellor[2].
- eviQ *Referral guidelines for cancer genetic assessment* recommend that people who have a cancer gene mutation in a blood relative, or a strong family history, or tumour pathology, warrant a referral to a family cancer clinic for genetic counselling and risk management advice[3].

People who undergo a genetic test outside of the referral groups may be exposed to increased risk or risk not considered when deciding to use a test, such as:

- Anxiety and psychological harm caused by receiving confirmation of genetic marker, especially if there is no known prevention, treatment or cure;
- Becoming complacent about future risk of disease if the result is negative;
- Information which potentially affect the ability to gain and coverage of travel insurance and other types of risk-rated insurance;
- Implications of this information for family members;
- Companies can include clauses which enable them to provide personal or health data to third companies;
- Out-of-pocket costs as self-funding of tests used outside of indication may not be available on the Pharmaceutical Benefits Scheme.

If regulated as a self-testing invitro-diagnostic device by the Therapeutic Goods Administration, either purchased by the doctor or directly by the consumer, predictive genetic self-tests require oversight by a range of health professionals including clinical geneticists and genetic counsellors. Also, these tests must prove comparable accuracy to point of care use. Variances such as compliance with collection and storage standard, and quality laboratory testing, may impact the ability to generate an accurate outcome.

Genetic self-tests to guide treatment and care options

Knowing the status of a genetic cancer marker can guide treatment eligibility and decisions, particularly important for access to publicly funded or subsidised options. In most situations, the decision to have genetic testing for this purpose will be made with the treating doctor, however, some patients may access genetic self-tests directly, particularly when they do not meet the criteria to be referred for testing by their doctor.

Acknowledging the Therapeutic Goods Administration classification system, as genetic self-tests represent a level three risk class for incorrect use, caution should be taken in the availability of genetic self-tests to identify risk of familial cancer or guide treatment decisions.

c. self-tests for determining the presence of other serious diseases (e.g. cancer, diabetes)

National population screening programs

Australia has two established national population screening programs which use a self-test to aid the early detection of cancer, the National Bowel Cancer Screening Program, and the National Cervical Screening Program. Self-test kits enable people to participate in these early detection initiatives which have comparable clinical effectiveness to point of care collection. Availability of self-tests to support participation in the National Bowel Cancer Screening Program and the National Cervical Screening Program should continue. Cancers detected through a national cancer screening program have shown to be less likely to cause death[4].

Self-tests for both the National Bowel Cancer and National Cervical Screening Programs are registered therapeutic goods, and therefore are safe, effective and of high quality for the indication/s they are registered. Notably, this in the population age groups in which they have been deemed most clinically effective. The risk mitigation strategies for both the bowel and cervical cancer National Screening Program self-tests, aligns with the discussion paper's requirements within the definition of a *serious disease*, as one that *where a self-test is available, it requires medical interpretation or follow up*[5]. These tests do not diagnose cancer but are used to identify indications of early disease for further investigation. These programs have pre-testing information, collection and testing standards, and defined follow up pathways involving health professionals.

Self-tests that provide information regarding serious diseases purchased directly by the consumer

Similarly to genetic self-tests, Australians can access non-genetic self-tests directly from local and overseas companies, for example CA-125. These health tests have received less public attention than genetic tests however, they are gaining more popularity. They are often marketed as screening tools to empower a healthy population to 'take control' of their own health, and can be purchased directly by the consumers, bypassing the person's usual general practitioner.

Non-genetic self-tests generally involve ordering pathology tests that are collected by people in laboratory. As there is no self-collection of the sample involved, these types of tests do not meet the definition of a 'self-testing invitro-diagnostic' under the Medical Devices Regulations (2002) for regulation by the Therapeutic Goods Administration[6]. Only collection devices used by the consumer in Australia are considered in vitro-diagnostics and can be regulated by the Therapeutic Goods Administration, not when collection is performed in laboratories.

Marketing as tests for information, rather than tests for medical decision making, enables direct-to-consumer non-genetic tests to by-pass usual quality control processes in Australia, including safety and efficacy review by the Therapeutic Drugs Administration prior to market availability. The *Therapeutic Goods Advertising Code 2018* aims to ensure that the marketing and advertising of therapeutic goods is conducted in a manner that promotes the quality use of the product, is socially responsible and does not mislead or deceive the consumer[7]. However, if tests are not Therapeutic Goods Administration regulated, companies are not required to comply with these advertising standards.

Self-tests to identify cancer markers can be problematic, negatively impacting on both the patient and health resources. Non-genetic (liquid biopsy) self-tests for determining or gaining information about the presence of cancer have limited clinical utility when used in isolation of other detection and diagnostic tools. Except for use as part of a National Cancer Screening Program, they often record false-positives and false-negatives, reducing their ability to conclusively detect the presence

of cancer. Liquid biopsies identify small amounts of DNA or proteins released into the blood stream from cancer cells, known as biomarkers or circulating tumour cells. While currently used in cancer care as part of surveillance after diagnosis, such tests are being used by otherwise healthy people to screen for cancer without a clear understanding of the benefits or harms, and the accuracy of these tests.

A few examples of the limited clinical utility of non-genetic self-tests as standalone diagnostic tools, and therefore problematic for direct-to-consumer access are:

- Prostate specific antigen for prostate cancer: This test in unable to differentiate between problematic and indolent cancers, therefore increasing detection, potentially leading to over-diagnosis and over-treatment. A study, using a Gleason score of >6 as an indicator of prostate cancer, found that over half of men who died from an unrelated event, died with undetected prostate cancer[8].
- CA-125 for ovarian cancer: This test has low predictive value which limits the ability to differentiate between cancer and usual physiological events. Elevated CA-125 is generally used as part of a tool kit for detecting ovarian cancer in asymptomatic women, however this marker is also elevated during menstruation[9]. Therefore, accurate interpretation of this result is critical.
- M2-PK for bowel cancer: Although sold online to consumers, M2-PK lacks diagnostic accuracy to identify the individuals who should be progressed for clinical follow-up and therefore, not a robust biomarker for identifying pre-cancerous bowel lesions[10].

Similarly, to the risks identified for genetic self-tests, the effects of inappropriate use of non-genetic self-tests could be the need for additional follow up tests, overdiagnosis, over-treatment, and conversely avoidance of doctors due to a false sense of their health.

2. Are there any particular tests that should not be available in Australia as a self-test? Please provide reasons why not.

Self-tests for determining the presence of serious diseases such as cancer should be able to be legally supplied in Australia subject to Therapeutic Goods Administration regulation and approval only where these tests form part of National Cancer Screening Programs and therefore the Excluded Purposes Specification should maintain an exception for these types of tests.

3. Do you have any suggestions on how potential risks to consumers could be mitigated?

<u>Adopt the European Union's extended definition of invitro diagnostic medical device for self-testing</u>

The definition of invitro-diagnostic medical device for self-testing in Australia should be extended to include *'devices used for testing services offered to lay persons by means of information society services'*[11]. This is an important step to address current concerns and emerging interest in consumers purchasing genetic and non-genetic self-tests, intended to provide health information about serious conditions. Referencing the discussion paper, this definition would apply to online companies selling direct-to-consumer services, where there is no self-collection device involved, for example where a consumer receives a pathology collection slip for collection at a laboratory. Therefore, also creating an opportunity for advertising standards to also apply.

<u>Introduce minimum standards for use of self-tests</u>

In addition to meeting requirements of safety, quality and efficacy, compliance with minimum standards could be introduced, including:

- Requires a doctor to order the test
- Requires medical interpretation or follow-up
- Accompanying patient information requirements, including emphasis on seeking health professional advice.
- Reference to general patient education produced by the Therapeutic Goods Administration and other independent sources which includes prior to decision to use and consultation with medical professional post such as *Understanding Direct-to-Consumer Genetic DNA Testing: An information resource for consumers.* A similar resource is needed for self-tests for serious diseases such as cancer.

In addition, for access to self-tests online, introduce and monitor standards for online consent forms, including the provision of information to make informed decisions. This would be a first step towards reducing exploitation online and determining what can and cannot be conducted online without face-to-face consultation.

Increase education and community awareness of self-tests and risk of use without health professional consultation

Information would need to be targeted at reaching people, including forums and websites where online companies advertise.

- Understand how people search on Google and position information from the Therapeutic Goods Administration at the top of these searches.
- Therapeutic Goods Administration develop education on the importance of the use of tests recommended by health professionals or registered on the Australian Register of Therapeutic Goods.
- Greater awareness of the potential risks of purchasing screening and diagnostic tests or services directly from commercial providers is required and options for regulation for consumer protection explored.

Potential introduction of advertising classification to display risk category of self-tests

The Black Triangle Scheme provides a simple means for practitioners and patients to identify certain types of new prescription medicines, including those being used in new ways and to encourage the reporting of adverse events associated with their use[12]. A similar concept could be considered for notification of high risk classified self-tests.

References:

1. Human Genetics Society of Australasia. Position Statement on Online DNA Testing. 29th August 2019. Accessed on 20th November 2019 via https://www.hgsa.org.au/documents/item/18
2. Cancer Council Victoria. Optimal Care Pathways for women with breast cancer. Accessed on 21st November 2019 via https://www.cancervic.org.au/downloads/health-professionals/optimal-care-pathways/Optimal_care_pathway_for_women_with_breast_cancer.pdf
3. Cancer Institute New South Wales. General practitioner referral guidelines for cancer genetics assessment. 14th March 2017. Accessed on 22nd November 2019 via https://www.eviq.org.au/cancer-genetics/adult/referral-guidelines
4. Australian Institute of Health and Welfare. 2019. Analysis of cancer outcomes and screening behaviour for national cancer screening programs in Australia. (p. 8&9) Accessed on 22nd November via https://www.aihw.gov.au/getmedia/0c4daae9-d0c6-422a-afbd-47a36c6c8697/aihw-can-115.pdf.aspx?inline=true
5. Therapeutic Goods Administration. September 2019. Review of the regulation of certain self-testing IVDs in Australia discussion paper. P. 13. Accessed on 22nd November 2019 via https://www.tga.gov.au/consultation/consultation-review-regulation-certain-self-testing-ivds-australia

6. Therapeutic Goods (Medical Devices) Regulations 2002. Accessed on 22nd November via https://www.legislation.gov.au/Details/F2017C00534
7. Therapeutic Advertising Code (no.2) 2018. Accessed on 22nd November 2019 via https://www.legislation.gov.au/Details/F2018L01524
8. Bell, 2015. Prevalence of incidental prostate cancer: A systematic review of autopsy studies. Accessed on 22nd November 2019 via https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4682465/
9. Mayo Clinic. CA-125 test. Accessed on 27th November 2019 via https://www.mayoclinic.org/tests-procedures/ca-125-test/about/pac-20393295
10. Keenan J, Aitchison A, Leaman J, Pearson J & Frizelle F. Faecal biomarkers do not always identify pre-cancerous lesions in patients who present in primary care with bowel symptoms. 2019 August 30;132(1501): 48-56 Accessed on 22nd November 2019 https://www.ncbi.nlm.nih.gov/pubmed/31465327
11. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. Accessed on 22nd November 2019 via https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0746
12. Therapeutic Goods Administration. Black Triangle Scheme. Accessed on 22nd November 2019 via https://www.tga.gov.au/black-triangle-scheme