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IVD Reforms
Medical Devices Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

30 November, 2018

To the Director, IVD reforms

Re: TGA Consultation: Proposal for the regulation of IVD companion diagnostics

MS Research Australia is the largest national not-for-profit organisation dedicated to funding and coordinating multiple sclerosis (MS) research in Australia. Our goal, as part of a worldwide effort, is to accelerate research into the cause, better treatments for, and prevention of MS, with the aim of ultimately finding a cure for MS.

A range of disease modifying medications are available for people with the relapsing form of MS. New medications for both relapsing and progressive MS are also in the pipeline and/or close to approval.

MS is a very variable disease, and people can have a range of responses to the available medications. The medications also have a range of potential risks and side-effects, which in some cases can be severe.

It is therefore crucial that we continually strive to improve the tools available to identify the most effective treatment and minimise risks for each individual. Some companion diagnostic tools are already available to help identify individuals with MS who may be at increased risk of adverse events with some MS medications (e.g. The John Cunningham (JC) virus assay for people considering or receiving treatment with Tysabri) and to monitor treatment response and adverse events (e.g. Bloodwatch which provides early identification and treatment of potential adverse events in people treated with Lemtrada). More are in development. There is also a great deal of work underway to help improve our ability to predict treatment responses in individuals.

As the TGA's consultation paper notes, 'precision medicine' is a rapidly growing field with a proliferation in the number and diversity of companion diagnostics, and this is not unique to MS.

For this reason we welcome the TGA's proposal to develop a regulatory framework for IVD companion diagnostic tests. This will help to ensure that these tests are as accurate and effective as possible, and enhance the safe and effective use of treatments for a wide range of health conditions.

We note that the TGA is currently limiting this regulatory framework to *in vitro* companion diagnostic tests (IVD CDx) and may later expand this to consider other types of companion diagnostic tests, such as imaging. Imaging capabilities are developing at a rapid rate, and in the field of MS are shaping up to provide accurate methods to prognosticate, and predict and monitor treatment outcomes. We would therefore recommend that the TGA keeps a close eye on this area and considers appropriate and timely regulation and oversight as required. However, this may perhaps fall under the 'in-house' category of CDx as discussed in Proposal 9.

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We support the proposed definition of IVD CDx (**Proposal 1**) and their alignment with the EU and FDA.

The meaning of "essential for the safe and effective use" of a therapeutic product is clear and appropriate (**Proposal 2)** and we agree that the IVD CDx should be appropriately referenced in the Product Information (PI) and Consumer Medicines Information (CMI) for the corresponding medicine or biological therapy. As noted below, some IVD CDx may be developed and evaluated by the TGA at a later time to the corresponding therapeutic product. However, it is important that the corresponding therapeutic product is clearly identifiable in the assessment of the IVD CDx and that the PI and CMI are updated accordingly.

Classifying all IVD CDx as Class 3 IVDs (**Proposal 3)** and the proposed amendment to Rule 1.3 is appropriate. We would like to note however, that under item *h*. it states "when there is a risk that an erroneous result will lead to a patient management decision resulting in an *immediate* life-threatening situation for the patient' – in some circumstances an IVD CDx medical device may detect serious risks where the effect is not *immediate.* For example the impact of ineffective use of a medication in MS may take months or years to evolve, and likewise, the emergence of an adverse event as a result of an inadequately monitored risk factor following long-term use of a medication. We would like to propose that the word *immediate* is removed from this item.

Proposals 4 and **5** are also appropriate. **Proposal 6** is also appropriate in that a fee should be applied for assessment of each IVD CDx where multiple devices are proposed for a single therapeutic good, and when a new intended purpose for a device is proposed. However, we recognise that this may lead to a significant burden for sponsors (particularly smaller biotech companies). Consideration could therefore be given to a reduced fee per device, where multiple devices that are substantially similar are being assessed in conjunction with one another.

The three scenarios for transitioning existing IVD CDx into the regulatory framework and the fee structures proposed under options a, b and c (**Proposal 7**) are appropriate. Regarding the feasible timeframe for this to occur (**Proposal 8)**, it would be more appropriate for industry stakeholders to comment.

We applaud the proposal to work with the NATA, RCPA and NPAAC to develop guidelines to be applied to in-house IVD CDx (**Proposal 9**). Any regulatory or oversight frameworks for these devices should ensure safety of consumers while also enabling and encouraging academic and 'in-house' laboratories to innovate.

While concurrent evaluation of a therapeutic good and its corresponding IVD CDx is ideal, as noted earlier this may not always be possible. We endorse the proposed options (**Proposal 10**) for a robust evaluation of IVD CDx with changed intended purpose or a new IVD CDx that was not used in the original clinical trials in order to demonstrate their performance is accurate and equivalent to existing devices.

Thank you for the opportunity to comment on this important area that will improve the safe and effective use of medicines and optimise treatment for all individuals.

Regards

Dr Lisa Melton
Head of Research, on behalf of MS Research Australia