Response ID ANON-CBS3-RZBF-Y

Submitted to Consultation: Proposed changes to the IVD medical device classifications and definitions
Submitted on 2025-05-22 12:10:53

Introduction

What is your name?

Name:
[redacted]

What is your email address?

Email:
[redacted]

What is your organisation?

Organisation:
[redacted]

Responding to this Consultation

Question 1(a): Do you agree with the proposals to change the Australian classification rules and principles that have an impact on approved products (as specified in the first Section of the paper), noting the changes are reflective of the regulatory scrutiny based on the associated health risks?

Respond to the question 1a:

No

Question 1(b): If no, which of the proposed changes do you not agree with? Please provide your reasons.

Respond to the question 1b:

Whilst the rationale is understood, the implications of the proposed changes have not been adequately addressed. Specifically one of the proposals indicates that immunohistochemistry testing would be changed to a Class 3 IVD. It is unclear from the example what this actually means. IHC may be used to assist in the classification of a tumour or to define a specific subset of tumour, however it may also be used to determine access to therapeutics such as ER testing for breast cancer. Laboratories are required to be assessed under accreditation but the majority of this testing comes under an in-house IVD. Therefore the requirements for each one of these assays may not be practical. Laboratories may have more than one hundred antibodies for testing.

Question 1(c): Are there any other classification rules and principles, relating to the IVD medical devices, that need to be considered as part of this proposal?

Respond to the question 1c:

No

Question 2(a): Do you agree with the proposals to adopt certain terminology in the Australian classification rules that have no impact on approved products (as specified in Appendix A of the paper), noting the changes are to improve clarity?

Respond to the question 2a:

Yes

Question 2(b): If no, which of the proposed changes do you not agree with? Please provide your reasons.

Respond to the question 2b:

Question 2(c): Do you agree the proposed changes in Appendix A of the paper, would not result in any impact on existing ARTG entries of IVD medical devices?

Respond to the question 2c:

Yes

Question 2(d): Are there any other classification rules, relating to the IVD medical devices, that need to be considered as part of this proposal?

Respond to the question 2d:

No

Question 3(a): Do you agree with the proposal to amend the Australian definitions as specified in Appendix B of the paper?

Respond to the question 3a:

No

Question 3(b): If no, which of the proposed changes do you not agree with? Please provide your reasons.

Respond to the question 3b:

The current and proposed changes to the classification of Class 3 IVDs for pathology laboratories to designate a CDx (Companion Diagnostic) poses an unacceptable patient risk and will result in an adverse outcome for patients.
This conclusion is based on patient outcomes before the inclusion of therapeutic options into pathology reports. Currently it is a requirement for the external QAP including RCPA QAP and EMQN to included therapeutic options in pathology reports for molecular testing in both somatic and germline cases if applicable. Failure to provide this information results in a nonconformance. The TGA proposal is to have laboratories remove this information which would be inconsistent with standard of care practice across the world.
The current proposed situation is that if a therapeutic drug is named in a pathology report it is classified as a CDx which requires correlation with the assay performed for the original clinical trial. Standard NATA accreditation allows the laboratory to report a result without reference to a specified drug. The proposed changes include removal of reference to a class of drugs.
1. When molecular testing was introduced for determination of patient response to targeted therapy, pathology laboratories refused to comment on the likelihood of response to either a class of drugs or a specific drug. This was evidenced by HER2 ISH testing where the result only was reported.
a) However, as more assays were introduced there was confusion about interpretation of the results by clinicians resulting in patient harm. The presence of a biomarkers is usually associated with a response to a therapeutic agent, however in the case of colorectal carcinoma, the presence of a KRAS or NRAS pathogenic variant is associated with a lack of response to EGFR monoclonal antibodies. Patients were given incorrect treatment due to a lack of understanding of the results. At this time, laboratories began to comment on the relevance of the molecular marker and the associated therapeutic options, to reduce the risk of patient harm.
b) The molecular changes that are detected for therapeutic options has become more complicated over time. For KRAS there are now targeted therapeutic options for tumours with KRAS G12C and G12D variants. This also varies depending on the origin of the tumour.
2. The assay that was used for the clinical trial may not be the most appropriate assay. The selection of the assay may be based on convenience, cost or availability of vertical integration of the pharmaceutical company rather than being the gold standard assay. In addition, improved assays may become available over the trial timeframe. The original BRAF assay used in the clinical trial for BRAF inhibitors in malignant melanoma was not endorsed by MSAC as the assay sensitivity was inferior to that of other assays that were available. For this reason, MSAC rarely requires a specific brand of assay as accreditation by NATA assesses the validation/verification of the assay to ensure the assay is fit for purpose and correlates with the original assay used.
3. The clinicians are not able to understand the complexities of the molecular results or the differences in variants without laboratory input.
a) For BRAF variants, there are 3 classes of variants, some of which can respond to BRAF inhibitors and some that do not.
b) Similarly, for EGFR there are rarer variants that have limited data available because there were few patients included in the clinical trials. EGFR resistance mechanisms and therapeutic response to first or third generation EGFR inhibitors may also depend on whether the resistance variant is present on the same allele (in cis) or the opposite allele (in trans) to the activating variant. Purely reporting the variant/s without indicating the appropriate therapeutic option will result in an increased risk of patient harm.
4. For HRD, the presence of HRD is a permanent change and cannot be used to determine if the tumour is sensitive/resistant to PARP inhibitors once the initial determination has been made to use PARPi. The presence of a BRCA1/2 reversion mutation does not change the HRD status. Clinicians will not be able to interpret the test results without the laboratory providing the appropriate therapeutic options.
The biological variability of the patient and the molecular alterations in the tumour have a far greater impact on the response to targeted therapies compared to differences in IVD assays where the assays have been appropriately validated/verified. The designation of CDx does not address any of these issues and the removal of therapeutic options or class of drug compound from a pathology report will lead to an increased likelihood of patient harm.

Question 3(c): Are there any other definitions, relating to the IVD medical devices, that need to be considered as part of this proposal?

Respond to the question 3c:

No

Question 4(a): Do you agree with the proposal to apply a 6-month transition period after the EU IVDR transition timelines for the proposed Australian amendments to take effect?

Respond to the question 4a:

No

Question 4(b): Provide reasons for your position.

Respond to the question 4b:

The proposed changes should not be implemented in the current form and the TGA should review the proposed changes with additional consultation as to the actual patient impact if the changes are to proceed. The proposed changes will result in increased patient harm based on the previous evidence. The transition period for the other proposed changes is too short to enable an appropriate implementation.

Question 5: Do you consent to your response being made publicly available on the TGA's Consultation Hub website? Please indicate your publishing preferences.

I consent to my submission being published anonymously (without my name or my organisation's name)

Question 6: If you consent to your submission being published, are there parts that you do not want published? Please specify which part(s). Please note – your contact email address and/or phone number will not be published with your submission.

Respond to the question 6:

No