AstraZeneca Pty Ltd – Response 11

CDx identification guide
"The CDx identification guide is a helpful reference for the sponsors. To further improve this guide, it would be beneficial if the TGA can provide guidance on where medicine/biological sponsors can present their conclusions on the required in-vitro testing. It would be helpful if the TGA can provide reference on the section where we can demonstrate that such testing aligns with mainstream pathology testing in Australia, and to provide confidence that the standard of care testing in conjunction with the medicine/biological will yield comparable clinical outcomes. For application involving in-vitro diagnostic testing for registration, there is a concern should the disagreement from the TGA emerges at the conclusion of evaluation. This could present significant challenges for the application. To help mitigate any unforeseen delays, it would be of value if the TGA could include a process to establish agreement on the outcome prior to submission or at an early stage of evaluation. Examples of mainstream testing Could the examples of mainstream testing include more contemporary examples such as EGFR, BRAF, HER2 or BRCA? Use of a Unique Product identifier (UPI) Additional information would be of value in this section to outline UPI assigned under IVDR can be considered as a suitable substitute. Mandatory application audit It would be of value if TGA can provide information on the suitability of FDA clearance or approval as a substitute."
Companion testing plan
"Companion testing plan The inclusion of a companion testing plan is valuable as it provides an overview of how the medicine or biological is used with the companion diagnostic. However, challenges arise in managing updates for companion testing plan through type H applications. The submission of any new or modified companion testing plans, as well as their removal, can be resource-intensive for both the medicine/biological sponsor and the TGA. A Category 1 application has a lead time of 12-15 months and with the ever-changing landscape of companion diagnostics, a more flexible regulatory solution for managing ongoing compliance would be beneficial. In cases where the intended in vitro diagnostic (IVD) test is considered a 'subsequent IVD', additional evidence is needed in the companion testing plan to establish its performance and comparability to the clinical trial assay. The challenge for the medicine sponsor lies in obtaining necessary performance and comparability data from the IVD manufacturer for inclusion in the medicine application, as these data may be confidential and inaccessible by the medicine sponsor. Exploring an alternative approach whereby the supplier can provide the information directly to the TGA would be favourable. Additionally, there is a need for clarity regarding whether the requirement for a commercial CDx to be included in the ARTG before legal supply in Australia applies to send-out testing, and if appropriately accredited overseas performed assays are mandated to be registered locally. In the guidance document, the “Please note” on page 8 states that a commercial CDx must be included in the ARTG before it can be legally supplied in Australia. It would be of value if the TGA could clarify whether this requirement apply to send-out testing (e.g., Myriad Genetics, FoundationOne), or is it specific only to local IVD and in-house IVD solutions? Our understanding is that appropriately accredited overseas performed assays are not mandated to be registered locally.

In a scenario where samples are sent overseas for testing as an interim measure, the cost of conducting these tests abroad may be prohibitive, potentially leading in patients being unable to access the medication while the local testing infrastructure is being established. It would be useful if the TGA could explore an alternative approach, where the evidence from the overseas sponsor, meeting the legislative requirements within their country of operation, could be considered as an alternative to full concordance."

Case studies

"The case studies serve as a practical guide for sponsors to consult when evaluating the requirements for CDx. However, it is important to note that some of these case studies may not accurately reflect real-world scenarios. Therefore, it is suggested to make Case Studies 2 and 3 more distinct, as they appear to be quite similar. Specifically, to differentiate Case Study 3, we recommend that the bridging study in this case should utilise specimens representative of those tested in the original pivotal clinical trials, particularly if the original clinical trial specimens are exhausted or inaccessible. This adjustment would bring the case study more in line with real-world conditions.

It is important to recognise that sourcing samples from the original trial does not reflect real-world practices. In reality, the sponsor of the medicine source alternative samples through other means.

Companion testing plan
Furthermore, we suggest the inclusion of companion testing plans that encompass various scenarios, providing comprehensive guidance for sponsors of the entire process, from the beginning to completion. This approach will help contextualising the process for the sponsors."

Further feedback

"TGA CDx list (with the inclusion of in-house IVDs)

Could the TGA please advise on the implementation date for the CDx list with the inclusion of in-house IVDs?"