Leica Biosystems – Response 4

CDx identification guide
• (Page 4) Re: Note "Examples of IVDs that are not captured under our definition of CDx include those consistent with FDA's consideration of complementary diagnostics". - Suggest including a definition or alternatively reference to relevant FDA guidance. • (Page 4) Re: "Note: CDx testing may be required for some therapeutic drug monitoring devices, not all. This will be determined during the application for the medicine." - Add additional guidance and cross reference to pre-submission process to encourage early interactions where it may be unclear. • (Page 7) What is the time lag between being added to ARTG and the update to the CDx list? If it could be significant, perhaps clarification needed i.e. some approved tests may not be included?
Companion testing plan
- (Page 8) Is there a template for what is included in the Companion testing plan? How is this submitted to TGA? • (Page 8) re: "If the medicine sponsor is aware of a concurrent application for inclusion of a corresponding CDx in the ARTG (or notification of an in-house CDx IVD), the companion testing plan can simply consist of a cross-reference to the relevant details." - suggest adding clarification of cross referencing within the device submission to CDx clinical data in the medicine indication registration submission. • (Page 8) Re: "The companion testing plan provides a mechanism for the TGA to evaluate the performance and validity of IVDs intended for companion testing, even when there is no concurrent application for inclusion of a CDx in the ARTG (or notification of an in-house CDx IVD). This approach recognises that there may be barriers to bringing a CDx to the Australian market for local supply, and Australian samples may have to be sent for testing internationally. While this is not preferred, the companion testing plan provides a mechanism for the TGA to appraise such testing and for a medicine or biological sponsor to take responsibility for it, until the registration or notification of a local testing option is possible." Please note - Sending of samples to an appropriately accredited overseas testing facility is considered acceptable by the TGA only if development of onshore testing with an ARTG-included or in-house (notified) CDx test is infeasible or incomplete. - Does this imply that routine testing of patient samples with the approved drug, where its CDx has not yet been applied and registered, must be conducted overseas until registration is completed? If so, why is there onshore testing with ARTG CDx? Is this ARTG CDx the equivalent of the one planned for registration? More clarification is needed on the "Please note -xxx" statement. • (Page 8) Re: "Sending of samples to an appropriately accredited overseas testing facility is considered acceptable by the TGA only if development of onshore testing with an ARTG-included or in-house (notified) CDx test is infeasible or incomplete" - Suggest adding clarification this statement is for testing of final IVD(CDx). i.e. not for clinical trial testing. - What is the process for sending Australia patient samples overseas? Is any approval or notification to TGA required before sending out the samples? - Request to clarify the registration process for clinical trial assays when Australia patient samples are shipped overseas for testing, i.e. no devices imported into Australia. • (Page 9) re: "evidence on performance and comparability to be submitted by the medicine or biological sponsor; within the medicine application." - Recommend clarifying mechanism for device sponsor/third party/lab to submit (or cross referencing) data to be used in medicines submission directly to TGA.
Case studies
Yes the case studies are helpful. - RE: Case study 2 and case study 3, and use of specimens used in the pivotal clinical trial re-tested. Request clarification to be added in body of text re: insufficient samples available from pivotal study for use in bridging.

Further feedback
"• (Page 7) re: ""we recommend consultation with TGA by requesting a pre-submission meeting with the Prescription Medicines Authorisation Branch"" - Recommend clarifying this is ahead of the submission and not at the time of submission. • (Page 7) re: ""Data to support evaluation of the clinical and analytical performance of the IVD used in generating the pivotal data (the clinical trial assay)"" - Recommend clarifying mechanism for device sponsor/third party/lab to submit (or cross referencing) data to be used in medicines submission directly to TGA. • (Page 8) RE: ""the TGA will perform a component evaluation of the clinical trial assay"" - Suggest clarifying what is meant by 'component evaluation' • (Page 12) Re: Fig 2. - Recommend adding clarification that foreign clinical IVD testing data can be used to support clinical performance data requirements. • (Page 13) Re: ""non-inferiority clinical study"" - Recommend using ""comparison"" terminology in place of ""non-inferiority"" • (Page 13) re: paragraph beginning: ""Applicants may use bridging and comparability studies to demonstrate comparability of analytical and clinical performance between the original CDx and the subsequent IVD."" - request adding clarification on acceptability of use of procured samples when e.g. clinical samples from pivotal study are not available."