Anonymous – Response 12

CDx identification guide
The guide is very helpful. We appreciate that standard of care local testing is permitted without a CDx indication for standard analytes such as HER-2 (as per case study 4). The guide does not consider how in-house tests influence the decision on whether a CDx is needed. We recommend that additional clarity is provided on in-house testing and how it influences the decision.
Companion testing plan
The sponsor of the medicine/biological is often not in direct control of the CDx (i.e. availability and accessibility). Therefore, we appreciate the recognition of the scenario in which developing a CDx in Australia is infeasible or out of control of sponsor of the medicine. We also appreciate the provision and requirements in the guideline for subsequent CDx and the ability to apply for modification of companion testing plan when an existing test becomes unavailable. From an access perspective, for the payer/HTA process in Australia (PBAC/MSAC), where a test is not MBS funded or included as part of routine care, a co-dependent application requesting funding for the test + drug is required. As part of the payer's consideration of the test, there is often uncertainty as to the capacity/capability of pathologists to implement a new test and meet the requirements of patient population. The companion testing plan will ensure this work/planning is conducted earlier and reassurance can be provided regarding the appropriate identification of patients for the medicine.
Case studies
The case studies are very helpful. In case studies #1-3, a CDx was required. Only in case study #4 was a CDx not required. It is not clear why it is important that the HER-2 test was an in-house test for case study #4. We suggest the addition of a case study for in-house NATA accredited CDx (non ARTG listed). This is because for many new/innovative tests this will rely on pathologists seeking NATA accreditation (in-house IVD) which requires substantial upfront investment to achieve approval. Reimbursement/MBS funding are granted for in-house NATA accredited CDxs too. Hence a case study will be helpful on this. In addition, we think more case studies will be required in future to help illustrate where the line is drawn regarding whether a CDx application is necessary. The situation may also evolve over time, as illustrated by the case study #4 where a test that was considered a CDx earlier may become a mainstream pathology test. How will this be addressed?
Further feedback
We appreciate the additional clarity provided in this version of the guidance. The CDx identification guide (Figure 1), aligns mostly with the considerations of the payer (PBAC/MSAC) when determining whether a fully integrated co-dependent submission (test+ drug) is needed. The clinical evidence for the CDx needs to consider the complete 4 quadrants (false positives, false negatives, true positives, true negatives) & test failure and its influence in identifying the appropriate patient and also the consequences of patients that miss out on treatment due to the inaccuracy of the test. Often these materials are missing/not conducted for payer files and integration to the regulatory process will assist with ensuring this evidence requirement can be met. Having early views from a regulatory body can help inform payer consideration of the CDx evidence. One such recent example of lack of preparedness for a CDx in the Australian setting was with

HRD testing for ovarian cancer, with NATA accreditation of the in-house test and implementation only occurring from Jan 2024, well after PARPi TGA registrations for Olaparib and Niraparib. Reimbursement of PARPis had been restricted to BRCAm, and expansion to BRCAwt HRD cohort was only achievable from the start of Jan 2024. Overall, while these requirements will increase the evidence burden for regulatory filing in Australia, the heightened consideration of the CDx component may increase the potential and accelerate the timelines to reimbursement.

One caveat to consider is that sometimes the development of CDx in Australia is not necessarily within the remit of the company applying for the medicine marketing authorization.

Also, the inclusion of evidence for CDx testing within a regulatory submission marks a significant shift in the requirements for medicine/biologics submissions. As such, the transition period for this requirement should be sufficient and flexibility allowed, i.e justified extensions for late-stage development products.