Comments on the proposed amendments to the new regulatory framework for *In Vitro* Diagnostic medical device (IVDs)  

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INTRODUCTION

The Australian Red Cross Blood Service (Blood Service) appreciates the opportunity to comment on the Therapeutic Goods Administration (TGA) proposed amendments to the new regulatory framework for *In Vitro* Diagnostic medical devices (IVDs) and supports the TGA’s initiative in addressing the complex issues identified since the introduction of the new framework.

The Blood Service has been working towards achieving compliance with the IVD requirements since implementation of the regulations in July 2010, however compliance in some areas, especially those requiring full conformity assessment of in-house IVDs, has proven to be challenging. The Blood Service has for many years used a combination of both commercial and in-house IVDs for both blood donor screening and reference services for patients, including complex red cell reference investigations, organ and tissue matching services, cadaveric and cord blood testing services and external client infectious disease screening services. The Blood Service supports the implementation of improved regulation of IVDs and is committed to compliance with the new regulations. However due to the complexity of some of our reference and supplementary testing services, and the class 4 in-house IVD registration requirements of IVDs used in this area, we have identified some potential difficulties in maintaining these services.

Therefore as part of the Blood Service approach to IVD compliance, focus has been placed on the conversion of in-house IVDs to commercial alternatives where available in the market. While this approach has proven to be feasible for the majority of the IVDs associated with blood donor screening, it has also identified some concerns for the Blood Service.

- The Blood Service is working towards the same IVD registration deadline as commercial suppliers. It is unknown if all commercial products currently in use, or planned for implementation as part of our commercialisation strategy, will achieve registration by the required date. It is also unknown if any changes made to the assays or their product inserts by the commercial manufacturer in order to comply with the IVD regulations will restrict their usage (including changing the product to Research Use Only). It is therefore feasible that the Blood Service would be left with no commercial assay option and no time to register an in-house version of the assay.
Gaps have been identified in the Australian commercial market where there are no suitable commercial class 4 IVD replacements (planned for inclusion on the ARTG) for some in-house IVDs currently used by the Blood Service. Therefore the Blood Service will be required to manufacture and register class 4 in-house IVDs with the TGA in order to continue to provide the same level of service.

The Blood Service is continuing to work towards full IVD compliance by using commercial replacements for many of our in-house IVDs. However, due to the issues identified above, we request that the TGA considers our response to the proposed changes to the IVD regulations and the additional comments provided.

**PROPOSAL 1A: Introduce a staged transition to the new IVD framework**

**PROPOSAL 1B: Retain the existing timeframe for transition to the new regulatory framework.**

The Blood Service supports Proposal 1A.

As a user of a large number of commercial IVDs critical to supply of blood components and blood products, patient reference services, and organ and tissue matching services within Australia, the Blood Service recognises the importance of continuity of IVD supply in Australia. As such, the Blood Service believes that the proposed staged transition to the new IVD regulatory framework will help support the successful implementation of these regulations. The additional time provided for commercial IVD manufacturers will help ensure there is no interruption to the supply of commercial IVDs currently in use at the Blood Service Proposal 1A provides the Blood Service with an important solution to one of the major issues associated with compliance with the IVD framework (that is, continuity of supply) and we support the adoption of this amendment.

The Blood Service does not support Proposal 1B and is concerned that retaining the existing timeframe for transition to the new regulatory framework would have a serious impact on the availability of some commercial IVDs and consequently on the supply of blood components and blood products, patient reference services, and organ and tissue matching services within Australia. The current implementation timeframe does not provide adequate time for the Blood Service to identify the gaps within the commercial IVD market and
subsequently design, register and implement in-house IVDs to ensure our current level of service to the community is maintained.

**Additional comment:** It is understood that current regulations require all new commercial IVDs to be included in the ARTG prior to the introduction to the Australian market. The Blood Service has been restricted in progressing the replacement of some class 4 in-house IVDs with commercial products as they are IVDs that have not previously been available in Australia. The Blood Service proposes that consideration be given to allow implementation of new commercial IVDs to address the gaps in the market in parallel with the manufacturer submitting the IVD to TGA for registration and with sufficient in-house validation demonstrating its performance.

**PROPOSAL 2A:** Introduce a modified conformity assessment procedure for the regulation of Class 4 in-house IVDs predicated on commercial IVDs, with staged timeframe for compliance.

**PROPOSAL 2B:** Introduce a modified conformity assessment procedure for the regulation of all Class 4 in-house IVDs, with staged timeframe for compliance.

**PROPOSAL 2C:** Retain the regulatory requirements for Class 4 in-house IVDs, with full conformity assessment procedures, with effect from 1 July 2014.

**The Blood Service does not support Proposal 2A.** The Blood Service notes that although Proposal 2A addresses issues faced by laboratories with regards to meeting conformity assessment requirements for Class 4 in-house IVDs predicated on commercial IVDs, it leaves other critical issues faced by the Blood Service unresolved.

Due to the gaps in the commercial market the Blood Service would have to retain a small number of class 4 in-house IVDs to continue provision of its specialised testing and reference services. As the in-house IVDs used by the Blood Service include *de novo* developed IVDs, under Proposal 2A these would still require full conformity assessment by the TGA. This requirement would continue to be a significant burden for the Blood Service. The current work undertaken to transition to commercially supplied IVDs is already a resource intensive and costly exercise, even without the added requirement to undergo full conformity assessment equivalent to that of a commercial diagnostic company. Therefore, the Blood Service is concerned that such a requirement for full conformity assessment of in-house IVDs could potentially lead to the organisation’s inability to continue to provide certain services if the requirements for conformity assessment cannot be met.
In addition, the Blood Service is also concerned that in this proposal the timeframe for regulatory compliance for de novo Class 4 in-house IVDs is the same as commercial Class 4 IVDs. As many commercial IVDs are yet to be evaluated by the TGA and are not currently included in the ARTG, it is unknown if a timely and successful regulatory approval can be obtained and whether there will any significant changes to the product information (i.e. usage instruction) that may be difficult for the Blood Service to maintain compliance with. Having the same deadline for in-house and commercial IVDs places immense pressure and unavoidable risks for laboratories, who may have to choose between progressing an in-house IVD application and selecting a yet to be ARTG included commercial IVD. Where a commercial option is chosen any issues with the IVD regulatory approval, or any significant changes to product information, could leave the laboratory without an IVD or a suitable IVD, and by then there may not be sufficient time to prepare a regulatory application to enable the laboratory to revert back to an in-house IVD.

If proposal 2A was to be selected, the Blood Service would strongly urge the TGA to consider the following further amendments.

- Provide additional time for in-house manufacturers to obtain ARTG inclusion for de novo class 4 in-house IVDs over and above the deadline for commercial IVDs. An additional 2 year transition period may provide sufficient time to undergo design control, conformity assessment and implementation of in-house class 4 IVDs developed de novo where a commercial alternative is not available or becomes unavailable.
- The TGA consider exemptions from the IVD regulations for certain class 4 in-house IVDs developed de novo, based on their intended use and risk level, where commercial alternatives are not available.

**The Blood Service strongly supports Proposal 2B.**

This proposal adequately addresses the issues the Blood Service has identified with regards to meeting the requirements for conformity assessment of Class 4 in-house IVDs (developed de novo or those predicated on commercial IVDs). This proposal provides the Blood Service with additional time to continue to effectively manage the replacement of in-house IVDs with suitable ARTG included commercial alternatives where available, and to address any gaps in the commercial market via a more manageable risk based conformity assessment process.

The Blood Service believes this proposal outlines the most appropriate conformity assessment approach for Class 4 in-house IVDs as it prescribes assessment requirements that are achievable for the laboratories, while at the same time ensuring that compliance with
the Essential Principles is verified. Noting that in-house IVDs used within the Blood Service are different to commercial IVDs in that they are:

- produced in small amounts, only sufficient to meet the laboratory network needs
- developed, produced and used by/with the oversight of laboratory scientists with knowledge and understanding of their performance and behaviour
- in most cases, produced in laboratories that have existing NATA accreditation. Compliance with ISO 15189, an international quality management system specific for laboratories, and compliance with various NPAAC standards (including *Requirements for the development and use of in-house in vitro diagnostic devices (IVDs)*), are mandatory parts of the accreditation process.
- assessed as part of NATA accreditation audit and TGA GMP inspections.

The Blood Service believes TGA evaluation of performance validation data would be sufficient to ensure appropriate regulatory oversight is maintained.

The Blood Service notes that as Proposal 2B specifies conformity assessment will consist primarily of an evaluation of the Class 4 in-house IVD performance validation data (based on risk) the additional one year beyond the commercial IVD deadline would be sufficient in most cases. However, without the specific requirements of a modified conformity assessment being detailed in the proposed amendments to the IVD framework, it is difficult to estimate the timeframes required to complete this process for all form of in-house class 4 IVDs and whether an additional 1 year extension beyond the commercial IVD inclusion deadline is sufficient, particularly where the in-house IVD must be developed *de novo*. It is therefore suggested that the TGA consider extending this to 2 years for in-house IVDs to ensure all validation and conformity assessment requirements can be met.

The Blood Service, as a manufacturer of therapeutic goods, is required to maintain a manufacturing licence for each site, including compliance to the *Australian Code of Good Manufacturing Practice – Human Blood and Tissues*. The Blood Service Quality Management System is currently assessed during annual TGA inspection of each processing centre. In addition, many of the Blood Service laboratories hold NATA accreditation and undergo triennial assessment by NATA audit. Therefore, the Blood Service believes that the quality management system should not require a distinct and additional assessment as is required by the current IVD regulatory framework.

The Blood Service acknowledges that Proposal 2B does not include a requirement for Class 4 in-house IVD entry into the ARTG. The ARTG contains products that can be lawfully supplied in Australia and, as in-house IVDs are not supplied outside a laboratory network, the Blood Service supports the proposal that the inclusion of such IVDs on the ARTG is not required. The regulation of Class 4 in-house IVDs would be sufficiently achieved through the
inclusion of approved Class 4 in-house IVDs in a TGA maintained database as in Proposal 2B.

The Blood Service appreciates the TGA taking a practical risk-based approach to conformity assessment and transition to the new IVD framework for all in-house IVDs and believes that proposal 2B will significantly assist in a successful transition for the Blood Service.

**Additional comment:** While the above proposal provides welcomed assistance with the complexity and timeframes for compliance with the IVD regulations, the focus is on class 4 in-house IVDs and does not address the flow on effect to the timeframe for regulation of class 1-3 in-house IVDs. While accreditation of class 1-3 in-house IVDs will be managed by NATA, the current transition period (30th June 2014), will be impacted on by the extension of commercial IVD (class 1-4) timelines to 30th June 2015 if proposal 1A is adopted. Therefore due to the same issues outlined above (proposal 2B) the Blood Service would like to request that the TGA consider an extension to the timelines for accreditation of class 1-3 in-house IVDs equivalent to that of the in-house class 4 IVDs in this proposal.

**The Blood Service does not support Proposal 2C.** This proposal makes it extremely difficult for the Blood Service to comply with the new IVD regulations due to both the complex requirements for conformity assessment of class 4 in-house IVDs for a non-commercial laboratory and the timeframes for compliance. This proposal does not help address any of the issues identified by the Blood Service and will put some supplementary and reference testing services provided by the Blood Service at risk.

**PROPOSAL 3: Introduce selective performance evaluation of Class 4 IVDs submitted for design examination.**

The Blood Service supports Proposal 3. The Blood Service agrees that the TGA should have the appropriate remit to undertake performance evaluation of a Class 4 IVD submitted for design examination, where the TGA has determined that the risks associated with the IVD warrant it.
PROPOSAL 4: Amend the definition of a medical device to include tests for predisposition and susceptibility.

The Blood Service has no objection to the amendment of the definition of a medical device to include predisposition and susceptibility tests. The Blood Service understands the potential ramifications of the results of these tests and agrees that these products should be regulated in a manner that reflects the level of risk they represent.

CONCLUSION

The adoption of proposals 1A and 2B will significantly address the issues that the Blood Service has identified with the current IVD regulations. Proposal 1A will facilitate the continuity of supply of commercial IVDs in the Australian market. Proposal 2B will allow the Blood Service to continue to provide specialised testing with reduced regulatory burden and cost, and with sufficient timeframes to accommodate regulation of in-house IVDs where commercial alternatives are not available, or become unavailable after the deadline for IVD registration.