Abbott comments on the Proposed amendments to the new regulatory framework for *In Vitro* Diagnostic medical devices

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Abbott
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Contents

Executive Summary

Abbott is pleased to provide comment on the Consultation Paper - "*Proposed amendments to the new regulatory framework for in vitro Diagnostic Medical Devices (IVDs)"* released on 30 April 2013.

In considering the proposals, Abbott is cognisant of the need to ensure the Australian community continues to have access to the same level of high quality pathology testing without interruption to supply. Abbott took into account the risk/benefit profile of each proposal and the continued alignment of the IVD framework with GHTF principles.

Abbott supports:

- **Proposal 1A - a staged transition to the new IVD Framework**. Whilst recognising that the Proposal as framed would achieve the objective of allowing Class 4 IVD and Australian manufacturers additional transition time, Abbott recommends the simplest implementation would be to extend the Transition Period for all IVDs to 30th June 2015.
- **Proposal 2A - a modified conformity assessment procedure for the regulation of Class 4 in-house IVDs predicated on commercial IVDs**. Abbott requires assurance from TGA that the level of scrutiny and fees applying to these modified CAs would be equivalent to a commercial IVD assessment, and recommends the TGA produce a prescriptive list of modifications that would be acceptable under this proposal.
- **Proposal 3 – Selective performance evaluation of Class 4 IVDs that are submitted for design examination.** The requirement to undergo local performance testing needs to be well justified and the manufacturer must be given the option to provide sufficient data to meet the Australian requirements in place of local performance testing.
- **Proposal 4 – Amend the definition of a medical device to include predisposition and susceptibility tests.** Abbott accepts changes need to be made to the definition of a medical device to ensure predisposition and susceptibility assays are adequately captured under the Therapeutic Goods Act.

Abbott cannot support Proposal 2B (A modified conformity assessment procedure for the regulation of all Class 4 in-house IVDs) as this would allow a different standard of assessment for *de novo* in-house Class 4 IVDs to that applied to equivalent commercial IVDs.

Background

Abbott is a global leader in *in vitro diagnostics* and offers a broad range of innovative instrument systems and tests for blood banks, hospitals, reference laboratories, point of care testing and self-testing. Abbott has helped transform the practice of medical diagnosis through science and research, particularly in the areas of hepatitis/retrovirus. Abbott's history includes first-of-a-kind products and significant technological advancements.

Abbott thanks TGA for the opportunity to comment on the consultation document *'Proposed amendments to the new regulatory framework for In Vitro Diagnostic medical devices (IVDs)'* released 30 April 2013.

Since the implementation of the new IVD regulatory framework on the 1st July 2010 Abbott has been diligent in ensuring compliance with the framework in the allowed 4 year transition period. To date Abbott has 6 of the 8 Class 4 inclusions on the ARTG and has a number of applications for conformity assessment pending with the TGA.

Since the inception of the IVD framework Abbott has advocated that Class 4 in-house assays should undergo the same level of regulatory scrutiny as commercial Class 4 assays.

While Abbott recognizes some of the proposals put forward by TGA affect Australian manufacturers and/or their IVDs, Abbott will primarily comment in the context of an overseas manufacturer.

Issue 1: timeframe for valid applications for inclusion in the ARTG.

Comments on the current situation regarding timeframes

The current regulations relating to the transition of Class 4 commercial IVDs requires the manufacturer to have obtained a TGA Conformity Assessment Certificate (CAC) as the only form of acceptable manufacturer's evidence before the sponsor submits an application for inclusion of a Class 4 IVD on the ARTG. The regulations state an IVD may continue to be supplied after the 30 June 2014 under the transition arrangements if a valid application for inclusion on the Australian Register of Therapeutic Goods (ARTG) has been submitted. However, for Class 4 IVDs a valid application cannot be submitted unless the CAC has first been issued by TGA.

The same situation applies to Australian Manufacturers supplying products in Classes 2, 3 and 4.

Abbott is concerned with only 13 months to the end of the transition period there are still a considerable number of IVDs requiring TGA CAC that have not yet been the subject of a CAC application and, from the limited number of Class 4 inclusions on the ARTG, even less TGA assessments finalized.

Two factors have a major influence on timing of manufacturers submissions. Firstly, the increased regulatory demands globally from previously unregulated countries and/or emerging markets, particularly in the Asia Pacific region. Secondly, while on-market performance has shown assays continue to be fit for purpose, regulatory submission requirements have changed since the launch of some routinely used products necessitating review of the original technical documentation to ensure it meets current regulatory submission requirements.

Given the current backlog of work within TGA (as presented to industry associations at the TGA IVD Working Group on 2nd May 2013) it is unlikely applications submitted over the next few months will be completed prior to 30 June 2014. There is a strong possibility a number of products may not have a valid application for inclusion by the end of the transition period because a Conformity Assessment Certificate has not been issued despite timely submission by the manufacturer of their application for a CAC.

This may mean a number of Class 4 diagnostic and screening assays currently used will not be able to be supplied past July 1st 2014, along with many lower class assays manufactured in Australia.

Abbott recognizes with Proposal 1A TGA's efforts to provide an extension of time to manufacturers to submit their CAC applications and for the TGA to process the applications within the (extended) transition period. Abbott is concerned Proposal 1A does not address the current TGA backlog of CAC applications and may result in many applications not being processed within the (extended) transition period and/or within the legislated 255 TGA working days for Design Examinations. If proposal 1A is not seen as addressing the backlog, then what other mechanisms are proposed by TGA to process all CA applications in order to prevent disruption of supply of IVDs to the Australian market?

As part of the negotiations between the TGA and the IVD industry on the new IVD framework, TGA agreed to set annual charges to $0 until 30 June 2014. If Proposal 1A is adopted this would allow some sponsors to avoid payment of the annual fee in the 2014/15 financial year by delaying application for inclusion until near 30 June 2015. This would penalize sponsors who have been diligent in getting their products included on the ARTG as they would pay annual fees in the 2014/15 financial year.

On 10 May 2012, TGA released a Regulation Impact Statement (RIS) on *'Changes to premarket assessment requirements for medical devices.'* The recommended option in the RIS (Option 2) includes proposal 3 which is the removal of the requirement for mandatory TGA CAC for Australian manufacturers (except Class 4 IVDs). Should Option 2 of the RIS be adopted, clarification will be needed on how the implementation of Proposal 1A would then apply.

While Proposal 1A focuses on Conformity Assessment, Abbott is concerned other lower class IVDs may not have a valid application for inclusion by 30 June 2014. For example, sponsors with large numbers of Class 3 products which are either not registered or not regulated as Class 3 in other countries may struggle to meet this timeline. These assays may require a mandatory technical file review and manufacturers must be in a position to be able to provide the technical files upon request.

Proposal 1A: staged transition to the new IVD framework

Abbott supports Proposal 1A to allow commercial manufacturers to submit valid applications for TGA CAC by 30 June 2014, and valid applications for inclusion in the ARTG by 30 June 2015. In fact, Abbott recommends extension of the transition period to 30 June 2015 for **all** IVD applications for inclusion on the ARTG as the simplest solution to ensure there is no disruption to supply of assays no matter what class or origin.

Abbott support is contingent upon:

- The extension of time must not penalize manufacturers who have been diligent in submitting their TGA CAC applications to date. Aside from new products, manufacturers would expect their applications to be processed ahead of applications submitted at a later time and, for design examinations, within the legislated timeframe of 255 working days.
- There must be a fast-track lane for new products (or new modifications) entering the Australian market to ensure these products are not disproportionately delayed during the latter part of the transition period. In particular Class 4 assays requiring Design Examination must be processed within the legislated timeframe of 255 working days. TGA has previously agreed to this proposal with the IVD industry.
- The current exemption from payment of Annual Fees for all IVDs must be extended to 30 June 2015 or an alternative arrangement which does not advantage or disadvantage any sponsor should be developed. Sponsors who have inclusions on the ARTG prior to 30 June 2015 must not be penalized nor should there be an incentive to sponsors to further delay submitting applications for inclusion onto the ARTG until close to the 30 June 2015 deadline.

The benefits of this proposal are:

- It allows manufacturers with a large number of assays requiring TGA CAC, particularly Class 4, additional time to prepare and submit high quality applications for CAC.
- It will ensure there is no disruption of supply of IVD products to the Australian market, particularly Class 4 assays used to diagnose high risk diseases and/or those used for donor screening.
- It provides a specific deadline for submitting a valid CAC application since currently there is no clear date which a sponsor can give a manufacturer to indicate they have passed a critical cut-off.

The risks of this proposal are:

- Some manufacturers will continue to delay submission of CAC applications creating a second backlog if large numbers of applications are submitted near the 30th June 2014.
- Sponsors will delay submitting applications for inclusion on the ARTG for assays in Class 1-3 where overseas manufacturer's evidence is being used. If proposal 1A is adopted as is, the TGA will need to make it clear to Australian sponsors the proposed extension of time only applies to IVD products where a TGA CAC is being used as Manufacturer's Evidence.

Additional comment:

Any overseas manufacturer may choose to apply for TGA CAC for Class 2 and 3 products. Proposal 1A as written could equally apply to these manufacturers. Sponsors and overseas manufacturers may choose to apply for TGA CAC for Class 2 and 3 IVDs rather than using overseas certification as Manufacturer's Evidence in order to delay submission of applications for inclusion on the ARTG beyond the 30 June 2014 deadline and/or to continue supply beyond this date. Clarification is needed on whether Proposal 1A is restricted only to Australian manufacturers and overseas manufacturers of Class 4 IVDs.

Does this proposal provide sufficient time for commercial manufacturers and sponsors of Class 4 IVDs to apply for inclusion in the ARTG?

Abbott would have sufficient time under Proposal 1A to complete all TGA CAC applications to meet the new deadline of 30th June 2014. Whether this allows enough time to apply for application for inclusion in the ARTG by 30 June 2015 is dependent on TGA processing of these applications.

Proposal 1B: retain existing timeframes for transition to new regulatory framework

Abbott does not support Proposal 1B. As stated above, Abbott has serious concerns about its ability to continue to supply certain Class 4 IVDs to the Australian market after the 30 June 2014 due to:

- An inability to accurately predict the exact date beyond which a Design Examination submission is 'too late' to meet the 255 TGA working days.*

  **Australian manufacturers of Class 2 and 3 products have even less ability to predict timeframes.*

- Additional 'stop clock' periods which may extend the submission time beyond the end of the transition period
- The age of some products to be registered means additional time may be required by the manufacturer to ensure the technical files meet current regulatory requirements.
- Potential delays in the issuance of TGA Conformity Assessment certificates not allowing sufficient time for Abbott to apply for inclusion on the ARTG for all its class 4 assays by 30 June 2014.

Provided the contingencies proposed above in Proposal 1A are met there is little benefit to Proposal 1B.

The risk of retaining the status quo is the high personal and public health risk posed to the Australian community given some Class 4 IVDs, including those for

diagnosis and screening of infectious diseases, will not be able to be supplied for some period of time post 30th June 2014.

Issue 2: Regulatory requirements for Class 4 in-house IVDs

Comments on current situation regarding Class 4 in-house IVDs

During the development of the current IVD framework Abbott was supportive of the requirement Class 4 in-house IVDs, particularly *de novo* assays, should undergo the same regulatory process for supply in Australia as commercial IVDs. The high level of risk posed by these assays coupled with the considerable cost and regulatory burden for commercial manufacturers justified this position.

Since the introduction of the IVD framework it has become clear there are a number of situations where it will be difficult for laboratories manufacturing Class 4 in-house IVDs to obtain a TGA Conformity Assessment Certificate for these assays. These include in-house assays based on a commercially supplied IVD which:

- incorporates a modification of the assay instructions for use; and/or
- are performed on sample types not covered by the manufacturer's intended use; and/or
- have an additional pre-analytical step; and/or
- use specimens outside the manufacturer's recommended storage conditions; and/or
- are intended as a Class 3 IVD by the commercial manufacturer but are used as a Class 4 assay for donor screening.

Abbott accepts in a number of these situations it will not be possible for laboratories to obtain the detailed design and development information required to prepare an application for a full TGA conformity assessment.

For TGA to undertake a full conformity assessment of an in-house assay derived from a commercial assay already registered on the ARTG, which has already undergone full conformity assessment, is a waste of TGA time and resources. The in-house modifications must not fundamentally alter the design of the commercial assay in these cases.

Abbott recognizes in some instances it would not be possible for laboratories to submit full manufacturing and design examination data without access to the original manufacturer's data files. In addition, the low volume of demand for certain testing means it will be difficult for laboratories to access sufficient

samples to provide adequate validation to satisfy TGA requirements for conformity assessment.

Abbott does however have concerns where laboratories are seeking to use Class 3 assays for donor screening purposes. Abbott accept the need for up-classification from the manufacturer's intended purpose for rare or non-routine assays but does not accept that laboratories should be able to up-classify in-house assays where there is an existing Class 4 commercial assay.

Additionally there are certain sample types/conditions manufacturers are unlikely to ever validate due to the lack of commercial benefit and/or the difficulty of undertaking such studies.

Proposal 2A: A modified conformity assessment procedure for the regulation of Class 4 in-house IVDs predicated on commercial IVDs

As indicated previously Abbott would prefer no changes to the agreed and legislated IVD framework. However this is clearly not practical at the present time with respect to some in-house IVDs based largely on the modification of commercially supplied IVDs.

In order to ensure modified commercial IVDs used as in-house IVDs can continue to be used, Abbott does not oppose Proposal 2A at this time.

Given Proposal 1A is adopted, a commercial IVD upon which an in-house assay is based may not be included onto the ARTG until 30th June 2015. Abbott accepts it will then be necessary to extend the time laboratories have to comply with the Conformity Assessment requirements. The proposed cutoff date of 30th June 2016 for inclusion of in-house Class 4 assays on the ARTG is acceptable.

The staggered timeframes for commercial and in-house Class 4 IVDs to comply with the IVD framework would mean laboratories undertaking in-house testing could continue to test 'off-label' until 30th June 2016. This would allow them to determine which commercial Class 4 assays (and related claims) had been included on the ARTG prior to deciding whether to undergo (modified) TGA conformity assessment for their own in-house IVD. Laboratories may then choose to use a commercial assay 'on-label' if available rather than register an in-house IVD.

In agreeing to Proposal 2A Abbott understands this proposal would **ONLY** apply to in-house modifications to commercial IVDs.

Abbott feels the following points are critical in managing this reform:

- While Abbott has specific examples of laboratory modifications to commercial IVDs which a manufacturer would be unlikely to include as a claim, allowable

modifications not considered to be fundamental changes to the design of the IVD must be very tightly specified. Abbott recommends a prescriptive list with an option to add to the list, as required, with due consultation.

- Dot point one in paragraph 4 on page 12 'a variation from the manufacturer's intended purpose..' is too broad a statement. While the three examples given which relate specifically to changes to sample type or processing may be acceptable modifications, other changes to the intended purpose could represent fundamental changes to the design of the IVD.
- In order to ensure the same level of safety to the Australian population, TGA assessment of the validation of the in-house modification must be equivalent to the assessment of the same modification by a commercial manufacturer. Fees related to assessment of the modification must be the same for an in-house assay and a commercial assay.
- Modifications considered to be fundamental changes to the design of the IVD must be clearly described and enforced. For example, the dilution of components in order to obtain additional tests per kit is a fundamental change to the assay but this is not clearly stated.
- Only rare or non-routine assays for which a commercial Class 4 assay does not exist should be allowed to be up-classified from Class 3 to an in-house Class 4 screening assay.
- Any manufacturer of a Class 4 assay should have stringent measures in place to ensure the assay continues to meet its claims to the end of expiry and does not compromise health and safety. Abbott would prefer to see laboratories producing in-house class 4 IVDs required to hold TGA GMP or equivalent to ensure an appropriate level of quality and safety.

Abbott seeks further clarification on the following points:

- Abbott is concerned the example given in dot point 4 in the same paragraph (Malaria IVDs) would potentially not have undergone any TGA pre-market assessment before being modified into an in-house Class 4 IVD. These assays are not mandated for audit upon application for inclusion on the ARTG unless adequate manufacturer's evidence is not provided. How does the TGA propose to address in-house Class 4 assays where the commercial assay has not been pre-market assessed?
- What is the liability on the original commercial manufacturer and sponsor if there is a problem related to the TGA approved in-house modification to the commercial Class 4 assay? No medico-legal responsibility can lie with the manufacturer or sponsor of the commercial assay for use of the assay outside the manufacturer's claims.

The benefit of Proposal 2A is the increased assurance of the availability of appropriately validated Class 4 assays for all testing critical to ensuring public health and safety in Australia.

The risk of Proposal 2A is incorrect results being produced for assays deemed to be high risk to either public or personal health due to modifications to the assay that have unintended consequences and/or are in fact fundamental changes to the design that are not properly validated and assessed.

Proposal 2B: A modified conformity assessment procedure for the regulation of all Class 4 in-house IVDs

Abbott cannot support Proposal 2B whereby all Class 4 in-house IVDs would be subject to a modified conformity assessment procedure.

Under this proposal Class 4 in-house IVDs could be developed from basic principles by laboratories with minimal scrutiny. Incorrect results from a *de novo* in-house HCV assay were one of the catalysts for the introduction of the proposed IVD regulatory framework in 2002.

The development of a *de novo* IVD is a lengthy undertaking and requires significant investment of resources in design, manufacture and validation in order to ensure the assay performs reproducibly and reliably. It also requires stringent manufacturing procedures to be in place to ensure the assay continues to meet claims and does not compromise health and safety. Given the high level of risk of Class 4 IVDs, these assays should be subject to the same level of TGA assessment as a commercial IVD as is the intention of the current IVD framework.

It is not acceptable to Abbott that laboratories manufacturing Class 4 IVDs would only be subject to routine NATA accreditation audits as a medical laboratory, ie *"maintain a Good Manufacturing Practice (GMP) license **and/or** NATA / RCPA accreditation…."*. Laboratories must have both GMP (or equivalent) and NATA accreditation if they are manufacturing Class 4 in-house IVDs which are being used for diagnosis or donor screening in Australia.

NATA accreditation is a peer-review process which could be open to bias and/or undue influence being placed on assessors. Commercial assays are reviewed by independent assessors to ensure the integrity of the assessment process and laboratories should have an equivalent oversight.

Abbott agrees if this proposal were to be implemented these assays should NOT be registered on the ARTG and available for supply to any and all laboratories. They should be assessed **prior to use** by the laboratories and a publically viewable, database maintained by TGA.

Proposal 2C: retain the current regulatory framework for Class 4 in-house IVDs

Abbott recognises a need to introduce a modified Conformity Assessment procedure for Class 4 in-house IVDs which are modifications of commercial assays. The risk of retaining the current framework for all Class 4 in-house IVDs is there may be no appropriately validated assays for certain testing critical to ensuring public health in the Australian community.

Issue 3: Performance evaluations for design examinations

Comments on Current Situation regarding Performance Evaluations

Currently TGA has the ability to request samples of Class 4 IVDs for evaluation but has no legislative remit to require or undertake a performance evaluation as part of a design examination for a Class 4 IVD. TGA has indicated this was an oversight when the IVD Regulatory framework was created.

Abbott recognizes the results of performance testing using Australian samples may be of value when assessing applications for design evaluation. In addition, TGA may be in a better position than manufacturers to source appropriate samples for testing.

Australia is less than 2% of the global market for IVDs and manufacturers may not be willing to source Australian-specific samples and undertake additional testing to supply such a small market. Conversely, the cost and resource expense of local performance testing to the sponsor and/or manufacturer is significant and, in Abbott's experience, can be more than the conformity assessment fees. Manufacturers must have the option to decide if local performance testing by the regulator, or the incorporation of Australian samples into the manufacturers performance testing is the preferred way to proceed.

With this in mind it is important the manufacturer clearly understands the requirements to be met by the performance evaluation, both in terms of sample types and protocols.

Proposal 3: Selective performance evaluation of Class 4 IVDs submitted for design examination

Abbott accepts the right of the TGA to amend the regulations to allow for local performance testing of IVDs that are the subject of a design examination. Abbott strongly agrees local performance testing is not required for all Class 4 IVDs and should not be undertaken routinely.

The requirement to undergo local performance testing needs to be well justified and should not duplicate data already provided by the manufacturer. Testing can be justified only where;

- there is good evidence the Australian population is significantly different to other parts of the world for the particular measurand; or
- there is good evidence new technology is significantly different to existing technology; and
- where the manufacturer has failed to provide adequate evidence to support the use of the assay or technology within the Australian population.

A prescriptive list of IVD markers is not justified and would lead to similar redundancy encountered under the previous TGA regulations whereby products were subject to performance testing, eg., monitoring assays, which under the current regulations is deemed unnecessary.

The introduction of a new marker in itself does not justify the cost and resource expense of a local performance evaluation. In addition, the statement in paragraph 3 under Proposal 3 '…a **new** IVD used to detect a serious infectious disease,..' should read '..an IVD used to detect a **new** serious infectious disease,…'. Post the IVD transition all IVDs will be new.

TGA should provide clear examples of exactly what constitutes a "new technology" or a "novel indication for use". In addition, an "IVD designed to detect a serious infectious disease" would not necessarily be classified as a Class 4 IVD, and hence would not be subject to the need for performance evaluation.

Unless the TGA can conclusively demonstrate why testing is required, there should be an option for manufacturers to supply data that would obviate the need for performance testing. Alternatively, TGA could arrange for provision of samples to be incorporated into the manufacturer's testing to allow the data to be collected as part of the assay validation. At a minimum TGA should supply guidance on testing protocols that will ensure Australian requirements are met.

Abbott understands the benefit to the Australian community of performance testing for markers where there is clear evidence of differences within the Australian population. However, the risk of this proposal is Class 4 IVDs will be subject to local performance testing by TGA at great expense to manufacturers and sponsors where there is no clearly no additional benefit to the Australian public.

Issue 4: Regulation of tests for predisposition or susceptibility to disease

As stated by TGA the intention of the new IVD framework was to include tests for predisposition or susceptibility to disease. Abbott has always understood this to be the intention. In drafting the regulations to include IVDs it appears such tests were overlooked when reviewing the definition of a medical device under section 41BD of the Therapeutic Goods Act (Act), particularly since they are incorporated in the definition of an IVD.

This oversight has created unintended ambiguity and requires correction given the significant consequences of potential patient management decisions that can be made on the basis of some of these tests, e.g., mastectomy based on a positive BRCA1 test.

Proposal 4: Amend the definition of a medical device to include predisposition and susceptibility tests

Abbott accepts changes need to be made to the definition of a medical device to ensure developments in technology such as predisposition and susceptibility assays are adequately captured under the Therapeutic Goods Act and are thus appropriately regulated.

Abbott supplies genetic tests for predisposition and susceptibility to certain diseases and conditions. Implementation of Proposal 4 will mean these tests must be registered on the ARTG either prior to 30 June 2014 (currently) and/or supply in Australia. Not undertaking Proposal 4 would mean a saving in fees and time to market as the products would remain exempt under the regulations governing 'other therapeutic goods'. However, Abbott has always understood the TGA intention to regulate these products.

Abbott supports the amendment of the definition of a medical device to incorporate these tests. Abbott does not believe the proposed change will have any effect other than to clarify the regulatory situation of these types of IVDs and provide a benefit in ensuring this technology can be appropriately regulated without confusion. We foresee no risks from the proposed change.

In response to the questions posed at the end of the TGA consultation, Abbott provides the following:

How might the proposed changes to the new regulatory framework for IVDs work most effectively?

As stated earlier the proposed changes would work most effectively if:

1. Proposal 1A is modified to extend the transition period for a valid application for inclusion on to the ARTG to 30 June 2015 for all IVDs. This should be in parallel with a requirement for valid applications for TGA conformity assessment certificate(s) to be submitted by 30 June 2014 for any products already supplied in Australia.

   TGA must, however, ensure all TGA Conformity Assessment applications can be processed to allow sponsors enough time to submit valid applications for inclusion by the 30 June 2015 deadline. New assays and/or manufacturers and newly modified assays must not be disproportionately delayed in getting to market.

   There must be no advantage to sponsors in delaying submission of applications for inclusion until the end of this new transition period to avoid paying annual fees.

2. Proposal 2A should be implemented with strict guidance on what is considered to be a fundamental modification to the design of a commercial assay and with a prescriptive (modifiable) list of what is not a fundamental modification to the design.

   Any modified conformity assessment process must apply equally to both in-house Class 4 and commercial Class 4 IVDs with the same fees applying to the assessment of a modification regardless of whether the sponsor is a laboratory or a commercial manufacturer.

   To minimise risk, laboratories manufacturing Class 4 in-house tests should be TGA GMP certified.

3. Proposal 3 should be implemented but allow the flexibility for the manufacturer to determine how performance testing requirements will be met. In addition, the manufacturer should be given adequate information (guidance) from TGA to be able to meet the performance validation requirements expected by TGA.

The most effective way to ensure performance validation requirements would be met is for TGA to arrange supply of samples and protocols for validation testing by the manufacturer.

4. Proposal 4 should be implemented to remove ambiguity and ensure that assays for predisposition and susceptibility testing are covered by the IVD framework as originally intended.

How do the proposals for change fit into the broader IVD framework?

Other than Proposals 2A/2B, the proposals do not fundamentally change the risk/ benefit balance of the IVD framework or at least the original intent. There is no additional burden on manufacturers and sponsors above what was originally expected from the IVD framework. In fact Proposal 1A has the potential to reduce the very real risk current implementation of the framework poses to the supply of IVDs critical to the health and well-being of the Australian public.

Proposal 2A provides a degree of flexibility in the regulation of in-house Class 4 IVDs based on the reality it is impossible for laboratories to undergo full conformity assessment for an in-house modified commercial assay. Abbott supported Class 4 in-house assays being required to undergo TGA CAC in the same manner as commercial IVDs. However, given there is greater risk from not having available appropriately validated Class 4 assays for all testing critical to ensuring public health, Proposal 2A is in keeping with the risk-based policy underlying the IVD framework.

Proposal 2B changes the risk/benefit profile of the framework by potentially increasing risk to public health. It also disadvantages commercial manufacturers of Class 4 assays who must undergo more stringent and costly regulatory requirements.

Of equal significance in this consultation is that the proposals do not increase divergence from the GHTF (IMDRF) guidelines on the regulation of IVD medical devices above what currently exists. Given the upcoming reforms to the European IVD Directive and the efforts of other member states to align with GHTF it is critical the fundamental concepts of the Australian regulations are not altered at this time. Despite all the efforts at harmonization, the increase in regulated countries over the past decade, all with varying degrees of divergence in regulations, continues to place a heavy burden on IVD manufacturers.

Regarding possible amendments to the new regulatory framework for IVDs, what are the highest priorities for you, or your organisation? Why?

Proposal 1A is the highest priority for Abbott in order to provide certainty that we will be able to continue uninterrupted supply of all assays to our customers and the Australian community.

Do the proposed changes pose any potential regulatory impact on your operation? If so, can you please give a clear indication of where there may be an associated cost.

Proposal 3 potentially provides the only direct regulatory cost impact due to the supply of instruments, reagents and support to allow TGA to undertake local performance testing.

In addition, if Proposal 4 did not proceed there would be a potential reduction in fees but only if adoption of the proposal reduced the number of 'kinds of devices' needing to be included. Minimal impact is likely here.

The indirect impact is the cost in both public health and commercial revenue of not having all Class 4 assays registered. In addition, the risk that some Class 3 assays may not be registered, will impact commercial revenue and may force greater reliance on in-house IVD manufacture in some pathology areas. There is also the potential liability to commercial manufacturers inherent in Proposals 2A/2B should a medico-legal issue arise involving an in-house modified commercial assay.

Conclusion

Abbott wishes to thank the TGA for the opportunity to comment on the proposed changes to the IVD framework. Abbott trusts these are of value and looks forward to further collaboration to ensure a mutually agreeable program of regulatory reform in the future.

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