Regulation of In Vitro Diagnostic Medical Devices

Transition to the New IVD Regulatory Framework

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Presentation to NSW Health Pathology
Background

New IVD regulatory framework implemented 1 July 2010

- IVDs regulated as a subset of medical devices
- Requirements apply to both commercially supplied and in-house IVDs
- Originally a 4-year transition - 1 July 2014 to comply with requirements
Key Features of the New Framework

• Four tier classification system based on different levels of risk for each class of IVD

• All IVDs to comply with a set of Essential Principles for quality, safety and performance

• All commercial IVDs & Class 4 in-house IVDs to be included in ARTG

• Class 1-3 in-house IVDs exempt from ARTG subject to conditions

• Provision for post-market monitoring
What is a Medical Device?

Supplied to be used for human beings for the purpose of one or more of the following:

• Diagnosis, prevention, monitoring, treatment or alleviation of disease;

• Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability;

• Investigation, replacement or modification of the anatomy or of a physiological process;

• Control of conception

[Therapeutic Goods Act 1989]
What is an IVD?

A reagent, calibrator, control material, kit, specimen receptacle, instrument, software, equipment or system

• Intended for the in vitro examination of human specimens for:
  – giving information about a physiological or pathological state
  – giving information about a congenital abnormality
  – determining safety and compatibility with a potential recipient
  – monitoring therapeutic measures

[Therapeutic Goods (Medical Devices) Regulations 2002]
What is an In-House IVD?

Manufactured by a laboratory for use in that laboratory or laboratory network

- Developed from first principles
- Developed or modified from a published source
- Developed or modified from any other source (e.g., commercial IVD, RUO products, ASRs)
- Used for a purpose other than the manufacturer’s intended purpose

[Therapeutic Goods (Medical Devices) Regulations 2002]
Classification of IVDs

Four classes, determined by the risk posed to health of an individual or to the public

Class 1 IVD – no public health risk or low personal risk
Class 2 IVD – low public health risk or moderate personal risk
Class 3 IVD – moderate public health risk or high personal risk

Class 4 IVD – high public health risk

[Classification rules – Schedule 2A, Therapeutic Goods (Medical Devices) Regulations 2002]
Classification Examples

• Class 1 IVDs: Microbiological culture media; instruments/analysers

• Class 2 IVDs: Pregnancy self-tests, H&E stain

• Class 3 IVDs: sexually transmitted diseases; genetic tests (inc FISH)

• Class 4 IVDs: screen blood donors for infectious diseases; ABO typing
Extension to Transition Timeframe

• Staged transition to allow additional time for compliance:

• Laboratories experiencing difficulties, particularly for those tests based on modifications to commercial IVDs
  – Laboratories need to know the commercial IVD has been included in the ARTG
  – Laboratories cannot submit applications for conformity assessment for Class 4 in-house IVDs unless commercial IVD is included in ARTG
### Key Transition Dates for In-house IVDs

<table>
<thead>
<tr>
<th>Deadline</th>
<th>Requirement</th>
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<tr>
<td>30 June 2016</td>
<td>Application for TGA conformity assessment for Class 4 in-house IVDs (only required if laboratory chooses this pathway)</td>
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<tr>
<td>30 June 2017</td>
<td>Application for inclusion in the ARTG for Class 4 in-house IVDs Notification of Class 1-3 in-house IVDs to the TGA</td>
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Can I Introduce New In-house IVDs During the Transition?

- **Class 1-3 In-house IVDs**
  - New Class 1-3 in-house IVDs can be introduced anytime before 1 July 2017
  - Notification as at 1 July 2017 must cover all the Class 1-3 in-house IVDs in use

- **Class 4 In-house IVDs**
  - Only considered transitional if in use prior to 1 July 2016.
  - New Class 4 in-house IVDs introduced after 30 June 2016 must be included in the ARTG prior to use
In-house IVD Reforms

• Additional reforms introduced in November 2015

• Modifications to the requirements for Class 1-3 in-house IVDs
  – Allow NATA accreditation to ISO 17025 for non-medical testing laboratories
  – Changes to the notification form to allow attachment of NATA test list
  – Removal of mandatory annual notification

• New alternative conformity assessment procedure for Class 4 in-house IVDs
  – Allows the use of NATA accreditation to ISO 15189 or TGA GMP licence
Regulation of Class 1-3 In-House IVDs

Exempt from inclusion in ARTG, conditional on:

- NATA accredited to:
  - ISO 15189 (medical testing laboratory)
  - ISO 17025 (non-medical testing laboratory)

- Meet NPAAC Requirements for in-house IVDs

- Notify TGA of in-house Class 1-3 IVDs
  - By 1 July 2017

- Renotify of new Class 1-3 in-house IVDs
  - By 1 July of subsequent years
Notification of Class 1-3 In-house IVDs

- Notification database – not publicly viewable

- All Class 1-3 in-house IVDs can be entered in the one notification form
  - selection of predetermined broad testing categories; and
  - attachment of NATA test list

- Notification fee applies each time a notification is submitted
Classification Rules – Class 4 IVDs

Rule 1.1: Detection of transmissible agents posing a high public health risk:

- IVDs intended to establish the safety of blood and blood components (ie, donor screening tests)
  - HIV, HCV, HTLV, Syphilis, CMV

- IVDs intended to diagnose infections that cause serious diseases with a high risk of transmission
  - HIV, HCV, HBV, HTLV
  - SARS, Smallpox, Ebola, highly virulent pandemic influenza strain
Classification Rules – Class 4 IVDs

Rule 1.2: Detection of red blood cell antigens & antibodies & non-red cell typing:

- Immunohaematology reagents (IHRs) intended to detect the following markers:
  - ABO system
  - Rhesus system – RH1-5
  - Kell – KEL1
  - Kidd – JK1, JK2
  - Duffy – FY1, FY2

- All other IHRs are Class 3 IVDs (or lower)

- IVDs for HLA tissue typing are also Class 3 IVDs
# Conformity Assessment - Class 4 In-house IVDs

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<thead>
<tr>
<th>Conformity Assessment (CA) Procedures</th>
<th>Requirements for Class 4 in-house IVDs</th>
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<tbody>
<tr>
<td>Option 1 – TGA CA</td>
<td>Same as for commercial Class 4 IVDs:</td>
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<tr>
<td></td>
<td>• TGA CA certification (Apply by 1 July 2016)</td>
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<tr>
<td></td>
<td>• Inclusion in ARTG</td>
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<tr>
<td>Option 2 – NATA accreditation (ISO 15189)</td>
<td>Apply directly for inclusion in ARTG (by 1 July 2017)</td>
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<td></td>
<td>• Subject to mandatory application audit</td>
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<td>Option 3 – TGA GMP licence</td>
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Fees for Class 4 In-house IVDs

• Application for inclusion in ARTG using TGA Conformity Assessment Certification (CAC)
  – Application fee for TGA CAC
  – QMS certification (additional fees if on-site audit required)
  – Design Examination for each kind of Class 4 in-house IVD
  – Application fee for inclusion in ARTG

• Application for inclusion in ARTG using NATA Accreditation or TGA GMP licence
  – Application fee for inclusion in ARTG
  – Mandatory audit fee
Reduction in Fees for Class 4 In-house IVDs

- In the majority of circumstances full fees would not be applied

- Only changes made to a commercially supplied Class 4 IVD would require assessment

- Fees can also be reduced by up to 70% if:
  - In the interests of public health; and
  - Would not be commercially viable if full fees were paid
‘Post-market’ Requirements

Laboratories must have procedures in place that allow for:

• Ongoing monitoring of performance of their in-house IVDs (eg, IQC, EQAP)

• Application of any necessary corrective actions

• Notification to the TGA of:
  – any adverse events
  – Any malfunction/deterioration in a Class 4 in-house IVD resulting in the need to recover the device (within a laboratory or laboratory network)
Exemption Provisions

- In-house IVDs only considered to be ‘supplied’ when used to test & report on patient
  - No exemption required to develop or stockpile an in-house IVD

- Automatic exemption to evaluate an IVD (commercial or in-house)
  - No reporting of patient results
  - TGA approval not required

- Other Exemption provisions
  - Special Access Scheme
  - Authorised Prescriber
  - Emergency Exemption
What Do Laboratories Need to Do?

- Identify your in-house IVDs

- Determine if you have any Class 4 in-house IVDs
  - Inclusion in ARTG required by 1 July 2017
  - Contact the TGA if unsure of which conformity assessment pathway to use

- Ensure laboratory is NATA accredited for Class 1-3 in-house IVDs
  - Notification to TGA required by 1 July 2017
  - Notification form under development – TGA to advise when available for use

- Understand ‘post-market’ requirements & have procedures in place for reporting adverse events