The Medicines and Medical Devices Regulation Review... and other regulatory reforms

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This talk

- The Expert Panel Review of Medicines and Medical Devices Regulation
- Reforms to the device regulatory system following the Review
  - Priority review of certain devices
  - Australian Conformity Assessment Bodies
  - Greater use of international regulators’ assessments
  - Strengthening postmarket monitoring
  - A new scheme for helping SMEs navigate the regulatory maze
  - TGA’s Advisory committees …. and what they do
- Compliance and Enforcement
  - Review of “low risk” therapeutic goods (including devices)
- Other reforms to the IVD framework
- TGA’s new clinical evidence guidelines
- Reforms to the European Device and IVD system
- Conclusion – a regulatory scheme fit for the 21st century?
Expert Panel Review of Medicines and Medical Devices Regulation

- **Review process** included discussion papers, submissions, workshops and interviews with key stakeholders by three experts.

- Public reports on *medicines and devices* and *complementary medicines and advertising* released during 2015.

- **Department considered reports** and stakeholder feedback and discussed implications with Minister and staff.

- **Minister** took preferred position to Cabinet.

- **Implementation design commenced in** May 2016 but **Government response only** publicly released on 15 Sept 2016.

- **Decisions were the Government’s to make**, but TGA was actively consulted.
Overarching principles for regulation as endorsed by the Government

- **Australia** maintain the capacity to undertake assessments of therapeutic goods for safety, quality and efficacy.
- The Australian Government **retain responsibility for approving the inclusion of therapeutic goods** in the ARTG.
  - Rather than automatically accepting international approvals.
  - However need to make much greater use of overseas evaluations.
- Need to introduce **greater flexibility in approval pathways** for both medicines and medical devices.
- TGA could **more appropriately align level regulation with the actual risk posed by the products** in certain areas.
Seven sets of reforms

1. Increasing Flexibility for Registration and Post-Market Processes for Medicines
2. Increasing Flexibility for Approval and Enhanced Post-Market Monitoring of Medical Devices
3. Increasing Flexibility for Pre-Market Approval and Increased Evidence of Efficacy of Complementary Medicines for Consumers
4. Simplified and More Effective Regulation of Advertising of Therapeutic Products
5. Streamlined Regulation of Patient-Specific Access to Therapeutic Products
6. Further Reviews
7. Rationalisation of TGA Statutory Advisory Committees
Review changes – Device regulation

- **Introduction of multiple pathways (and timeframes):**
  - Conformity Assessment within Australia by TGA (current)
  - Conformity Assessment within Australia by a separate body designated by TGA
  - Utilisation of overseas marketing approval *accepted in principle by Government* where the device has been:
    - Conformity Assessed by a body that has been designated by a comparable overseas Designating Authority; or
    - Approved by a comparable overseas regulatory authority

- **Expedited review process** for certain novel devices
Accelerated assessment of devices

- Medical devices designated for Priority Review will be allocated front-of-queue priority, with **no truncation of assessment processes**
- Involves **faster processing** of conformity assessment and/or ARTG inclusion
- **Priority Review designation for a device will lapse** where timeframes for submission of the application or requests for information in assessment processes are not met
- **There will be a fee** for designation applications additional to the current fees for inclusion or CA
- **Planned Jan 2018 start date** but this will depend on approval of new regulations by Government
Consultation feedback

• **Consultation paper** open for public comment from Nov 2016 to Jan 2017. Major stakeholder feedback incorporated into plans:
  
  – two week sponsor alert period and a four week assessment of request for priority designation
  
  – designations would lapse if the related application is not received within six months (aligns with arrangements for medicines)
  
  – positive decisions for medical devices eligible for Priority Review designation published on the TGA website
  
  – clarification of eligibility criteria (such as the definitions of terms, evidence requirements, etc), to be addressed through guidance documents
Proposed criteria for priority designation

• Device intended for the treatment, prevention or treatment of a life threatening or seriously debilitating disease or condition; AND
• Device addresses an unmet clinical need in Australian patients; AND
• Breakthrough technology/ clinical advantage/ public health (IVDs only)
• Meets at least one of the following:
  – The device represents a breakthrough technology with evidence of a major clinical* advantage over existing technology; OR
  – There is evidence that the device offers a major clinical* advantage over existing alternatives included in the ARTG; OR
  – For IVDs, early availability will result in a major public health benefit

*Engineering or pre-clinical evidence is insufficient on its own; there must be evidence of a major clinical advantage
Stakeholders indicated that their usage would be limited

- Under 10 priority review applications expected a year, but no limit enforced from TGA
- Plus companion IVDs for all medicines assessed as eligible under the medicines priority review pathway
- There will be an application fee for designation of around $10k
At present conformity assessment can either be from TGA or from a EU Notified Body

- **Independent commercial entities in Europe** (Notified Bodies) are authorised by governments in each EU country
  - mandatory TGA audits for class III / AIMD devices, certain contraceptives, device disinfectants, and intraocular devices
  - **TGA can do audits** for other devices if there are concerns

- **TGA MUST do conformity assessment**
  - **of devices** containing medicines, animal, biological or microbial tissues and of Class 4 IVDs
  - **sponsors can also ask TGA** to carry out conformity assessment of other devices
Designation of Australian Conformity Assessment bodies

- Government agreed to allow bodies designated by the TGA to be able to undertake conformity assessment certification in Australia.

- Public consultation paper from Nov 2016 to Jan 2017, which outlined proposed details for:
  - the TGA designating authority function
  - designated conformity assessment bodies, and
  - a designation process, including designation criteria

- The requirements for conformity assessment bodies may draw from both European arrangements for notified bodies and Medical Device Single Audit Program (MDSAP) requirements.

- To start in mid 2018
What will the demand for Australian bodies be? Build it and they may come?

Montreal Mirabel International Airport
Built for the 1976 Olympics
What will it cost?

- No **commercial conformity assessment bodies** currently exist in Australia
- Fees that **Australian notified bodies charge** will be up to the market
- **TGAs costs in designating Australian notified bodies** still to be determined, and have to reflect competitive neutrality principles
- Unclear if there will be an **impact on current TGA conformity assessment fees**
- We are **engaging an external consultant** to undertake business analysis of the cost impacts and risks associated with the proposed designating authority function
What is competitive neutrality?

- Aims to promote efficient competition between public and private businesses
- To ensure that government businesses do not enjoy advantages over private sector competitors simply by virtue of public ownership
  - These could range from tax breaks to improved purchasing power to absence of the imperative to make a profit
  - Government businesses also face disadvantages such as compliance and administrative overheads, recruitment rules
- There is an Australian Government Competitive Neutrality Complaints Office
Using other regulators’ evaluations

- System is already built on use of EU notified bodies
- Being done together with confidence building in EU notified bodies if there are to be fewer audits
- EU system also undergoing significant change
- Main focus is potential use of Canadian and US evaluations
- But these device and IVD regulatory frameworks are quite different to Australia
- Will consult on process in mid 2017
Strengthening of post market monitoring: device recommendations accepted

- Better integration and timely **analysis of available datasets** (including matched de-identified patient administrative data)
- **Electronic reporting** of adverse events
- **Pharmacovigilance inspections** of sponsors
- **Public reporting of all laboratory testing results**
- **Enhanced** information - sharing with overseas regulators
- Also continued roll out of InSite Hospital program
Changes to committees

• New **Advisory Committee for Medical Devices** from Feb 2017
• Has pre-market and post-market functions of two previous committees
• The Medicines committee looks at all novel prescription medicines (new chemical entities), but there are too many devices to do this!
• **So what do they do?** Some examples:
  – Usually focus on the highest risk devices, and contentious issues such as MRI conditioning of implantable devices
  – Extrapolation of short-term clinical data to long term implantation
  – Breadth of indications proposed versus narrow clinical data
  – When clinical assessment based on other clinically equivalent devices
  – Extrapolation of mechanical data, modelling versus product testing
  – Where applications focused only on postmarket data from other countries
Further reviews being undertaken

- Regulation of lower-risk medicines and class I medical devices to determine whether:
  - they may excluded from regulation by TGA
  - or better regulated by TGA according to risk

- Several other low risk products such as hard surface disinfectants classified as devices or other therapeutic goods
SME regulatory assistance and clearer regulatory guidance

- To help small business navigate the “regulatory maze” through
  - advice phone and email lines
  - better guidance documents
  - training workshops
  - and “signposting” to information

- Would not replace detailed product-specific advice provided by commercial consultants
- We have worked closely with AusBiotech, MTP connect, ARCS etc. to duplicate offerings
- Will be launched soon!
Compliance and enforcement

• The Review recommended that “TGA implement stronger compliance and enforcement powers to protect the public, and provide for graduated penalties that allow the TGA to respond appropriately to the full range of non-compliant behaviours”

• Public consultation on these powers close on 31 May 2017

• Proposed to incorporate, with some modifications, provisions from the Regulatory Powers (Standard Provisions) Act 2014 into the Therapeutic Goods Act to bring TGA’s powers on monitoring, investigation, infringement notices and injunctions, into line with other Commonwealth regulators

• Proposed to remove the current requirement to prove harm or likelihood of harm, from strict liability offences in the Therapeutic Goods Act, and reduce the penalties for these offences
Other reforms to the IVD framework

- Implementing in-house (laboratory-developed) IVD framework by 1 July 2017
  - NATA accreditation & compliance with NPAAC standard on in-house IVDs for Class 1-3 in-house IVDS. Notification to TGA.
  - Class 4 in-house IVDs included in ARTG
- Updated guidance on regulatory requirements for IVDs
- Annual charges for IVDs effective from 1 July 2017
  - Applied to postmarket monitoring issues – e.g. in 2016 comprehensive assessment of home pregnancy tests performance
  - Transition period for the IVD framework ends 30 June 2017
- Wording of regulations around access to unapproved IVDs through the Special Access Scheme / Authorised Prescriber to be amended to better reflect how IVDs are used
What else is on the horizon?

- Implementation of **TGA clinical evidence guidelines** for devices
- **Regulation of 3D printed devices**
- **Companion diagnostics** – how to align medicine and IVD reviews?
- **Software as a medical device**
- **Risks of device hacking**
- **European reforms** to medical device regulation

**MMDR Rec 20** - Regulation of medical devices by TGA is, wherever possible, aligned with the European Union framework including in respect of the:

- Classification of medical devices
- **Essential Principles/Requirements**
- Adoption of a risk-based approach to variations to medical devices
- Should TGA apply specific requirements, there must be a clear rationale
Many more oncology drugs means more companion diagnostics

- 2017 - over 50% of **global meds industry revenue** (AUD $700 billion) will be from oncology drugs
- Histology-based diagnosis and chemotherapy are becoming increasingly redundant
- **Greater use of bio-markers** for determining target populations
- Drove much of the impetus for **priority review** and **provisional approval pathways for medicines**
- Move from organ-based to **molecular definitions** of cancer has driven companion diagnostics and **many submissions for extension of indications**
- **TGA required to align parallel pathways of product evaluation** – logistically complex if different sponsors and issues arise with one product
Regulation of 3D printed devices

• “Patient – specific technology”, 3D bio-printing and personalised implants may fit the definition of a custom-made device under the Therapeutic Goods Act
  – Custom-made devices are exempt from inclusion on the ARTG,
  – But the Australian manufacturer or importer must notify its details to TGA
  – And they are still required to report adverse events

• How does regulation keep up with technological change?
  – What evidence should a clinical trial for 3D printed device collect?
  – How to manage innovations such as customised joint implants?
  – e.g. FDA now requires “patient-matched” 3D printed devices to undergo pre-market assessment

• TGA/ industry /researcher workshop planned for mid-year
Networked medical devices

- **Examples include** - weight scales, pulse oximeters, glucometers, insulin pumps, blood pressure monitors, diagnostic ECGs, sleep apnoea test devices and home INR tests

- **Small, flexible, wearable sensors** useful for monitoring chronic diseases

- **WiFi and Bluetooth** can turn many devices into over-the-counter products
Yet device vulnerability through hacking has become an issue of real concern

Especially of concern with:

1. newer cardiac devices such as pacemakers, implantable cardioverter defibrillators, cardiac resynchronisation devices
   - some hacks can control the pace of the devices
   - other hacks can drain the long life battery

2. certain 3-D printed devices
   - hacking could change the way the device is printed, changing the shape, strength and properties of the printed device
   - also access to confidential patient information related to the device

• FDA have developed guidance around cybersecurity controls
Developments create regulatory dilemmas

**Medical Apps**: software is considered a medical device if used for diagnosis, prevention, monitoring, treatment or alleviation of disease...

- **Apps that analyse clinical data**, e.g. results of blood tests or ECGs
- **Embedded software** in monitors, defibrillators, pumps and implantable devices

Software that just **presents or manages information** e.g. medical records, dosage calculator is not a device
A regulatory scheme for the 21st century?

- Implementation of the MMDR is phased over 2017 to 2019
- TGA has been asked to work out the detail on how changes could be implemented in consultation with stakeholders
- Government agreed that we could use TGA reserves to pay for cost of design of reforms
- Two major sets of changes to our legislation are needed while some other reforms are just to internal processes/ new IT
- We will need to get government policy approval, in particular where changes to the Act or Regulations are needed
- Need to implement review recommendations in parallel with business as usual and implementing several other reforms
Appendix: Schemes to access unapproved devices

- Schemes **enable health practitioners to supply certain unapproved therapeutic goods** through the **Special Access** or the **Authorised Prescriber Schemes**

- Changes will allow certain products with a **safe history of use** in similar countries to be provided to patients by way of notification to the TGA, rather than requiring pre-approval under SAS Cat B

- **Some risk** – is the SAS Cat A scheme currently being used inappropriately because it is an easy route?
  - SAS A notifications for devices increased 606% between 2011-16, while SAS B applications have decreased by 56%
  - Do we need to increase auditing of these pathways, or impose other controls?
Streamlined Regulation of Patient-Specific Access to Products

• Streamline access to medicines and medical devices that have not been approved in Australia
  - Some applications for Special Access to proven but unregistered products to be subject to automatic approval
  - Online system for notifications, approvals and reporting

• Implement improvements to Authorised Prescriber Scheme