Australian Government
Department of Health
Therapeutic Goods Administration

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 21 st 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 G**overnment 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 <u>at least</u> 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 c**lass III / AIMD devices, c**ertain **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 a 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

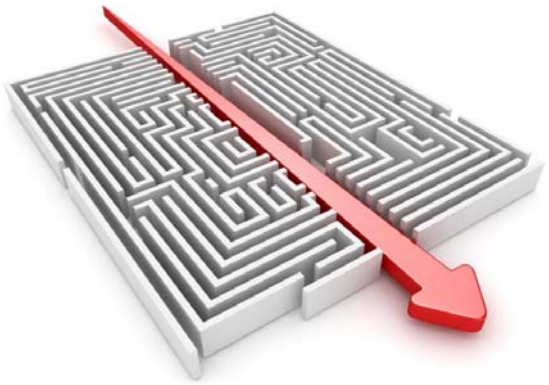
Further reviews being undertaken

- **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 i**n-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

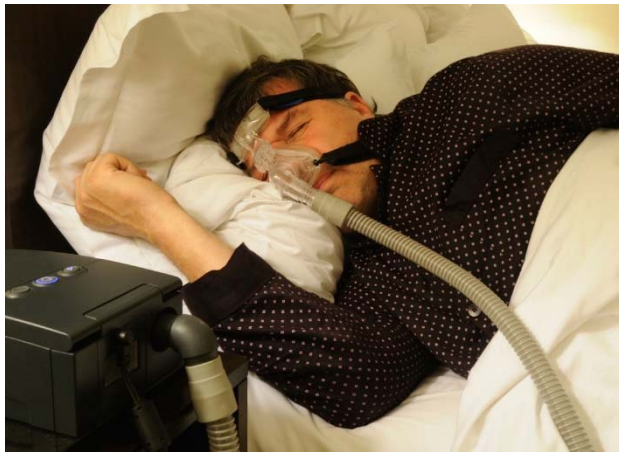
- 2017 - over 50 % of **global meds industry revenue** (AUD $700 billion) will be from oncology drugs
- Histology-based diagnosis and chemotherapy are becoming increasingly redundant
- **Greater use of bio-markers** for determining target populations
- Drove much of the impetus for **priority review** 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