



Australian Government
Department of Health
Therapeutic Goods Administration

The world of Regulatory convergence: an Australian reflection

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TGA Health Safety
Regulation

- I've spoken at the 2013 and 2014 ARCS meetings on convergence but now it's really gaining momentum!
- PM's announcement in October 2014
- Future directions of international regulatory convergence activities will depend on the Government's response to recommendations of the Expert Review of Medicine and Medical Device Regulation
- Several issues were raised in the review discussion paper on regulatory convergence, and use of other evaluations
- Work underway – medicines and devices
- New collaborations and some concrete results

Expert Review of Medicine and Medical Device Regulation

- **First report (prescription and OTC medicines, devices)** was reported to Government on March 31 2015 and the next steps are under now consideration by Government
- **Second report (complementary medicines and advertising)** will be submitted to Government by June 30 2015
- **Collaboration with international regulators** featured heavily in the Review Panel's discussion paper of November 2014
- **Strong focus on international cooperation** follows PM's statement in October 2014

PM's Media release 14 October 2014



*“ if a system, service or product has been approved under a trusted international standard or risk assessment, then **our regulators should not impose any additional requirements for approval** in Australia, unless it can be demonstrated that there is a good reason to do so.....*

*As an important first step, the Government will enable **Australian manufacturers of medical devices the option of using EU certification in place of TGA certification.**”*

Some questions raised on international convergence in the Nov 2014 discussion paper

- Should Australia **recognise other international regulators** as ‘trusted’ for medicines and device approvals ?
 - how to determining whether an overseas regulator is “trusted” ?
 - how would their evaluations or decisions be used in practice ?
- Should **accelerated or provisional approvals** be implemented ?
 - would this alter how decisions by other regulators should be used ?
- Are there aspects of safety, quality or efficacy that need to be considered in the **Australian context** ?
- Should we maintain **Australian specific requirements** with respect to labelling and post market monitoring?

Medicines



How greater international medicines collaboration could work in practice?

Issues in the discussion paper and review submissions

- Predicated on the Australian applicant **providing full data package and full, unredacted copies of evaluation reports** to TGA
- **What Australia-specific work would be done** – e.g. Aust medicine use patterns, RMPs, pregnancy classification, labelling, AusPARS ?
- More straightforward if overseas submission is for **same product and clinical context** - what about similar but not identical products?
- **Sponsors should not be compelled** to use an overseas evaluation - in a number of cases this would delay registration
- Retention of **sovereign decision making** by Australia
- Recognition that **Australia needs to contribute** evaluation reports and participate in worksharing initiatives too

Current major medicines collaborations

- **ICH** (International Conference on Harmonisation...)
- **PIC/S** (Pharmaceutical Inspection Coop'n Scheme)
- **International Generic Drug Regulators Pilot**
- **ACSS** (Australia, Singapore, Switzerland, Canada) and **Australia - Canada Regulatory Cooperation:**
 - Manufacturing compliance and enforcement
 - Generic medicines
 - Good review practices
 - Risk benefit assessment / communication methodology
 - Secure portal for information exchange
 - OTC medicines (Australia-Canada)

International Coalition of Medicines Regulatory Agencies – formed Dec 2013

- **First regulatory coalition at agency head level**
 - 23 countries plus EMA, EU and WHO
- **Leverage/strategic oversight of existing initiatives**
- **Initial priorities:**
 - Better information sharing mechanisms between regulators (e.g. IT systems, commercial-in-confidence)
 - United industry engagement
 - GMP Inspection worksharing
 - Generic medicines convergence and worksharing
 - Capacity building of emerging regulators

Generic medicines collaboration

- Access to generics very important in managing health care costs
- But there are increasing numbers of submissions and complexity of products
- So need to **increase the efficiency of regulatory review**
 - More **consistent dossier/ product requirements** across countries
 - Collaboration between regulators on aligned submissions **could** provide faster evaluation times and reduced fees
 - **Potential** for move away from requirement for local reference products



Response: a new, integrated approach

International Generic Drug Regulator's Programme (IGDRP)

- Senior scientific staff of 13 regulators
- Convergence of specific technical requirements e.g. bioequivalence, biowaivers, choice of foreign reference products
- Assessment of drug master files and report structures so that the evaluations of other regulators can be used in worksharing

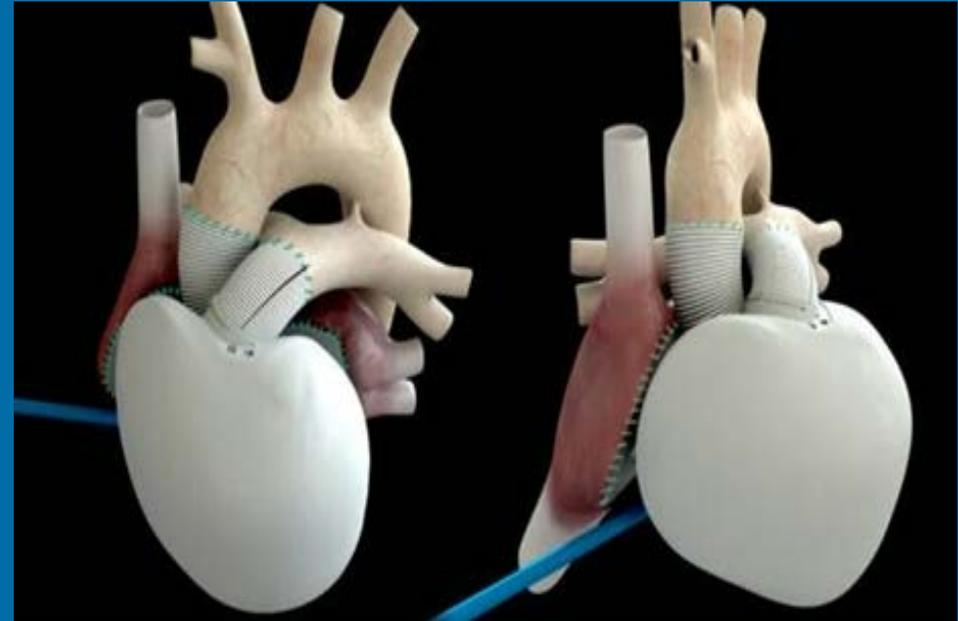
International Coalition of Medicines Regulatory Authorities

- Generics project focuses on **strategic issues to establish a framework** for routinely exchange evaluation reports:
 - Regulator business processes/ confidential information
 - Legal frameworks
 - Secure platforms for sharing confidential information
 - Analysis to identify additional opportunities for worksharing

Pilots being implemented by TGA

- **Information exchange on medicines which either** have recently received market authorisation (**share reports**) OR under consideration and **suitable for worksharing**
- **EU Centralised and Decentralised Procedure on evaluation of generic drug applications**
 - an application submitted under EU DCP will be submitted at the same time to TGA
 - offers applicants the potential to seek market authorisation in a number of markets at the same time
 - Australian registration decision is made by TGA
- **ACSS and TGA-Canada Collaboration**
 - Collaborated on over a dozen applications in 2014/15
 - Collaboration on complementary medicines ingredients

Medical devices



Some specific devices questions raised in the Review discussion paper

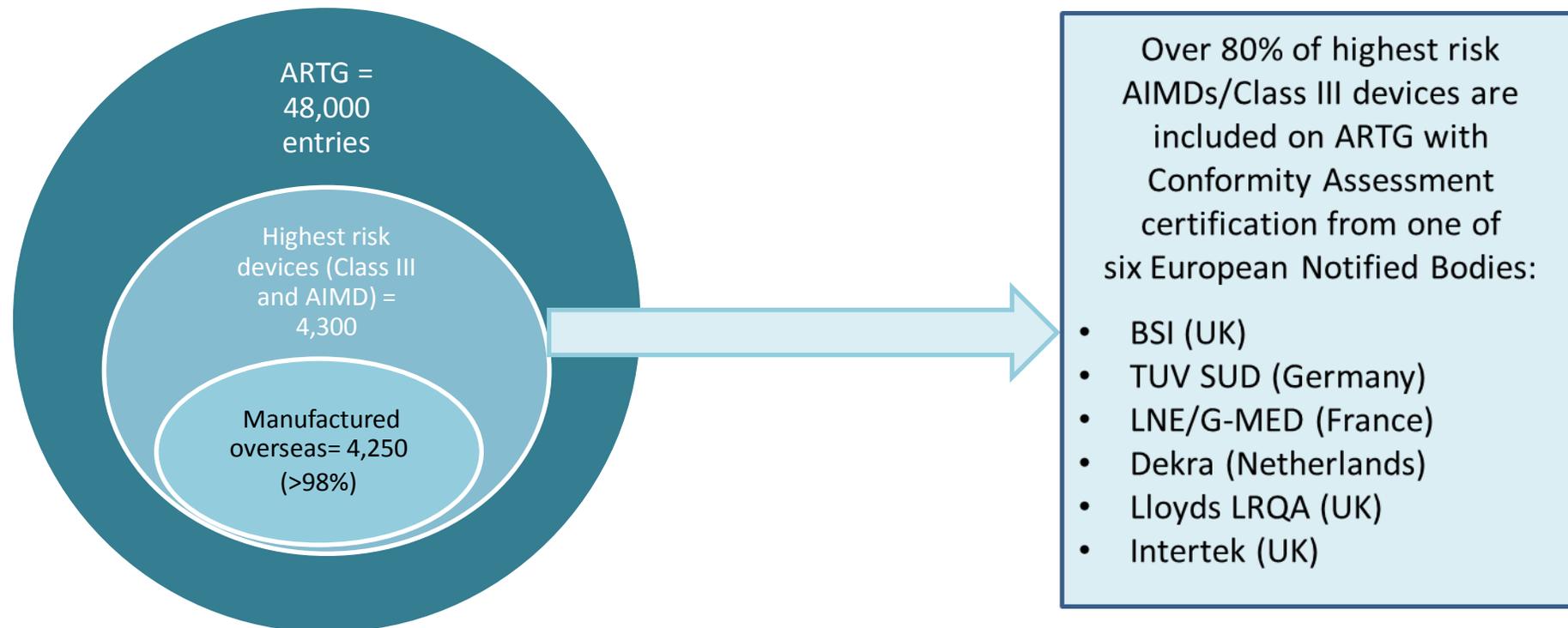
- Should the TGA undertake its **own assessment** of the competence of European Notified Bodies?
 - i.e. “go it alone” vs “piggybacking” on EU assessments
- How could concerns about the **quality of some overseas conformity assessments** be managed?
- Should Australia be able to **recognise decisions by FDA** and “trusted” non-European systems?
- Should Australia **adopt the EU classification system for devices?**

The European System: a quick recap

- European Union ‘directives’ = Therapeutic Goods legislation and regulations
- Independent commercial entities (Notified Bodies) are designated (authorised) by the government regulator in each EU country to apply conformity assessment procedures (examine safety and efficacy information, assess clinical data)
- Conformity assessment certification leads to a “CE mark”, which provides authority to market within Europe, but TGA undertakes application audits of higher risk devices
- New, more stringent EU regulations may be adopted as soon as 2016 – but 31 countries are involved in negotiations!

How does this impact Australia?

TGA accepts CA certification from Notified Bodies to support applications for ARTG inclusion, **but highest risk devices have application audits**



What is confidence building?

- Recent events (e.g. PIP implants, metal-on-metal hips, gynae meshes) highlighted need for closer scrutiny of Notified Body processes and outputs
- Australia needs to be confident that Notified Bodies have appropriate:
 - operating procedures
 - quality management systems
 - data management processes
 - evaluators with appropriate technical qualifications
- The issue is how do we go about confidence building?

Australia's approach (pending report of Review of Medicines and Medical Devices regulation)

- Participation by TGA staff as observers in EU joint assessments of targeted Notified Bodies is already underway
- Continue development of clinical evidence assessment guidelines
- Enhanced effort to build confidence in clinical assessments of targeted Notified Bodies
- Policy meetings in Europe with major designating authorities (UK, Germany, Netherlands), notified bodies, Team NB (industry representative body) and European Commission held by TGA in November 2014
- MDSAP also contributes to confidence building (see later)

International Medical Device Regulators Forum (IMDRF)

- IMDRF was established in 2011 to **build on Global Harmonisation Taskforce (GHTF) guidance**
- Adoption of GHTF guidance facilitates mutual recognition of most areas of device regulation across the product life-cycle
- **Members:**
Australia, Brazil, Canada, China, EU, Japan, Russia, USA
- **Observers and Affiliates:**
WHO, APEC's Life Sciences Innovation Forum, Regulatory Harmonization Steering Committee, Asian Harmonization Working Party, Pan American Health Organization

IMDRF work program

- **Medical Device Single Audit Program**
- Review system for **confidential exchange of information on serious adverse events**
- Implementation of **Unique Device Identification** system
- Review of **recognised standards for devices** to increase consistency
- **Regulated Product Submission**
- **Software** as a Medical Device
- Integrating **Patient Registries** and tools for enhanced device evaluation and tracking



MDSAP

- Medical Devices Single Audit Program will allow a single regulatory audit of a medical devices manufacturer **to satisfy needs of multiple regulators** (Australia, Brazil, Canada, USA)
- Developing a **standard set of requirements** for auditing organizations performing regulatory audits of medical device manufacturers' **quality management systems**
- Several Notified Bodies and manufacturers have agreed to participate and several audits already carried out
- Now encouraging more manufacturers to participate

GMP inspection collaboration

- Involvement in **PIC/S**
- **Widespread use of GMP clearances** already significantly reduces the number of overseas inspections required
- **Joint inspections** with other regulators
- But **better sharing of confidential information** such as inspection plans and reports is needed



Post market vigilance – the forgotten cousin of international collaboration

- **Needs to be strengthened** if more product approvals made on less complete evidence, and/or if provisional approval is adopted
- **Long-established and prompt communication between regulators** on incidents and decisions but some groups now developing to discuss potential regulatory actions
- **Strong media interest** when regulators reach different conclusions on the need for product withdrawal, rescheduling or change to the PI - informal communication is critical
- **Opportunities for greater international collaboration** - e.g. mining bigger pharmacovigilance data sets and registry data
- **New WHO ADR database** (www.vigiaccess.org) valuable but does not have data on numbers of people exposed to each drug and frequency of reporting varies by country

Different regulators may still reach different conclusions using similar data... including on market authorisation or particular indications



To conclude

- **Increasing global cooperation between regulators** is now happening, and industry is starting to see the benefits
- The **future direction of international collaboration activities** and of medicine and device regulation overall will depend on the Government's response to recommendations of the Expert Review
- **Work is nonetheless continuing** on several fronts – generic and complementary medicines, OTC monographs, device confidence building and inspections, GMP systems and inspections
- But establishing systems for **global collaboration on New Chemical Entity evaluation** is the biggest “prize”
- **Being able to share experiences with other international regulators** on “what works” is also very important



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