Australian Government
Department of Health
Therapeutic Goods Administration

Trends in Australian and international regulation and regulatory cooperation

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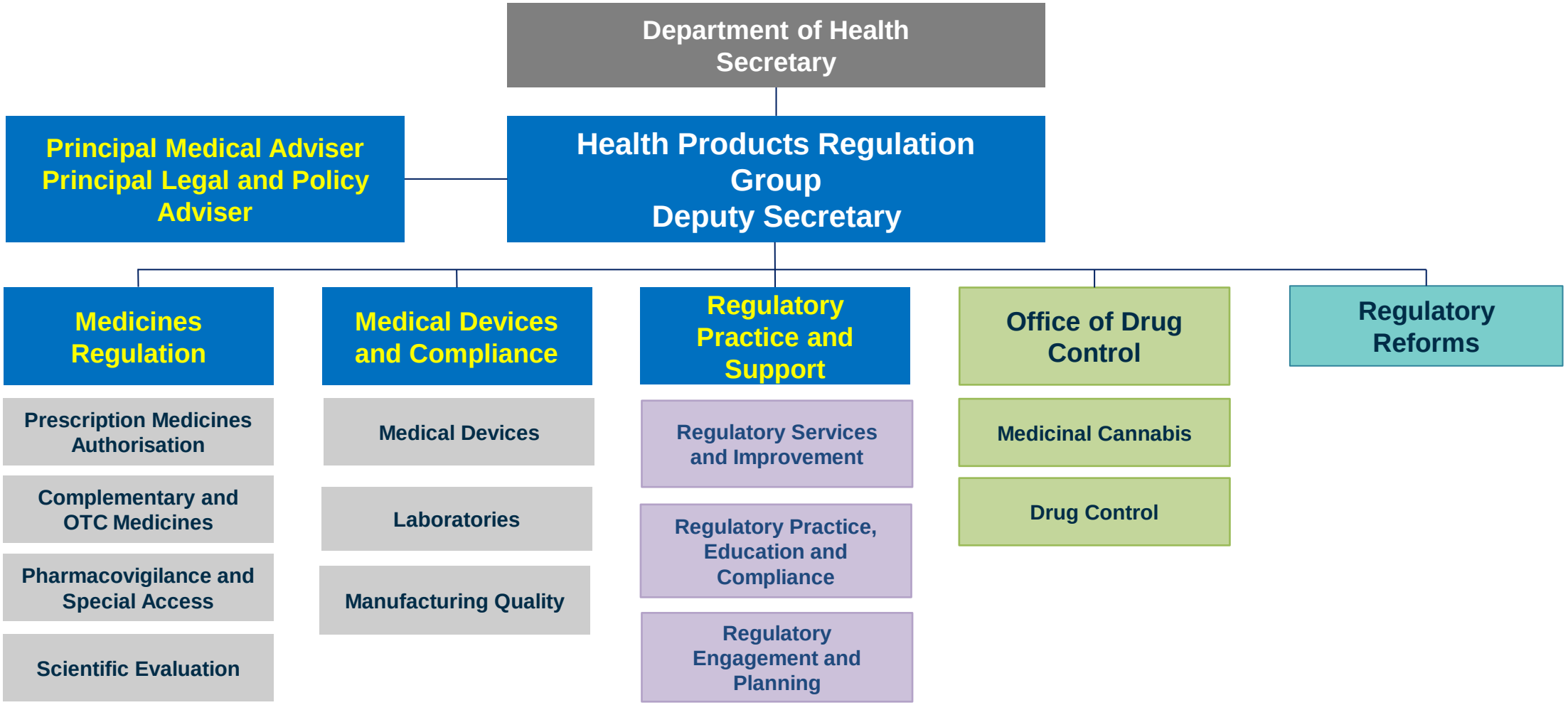
ARCS Scientific Congress Canberra 2016

TGA Health Safety Regulation

This presentation

- The **Health Products Regulation Group**
  - Therapeutic Goods Administration and the Office of Drug Control
- But first – where is the **Medicines and Medical Devices Review** up to ?
- **TGA Stakeholder Survey 2016**
- Recent developments at some of the major **overseas regulators**
- Update on **TGA's international collaborations**
- **Conclusion**

Health Products Regulation Group Structure



But first…. Where is the MMDR up to ?

"Improving the Regulation of Therapeutic Goods in Australia" is a May 2016 budget measure

"The Government will provide $20.4 m over four years from 2016-17, including $9.5 m in capital funding, to improve the regulation of therapeutic goods in Australia in response to the Expert Panel Review of Medicines and Medical Devices Regulation. The funding will improve access to therapeutic goods for consumers and introduce more flexible and timely regulatory processes for the therapeutic goods industry."

While this is technically "government" money it is fully industry funded from TGA reserves and not additional taxpayer funds

What was publicly released on budget night ?

www.health.gov.au/internet/budget/publishing.nsf/Content/budget2016-factsheet23.htm

Prescription medicines and medical devices

- Sponsors able to add medicines and devices to the ARTG through **new approval pathways**
- New medicines such as cancer drugs will enter the market sooner, through **new provisional approvals** and making **greater use of overseas assessments**
- **New medicines and devices will be approved faster** in certain circumstances, based on criteria to be developed in consultation with consumers, health professionals and industry
- Assessment times will be reduced by up to three months through utilising work carried out **by comparable overseas regulators**
- There will be **greater focus on post-market reporting** to ensure safety and efficacy is maintained which will include enhanced electronic reporting and a risk communication strategy
- **Commercial bodies approved by the TGA** will be allowed to undertake device assessments

What was publicly released on budget night ?

Complementary medicines

- A catalogue for **approved ingredients** and **permitted indications** will be established

Product access

- **Scheduling Policy Framework** to be reviewed in consultation with state and territory govts
- **Pre-approval will be introduced under Special Access Scheme (B)** for low-risk products that have specific and well-established patterns of use for patients with a non-terminal condition.

Advertising

- Advertising regulations will be **more consistent** across the range of medicines and devices
- **TGA investigation and enforcement powers** will be strengthened, and a new compliance education program for industry will be introduced

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Advisory committees

- **The Government will reduce the number of statutory advisory committees** that provide independent expert advice to the TGA from 11 to seven
- The **new committees** will advise on medical, chemical and scientific matters, market approval of new therapeutic goods, and product safety issues

Enforcement

- **TGA's enforcement and compliance powers will be strengthened**.
- Compliance activities will make greater use of data analytics to target areas of concern

Funding design of the reforms

- Design and IT systems changes will be **drawn from reserves** in the TGA Special Account.
- An **increase in TGA fees and charges will not be required**

We have started work

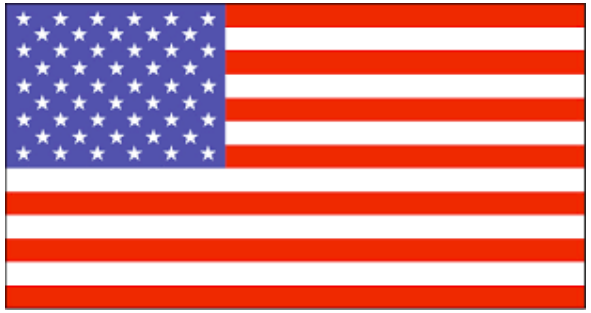
- **Teams have been established** to work on the government's decisions in each area
- Strong **IT systems design** component to the reforms
- **Once the Government announces** the detailed response to the review
  - Communication materials explaining the government's intent will be released
  - Stakeholder consultations will commence - consultations will be clustered to avoid stakeholder overload
- **Implementation of several recommendations** will require changes to the Therapeutic Goods Act and/or Regulations

TGA stakeholder survey 2016

- A reporting requirement for the Government's **Regulator Performance Framework**
- **2810 responses** including 449 healthcare professionals, 65 consumers and 1628 from industry
- Results remarkably positive in terms of **trust and confidence in the regulator**
  - 79 % of industry have high/very high confidence in TGA safeguards
  - 61 % of community/ consumer groups with 27 % ambivalent/ unsure
- **Positive about engagement** – (users satisfied or very satisfied) with TGA consultations (63%), exhibitions (75%) and information sessions (82%) respectively.
- Main area for work is to **TGA to engage more actively with consumers**
  - They are aware of, and have a generally favourable perception of the TGA, but many unsure
  - Consumers also felt least engaged in TGA policy consultations

Some international regulatory developments

Some FDA developments

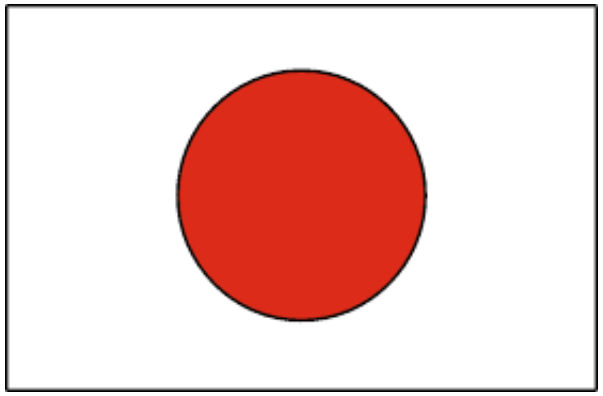


- **FDA-EMA cooperation** on inspections, more broadly
- **Reduction in fees** – NCE only AUD $ 2.7m, generic $ 310 k
- Strong focus on **real world data** and involvement of patient centred outcomes
- Evaluation of **breakthrough designation schemes** for medicines
- **Biosimilar framework** emerging
- **Greater use of real world / big data** in medicine clinical trials and devices evaluations
- **Device reforms** – low risk devices exempt from regulation, streamlining device approval times
- **Zika virus** – blood supply, diagnostics
- **Integration of drug and biomarker development** for cancers
- **Focus on challenging conditions** for drug development – e.g. Alzheimers, diabetes
- Concerns re **prescription opioid abuse**

Some EMA developments

- **PRIME (PRIority MEdicines) system** – enhance development of medicines that target unmet medical need – proactive early dialogue
- Review of experience with **provisional / adaptive licensing pathways**
- Enhancement of **scientific advice to medicines developers** around clinical trial design
- **Parallel scientific advice** with European Health Technology Assessment Bodies
- **Increased focus on transparency**, especially access to clinical trials data
- Review of regulation of **“first in man” clinical trials**
- Focus on **updating safety advice** for medicines
- **Track and trace** of medicines throughout the supply chain
- Approval **on-line pharmacies** (easily recognisable logo)
- **BREXIT** and future location of the EMA ?
- **New European medical devices/ IVD regulatory framework** inches forward

Some PMDA Japan developments



- Now has the **fastest average medicine approval time** globally following tripling of evaluator staff over the last decade
- **New regulatory framework** for innovative products (SAKIGAKE)
- Provisional licensing of **cell and tissue therapies**
- Increased amount of information published in **English**, but most evaluations only in Japanese
- **Increased emphasis on funding regulatory research** projects and collaboration with universities and research institutes
- **Innovative approaches to post-market pharmacovigilance**
  - stimulated reporting for new medicines
  - publication of risk management plans
  - MIHARI collaboration on the use of electronic health data

Some HPFB Canada developments

- **Strong emphasis on regulatory transparency**
  - **GMP Inspection information** and reports published
  - **Enforcement information** such as advertising complaints
  - Publishing **information on NCEs under review**
  - **Information on positive and negative decisions** for medicines and high-risk medical devices, and summary of basis of decision
  - Increased powers to **disclose safety risks and recalls**
- Requiring healthcare institutions (as well as sponsors) to **report adverse events**
- Plain language **medicines labelling**
- Mandatory reporting of, and expanded information on **medicines shortages**

Australia is the only country we know where international regulatory cooperation is formal Government policy

" 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".

Prime Minister's media release 14 October 2014

GMP inspection collaboration

- Involvement in **PIC/S**
- **Widespread use of GMP clearances** already significantly reduces the number of overseas inspections required
- **More joint inspections** with other regulators being undertaken
- Mechanisms to improve **sharing of confidential information** such as inspection plans and reports being developed through ICMRA

International Coalition of Medicines Regulatory Authorities (ICMRA)

- **First regulatory coalition at agency head level** – commenced Dec 2013
  - 23 countries plus EMA, EU and WHO
- **Initial projects completed:**
  - Establishment and governance
  - Generic medicines information sharing and commercial-in-confidence processes
  - Documentation of capacity building initiatives
- **Projects underway**
  - Establishment of systems to enable GMP Inspection reports from one regulator to be recognised by a second regulator – avoid need for separate inspection
  - Pharmacovigiliance collaboration
  - Supply chain security and crisis management

ICMRA Pharmacovigilance project

- Identify **areas for sharing of learnings and structured collaboration**
- Assist **policy discussions** by agency heads (and subject experts)
- There are well-established national and WHO pharmacovigilance systems, and this project is NOT about establishing new systems
- **Three priorities** were identified for initial work:
  - **How to best utilise "big data"** for pharmacovigilance purposes?
  - What policy approaches are most successful in **increasing the rates of adverse events reporting**, in particular from health care professionals?
  - Are there workable approaches by which the **existing pharmacovigilance systems can be better linked?**

ACSS Consortium

Australia-Canada-Singapore-Switzerland Consortium

A practical implementation approach to test feasibility of worksharing – complements bilateral cooperation with Canada

- Common template and safety assessment of **complementary medicine** ingredients
- First worksharing trial for a **generic medicine** underway
- Information sharing on **New Chemical Entity** submissions and planning for worksharing
- **Good review practices**, Risk benefit assessment and communication methodology
- **Manufacturing compliance** and joint inspections
- **Secure portal** for confidential information exchange developed
- **Staff exchanges**

IGDRP
International Generic Drug Regulators Programme

Dr Mariana Gebara-Coughlan will talk more about IGDRP in a separate ARCS presentation

- Australia, Brazil, Canada, Chinese Taipei, CMDh (EU), EDQM, Japan, Korea, Mexico, Singapore, South Africa, Switzerland, USA, WHO
- **Comparison of review process** – legislation, key regulatory guidelines, phases of the application process, timelines, user fees
- IT platform and central repository
- **Information and Work Sharing models** - sharing of assessment reports in “real time”
- **Quality Working Group** - establish frameworks and mechanisms for information sharing and work sharing on quality – ASMF / DSMF
- **Bioequivalence** - develop tools to aid in assessment, cooperation on biowaivers

Collaboration with other regulators is already happening with generic medicines

- Since late 2013, several generic medicines have been registered by TGA **following the exchange of reviews with Health Canada**
- **TGA involvement in a pilot of EU Decentralised Procedures** for evaluation of applications now extended to those submitted through the **Centralised** Procedure
- **ACSS worksharing pilot** underway – TGA evaluation reports shared with other agencies for their assessment
- Generics cooperation is **also a test case** for broader cooperation between regulators on New Chemical Entities (New Prescription Medicines)

How could use of an international evaluation speed evaluation of a new prescription medicine?

A range of alternatives exist:

1. **Work sharing** - If two regulators received the same application, share workload by evaluating different parts of the dossier
2. **Information sharing –** use of the evaluation report of another trusted regulator to reduce re-work
3. **Streamlined acceptance** based on a decision by a trusted regulator

- Some countries (e.g. Singapore, Mexico, Taiwan) already **provide industry with a range of alternatives** like these
- **Timely sharing of reports critical** for faster review – otherwise it's slower !

How could streamlined acceptance based on a decision by a trusted regulator potentially work ?

- Where the overseas regulator has approved the **same** medicine, TGA could avoid **(re-)evaluation** of its quality, safety or efficacy
- Only the **Australian-specific requirements** would be assessed, e.g.:
  - Product Information, Consumer Medicine Information
  - Australian clinical guidelines/ context of use,
  - Risk Management plans, Scheduling and Australian labelling requirements
- Would require the company applying for local approval to provide them with the **full data package and full overseas reports** on the medicine
- So as to enable the basis of decisions on indications and risks to be understood and **manage potential risks** once the medicine is in the market

IMDRF International Medical Device Regulators Forum

- Aims to accelerate international device regulatory harmonisation and convergence
- Established in 2012 to build on foundational work of GHTF (Global Harmonization Taskforce on Medical Devices)
- Members: Australia, Brazil, Canada, China, EU, Japan, Russia and USA
- Asian Harmonization Working Party and PAHO are affiliates and WHO and APEC are observers

IMDRF Medical Device Single Audit Program

- Pilot to p**romote greater alignment** of regulatory approaches and technical requirements
- Develop a standard set of requirements for **third party organisations** performing audits of manufacturers' QMS on behalf of regulators
- **Benefits manufacturers** through a reduced number of audits, reduced annual cost, an increase in the predictability of outcomes, and opportunities for export markets.
- **Benefits Sponsors** as an additional basis for ARTG entry
- **Enable TGA to be focused** on problematic devices, manufacturers that are not in compliance with regulations, and oversight of third party auditors

Keith Smith will talk more about MDSAP in a separate ARCS presentation

Other IMDRF projects

- Development of a comprehensive and consistent **Regulated Product Submission structure** as an international format for device evaluation
- **National Competent Authority** system - to facilitate exchange of post market safety information
- Harmonised approaches to treatment of **Software as a Medical Device**
- **Integrating Patient Registries** for enhanced device evaluation and tracking
- Medical **device adverse event terminology**
- **Good regulatory review practice** – competence and training requirements
- Improving quality of **international device standards for regulatory use**

Draft clinical evidence guidelines

Dr Cheryl McRae will talk more about this in a separate ARCS presentation

- Significant interest from other international regulators!
- **Outline current TGA expectations** for:
  - clinical evaluation reports
  - underlying evidence to be held by medical device manufacturers
- Written for manufacturers and sponsors (also important for clinicians, evaluators)
- **Aim is to clarify requirements** but not change the requirements
  - reduce numbers of errors in clinical evidence reports received by TGA
  - multiple rounds of review delays decisions and wastes time and resources

Summary

- The MMDR "Improving the Regulation of Therapeutic Goods in Australia" 2016 budget measure sets **high-level direction for reforms**
  - Significant but staged consultation with stakeholders will be undertaken soon
  - Several other reforms are also in train – e.g. medicines labelling, orphan drugs, stem cells, IVD transition
- Priorities of TGA and overseas regulators have **much in common**
- **International regulatory collaboration** is Australian Government policy
  - TGA is in a leadership role for several initiatives
  - In time, there will be benefits for industry, patients and TGA
  - Several initiatives in place, but all are dependent on desire from partners to collaborate
  - Integration of international collaboration projects into "business as usual" will take time

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