Australian Government
Department of Health
Therapeutic Goods Administration

Regulatory affairs – the Australian and international landscape

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ARCS Plenary presentation

21 August 2018

TGA Health Safety Regulation

"Talk about the current and future regulatory environment….how it is evolving in response to global shifts …and challenges faced by regulators"

- Focus is on **prescription medicines and medical devices**
- The **Expert Panel Review of Medicines and Medical Devices Regulation** responded to major international developments
- Where we are up to with **implementation of the government-endorsed recommendations of the Expert Panel Review**
- **Other changes are coming soon**, and **some reflections**
- Some other responses to the changing **international regulatory environment**

The global regulatory environment is evolving

- **“Regulatory nationalism”** – UK Brexit/ Europe/ North America
- Yet **worksharing** is gaining real momentum for mid-sized regulators
- US working to become **first country for submission** of device applications
- Slow evolution of Asian systems towards **alignment** vs African Harmonisation
- **“Medicines” have evolved** from small molecules to proteins to cells
- More **flexible access pathways** for medicines and devices
- Move from an NCE to an EOI to a biomarker model ?
- **Personalised medicine-** more orphan drugs and devices for small populations
- **Regulation and innovation** more closely linked – initiatives such as SME assist

Prescription medicines

Comparable overseas medicines regulators

- Countries able to specified in regulation
- **Guidance documents** specify what reports are needed from each country
  - Canada
  - Singapore
  - Switzerland
  - United Kingdom
  - United States
  - European Union

Two pathways

- TGA will usually only evaluate data generated specifically for Australian context
- **COR-A (120 working days) pathway:**
  - identical medicine and manufacturing site, evidence of compliance with GMP
  - foreign marketing approval no older than 1 year
  - no additional evaluation of Australian specific data is required other than labels, product information and consumer medicine information
- **COR-B (175 working days) pathway:**
  - TGA decision still mostly based on review of overseas reports.
  - Additional data that may be reviewed include
    - updated stability data
    - validation data for an additional manufacturing site and
    - updates to pivotal clinical studies and new safety data

Reflections - Comparable overseas regulators

- **Internal cultural change** and trust by our evaluators is critical
- **Onus is on the company** to provide information
- **Hard to obtain un-redacted reviews** from the USA although about 1 in 3 medicines are approved by FDA before they are submitted to TGA
- Full eCTD implementation could change submission lag, but **is submission lag deliberate …..**
  - To see how the review goes with the biggest regulators first ?
  - To avoid dealing with several sets of questions at once ?
- **Indications also may differ** somewhat between countries
- **Several applications now received for the COR B pathway,** but most sponsors are submitting full applications to TGA

Expedited pathways for prescription medicines

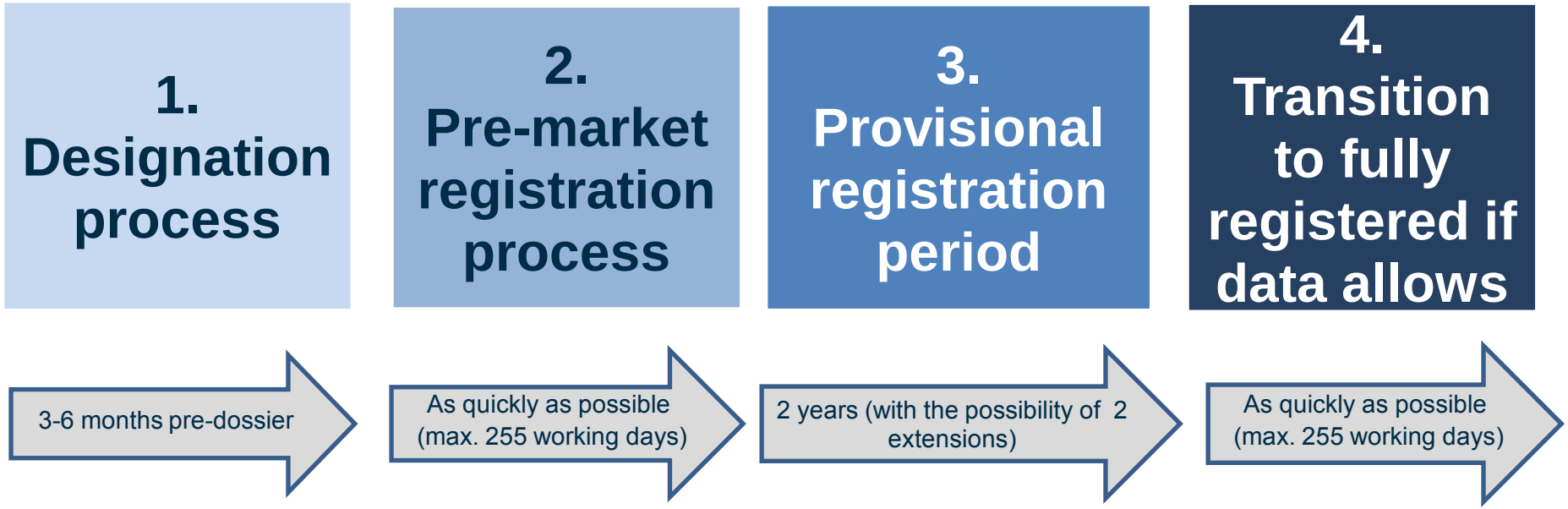
- **Priority Review** (max 150 wkg days) of complete data – full approval
- **Provisional Approval** (max 255 wkg days, but will aim for faster) on the basis of early data on safety and efficacy
- Some **eligibility criteria** for Priority Review and Provisional Approval similar:
  - serious condition
  - major therapeutic advance
  - comparison against existing therapeutic goods
- Others are **quite different** - eligibility for:
  - **Priority Review** based on '*substantial evidence*'
  - **Provisional Approval** based on '*promising evidence from early clinical data*'

What did we take into account?

- **TGA only formerly had a standard pathway**
  - approval times for this pathway were competitive (200-250 working days)
  - faster than EMA approvals and same as FDA standard pathway
- Strong industry and patient **calls for new facilitated pathways**
- **Design considerations**
  - learnings from **other regulators' facilitated pathways**
  - as a **medium sized** regulator we shouldn't routinely influence development pathway / clinical trial design, so sponsor interaction can start later
  - provision in law that sponsors can **seek review** of the designation decision
  - planned to **publish priority designations** on the TGA website

Small regulator syndrome?

Provisional approval pathway



Reflections – priority review and provisional medicines designation

- **Publication of successful priority review designations** has led to pressure for TGA to publish all NCE submissions
- Many priority designations are for **extensions of indications**
- We have managed to approve several priority designated medicines **well ahead of the legislated timeframe**, but it has put pressure on other timeframes
- **TGA provisional pathway constructed** to avoid risk of it becoming a pathway for approval of “medicines that just miss out full approval”
- **Government still to consider reimbursement** policies for provisional approvals
- **Fixed timeframes** mean that companies need to be advanced in confirmatory trial plans and able to implement postmarket monitoring requirements

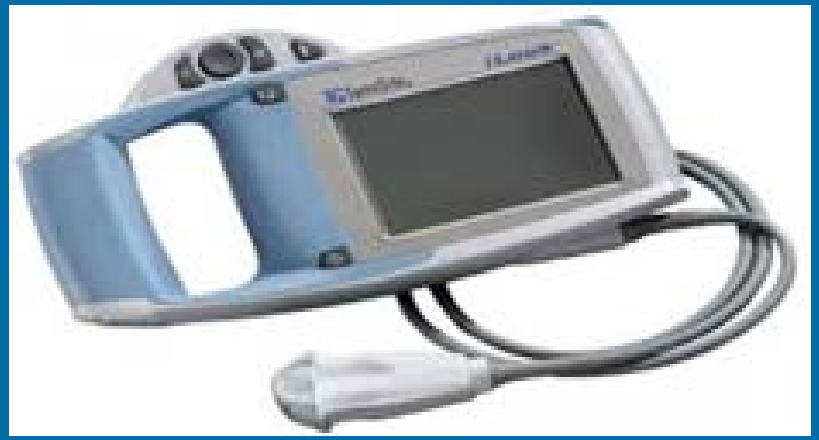
Enhanced postmarket monitoring

- Better integration and timely **analysis of datasets**
- Adverse Event Management **IT System**
- **“Black triangle”** scheme to alert practitioners and consumers
- **Pharmacovigilance inspection scheme**
- **RMP Compliance** Monitoring Program
- **Revision of Product Information (PI)** templates
- Enhanced **international collaboration**

Other major areas of work underway

- **Special Access Scheme** – online submission portal
- **Medicine shortages** - mandatory reporting, triage and systematic management
- **Opioids** - reducing pack sizes of prescription medicines to treat acute pain more appropriately, review indications, CMI changes, better information for healthcare professionals and consumers
- **Generic medicines** – prioritisation, pathways and GMP clearances
- **Good Clinical Practice** (GCP) clinical trial inspections
- **Fecal microbial transplants**

Medical devices



Introduction of multiple device pathways - MMDR

- **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

- Priority Review devices will be allocated front-of-queue priority, with **no truncation of assessment processes**
- Involves **faster processing** of conformity assessment and/or ARTG inclusion
- Selected devices will receive a **time- limited priority review designation**
- **Available from Jan 2018** but no applications received as of early Aug 2018

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 (not just engineering) 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

At present conformity assessment can either be from TGA or an 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

Australian Conformity Assessment bodies

- We now **allow bodies designated by the TGA to be able to undertake conformity assessment** certification in Australia
- **Requirements for Australian CA bodies** draw from both European arrangements for notified bodies and MDSAP
- **Regulations commenced in March 2018** and set out the criteria for qualifying to become a designated body; how to apply to become a designated body; and inspection and monitoring requirements.
- **Supporting guidance material** is being finalised and will be published soon following incorporation of feedback from industry

Reflections – medical device reforms

- **No priority device review applications yet** – as the system is not a provisional/ breakthrough scheme, it may be less attractive to industry
- Still need to see whether there is real **demand for Australian CA bodies** – most notified bodies are busy adapting to the changes in Europe
- Maintaining the **ability for TGA to carry out Conformity Assessments** was a good move given the pressures on EU notified bodies
- We will **continue to streamline application audit processes**, but variability in the quality of clinical evidence remains a challenge

What will the demand for Australian bodies be? Build it and they may come

Montreal Mirabel International Airport built for the 1976 Olympics

Using other regulators' evaluations

- **Australian system already built on use of EU notified bodies**
  - so a tradition of using other evaluations to support device inclusion exists
- **But some differences** in device and IVD regulatory frameworks between Australia and other countries
- So establishing **comparable overseas regulators** is more complicated than with medicines
- Evidence submitted should be for the **same medical device** as being applying for in Australia (i.e. same design/ intended purpose/ indications).

Using other regulators' evaluations

- Specific evidence and documentation, will be considered in **abridging** TGA conformity assessments or applications for ARTG inclusion:
  - Certificates issued by designated **EU Notified Bodies**
  - Decisions of the **United States FDA**
  - Licences issued by **Health Canada**
  - Pre-market approvals from **Japan**
  - Certificates/reports issued under the **Medical Device Single Audit Program**
- **Detailed guidance** on how particular reports could be used has undergone industry consultation over last few months
- **Instruments** listing the comparable overseas regulators and preliminary assessment requirements will be made soon, and the guidance released

Other MMDR device reforms - coming soon

- **Strengthened postmarket monitoring**
  - Better integration and timely **analysis of available datasets** (including matched de-identified patient administrative data)
  - **Electronic reporting** of adverse events
  - **Enhanced** information - sharing with overseas regulators
- **Target timeframes** for all device pathways
- Completion of **class I medical device classification review**
- Greater **alignment with the EU medical device framework**
- National **Clinical Quality Registry** Strategy

Other Device reforms – coming soon (ish)

- **Patient cards and product information** for implantable devices
- UDI for devices
- New regulatory frameworks for **3D printed devices**
- Review of **software as a device and cybersecurity**
- Other **aspects of the medical devices framework** will be aligned with the EU regulations wherever possible
- **Companion diagnostic** regulatory framework

Conclusion - new pathways – interest thus far

Strong interest from industry

- Priority medicines review
- New orphan medicine pathways
- Notifiable medicines variations

Moderate interest

- Provisional medicines approvals
- Using overseas medicines evaluations

Interest unclear

- Priority medical device pathways
- Australian notified bodies
- Using overseas medicines evaluations

Conclusion

- MMDR brings the **most sweeping change to regulation in 25 years**
- **A range of other reforms** are also being implemented
- **Importance of consultation** on proposed changes
- **Communication / education and review** of implemented changes
- **Consumer engagement** will require greater effort
- **Business as usual** remains critical
  - TGA publishes detailed reports on our regulatory performance
  - Staff, budget and IT constraints makes carrying out reform while managing BAU challenging