GMTA/DITTA Workshop on Reliance

• **Scene Setting:** What is reliance and why is it important?
• **Session 1:** Reliance in a premarket setting
• **Session 2:** Reliance in a post market setting
• **Next Steps**
Session 1: Reliance in a premarket setting

*Case studies in premarket reliance implementation*

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Outline

- Reliance vs recognition?
- How do we use reliance in the Australian context (maintaining sovereign decision making)
  - Comparable overseas regulators framework
  - Observations on IVDs vs non-IVD devices
- Benefits, Lessons and Challenges
- Case Studies and the Future
Australian context - Comparable overseas regulators framework
Criteria for comparable overseas regulators - TRUST and CONFIDENCE

1. Comparability of the regulatory framework
2. IMDRF membership
3. Life cycle approach and post-market vigilance
4. Communication and cooperation with overseas regulators
5. Expertise of the overseas regulator

Note: Decision is made by the Australian Government
The TGA advises the Government based on the above criteria after significant liaising with the other regulator and the outcome is expressed in a Determination (legal instrument).
Legislation to support reliance

- **Therapeutic Goods (Overseas Regulators) Determination 2018**
  This instrument lists entities determined to be overseas regulators under the Therapeutic Goods Act

- **Therapeutic Goods (Medical Devices—Information that Must Accompany Application for Inclusion) Determination 2018**
  This instrument lists the kind of information that must accompany an application for inclusion in the Australian Register of Therapeutic Goods (ARTG)
## COR evidence accepted for Device Classifications - Class III Example

<table>
<thead>
<tr>
<th>Comparable Overseas Regulator</th>
<th>Documents required by TGA to support a Class III Medical Device application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Canada</td>
<td>MDSAP + Medical device licence Class IV</td>
</tr>
<tr>
<td>Japan – Ministry of Health, Labour and Welfare</td>
<td>MDSAP + Pre-market approval certificate</td>
</tr>
<tr>
<td>EU MDR</td>
<td>Annex IX(QMS) + Annex IX (Technical documentation)</td>
</tr>
<tr>
<td>EU MDD</td>
<td>Annex II.3 + II.4 (design exam)</td>
</tr>
<tr>
<td>US FDA</td>
<td>MDSAP + PMA</td>
</tr>
<tr>
<td>Singapore – Health Sciences Authority</td>
<td>Form supporting entry in Singapore Register of Health Products as a Class D medical device</td>
</tr>
</tbody>
</table>
ARTG entries for Medical Devices

Less than half of ARTG entries for medical devices (IVDs and non-IVDs) require supporting CA certification

- Non-IVD Medical Devices with CA certification: 41.9% (26,077)
- IVD Medical Devices with CA certification: 3.3% (2,028)
- System or Procedure Packs without CA certification: 1.1% (700)
- Medical Device (IVD and non IVD) ARTG entries without CA certification: 53.8% (33,488)

Percentage of medical device (IVDs and non-IVDs) ARTG entries (62,293 total)
ARTG entries supported by overseas certifications for medical devices (non-IVDs)

Manufacturer Evidence Supporting Medical Device ARTG entries (non-IVD) by Certification Type (at February 2024) (42% of all ARTG entries)

<table>
<thead>
<tr>
<th>Certification Type</th>
<th>Percentage</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan QMS</td>
<td>0.1%</td>
<td>14 (0.1%)</td>
</tr>
<tr>
<td>US FDA</td>
<td>0.1%</td>
<td>26 (0.1%)</td>
</tr>
<tr>
<td>Singapore HSA</td>
<td>0.1%</td>
<td>37 (0.1%)</td>
</tr>
<tr>
<td>TGA Certification</td>
<td>3.5%</td>
<td>912 (3.5%)</td>
</tr>
<tr>
<td>MDSAP</td>
<td>6.5%</td>
<td>1,702 (6.5%)</td>
</tr>
<tr>
<td>EU MDR</td>
<td>9.1%</td>
<td>2,370 (9.1%)</td>
</tr>
<tr>
<td>EU MDD/AIMD/AIMDD</td>
<td>80.6%</td>
<td>21,016 (80.6%)</td>
</tr>
</tbody>
</table>

Percentage of Certification Type for ARTG entries supported by ME certification (26,077 total ARTG entries)
### Manufacturer Evidence supporting IVD ARTG Entries by Certification Type (at February 2024) (3.3% of all ARTG entries)

<table>
<thead>
<tr>
<th>Certification Type</th>
<th>Percentage</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU IVD Regulation 2017/746 (EU IVDR)</td>
<td>1.6%</td>
<td>32</td>
</tr>
<tr>
<td>Directive 98/79/EC (IVDD)</td>
<td>6.8%</td>
<td>138</td>
</tr>
<tr>
<td>TGA IVD Conformity Assessment Certification</td>
<td>10.7%</td>
<td>217</td>
</tr>
<tr>
<td>Other ISO 13485</td>
<td>34.9%</td>
<td>708</td>
</tr>
<tr>
<td>MDSAP</td>
<td>46.0%</td>
<td>933</td>
</tr>
</tbody>
</table>

Percentage of Certification Type for IVD ARTG entries supported by ME certification (2,028 total ARTG entries)
<table>
<thead>
<tr>
<th>Benefits</th>
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<tbody>
<tr>
<td>• Faster access to technology to improve the health of Australians</td>
</tr>
<tr>
<td>• Reduced duplication of regulatory effort and costs to companies</td>
</tr>
<tr>
<td>• The TGA is better able to channel its resources to areas of need</td>
</tr>
<tr>
<td>• Better export access for Australian companies</td>
</tr>
<tr>
<td>• Introduction to the latest emerging devices</td>
</tr>
<tr>
<td>• We are part of the global regulatory infrastructure</td>
</tr>
<tr>
<td>• Shared regulatory science - knowledge and relationships</td>
</tr>
</tbody>
</table>
Lessons and challenges

- Need Government support
- Positive ongoing relationships with other national regulators are crucial to success
- Late night meetings and travel – it is hard work being distant from regulatory partners!
- Domestic stakeholders may see reliance as a threat to sovereignty
- Need broad support from domestic industry and health care to resist bespoke requirements
- Often challenging to meet expectations of the stakeholders
- Differing interpretation of legislation and/or guidance across jurisdictions
- Other mechanisms such as information sharing agreements, Mutual Recognition Agreements and Memorandum of Understanding
Case Study 1

Class IIb application – cardiac system generator supported by EU MDR

- TGA checking of application showed:
  - Details in application and certificates were complete and correct
  - No further information was required
- Outcome:
  - Application was approved within the legislated 20 working days
Case Study 2

Class IIb application - skin contouring radio-frequency system supported by MDSAP and US FDA 510k

- TGA checking of application showed:
  - IFU did not comply with EP 13.4 (information that must be provided with the device)
  - Intended Purpose stated in the original application was inconsistent with the IFU and 510(k).
  - The entity the 510(k) was issued to did not match the manufacturer name as stated on the MDSAP certificate.

- Outcome:
  - The 510(k) Establishment Registration & Device Listing entry showed the registered establishment was the MDSAP certificate holder.
  - An updated Intended Purpose was provided for the application.
  - The IFU was amended to comply with EP 13.
  - Application was approved within 33 working days
Case Study 3

Class III applications (Mitral Valve Clips) supported by EU MDR - with inadequate supporting documents (group of 3 applications)

- TGA checking of application showed:
  - Clinical evaluation report, IFU and labels of the devices were not provided.
  - These documents are needed for preliminary clinical assessment to determine the risk/benefit ratio of the devices.

- Outcome:
  - Information requested was provided promptly to the TGA.
  - New information received was adequate to proceed to delegate’s decision.
  - The applications were approved within 20 working days.
Case Study 4

Class III applications (Breast implant support materials)- supported by EU MDR (group of 3 applications)

• TGA checking of application showed:
  ▪ Insufficient clinical evidence to establish the safety and performance of the devices for use in breast reconstructive surgery.
  ▪ Lack of robust, long-term comparative safety data for use.
  ▪ Adverse events poorly reported by surgeons outside of clinical trial.

• Outcome:
  ▪ Since November 2021, one application has been withdrawn
  ▪ Full Clinical review required by the TGA:
    ▪ Narrow intended purpose to use in reconstructive breast surgery only.
    ▪ IFU/PILs updated with comprehensive list of adverse events.
    ▪ Ongoing PMCF plan with registry data for the next 7-years.
Future

• The TGA continues to build experience with comparable overseas regulator approvals (including EU MDR & IVDR)
• UK MHRA – reliance & recognition discussions underway
• Reviewing potential expansion of reliance mechanisms with existing regulators (eg: USFDA, Health Canada, Japan)

KEY MESSAGES
1. Trust and Confidence takes time and collaboration
2. Significant benefits can be realised