Australia and Asia Pac Regulation of Orthopedic Devices

OSMA Summer 2019, Denver CO

What We Do

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- **Regulatory Compliance, Strategy & Submissions**
- **Reimbursement – Strategy, Advice and Major Submissions**
- **Clinical Trial Management**
- **Quality Management Systems**
- **Authorised Representation, Sponsorship & Distribution Management**
- **Post Market Compliance & Surveillance**
- **Health Economics – Economic Models and Market Analysis**
- **Prescription, Biotech, Consumer & Generic Pharmaceuticals**

Your Presenters

Luis Jimenez

- VP Business Development LA Office
- Ex President & COO for Class III Implantable medical device company doing regenerative medicine
- Chemical Engineering/MBA, experienced with quality systems, technology transfer and production validation
- Board positions OCRA and several start-up companies

Arthur Brandwood

- Director and Principal Consultant
- Ex Director of Device Evaluation, TGA
- Biomaterials Engineer – Orthopedic and Cardiovascular
- Biocompatibility Specialist (ISO 10993 participant 27 years)
- Senior Adviser AHWP
- Professor – University of Sydney

The Brief...

Deep Dive on TGA Changes	Some Specific Questions: Re-classifications – TGA approaches and consequences
	Impact on products already approved
	Continuing approach for CER
Impact of MDR on Asia Pac (ex China)	Current consultations – up-classifications of spinal devices, custom devices
	Timelines and fees on expanded recognitions of international regulators
	TGA transitional period and MDD applications still in progress
ASEAN Update: MDR Impact and pending UDI Requirement Expectations	Device lifetime and safe disposal – ASEAN approach
	Japan and Korea – approach to Biocompatibility

Agenda

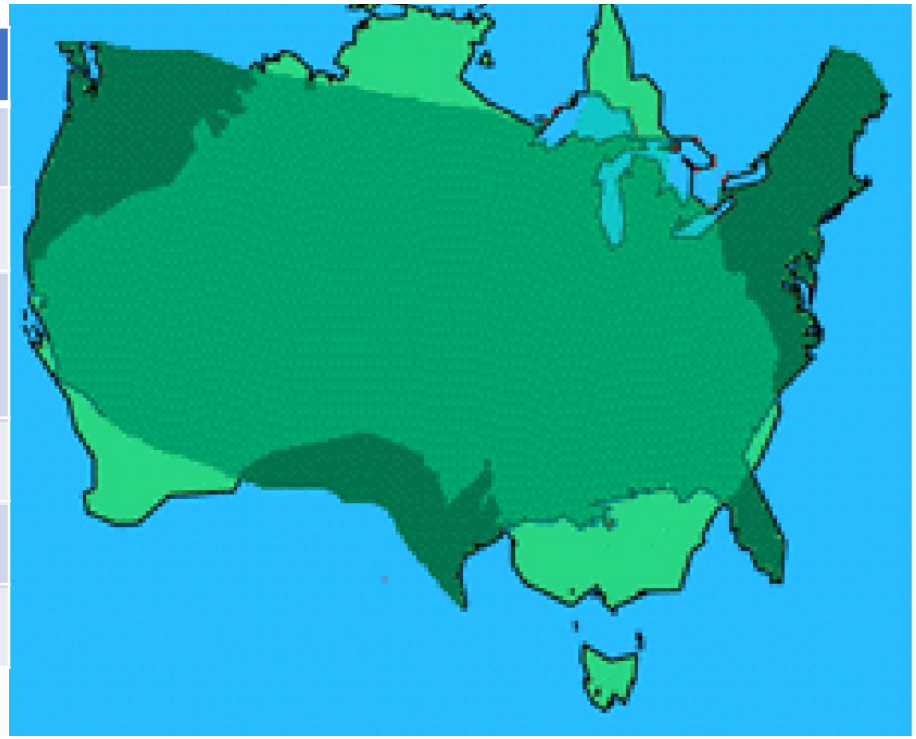
- Introduction – Australian Market
- TGA Fundamentals
- Recent Changes
- Current TGA Consultations
- Impact of MDR transition (TGA & APAC)

Australian Medtech Market

Sophisticated healthcare system with hybrid public/private delivery

Australia General Statistics

	2018
Population	25 million
GDP:	US$ 1.2 trillion
GDP Growth Rate (2017):	2.75% (26 years)
Unemployment:	5.5%
Inflation rate:	2%
Exchange Rate	$US.75=A$1



Australian Market Statistics

- The Australian medical technology industry (2018):
- ~$11.8B in 2012-13 (including IVDs and dental)
  - 80% is imported
  - 54K entries on the ARTG
  - For 2.9K Companies only 800 Australian
- 70% Federal and State government spending accounts.
- 30% individuals and private health insurance

Clinical Trials In Australia

Stable political environment

Strong legal, financial and business services

Well-developed infrastructure (medical research facilities and Trial support services)

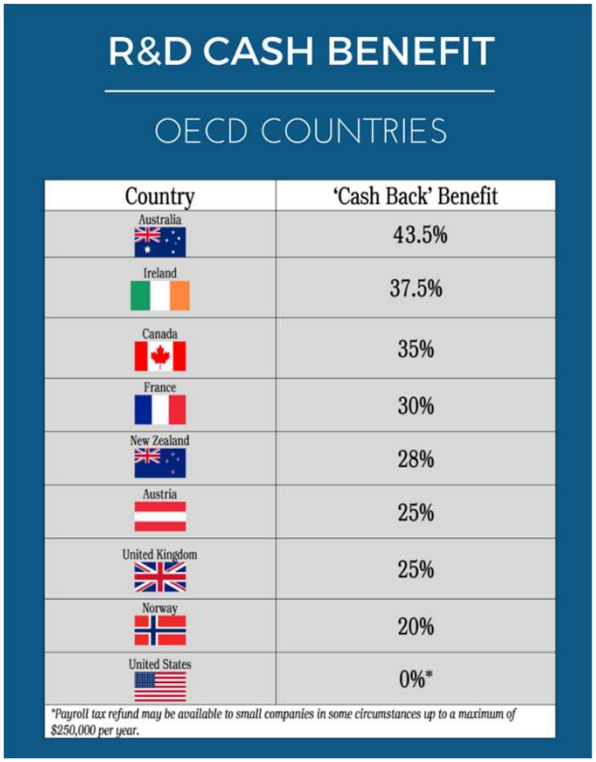
World-class science, capacity for international partnerships

- ✓ Accepted in Europe for CE Mark Applications
- ✓ Accepted in US as Early Feasibility Data
- ✓ International recognition for quality research (substantiation studies)

R&D Tax Incentives

- Excellent Tax Offset for R&D
  - 43.5% tax offset (<A$20M turnover) or indexed ratio (>A$20M turnover)

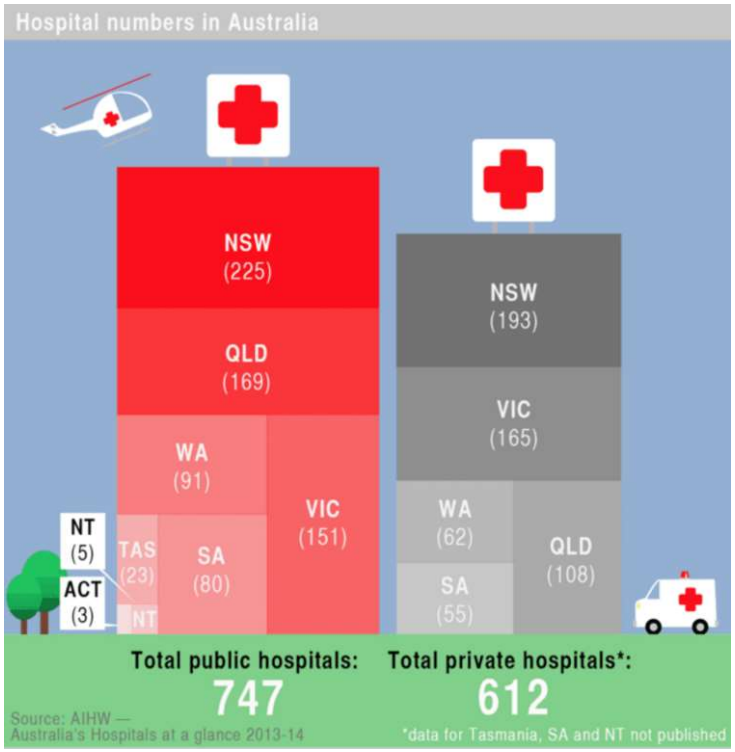
- Eligible Entities
  - Australian companies
  - Foreign companies in countries with double tax agreement which have permanent establishment in Australia



Source: Swanson Reed (www.swansonreed.com.au)

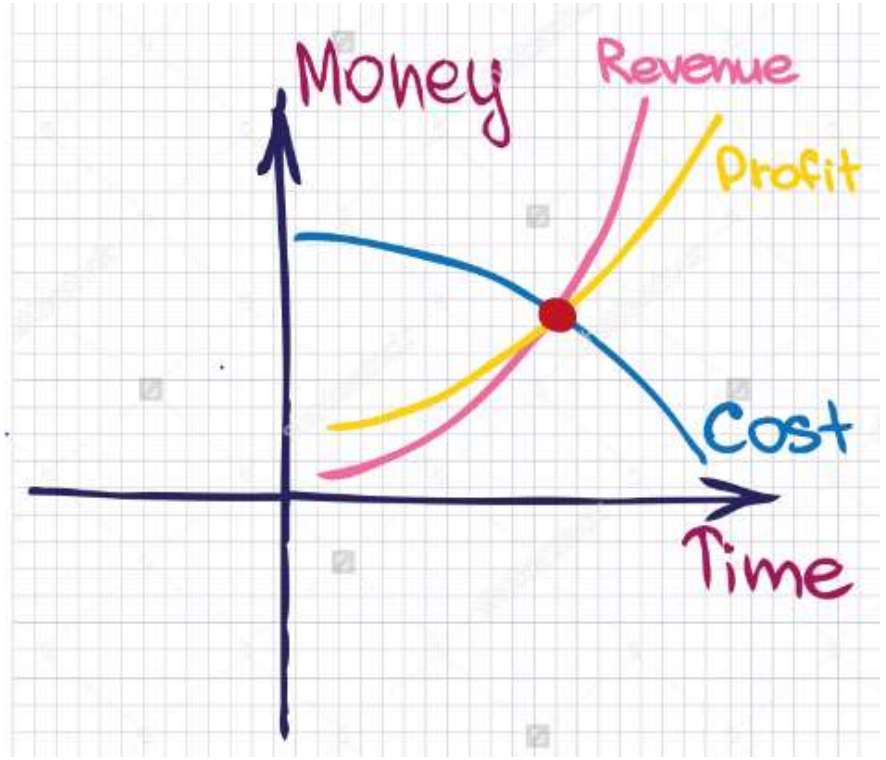
Australian Hospital Systems

- **Medical Benefits Schedule (MBS)** - list of medical procedures subsidised by **Medicare**
- A procedure must be included on MBS to be covered by Private Health Insurance (PHI)
- Implantable devices –receive a payment over and above any other reimbursement – **PROSTHESES LIST**



Australian Value-Based Reimbursement

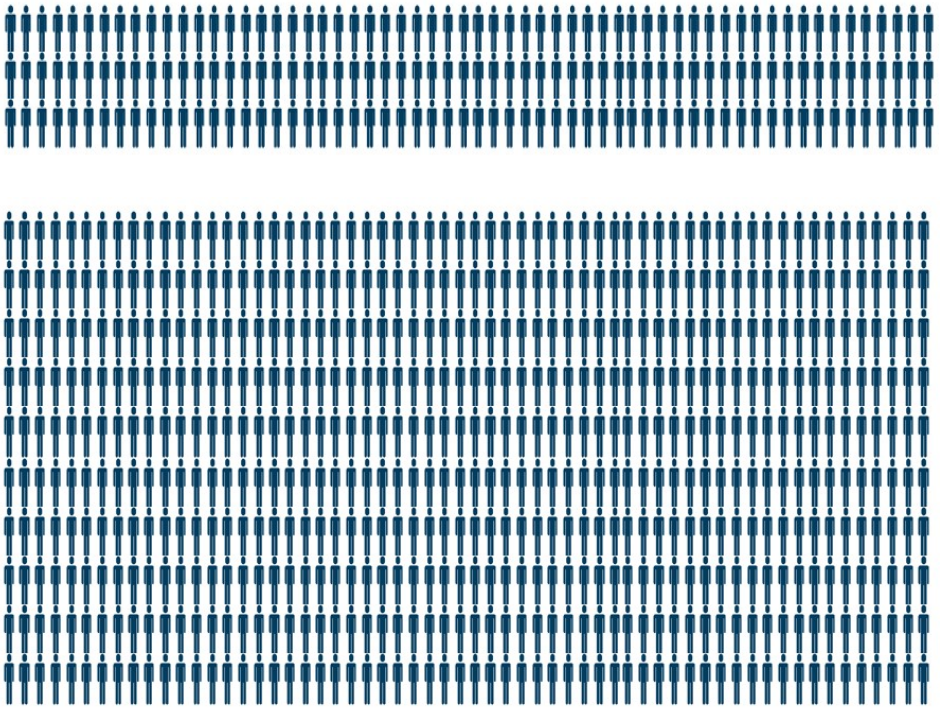
- MSAC critically evaluates both:
  - Clinical outcomes
  - Detailed cost analysis
- Only procedures that represent good value will be reimbursed
- Value based reimbursement requires a detailed economic model
  - Incentivizes adoption of novel cost saving and clinically superior procedures



TGA Fundamentals

Regulations closely modeled on the European Directives

Agency Resources



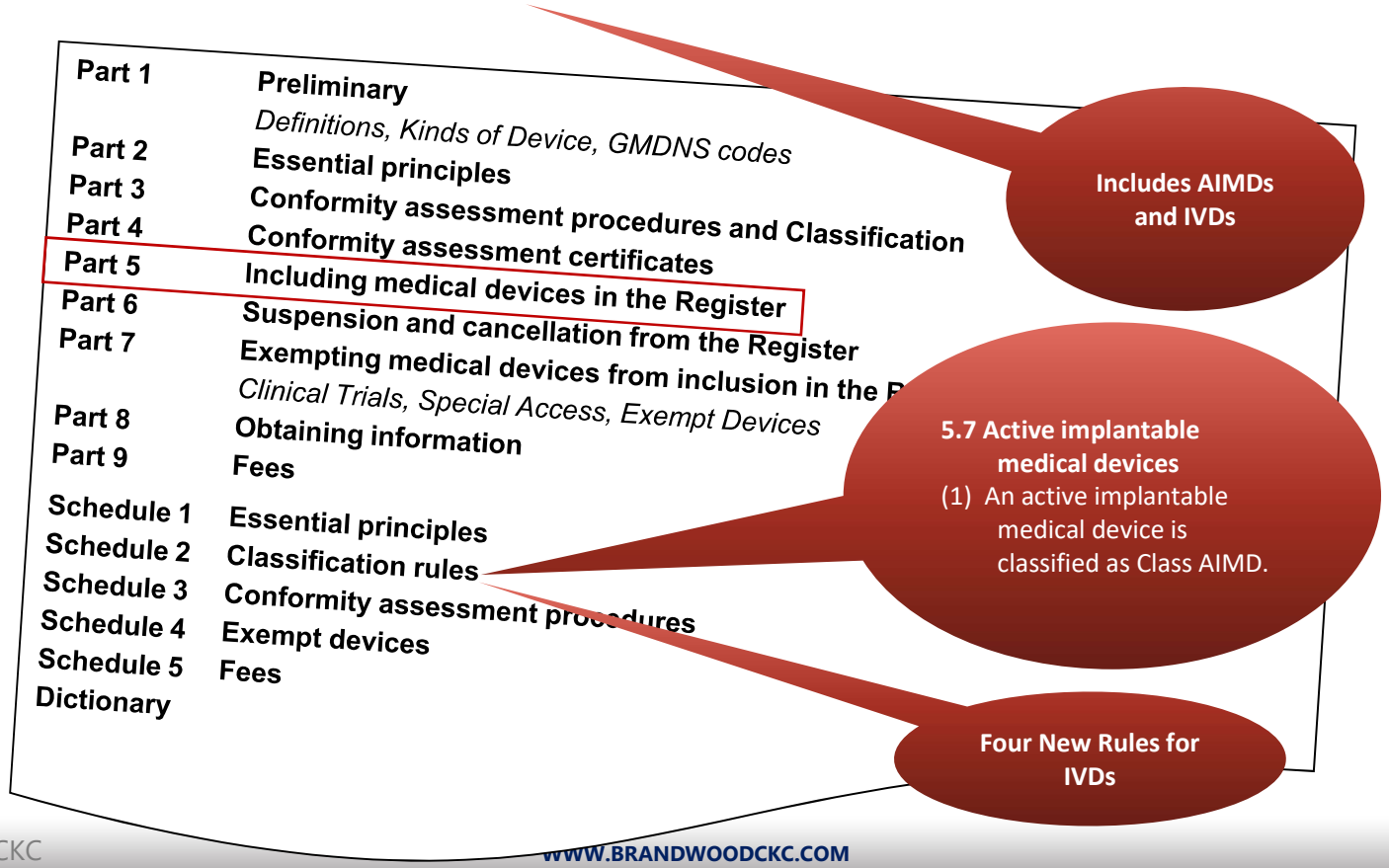
1,500

5,000

100

= 10

Therapeutic Goods (Medical Devices) Regulations 2002



EU reference 93/42/EEC (MDD) and/or 90/385/EEC (AIMDD)	Australian reference Therapeutic Goods (Medical Devices) Regulations 2002 – Schedule 3
Annex II	Part 1 – Full quality assurance procedures
Annex II.4	Part 1, Clause 1.6 – Examination of design of Class AIMD or Class III
Annex III	Part 2 – Type examination procedures
Annex IV	Part 3 – Verification procedures
Annex V	Part 4 – Production quality assurance procedures
Annex VI (MDD only)	Part 5 – Product quality assurance procedures
Annex VII (MDD only)	Part 6 – Declaration of conformity procedures
Annex VIII & Article 12 (MDD only)	Part 7 – Procedures for medical devices used for a special purpose

The Australian Register of Therapeutic Goods (ARTG)

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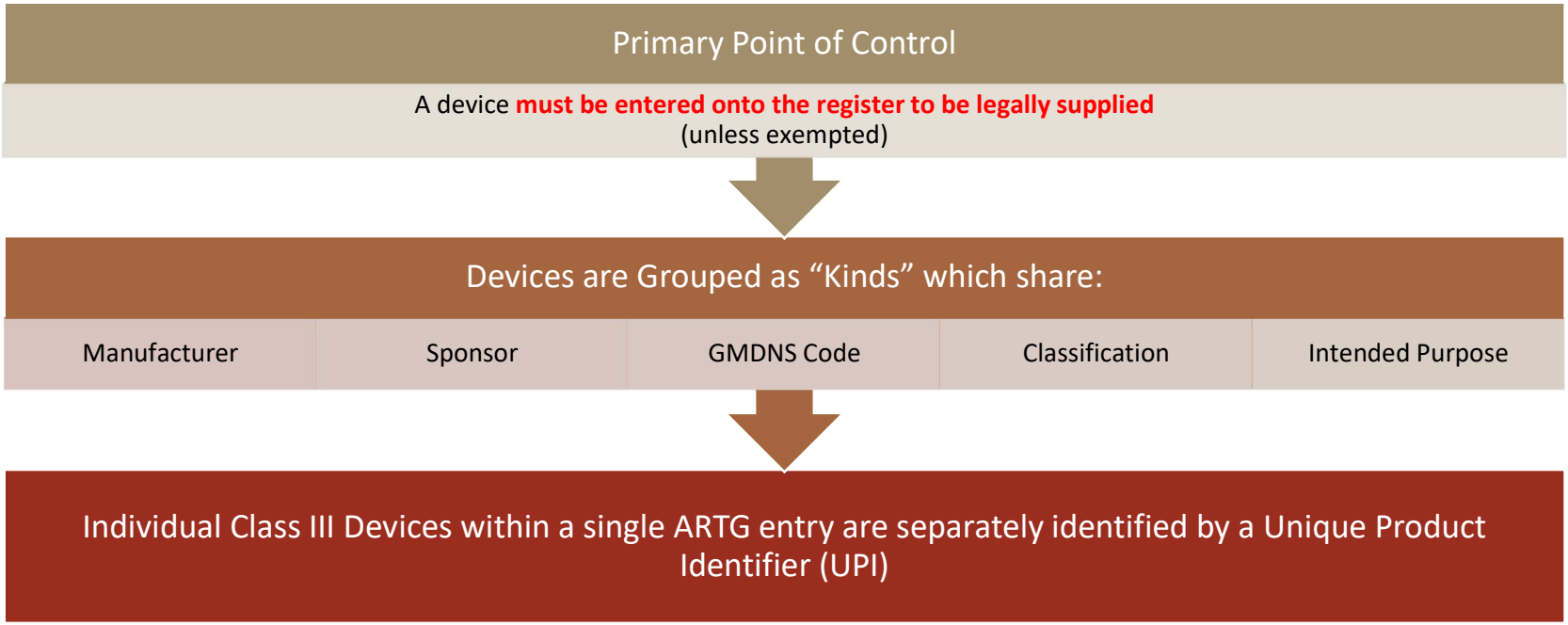

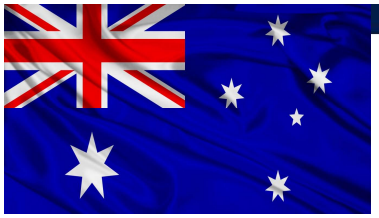

Paths to Market - Australia

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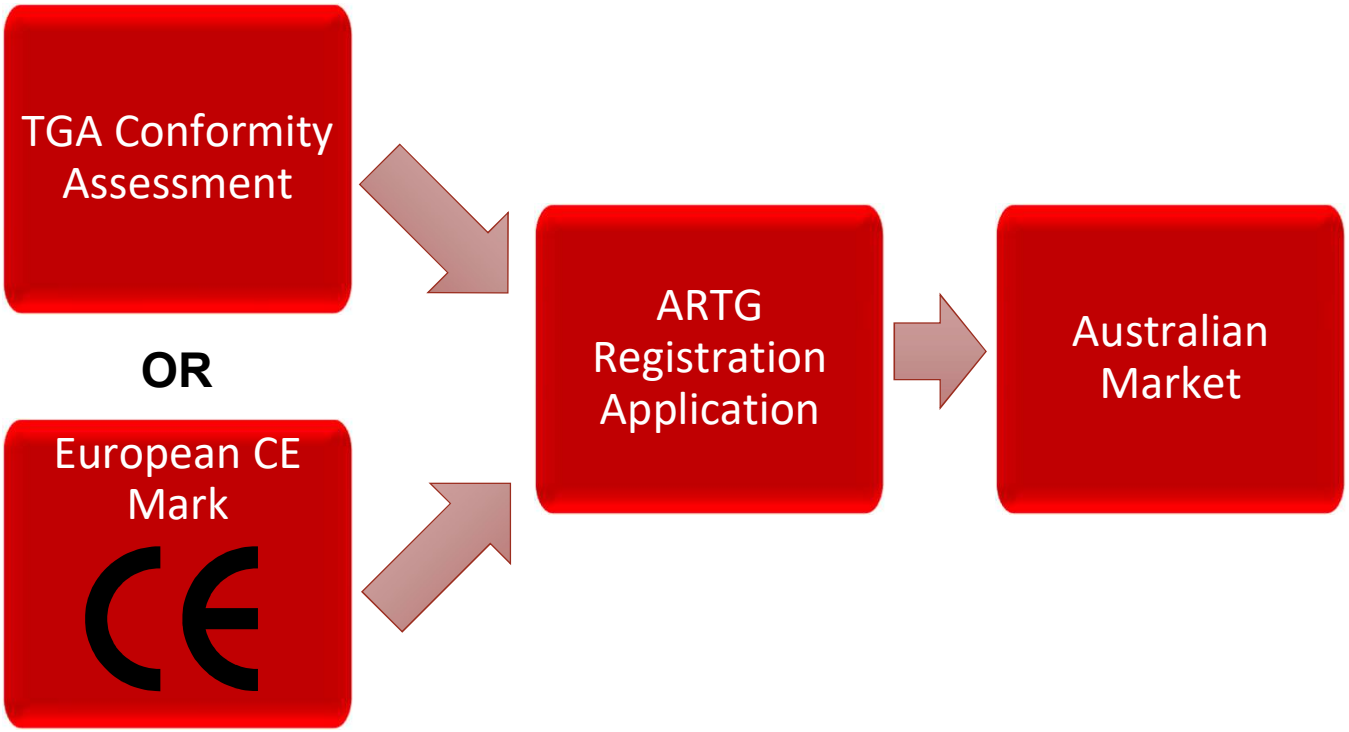
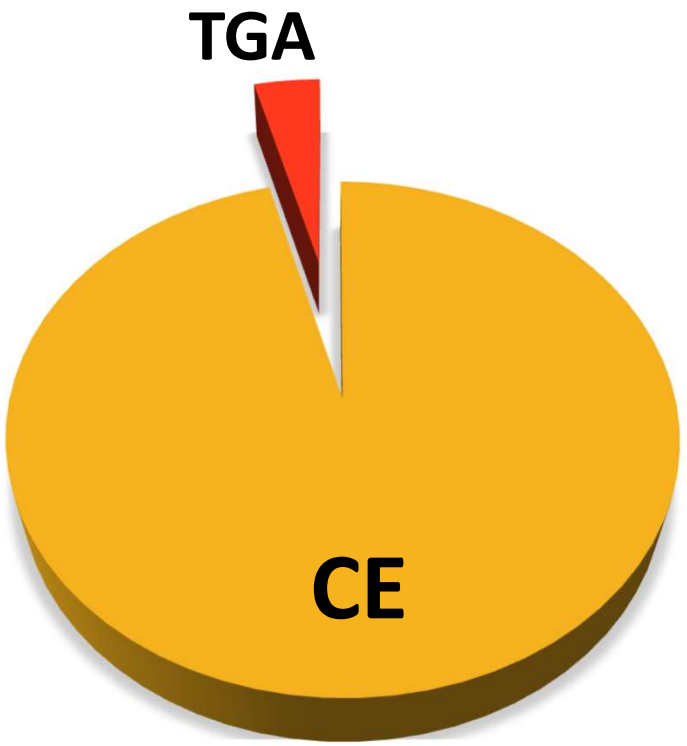


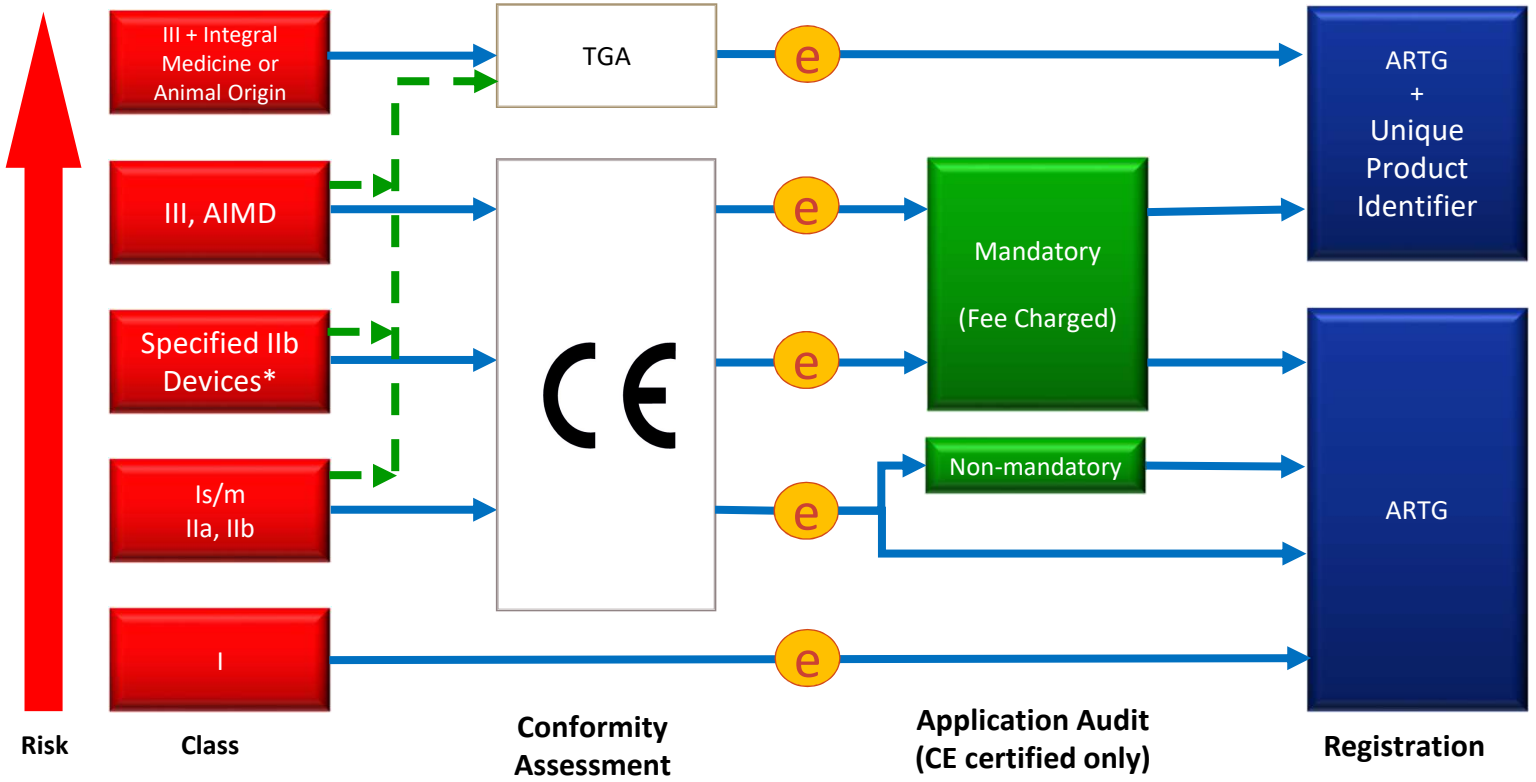


More than

90%

of Devices Subject to Australian TGA review are registered based on CE certification

TGA Processes (pre August 2018)



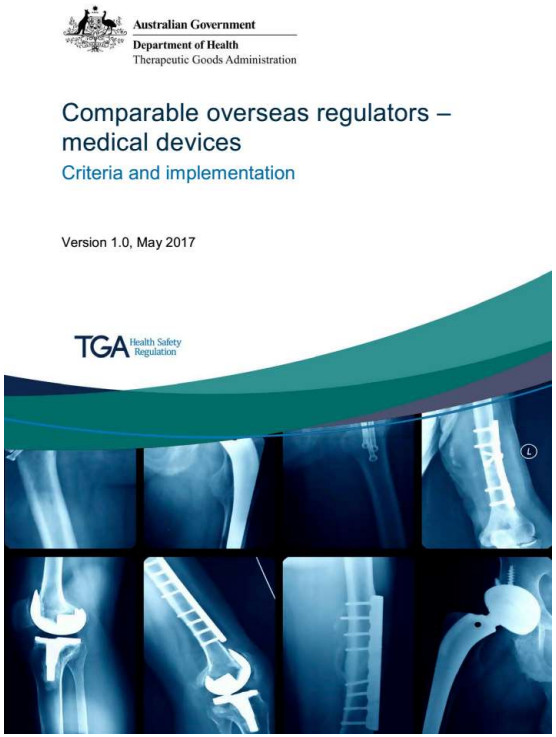
Application Audit is a review of

- CE certification and Declaration of Conformity
- Risk Assessment
- Clinical Evidence report
- Labelling & IFU

*Barrier Contraceptive (not condoms), Disinfecting Device, Intraocular Lens or Fluid, Non-saline Breast Prosthesis

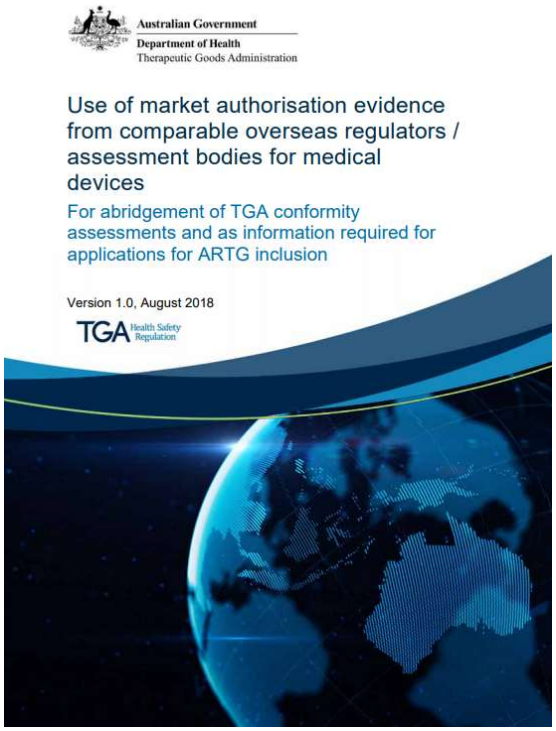
Recent Changes

Wider Acceptance of International Data



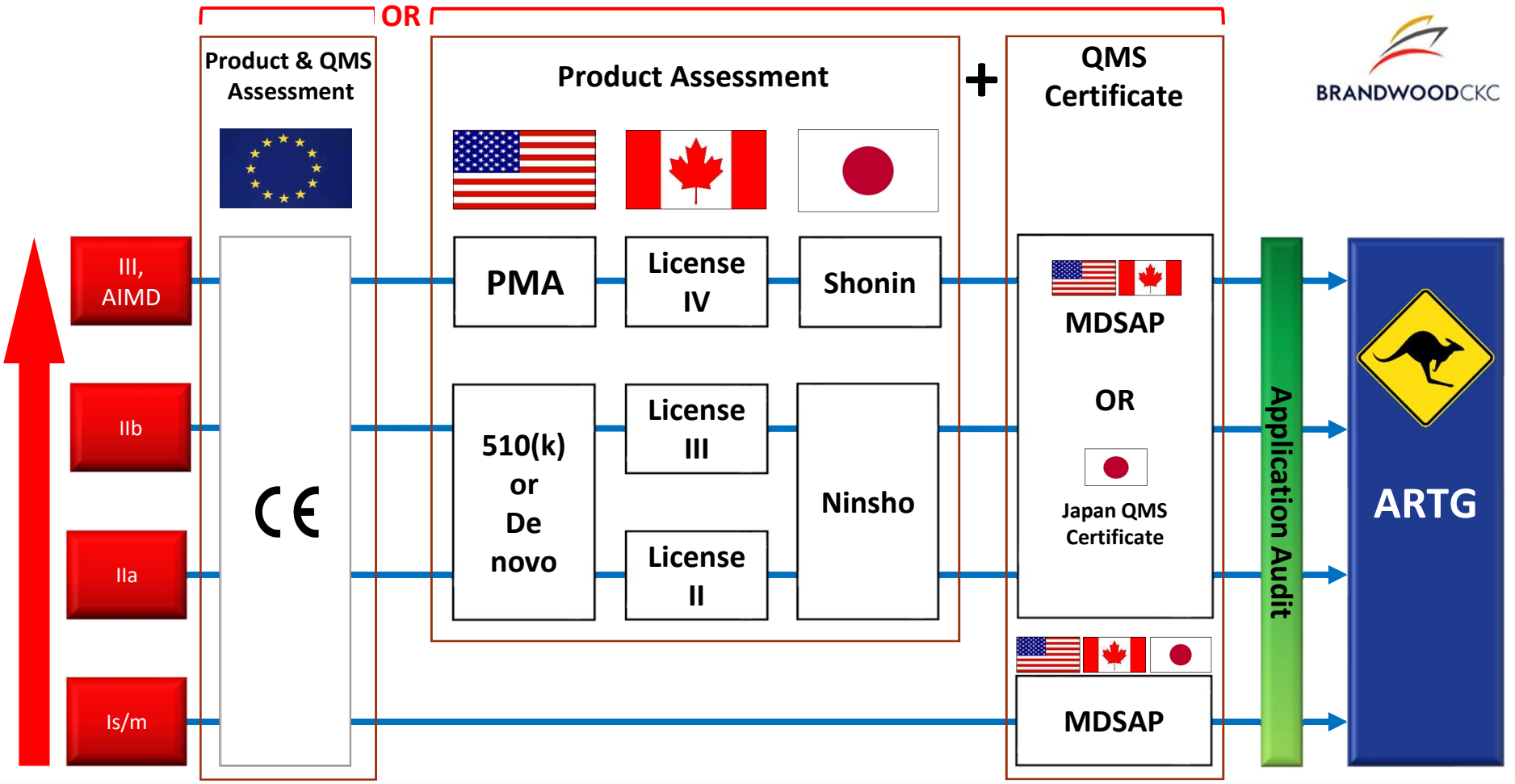
TGA Consultation on Comparable Overseas Regulators

May 2017

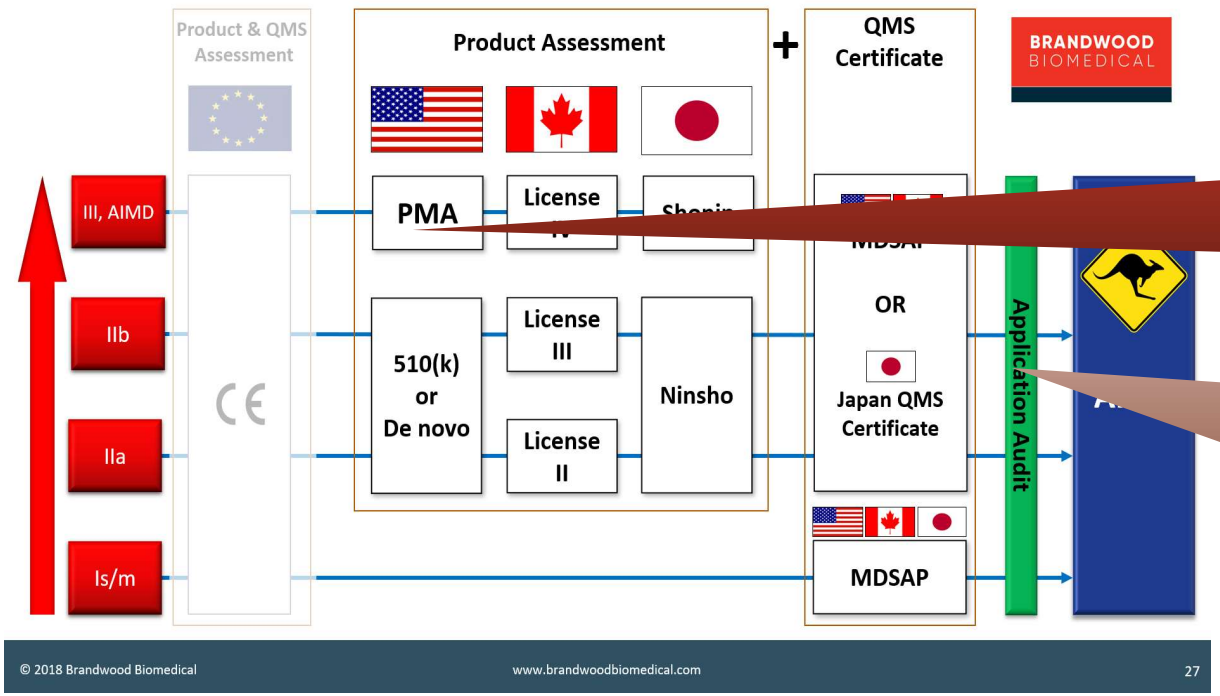


TGA Policy on Use of Overseas Evidence

August 2018



Challenges to Acceptance of International Evidence



Classification

Many Class III Devices in Europe/Australia are NOT PMA in US

Clinical Evidence

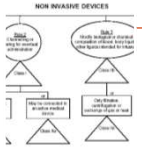
Often Not available for 510(k) cleared devices

Impact of MDR

Regulations closely modeled on the European Directives

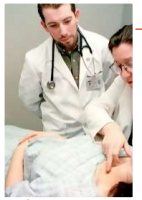
What's Changed in MDR

Safety and Performance Requirements



Updated Classifications

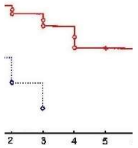
More Data



Clinical Evaluation Strengthened

Scrutiny Process

Stricter Review



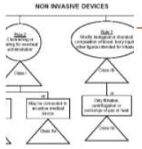
Postmarket Surveillance

Transparency - EUDAMED

Continuous Vigilance

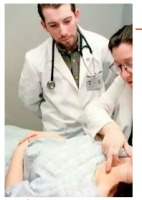
Impacts on TGA?

Safety and Performance Requirements



Updated Classifications

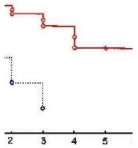
TGA will need to update to match



Clinical Evaluation Strengthened

Scrutiny Process

TGA's view is that Europe is catching up with Australia

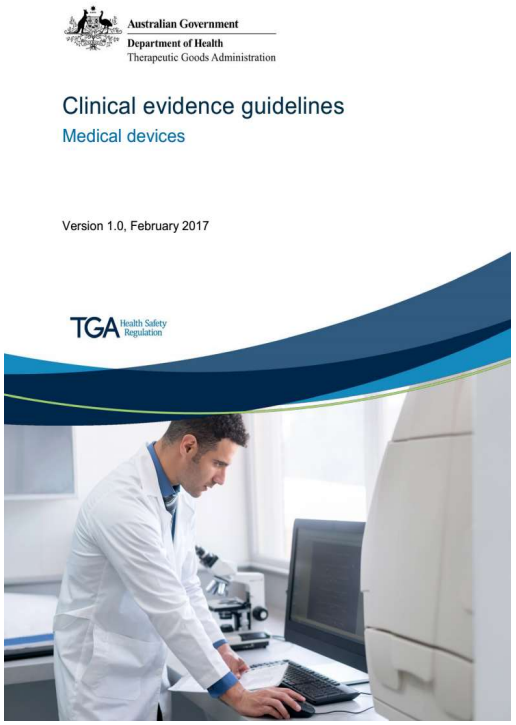


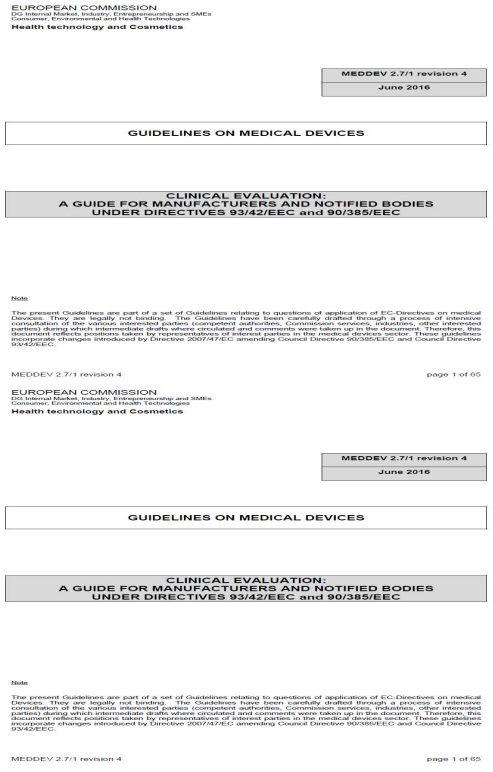
Postmarket Surveillance

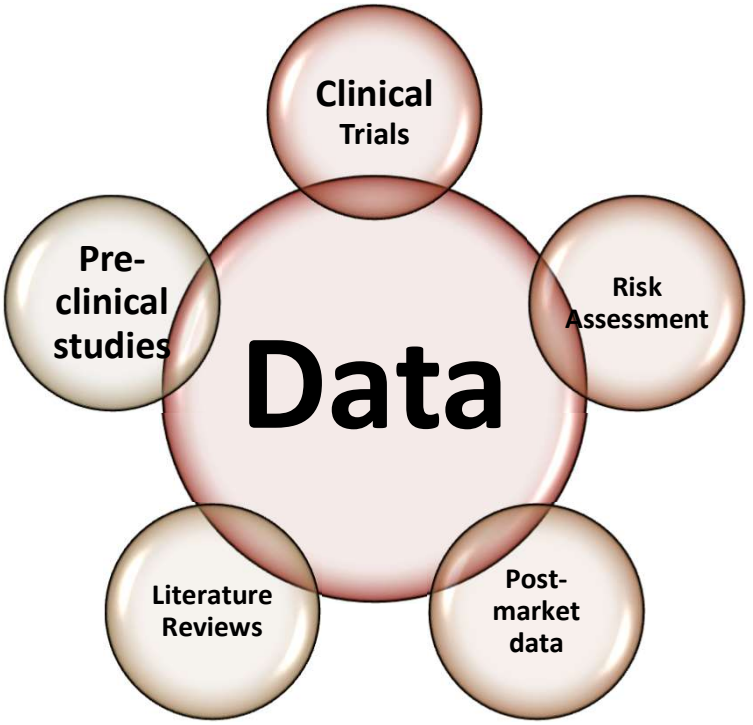
Transparency - EUDAMED

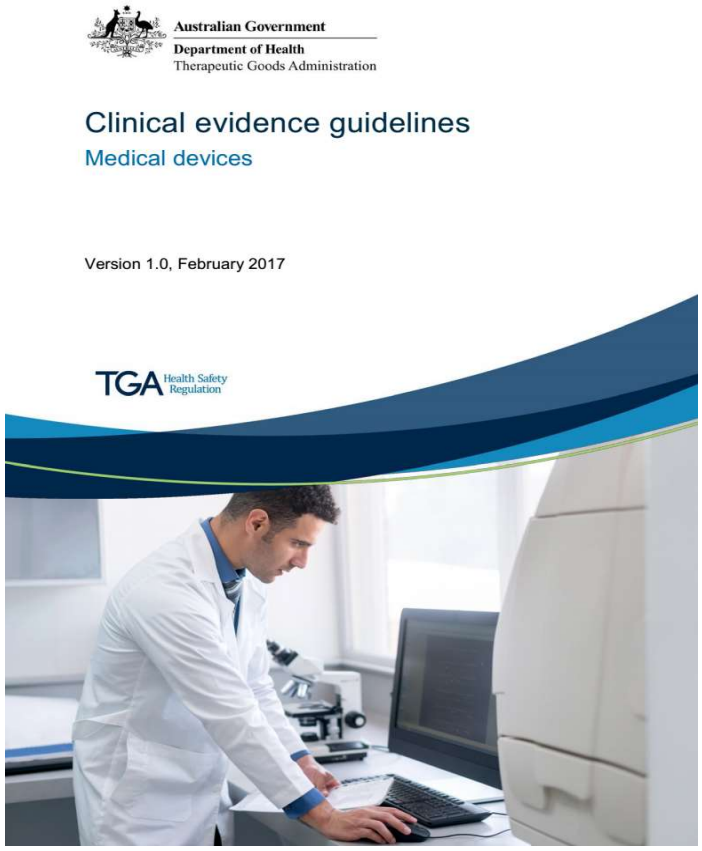
TGA local systems already exist – no significant change?

Clinical Evidence









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Legislative basis

Clinical evidence

- *Key definitions and concepts*
- *Clinical data*

Clinical evaluation report

- *Format*
- *Supporting documents*
- *Common errors in the clinical evaluation report*

Demonstrating substantial equivalence

- *Clinical evidence requirements*
- *Predicate and similar marketed devices*
- *Substantial equivalence*

https://www.tga.gov.au/sites/default/files/clinical-evidence-guidelines-medical-devices.pdf

Common Errors

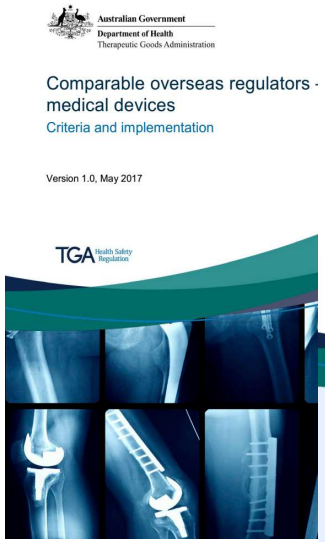
- Absence of the required components of the CER and/or referenced attachments and appendices missing
- Intended purpose(s), indication and claims inconsistent between documents i.e. application, IFU and CER list different intended purpose(s)
- Intended purpose(s), indication and claims not supported by clinical data
- Lack of information about the regulatory history of the device in other countries, for example recalls, withdrawals, removals from market, suspensions and cancellations and the reasons for these in any jurisdiction
- Information on predicate or previous related devices not included and/or substantial equivalence not demonstrated (if relevant)
- Insufficient or incomplete clinical investigation(s) data, literature and post-market data with the device or predicate/similar marketed device if relevant.
- In submissions where a literature review is provided:
    - Little or no synthesis and critical evaluation of the clinical investigation data, results of the literature review and post-market data
    - Inadequate critique and summary of the totality of evidence provided for the device
- No post-market data including adverse events, vigilance reports, complaints, failures in cases where this information is available
- More than one CER
- Author of CER not included, totality of clinical data not evaluated by competent clinical expert, CER not endorsed/signed by clinical expert
- CER not dated or out-dated
- Inappropriate selection of clinical experts.

TGA Responses to MDR

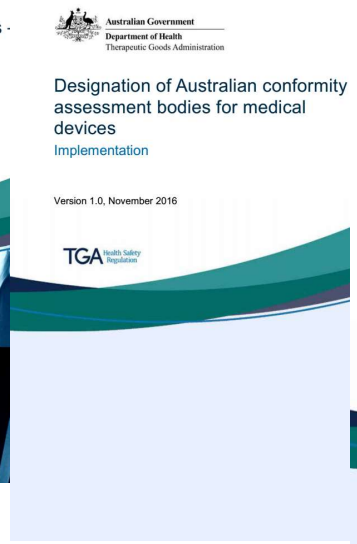
- Re-classifications. May run AHEAD of Europe on some changes
- No guarantee of complete alignment
- Active engagement with IMDRF on some areas (Software, Custom devices)
- Context of TGA Action Plan
- Capacity Building across pre and postmarket. Raise consumer awareness and involvement

Real World Capacity of TGA

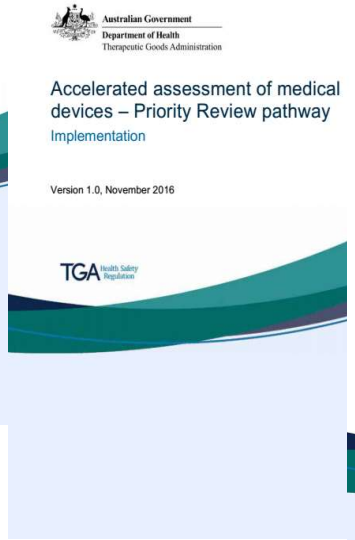
Public mistrust and demands for greater scrutiny



Recognising International Decisions



Australian 3rd Party Assessors



Priority Review Pathway

Classification Changes

Software as a Medical Device

TGA's 3 Action Plan Strategies

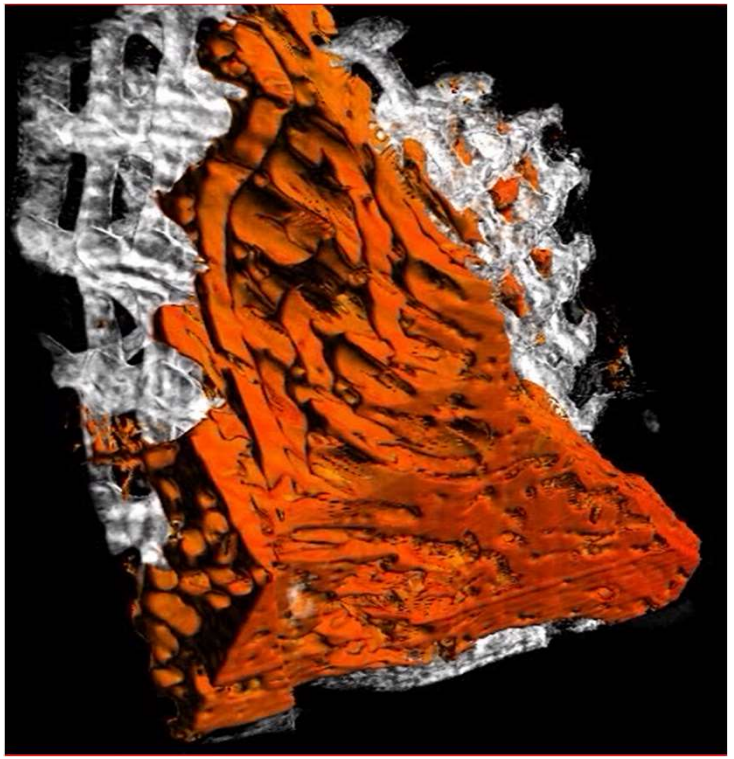
1. **Premarket**
   - Expand assessment of 3D printed devices, software.
   - Cybersecurity
   - Review of low risk device self declaration
   - New specialist review teams
   - Possible increase in Clinical Evidence for certain high risk devices: ***spinal implants***, *devices that make diagnoses, diabetes management devices, medical devices used for IVF, and companion diagnostics*
2. **Postmarket**
   - Mandatory reporting from hospitals and clinics?
   - Enhanced recall and de-registration powers
   - Patient implant cards, UDI
3. **Patient Information**
   - Greater publication of process
   - Expert Working Groups with Consumer co-chairing

TGA's Plan is to consult and implement by end of 2019

Low Risk Devices?

"Custom made devices are not required to undergo premarket assessment by the TGA or to be included on the ARTG before supply. This is because of the relatively low risk associated with the use of custom made devices such as prescription glasses and dental crowns, as well as the impracticalities of the TGA assessing such devices."

https://www.tga.gov.au/custom-made-medical-devices



Spinal Implants: a recent TGA – Stakeholder Workshop

Detailed Presentation from Surgeons

- Spinal fixation cases, implants were not the issue in most failures - it was surgeon technique.
- But for dynamic constructs there was a clear higher risk.
- Fusion implants (screws, plates, wedges, cages, hooks, rods, couplings and clamps) are only performing a temporary function while the bone fuses and should stay IIb.
- Disc replacements, expandable cages and other dynamic fixation implants, should be Class III.

Outcome?

- TGA and Consumer Health Forum both changed view after discussion to shift towards the EU Notified Body proposal
- TGA likely to announce a final position more moderate than previously

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ASEAN – let's all dance together?

Progress on AMDD Implementation across ASEAN

Member	Status
Indonesia	▪ Ratification of AMDD is targeted for end of 2019 (already passed to Parliament) ▪ Current Medical device regulation is already in line with AMDD
Malaysia	▪ Mandatory period for Product Registration has started on 1 July, 2016 ▪ Final draft of the 2nd part of regulations has been finalized on 6 March,2017. ▪ Target for completion of ratification process by 2019
Philippines	▪ Submission for ratification in 2018 ▪ Implementation of the guideline in 2019
Singapore	▪ Instrument of ratification was submitted on 10 Nov 2015 ▪ Has fully implemented AMDD
Thailand	▪ AMDD has already been approved by parliament ▪ Target for ratification of AMDD is expected by 2019
Vietnam	▪ Has ratified AMDD in 2016 ▪ Has developed Decree 36 on management of medical devices in harmony with the international commitments

Local Differences

Category

- Device or Drug or Exempt?

Classification

- Local Idiosyncrasies e.g. IVDs are medicines in Vietnam.

Process

- Local frameworks are highly varied

Dossier

- Some have adopted the AHWP CSDT format, but with local differences

Asian Harmonization Progress

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Very slow!

- AHWP is starting to contemplate guidance on UDI – but expect 2-3 years before something emerges
- ASEAN members are still developing national regulations to follow the ASEAN MDD – which is closely based on EU MDD
- Realistically, there is little prospect of update to match MDR in near future

But Note:

- Many APAC jurisdictions abridge assessments for CE marked or GHTF member approved devices (e.g. Singapore, Malaysia, Taiwan, Indonesia)
- As MDR is more rigorous than MDD, CE marks will still have validity in APAC or abridged assessments

Some Specific Questions:

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- Re-classifications – TGA approaches and consequences
- Impact on products already approved
- Continuing approach for CER
- Current consultations – up-classifications of spinal devices, custom devices
- Timelines and fees on expanded recognitions of international regulators
- TGA transitional period and MDD applications still in progress
- Device lifetime and safe disposal – ASEAN approach
- Japan and Korea – approach to Biocompatibility – mandatory biological testing?

Time for Q&A…

Think of something later?
Ask us by email…

help@brandwoodCKC.com

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