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HBD EAST 2023

CURRENT SITUATION: MEDICAL DEVICE REGULATIONS OUTSIDE OF JAPAN AND THE US

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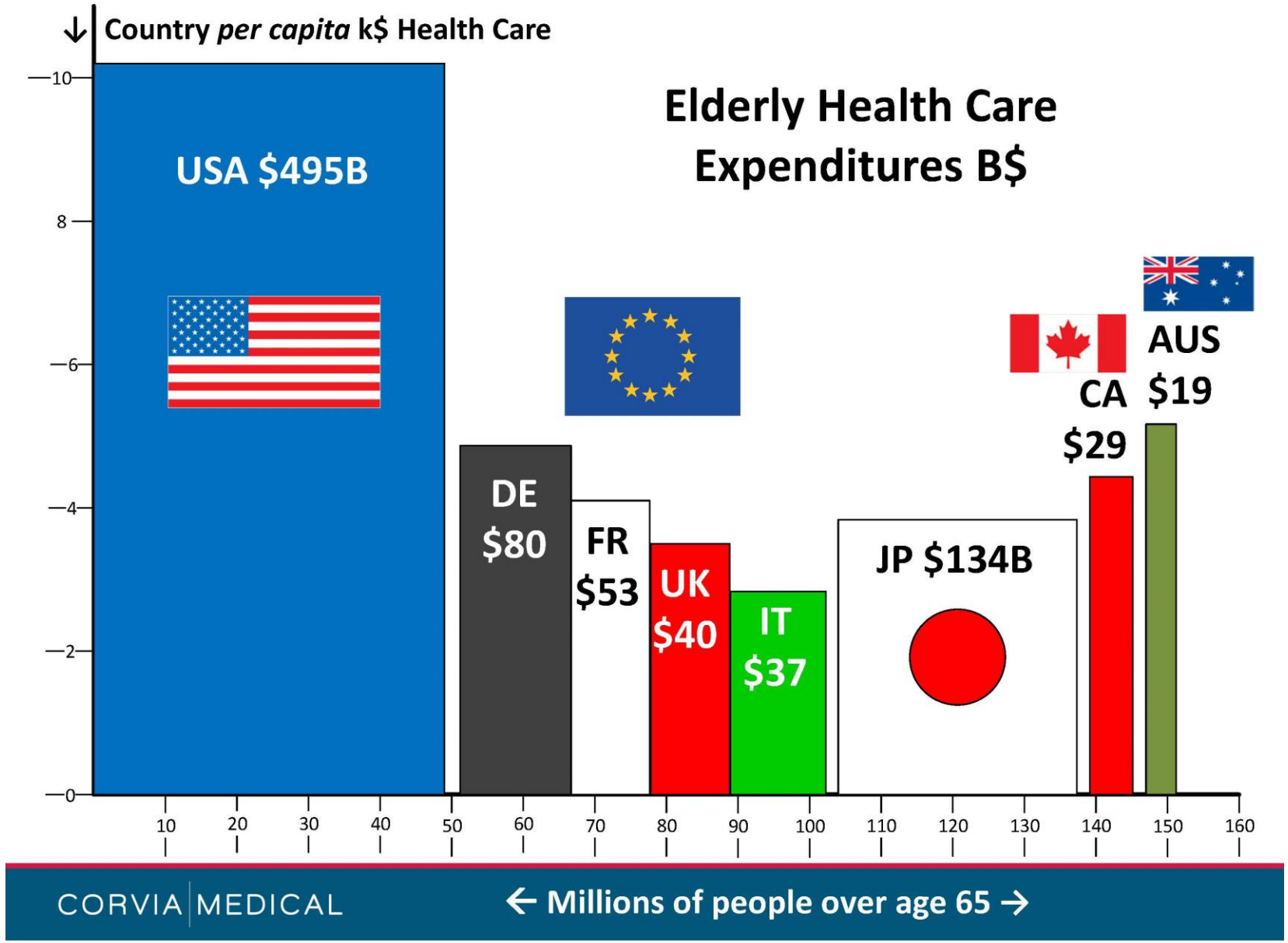
MEDICAL DEVICES

Recent Updates

- European Union
- Canada
- Australia
- South America
- China
- India



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EUROPEAN UNION

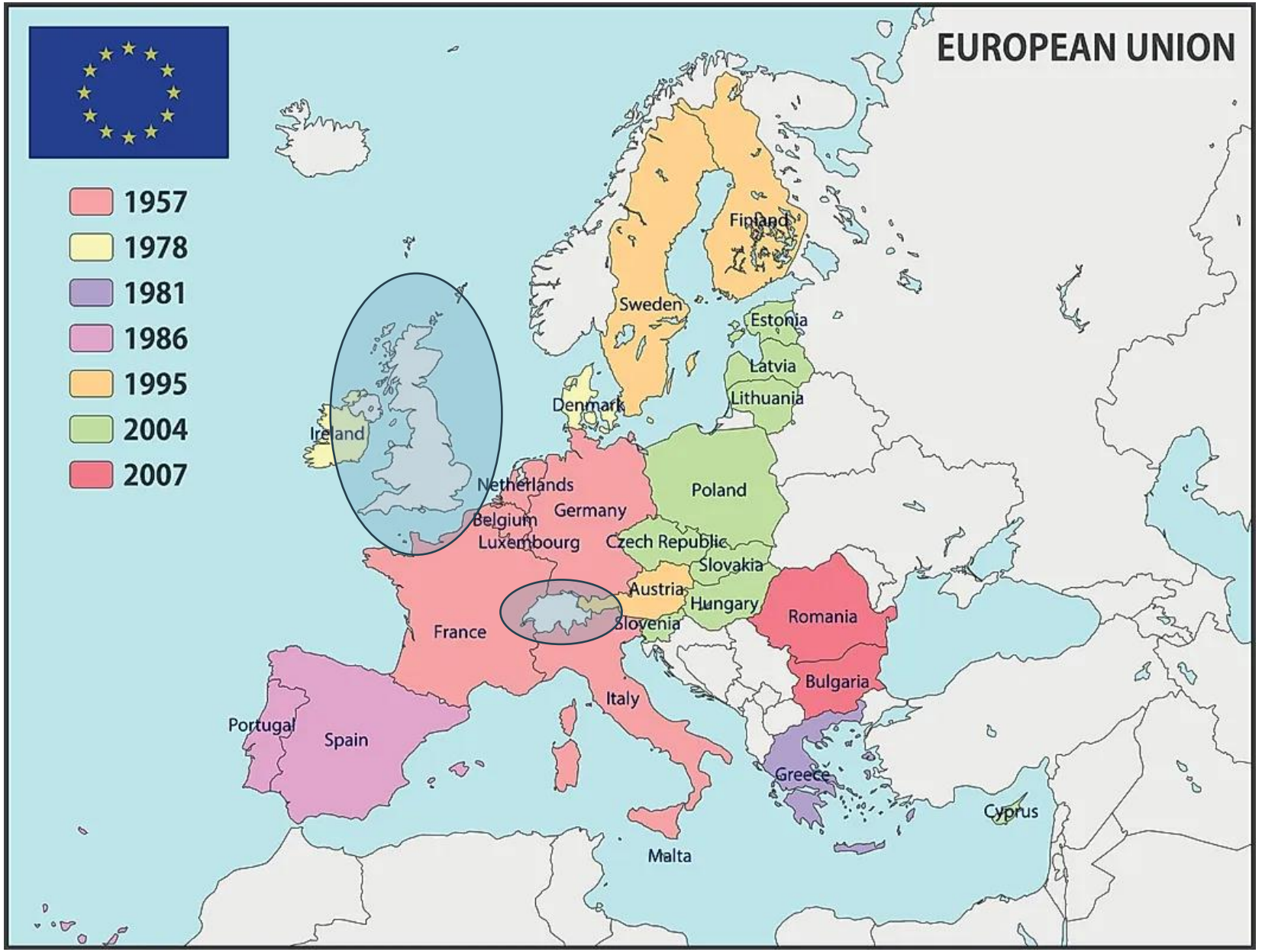
A bit of a moving target….

Switzerland

- SW now accepting market clearance applications from FDA-approved devices as well as CE Marked devices

United Kingdom

- BREXIT happened
- UKCA requesting certification to the UK MDR 2002 / 2019
  - More work/$ for Notified Bodies
  - Additional symbol on labels
  - Additional Authorized Representative = UKRP



EUROPEAN UNION

Progress towards implementation of the EU Medical Device Regulation (EU MDR)

- **Capacity constraints** with Notified Bodies (NB) due to fewer NBs, new NB training and certifications, new internal procedures development
  - 38 Notified Bodies
  - 43% increased work per certificate
  - 18 months average time QMS + Device
  - 85% of Tech Dossiers incomplete
- **Therapy Effectiveness** now reviewed - 100% of medical devices need complete reviews
  - Not every NB has "scope"
- **17,000 Certificates expire in 2024**
  - Many NBs refusing new applications
  - Most NBs refusing new customers
  - Certificates, Applications, and Refused Applications, on the rise….
  - Legacy MDD Class III devices now have until 2027-12 to transition to the MDR

Technical File

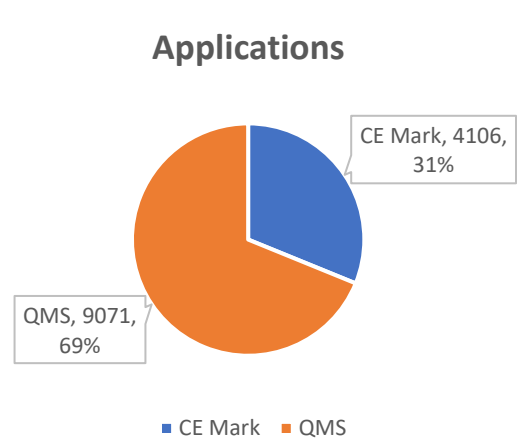
- Clinical Evaluation Process, PMS
- New Labeling Requirements, UDI

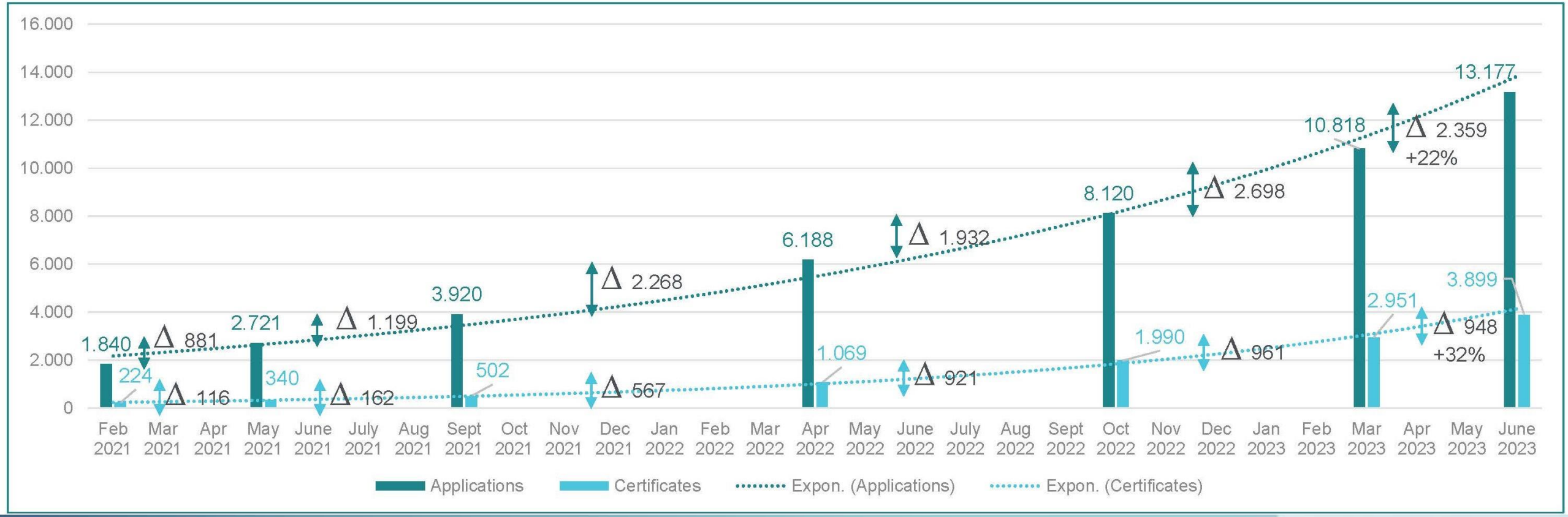
Quality Management Systems

- EU MDR doubles the on-site QMS inspection subjects vs. ISO13483(2016)

EUROPEAN UNION

June 2023
MDR Applications: 13.177
MDR Certificates: 3.899





CANADA – HEALTH CANADA

Market Clearance

- Many proposed amendments in review
- Multiple new draft guidances in development
  - Machine Learning & SaMD
  - Establishment Licensing
  - Device Classification
  - Agility for Emergencies
- eSTAR (electronic submission) pilot fully enrolled 2023-10-31
  - FDA joint applications & CA only
  - IMDRF Medical Device Table of Contents

Quality System

- **MDSAP** is alive and well and living in Canada, Brazil, Australia, Japan & USA
  - MDSAP **ISO 13485 (2016)** Certificate before Market Access as of 2019-01, *no more CMDCAS*
  - 13 Recognized providers
  - All Health Canada registrars are now authorized to perform Medical Device Single Audit Program audits

AUSTRALIA – TGA – THERAPEUTIC GOODS ADMINISTRATION

Market Clearance

- Comply with AUS MDR 2002
  - Essential Principals - Conformity
- TGA Application + Audit
  - Audit reduced with FDA PMA or EU-MDR Market Authorization
- ARG MD Update 2023-11-02
  - Additional recognition for EU-MDR Device & QMS certs
  - EU Device Codes & AE reports
  - Revised Market Access checklist
- Transparent process but complex

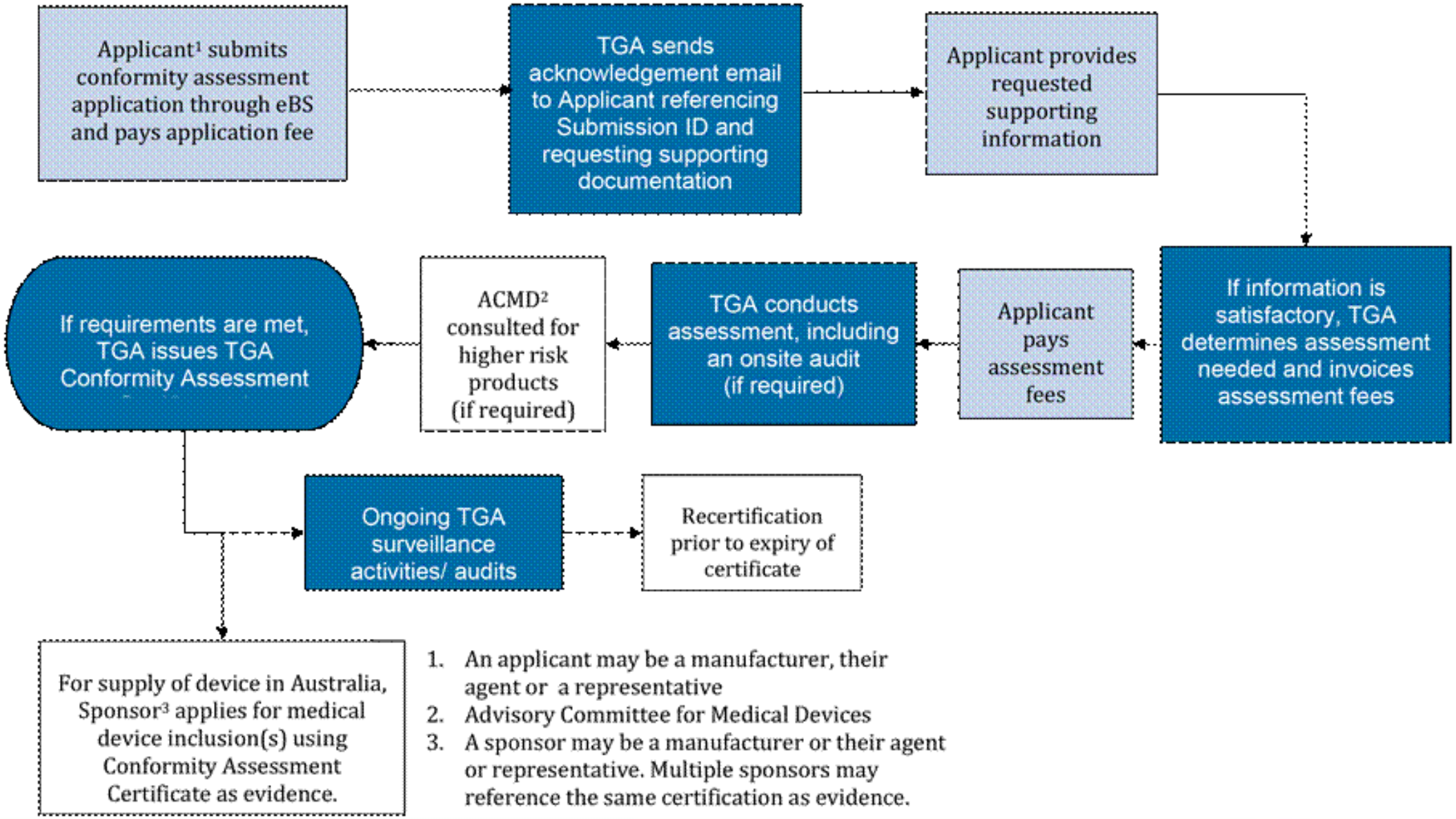
Revised Guidances

- Conformity Assessment application
- Software as a Medical Device
- Adverse Event reports
- Off-label use of Medical Devices
- Auditing of Medical Devices
- Device classification

Quality Systems – *Get a Certificate*

- See the Essential Principals Checklist
  - Risk Management
  - Biocompatibility
  - Clinical Evidence

Flowchart Describing the AUS TGA application process for Conformity Certification



1. An applicant may be a manufacturer, their agent or a representative
2. Advisory Committee for Medical Devices
3. A sponsor may be a manufacturer or their agent or representative. Multiple sponsors may reference the same certification as evidence.

LATIN AMERICA – THEY'RE ALL A LITTLE DIFFERENT

Brazil - ANVISA

- Very large market, 214M people
- *Member of MDSAP, IMDRF*
- High Risk Device requires registration
  - Tech File with expert assessment
  - Attention to measurement & electronics
  - Revalidation @ 10 yrs
  - Brazil GMP Certification

Columbia - INVIMA

- Large market, 51M people
- Local Representative
- QMS – GMP
- Application with Columbia-specific format

Mexico – COFEPRIS

- Very large market, 127M people
- Leverage Health Canada or FDA approval
- Import permit required for implantables
- *New regulations for Nano Materials & SaMD*
- QMS - ISO 13485 Certification required

Argentina - ANMAT

- Large market, 45M people
- Authorized Representative required
- Home Country Approval
- Essential Requirements Checklist
- QMS – GMP aligned with ANMAT
- Adverse event reporting

CHINA – AIMING FOR GLOBAL CLINICAL LEADERSHIP

Market Clearance - NMPA

- Since 2017, emphasis on lifecycle management
- International harmonization
  - Product registration dossier
  - Clinical data / evidence requirements
- Pathways to registration:
  - "on the exempt list"
  - Class II and III (like PMA products) CER
  - Overseas data accepted – if ethical, legal & scientific
  - Real-world data (2019)
  - Clinical Trials

Investments in Transparency

- Exempt List – 1000 medical devices
  - Mechanism of action – clear
  - Design & production – mature
  - No/low SAEs
  - Safe & effective with existing data support
- Technical Review – Chinese standards
  - Multiple observation endpoints
  - GMP

Real-world Data

- HaiNan Province RWD Zone Pilot 2018
- Published RWD guidance document

CHINA – PATHWAYS TO NMPA REGISTRATION

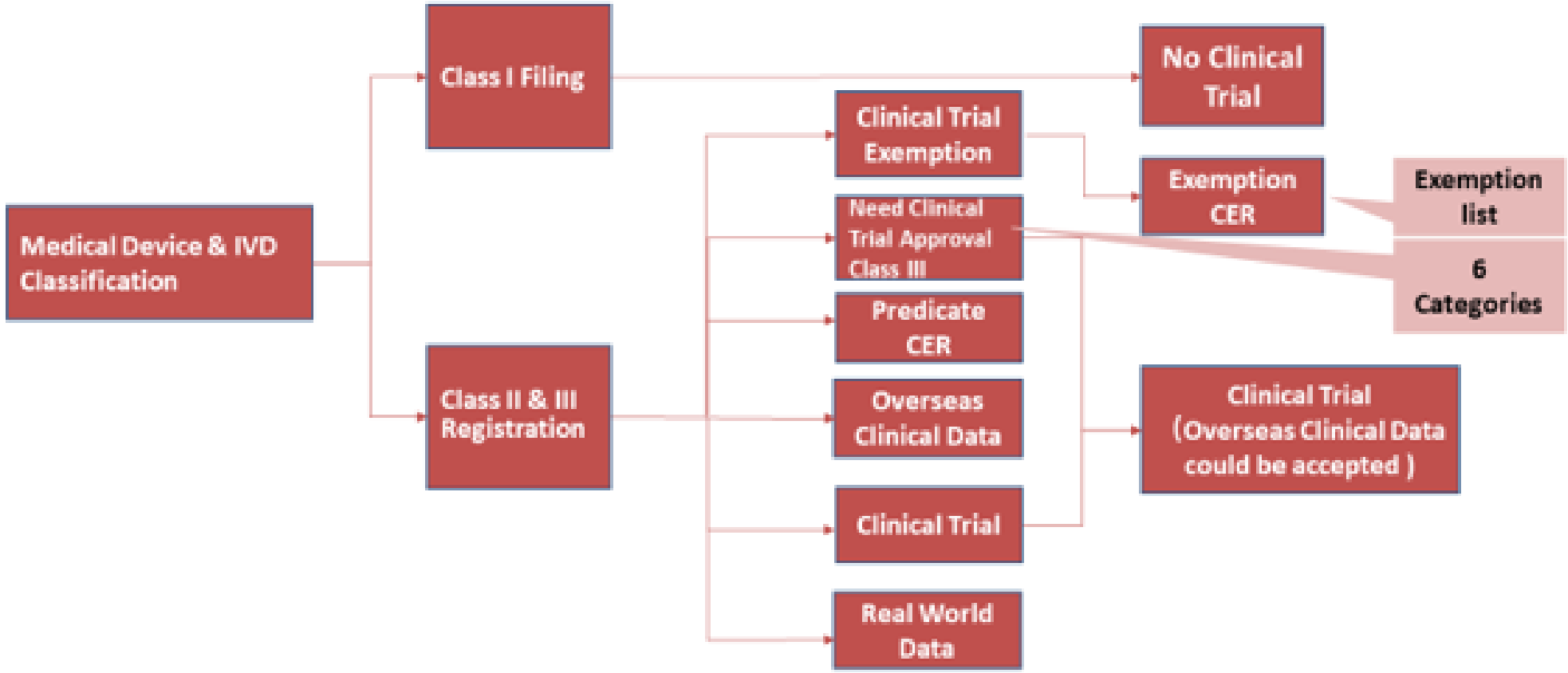


FIGURE Key clinical pathways and decision tree for device registrations with the China National Medical Products Administration.[9]

INDIA – ALL MEDICAL DEVICES "SOON TO BE FULLY REGULATED"

Market Clearance - CDSCO

- 2023-10-01 - Devices of all classification need a license
- Technical Dossier
  - device master record
  - factory file (GMP)
  - technical presentation
  - a 9-month review process.
- Apply to DCGI prior to registration
- Or get a "No Objective Certificate"
- Local agent required.

- Draft regulations for **device classification**
  - Class A & B import license with country of origin approval
  - Class B, C, & D *require clinical data*
  - Class D – High Risk (heart valves and other implantables)

CONCLUSIONS – SMALL COMPANY POINT OF VIEW

Common Issues

- Regulations are proliferating faster than harmonization as countries gain economic strength & need for medical devices
- Difficult to know all regional specifics in countries of commercial interest
- Fast Growth in post-market surveillance expectations – *but no one wants to pay for registries & infrastructure*
    - Patient Tokens?

Company Efficiencies

- More use of consultants & part time work
    - Stop growing the company head count
    - Provides access to regional specialists
    - Work-from-home technologies enable qualified specialists available off-site
- More emphasis on Matrix Management
    - Therapy specialists
    - Regional specialists
    - Surveillance specialists
- More use of information management systems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