Medtech: Global Regulatory Strategy in Medical Device Product Development

We contribute to healthcare

Asia Regulatory & Quality Consultancy
For Medical Device & Drug

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Regulatory & Quality Consultant
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Profile

May Ng

• Founder for ARQon (Asia Regulatory & Quality Consultancy), 3 years
• 2 years as Product Manager for In Vitro Diagnostics (IVDs), Poison & Radiation
• 10 years in Singapore Health Science Authority (HSA), established Singapore registration, approved ~1400 devices, key authoring guidances ie CSDT, GDPMDS.
• 4 years in Biosensors, Regulatory Director drug-eluting stent manufacturer for:
  o Product registration for Asia and global countries
  o Regulatory compliance from product design, manufacturing and distribution (DHF/DD/TF, Clinical trial, Customs, Labelling, Product & process change, Recall)
  o Site compliance from regulator audit (EU DEKRA, TUV SUD, TUV NORD, KR MFDS, AU TGA, JP PMDA, BZ ANVISA, SG HSA)

Education
• BSc (Biochem & Microbio) in UPM, MSc (Biomed. Eng) in NTU, Grad Dip (Medtech Manufacturing) in A*Star Simtech

External roles
• SMF-MTIG - Deputy Chair, MTIG and Program/SME
• ASEAN Medical Device Industry Association (ASEANMed) - Singapore Rep
• China-ASEAN Medical Cooperation Committee - Singapore Rep
• APACMed – MTIG Rep
• Trainer to Authorities: Taiwan FDA, Thai FDA, HK MDCO, S. Arabia FDA, others
• Past committees: AHWP, ACCSQ-MDPWG, ARPA, RAPro, PMO’s TEC
- **Global regulatory control**
- **Medical device definition**
- **Medical device design and development phases**
- **10 Regulatory Strategy considerations**
Global Harmonization

Management Committee (Regulators)
1. Australia
2. Brazil
3. Canada
4. China
5. EU
6. Japan
7. Russian Federation
8. Singapore
9. USA

Official Observers

Affiliate Organizations

World Health Organization

Pan American Health Organization

Asia Pacific Economic Cooperation

Life Sciences Innovation Forum

Regulatory Healthcare Steering Committee (APEC LSIF RHSC)

Global Harmonization Working Party

Below: Not affiliates. Information exchange
ASEAN AGREEMENT ON MEDICAL DEVICE DIRECTIVE

The Governments of Brunei Darussalam, the Kingdom of Cambodia, the Republic of Indonesia, the Lao People's Democratic Republic, Malaysia, the Republic of the Union of Myanmar, the Republic of the Philippines, the Republic of Singapore, the Kingdom of Thailand and the Socialist Republic of Viet Nam, Member States of the Association of Southeast Asian Nations (ASEAN), hereinafter collectively referred to as “Member States” or singularly as “Member State”;

MINDFUL that in the year 1992, the ASEAN Heads of Government declared that an ASEAN Free Trade Area (AFTA) shall be established in the region and that in 1995, they agreed to accelerate its implementation to the year 2003;

ASEAN
Medical Device Directive (AMDD)

Signed 21 Nov 2014
Enforced 1 Jan 2015
AEC 2015

AMDD
Each Member States Implementation to be ratified to ASEAN Secretariat by end 2019 (latest)
The AEC blueprint combines 625 million people into one integrated market and production base where the flow of goods, services, investments and skilled labour is free. Between 2008 and 2013, intra-regional trade jumped by 33 per cent from US$458.1 billion (S$637.9 billion) to US$608.6 billion.

What ASEAN will be saying in December is that most of the necessary measures for South-east Asia to evolve into an economically-integrated region have been taken. Since early this year, it has been claimed that as much as 97.3 per cent of traded products within the region are duty-free.

Measures still awaiting completion most importantly involve removing non-tariff barriers. The significant ones are simplifying custom procedures, harmonising standards, minimising multiple testing of products and labelling requirements.
Figure A4.5 Interrelation of (medical) products inside and outside health care

"Health technologies" refers to the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives. (WHA 60.29.)
‘Medical device’ means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices,
- providing information by means of in vitro examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

*Source: IMDRF*
1. Active implantable devices
2. Anaesthetic and respiratory devices
3. Dental devices
4. Electro mechanical medical devices
5. Hospital hardware
6. In vitro diagnostic devices
7. Non-active implantable devices
8. Ophthalmic and optical devices
9. Reusable devices
10. Single-use devices
11. Assistive products for persons with disability
12. Diagnostic and therapeutic radiation devices
13. Complementary therapy devices
14. Biologically-derived devices
15. Healthcare facility products and adaptations
16. Laboratory equipment
No one size fits ALL

Which countries to penetrate
- no regulation vs stringent regulation/regulators,
- local vs global

Regulatory requirements
- from design (Phase 1) to commercialization/post-market surveillance

Who do you need in the Product development team
- Engineering/Science, Clinical, Marketing, Regulatory

Estimating timeline – from concept (Phase 0) to commercialization
*Basic elements for medical devices legislation. Premarket, placing on the market and postmarket.

58% of WHO member states (of 194 countries) with regulation

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Medical Device Design and Development phases

0 Initiation, Concept & Feasibility
Regulatory Strategy

1 Design Phase
Regulatory review and documentation

2 Design Verification & Validation Phase
Regulatory Submission

3/4 Final Validation & Design Transfer Phase
Regulatory Approval

5 Post-Market Phase
Regulatory Surveillance & Vigilance reporting

**Regulatory strategy**
- Device Name
- Device Description
- Intended Use
- Country of Interest
- Device classification
- Product Registration/Timeline
- Technical Documentation
- Quality Management System
- Clinical Assessment
- Reimbursement Assessment

**Design freeze** early for target to market early, other features in next generation or revise Design input documents

- Country-specific tests, standards
- Clinical Evaluation planning
- Reimbursement planning for specific product
- Country-specific QMS, in addition to ISO13485
- Technical Documentation to build during design control phases
Medical Device Design and Development phases

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- Regulatory Strategy

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Regulatory strategy
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1. Device name
- As stated on the product labelling
- [Product Owner][Tradename][descriptor]
  eg. Biosensors BioMatrix drug coated balloon

2. Device description
- Device principles of operation for its intended purpose
- Substantial equivalent devices in the market, if any
  eg. Physical vessel opening or for drug delivery

3. Intended use
- Objective intends of the manufacturer regarding the use for the medical purpose
- Defined the device classification
  eg. treat, diagnose, aid
Sec. 890.5380 Powered exercise equipment.

(a) Identification. Powered exercise equipment consist of powered devices intended for medical purposes, such as to redevelop muscles or restore motion to joints or for use as an adjunct treatment for obesity. Examples include a powered treadmill, a powered bicycle, and powered parallel bars.

(b) Classification. Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter, subject to the limitations in 890.9.
4. Countries of Interest
- No/Least regulation vs stringent requirements
- Some with abridged approval process with predicate device, local made,
- Regional and international harmonization
- Eg 510k vs PMA, Hong Kong vs Singapore,

5. Device classification
- Lower to higher risk class: Class A, B, C, or D (IMDRF/ASEAN) and I, IIa, IIb, III (EU)
- Based on intended use and function of the device
- Risk posed to the patient and/or user
- Device class will determine:
  - Product registration
  - Technical Documentation
  - Quality management system
Countries of Interest

Medical device market

Source: Euromonitors
Product risk classification

Figure A4.1 Impact of device classification on regulatory scrutiny

Note: As the regulatory requirements increase, so does the scrutiny by the regulatory authority.
Source: Reproduced from Principles of medical devices classification (2).
Product risk classification

In Vitro Diagnostic Device

- Duration of device contact with the body
- Degree of invasiveness
- Body system affected
- Local vs. systemic effects
- Electrical/Active

Medical Device

- By test type (Intended use & indications)
- User & impact of results

List A (Class D)

List B (Class C)

Self-testing (Class C)

General (Class A, B, C, D)

Class III (Class D)

Class IIb (Class C)

Class IIa (Class B)

Class I (Class A)
Product risk classification – General Medical Device

Source: IMDRF
Product risk classification - In Vitro Diagnostic (IVD) medical device

Source: BSI
### Table A4.1 Examples of medical devices by risk class

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low</td>
<td>Syringes, examination gloves, patient hoists, stethoscopes, wheelchairs, IVD instruments, microbiological culture media</td>
</tr>
<tr>
<td>B</td>
<td>Low—moderate</td>
<td>Surgical gloves, infusion sets, pregnancy tests</td>
</tr>
<tr>
<td>C</td>
<td>Moderate—high</td>
<td>Condoms (unless with spermicide (class D)), infusion pumps, neonatal incubators, therapeutic and diagnostic X-ray, lung ventilators, haemodialysers, anaesthesia equipment, self-test glucose strips, IVDs for the diagnosis of Neisseria gonorrhoea</td>
</tr>
<tr>
<td>D</td>
<td>High</td>
<td>Implantable cardioverter defibrillators, pacemakers, breast implants, angioplasty balloon catheters, spinal needle, IVDs for the diagnosis of HIV, hepatitis C or hepatitis B</td>
</tr>
</tbody>
</table>

*The actual classification of each device depends on the claims made by the manufacturer for its intended use and the technology or technologies it utilizes. As an aid to interpreting the purpose of each rule, illustrative examples of medical devices that should conform to the rule have been provided in the table above. However, it must be emphasized that a manufacturer of such a device should not rely on it appearing as an example but should instead make an independent decision on classification taking account of its particular design and intended use.*
6. Product registration

- Exempted or registration
- Voluntary or Mandatory
- Abridged approval process with predicate device, local made
- Regional and international harmonization
- Green channel or priority route
- eg 510k vs PMA, Hong Kong vs Singapore
7. Technical Documentation

- Applies to all medical device
- Format based on EU MDD/MDR, GHTF STED, ASEAN CSDT (product information, risk management, Essential requirements related to preclinical, clinical, manufacturing, labelling)
- Country specific requirements – preclinical and local testing, local clinical trial, overseas manufacturing audit, local labelling, Legalization of documents, Country of Origin/Free Sale certificate

8. Quality management system

- No Certification or Certification required
- Organization structure, responsibilities, procedure, process, resources
- Certification for Manufacturer License and Product registration
### Global regulatory control

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>United States</th>
<th>Europe</th>
<th>Canada</th>
<th>Australia</th>
<th>Singapore</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philosophy</td>
<td>Risk based Classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Reg. Framework | • Food, Drug & Cosmetics Act 1976  
• Code of Federal Register (CFR) | • AIMD 90/385/EEC  
• MDD 93/42/EEC  
• IVDD 98/79/EEC  
• MDR & IVDR | • Food & Drugs Act  
• Medical Device Regulations | • Therapeutics Good Act 1989  
• Therapeutics Good (MDs) Regulations 2002 | • Health Products Act  
• Medical Device Regulations |
| Classification Systems | Class I (Exempt + General Controls)  
Class II (Gen + Special Controls)  
Class III (Gen + Special Controls+PMA) | Class I, IIA, IIB, III Class A, B, C, D (4 Classes)  
| Conformity Assessment | • Premarket Approval (PMA) by FDA  
• Premarket Notification (510k) by FDA and 3rd parties accredited by FDA  
• Quality System  
• Vigilance Reporting | • Evaluation by Notified Bodies  
• Conformity assessment/MQM S/ Type Testing  
• Vigilance Reporting | • Evaluation by Health Canada  
• Quality System (ISO13485 mandatory)  
• Vigilance Reporting | • Evaluation by Notified Bodies or Competent Authority for Class III, Combinations, Local manufactured  
• Conformity assessment/QMS/ Type Testing  
• Vigilance Reporting | • Full Evaluation  
• Abridged Evaluation (Benchmarked GHTF)  
• Quality System  
• Vigilance Reporting |
Global product registration

**Global/CE ASEAN**

- **CLASS I CLASS A**
  - Discussion to ascertain product class grouping, exemption/registration, documents, lead time

- **CLASS IIa CLASS B**
  - Preparation of Technical Documentation

- **CLASS IIb CLASS C**
  - Appoint Local Authorised Representative (ARQon)
    - Some countries require the AR/importer/distributor to have AR/importer/distributor licenses and/or certified Quality Management System

- **CLASS III CLASS D**
  - Product registration by Local Authorised Representative – Some countries require conformity assessment on manufacturers’ product and/or manufacturers’ QMS

**Product Approval**
Global Product registration – CE MDD

Medical Devices Directive 93/42/EEC Conformity Paths

- Annex 2
  - EC Declaration of Conformity
  - Full QA System Audit
  - EC Design Examination
  - Audit Decision
  - Surveillance

- Annex 2
  - EC Declaration of Conformity
  - Full QA System Audit Except EC Design Examination
  - Audit Decision
  - Surveillance

- Annex 3
  - CE Type Examination
  - CE Type Examination Certificate

- Annex 4
  - EC Verification Statistical Sampling
  - Surveillance

- Annex 4
  - EC Verification Product Testing
  - Surveillance

- Annex 5
  - EC Declaration Production QA System Audit
  - Surveillance

- Annex 6
  - EC Declaration Product QA System Audit
  - Surveillance

- Annex 7
  - EC Declaration of Conformity Class I Sterile or Measurement

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Global regulatory control – product lifecycle

Pre-market
- Dealer licence
  - Importer
  - Distributor
  - Registrant
  - Manufacturer
- Product licence
  - Notification
  - Registration
- Updates
  - Changes
  - Renewal
  - Periodic report

Post-market
- Complaint handling & records keeping*
- Distribution & records keeping*
- Adverse incident reporting*
- Field safety corrective action reporting*
- Advertisement permit (if applicable)

* Supporting role

RA and other depts.:
- R&D & Engineering
- Clinical
- Purchasing

Development:

Production:
- Production QA/Vendor
- Sales & Marketing
- Customer Service
- QA/Clinical
- Distributors
- Corporate

Distribution:

Product Use:

End-of-life:

Changes/Improvements

Raw materials

Waste
Global regulatory control – product lifecycle

RA and other depts.
- R&D & Engineering
- Clinical
- Purchasing

Development

Production
- QA/Vendor

Sales & Marketing
- Customer Service
- QA/Clinical
- Distributors

Corporate

Distribution

Product Use
- Sales & Marketing
- Customer Service
- QA/Clinical
- Distributors

End-of-life

Changes/Improvements

Pre-market

Post-market
- Complaint handling & records keeping*
- Distribution & records keeping*
- Adverse incident reporting*
- Field safety corrective action reporting*
- Advertisement permit (if applicable)

* Supporting role

Raw materials

Clinical trial*

Technical Documentation & review*

Standards Compliance*

Labelling

Clinical
- Special-access for hospital
- Emergency-access
- Custom-made device
- Refurbished device
- Parallel imports
- Re-export
- Hospital tender
- Reimbursement
- Personal Use

Non-clinical
- Sample not for human use eg. demo, marketing, test
Device Info

Device Name: Abbott AxSYM® Free PSA Assay (LN 7K54, LN 7K89) [Abbott]
Description: The AxSYM Free PSA assay is a Microparticle Enzyme Immunoassay (MEIA) for the quantitative measurement of free prostate specific antigen (PSA) in human serum. It is intended to be used in conjunction with the AxSYM Total PSA assay in men aged 50 or older with total PSA values between 4 and 10ng/mL and non-suspicious DRE to determine the % free PSA value. Can be used as an aid in discriminating between prostate cancer and benign disease. Use with Abbott AxSYM Analyzer.
Medical Specialty Area: Immunology
Medical Device Class: Class C IVD
Device Registration No: DE0000802
Registration Date: 09/06/2005
Change Notification Approval Date: 25/03/2014

Product Owner


Registrant

1. ABBOTT LABORATORIES (SINGAPORE ) PRIVATE LIMITED 3 FRASER STREET, DUO TOWER, #23-28, SINGAPORE 189352

Imported By

No records found

Models

<table>
<thead>
<tr>
<th>No.</th>
<th>Model Name</th>
<th>Identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Reagent Pack</td>
<td>LN 7K54-20</td>
</tr>
<tr>
<td>2</td>
<td>Master Calibrators</td>
<td>LN 7K54-30</td>
</tr>
<tr>
<td>3</td>
<td>Controls</td>
<td>LN 7K89-10</td>
</tr>
<tr>
<td>4</td>
<td>Calibrators</td>
<td>LN 7K89-01</td>
</tr>
</tbody>
</table>
9. Clinical assessment

- Literature, Clinical experience and/or Clinical investigation/trial?
- Assessment and analysis of clinical data for the clinical safety and performance

=> Clinical Evaluation report

10. Reimbursement assessment

- Reimbursement approval to supply in the government hospital and selling price
- Government healthcare payment infrastructure for the use of the device and treatment method
- Controlled by Health Technology Assessment authority

=> Core Value Dossier (for new reimbursement code)
Other considerations

- Project and Documentation workplan
- Teamwork
- Regulatory Strategy
- Marketing Strategy
- Awareness on changes on regulatory, technology and IP
"Sure, it's a great invention, but does it comply with all government guidelines?"
Contacts & Thank you

Key offices: HQ-Singapore, ASEAN-Malaysia, Vietnam, ASIA- Taiwan, AU-Victoria, EU-Switzerland, US - California

Partners: CHINA-Guangzhou, Shanghai, JAPAN-Tokyo, LAMER – Brazil, MIDDLE EAST/N.AFRICA-Dubai, GLOBAL

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