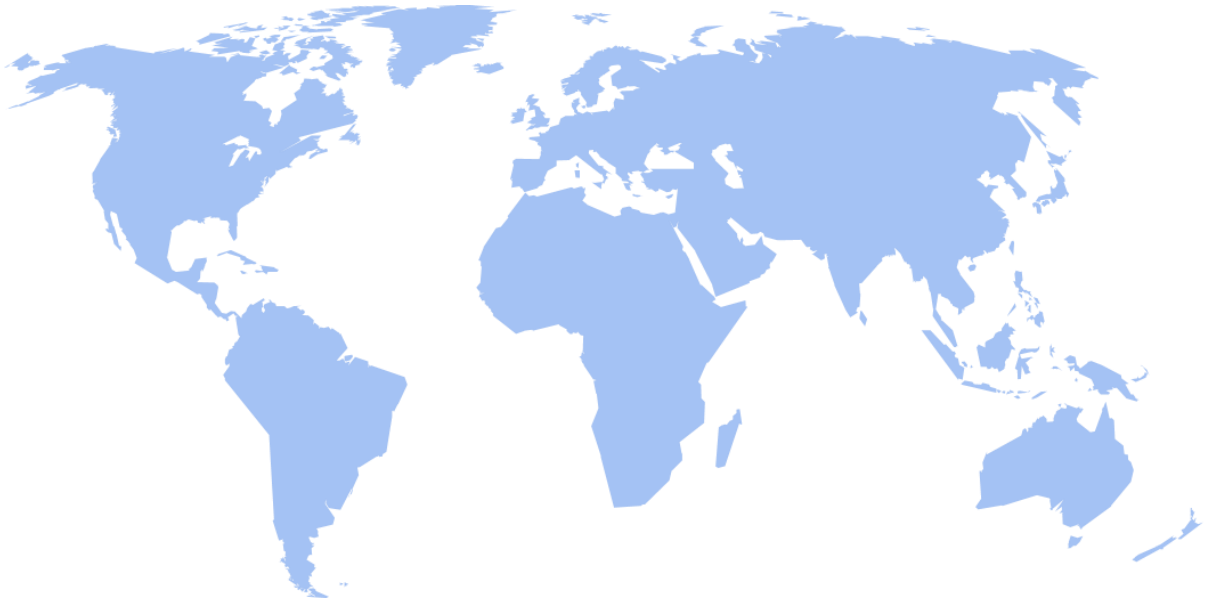


Medtech: Global Regulatory Strategy in Medical Device Product Development

We contribute to healthcare

Asia **R**egulatory & **Q**uality **Con**sultancy
For Medical Device & Drug

May Ng

Director,
Regulatory & Quality Consultant
may.ng@arq-on.com

Disclaimer:

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**:
  - ***Product registration*** *for Asia and global countries*
  - ***Regulatory compliance*** *from product design, manufacturing and distribution (DHF/DD/TF, Clinical trial, Customs, Labelling, Product & process change, Recall)*
  - ***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

CONTENT

- Global regulatory control
- Medical device definition
- Medical device design and development phases
- 10 Regulatory Strategy considerations

Global Harmonization

IMDRF International Medical Device Regulators Forum

Official Observers

World Health Organization

Asia Pacific Economic Cooperation
Life Sciences Innovation Forum
Regulatory Healthcare Steering Committee (APEC LSIF RHSC)

Management Committee (Regulators)

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

Affiliate Organizations

Pan American Health Organization

Asia Harmonization Working Party

Below: Not affiliates. Information exchange

Global Medical Technology Alliance
Innovating for a Healthier World

DITTA GLOBAL DIAGNOSTIC IMAGING, HEALTHCARE IT & RADIATION THERAPY TRADE ASSOCIATION

OECD

APACMed ASIA PACIFIC MEDICAL TECHNOLOGY ASSOCIATION

RAPS REGULATORY AFFAIRS PROFESSIONALS SOCIETY
Driving Regulatory Excellence™

ASEAN MDD

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)

ASEAN MDD

comment & analysis

CAN GROUPING KEEP PACE WITH THE WORLD?

Why ASEAN's integration is through the economic route

OOI KEE BENG

Just 20 months short of turning half a century old, the Association of South-east Asian Nations (ASEAN) will officially become an integrated community. On Dec 31 this year, rotating ASEAN chair Malaysia

been and will continue to be in the field of economics. ASEAN has been ambitious and proactive in creating a common market and production base. Other areas of integration, however, by comparison and by design, take a backseat, and events there have been more ad hoc and opportunistic.

Given the way things work in this part of the world, understanding this reality requires a historical take that highlights the region's uniqueness.

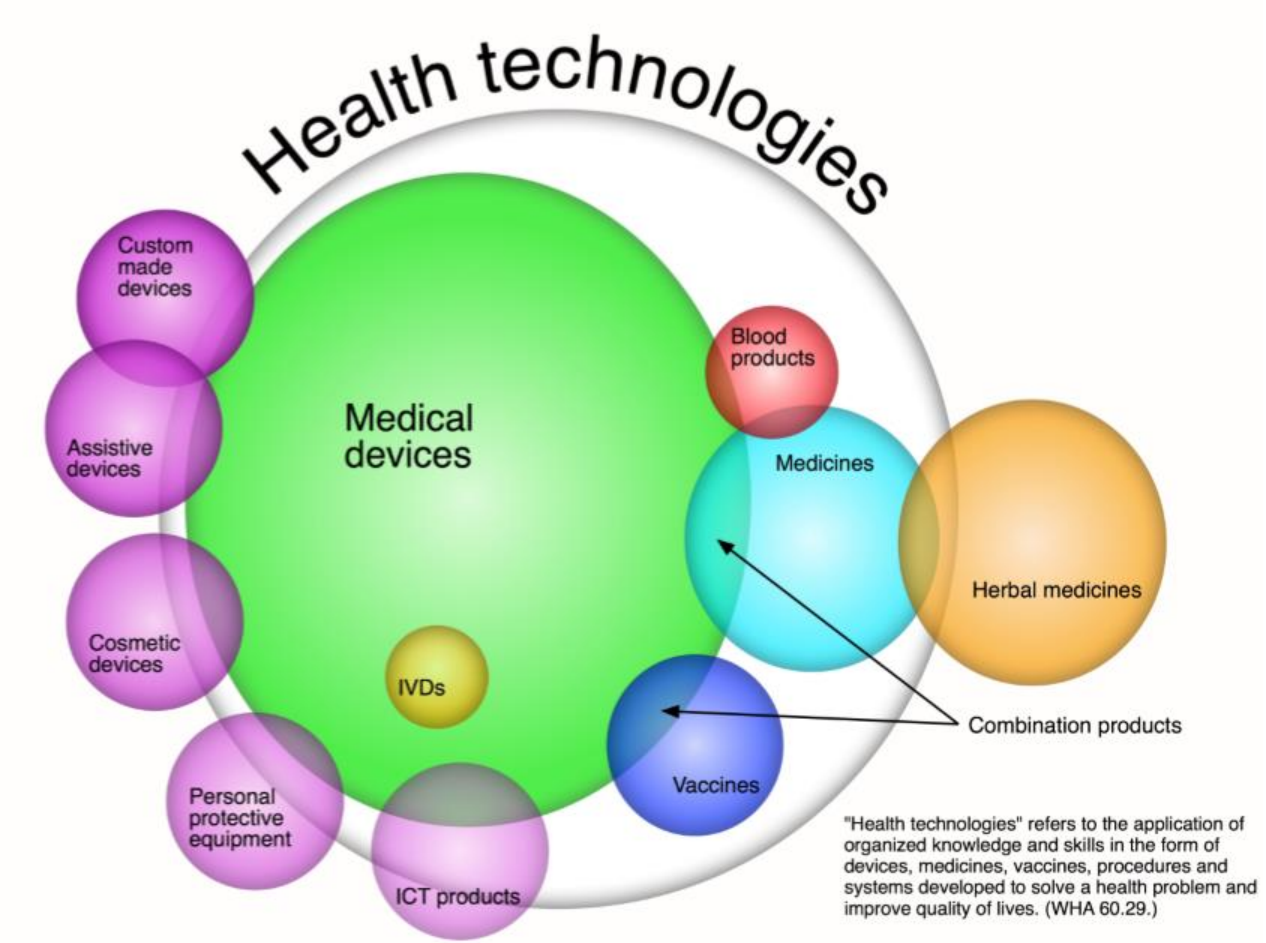
The AEC blueprint combines 625 million people into one integrated market and production base where the flow of goods, services, investments and skilled labour is free. Between 2008 and 2013, intra-regional trade jumped by 33 per cent from US$458.1 billion (S$637.9 billion) to US$608.6 billion.

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. As

Medical Device Definition

Figure A4.5 Interrelation of (medical) products inside and outside health care



Medical Device Definition

'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:

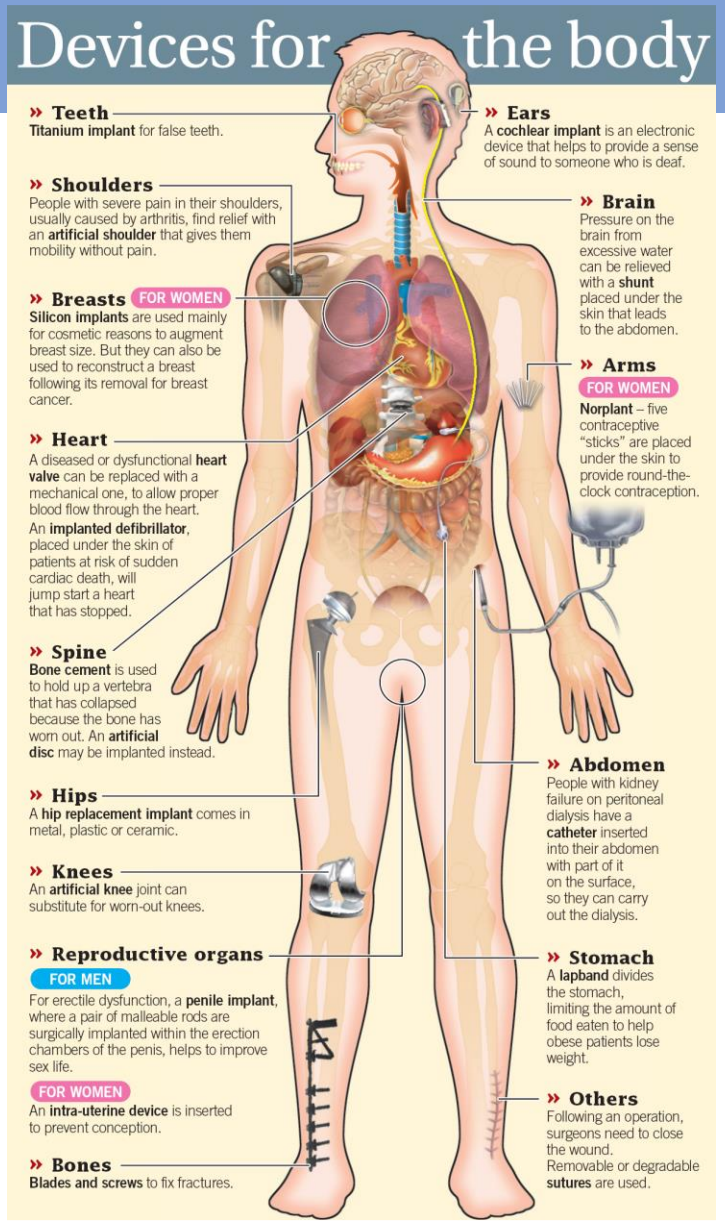
- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of 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

Medical Device Categories

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



Source: Strait Times

Why Regulatory Strategy & Why GLOBAL?

- **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

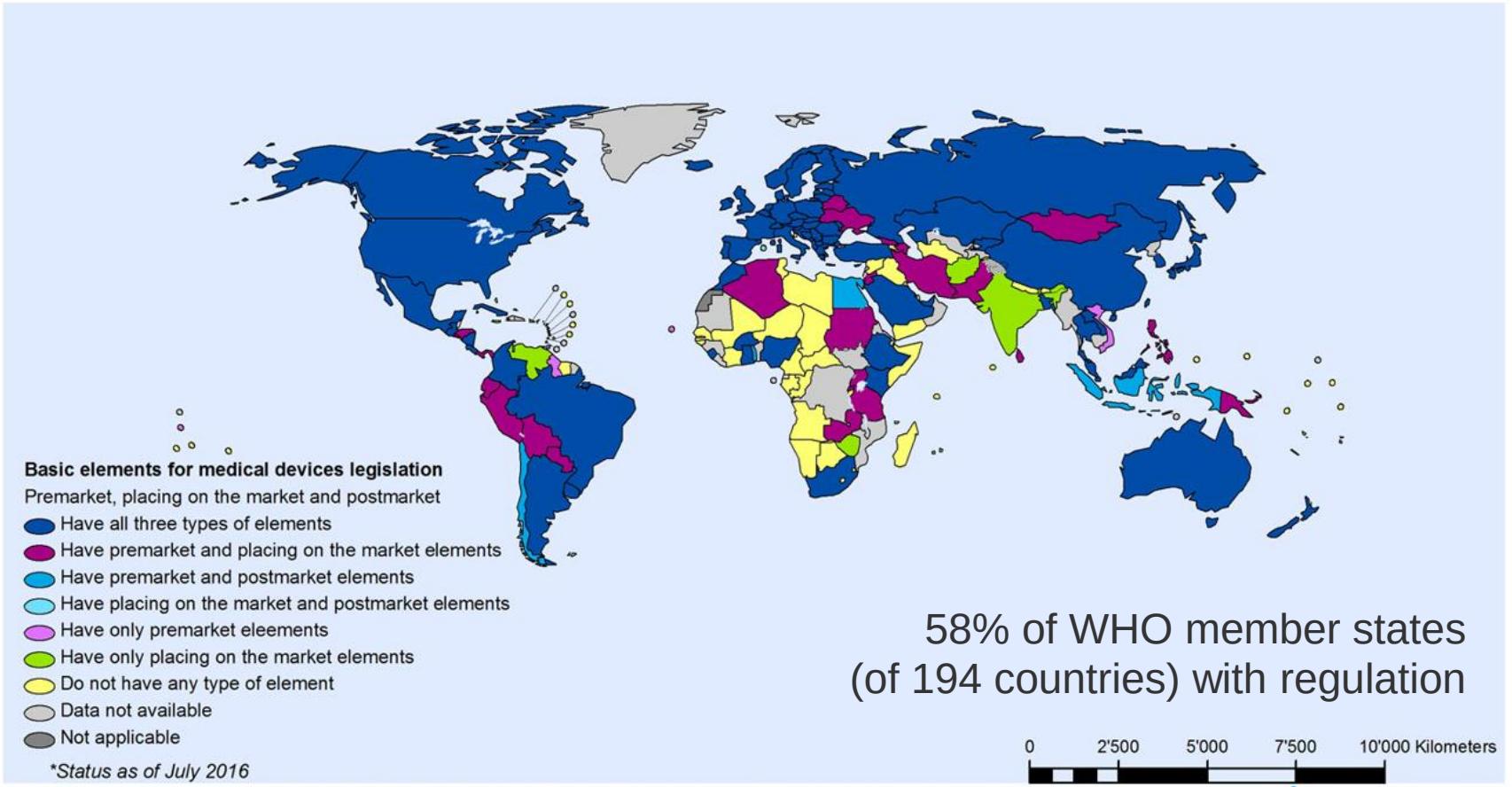
- **Who do you need in the Product development team**

  - Engineering/Science, Clinical, Marketing, Regulatory

- **Estimating timeline** – from concept (Phase 0) to commercialization

Global regulatory control

***Basic elements for medical devices legislation.**
Premarket, placing on the market and postmarket.



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.

Data Source: WHO Regulatory Status desk survey
July 2016 update
Map Production: Department of Essential Medicines and Health Products
World Health Organization

World Health Organization

Medical Device Design and Development phases

0 Initiation, Concept & Feasibility

Regulatory Strategy

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

1 Design Phase

Regulatory review and documentation

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

2 Design Verification & Validation Phase

Regulatory Submission

3/4 Final Validation & Design Transfer Phase

Regulatory Approval

- 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**

5 Post-Market Phase

Regulatory Surveillance & Vigilance reporting

Medical Device Design and Development phases

0 Initiation, Concept & Feasibility

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5 Post-Market Phase

Regulatory Surveillance & Vigilance reporting

Considerations in Regulatory Strategy

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

Intended use

New Search | Help | More About 21CFR

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of April 1, 2016]
[CITE: 21CFR890.5380]

See Related Information

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

PART 890 -- PHYSICAL MEDICINE DEVICES

Subpart F--Physical Medicine Therapeutic Devices

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.

Source: US FDA

Considerations in Regulatory Strategy

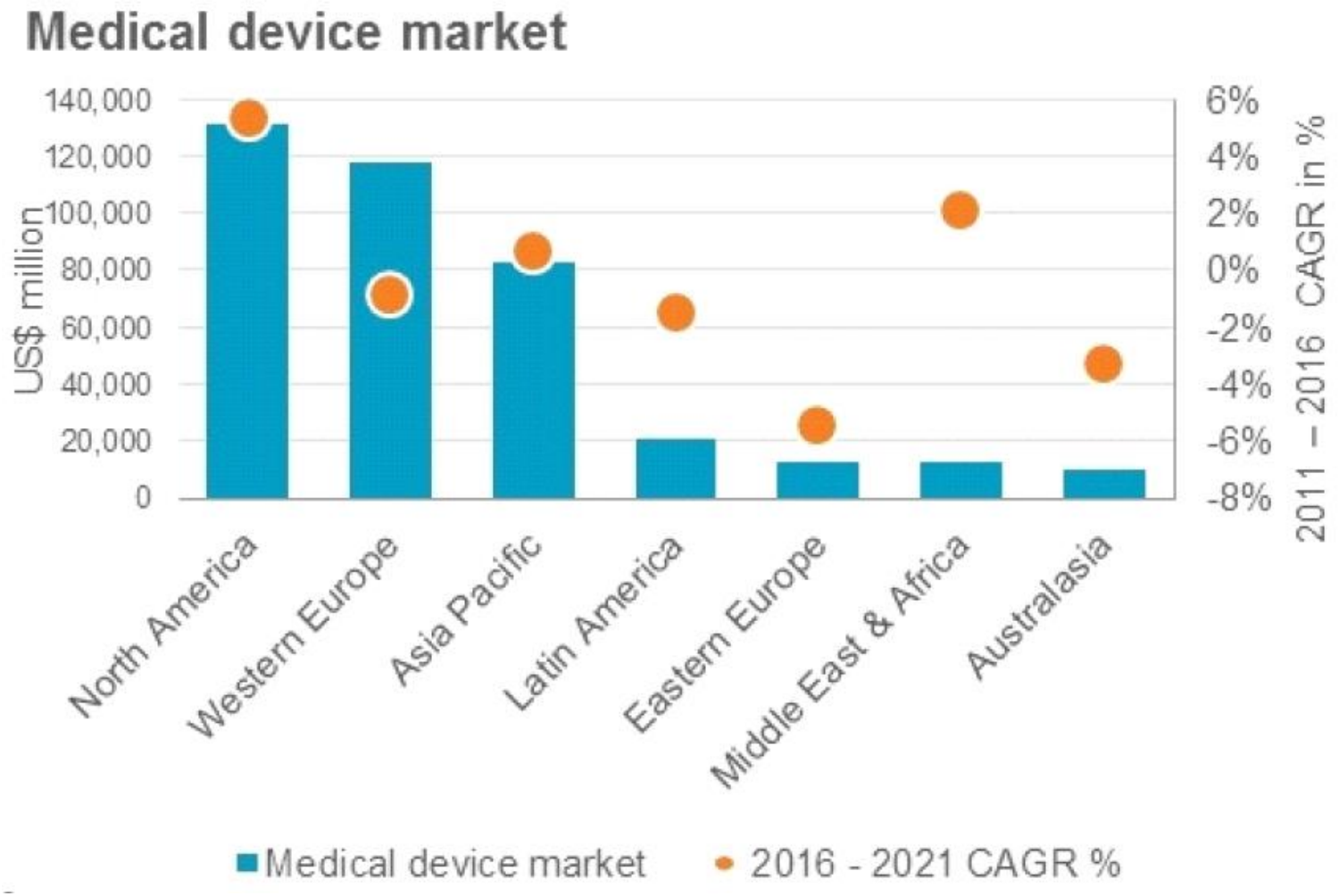
4. Countries of Interest

- 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**

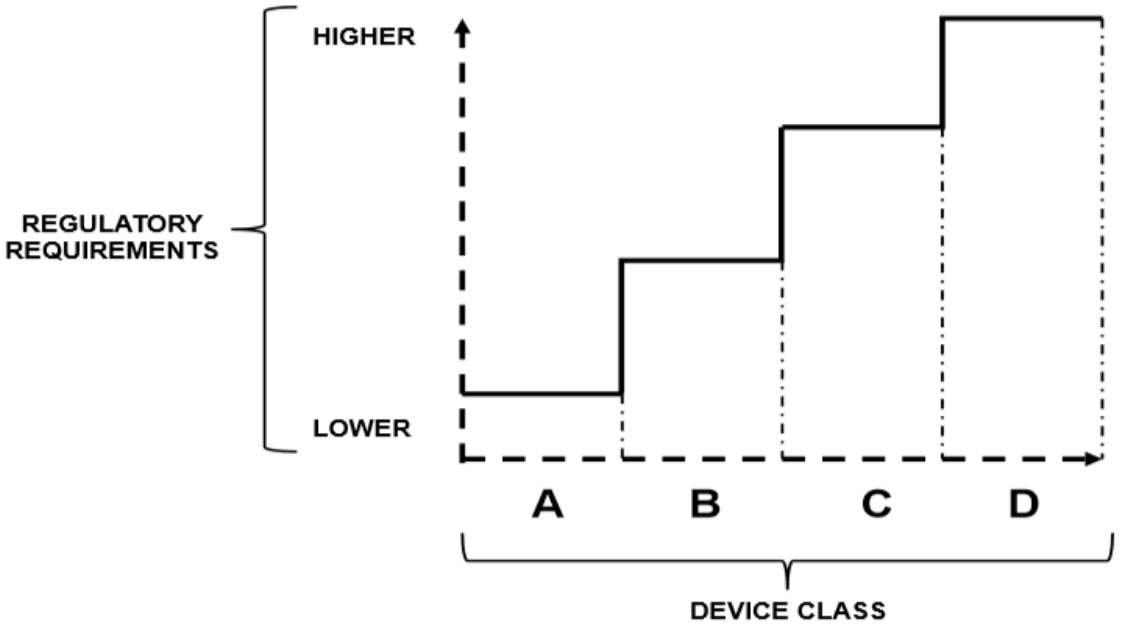
Countries of Interest



Source: Euromonitors

Product risk classification

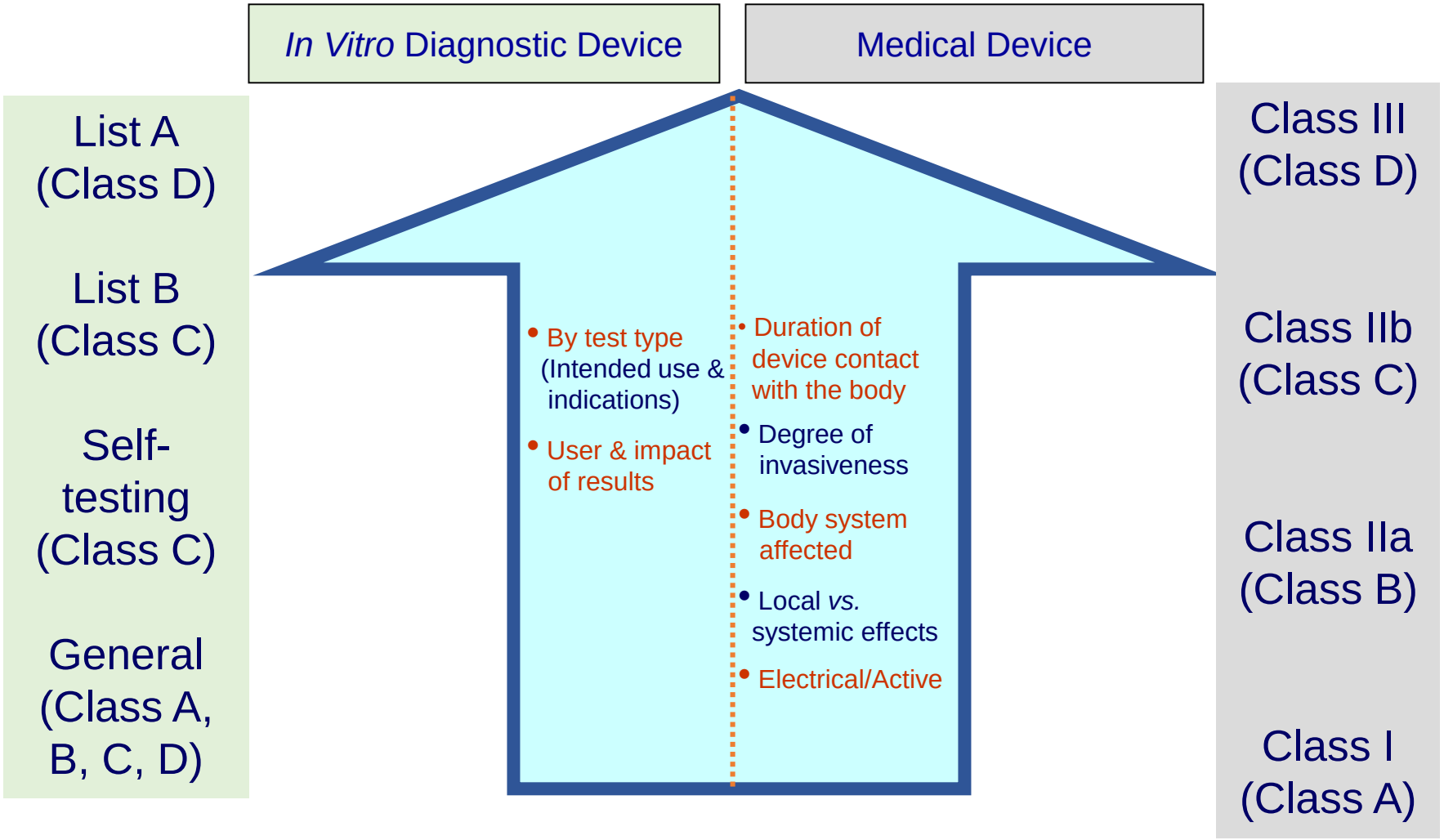
Figure A4.1 Impact of device classification on regulatory scrutiny



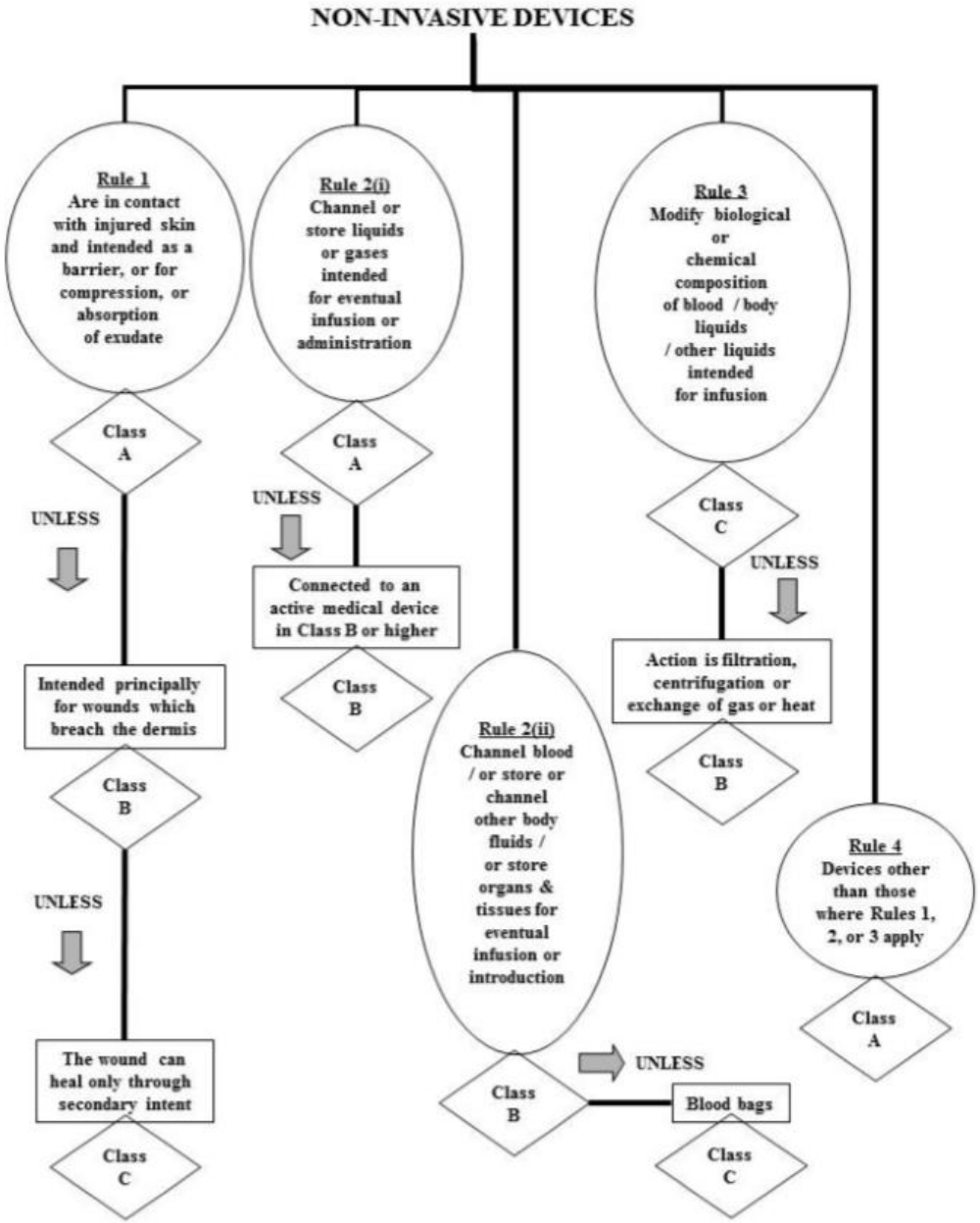
Note: As the regulatory requirements increase, so does the scrutiny by the regulatory authority.
Source: Reproduced from Principles of medical devices classification (2).

Source: IMDRF

Product risk classification

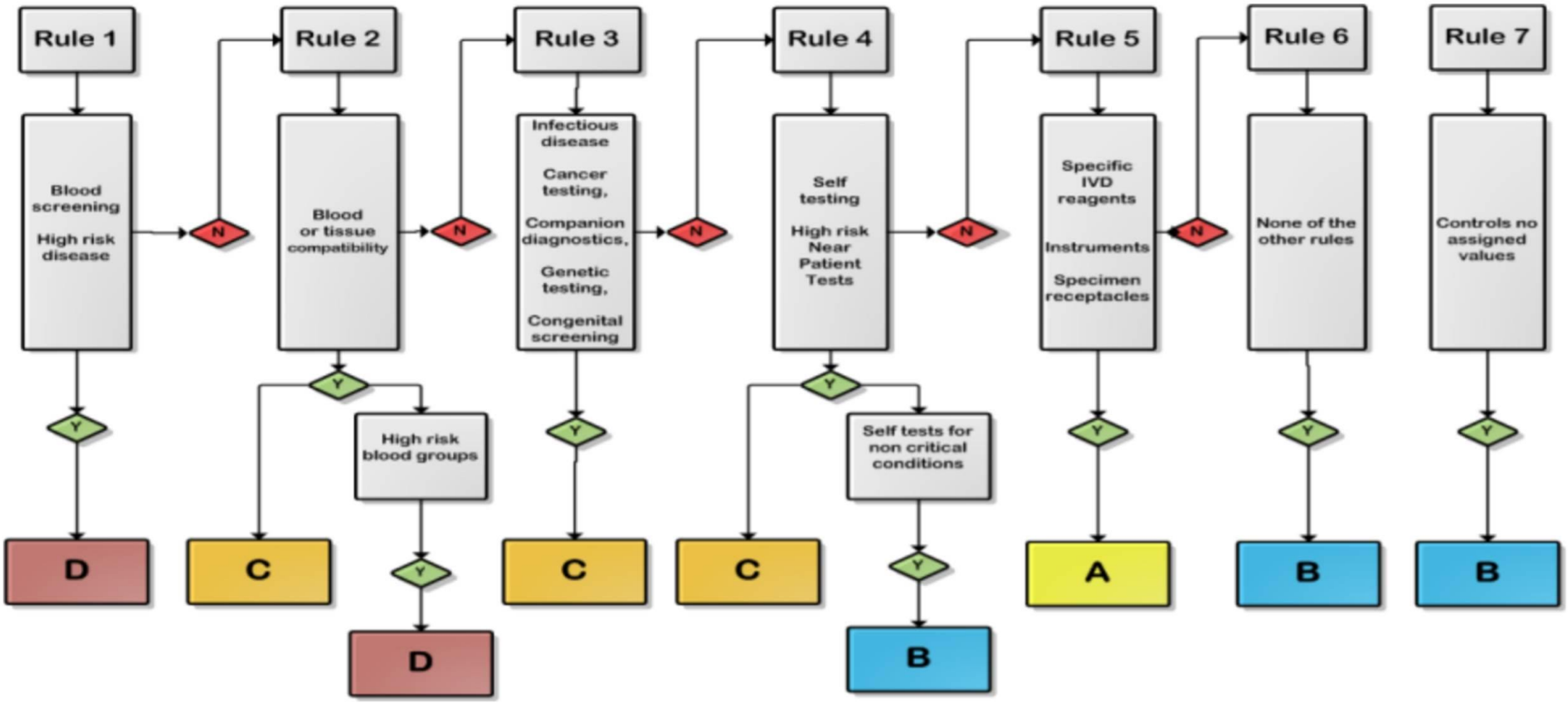


Product risk classification – General Medical Device



Source: IMDRF

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



Source: BSI

Product risk classification - Overall

Table A4.1 Examples of medical devices by risk class[a]

Class	Risk	Examples
A	Low	Syringes, examination gloves, patient hoists, stethoscopes, wheelchairs, IVD instruments, microbiological culture media
B	Low–moderate	Surgical gloves, infusion sets, pregnancy tests
C	Moderate–high	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
D	High	Implantable cardioverter defibrillators, pacemakers, breast implants, angioplasty balloon catheters, spinal needle, IVDs for the diagnosis of HIV, hepatitis C or hepatitis B

[a] 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.

Source: IMDRF

Considerations in Regulatory Strategy

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

Considerations in Regulatory Strategy

7. Technical Documentation

- Applies to all medical device
- Technical documentation – Technical File/Design Dossier (CE), Design History File (US), Country dossier
- 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

COUNTRY	United States	Europe	Canada	Australia	Singapore
Philosophy	Risk based Classification				
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)	Class I, II, III, IV (4 Classes)	Class I, IIA, IIB, III Class A, B, C, D (4 Classes)	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/MQMS/ 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	CLASS IIa CLASS B	CLASS IIb CLASS C	CLASS III CLASS D

Discussion to ascertain product class grouping, exemption/ registration, documents, lead time

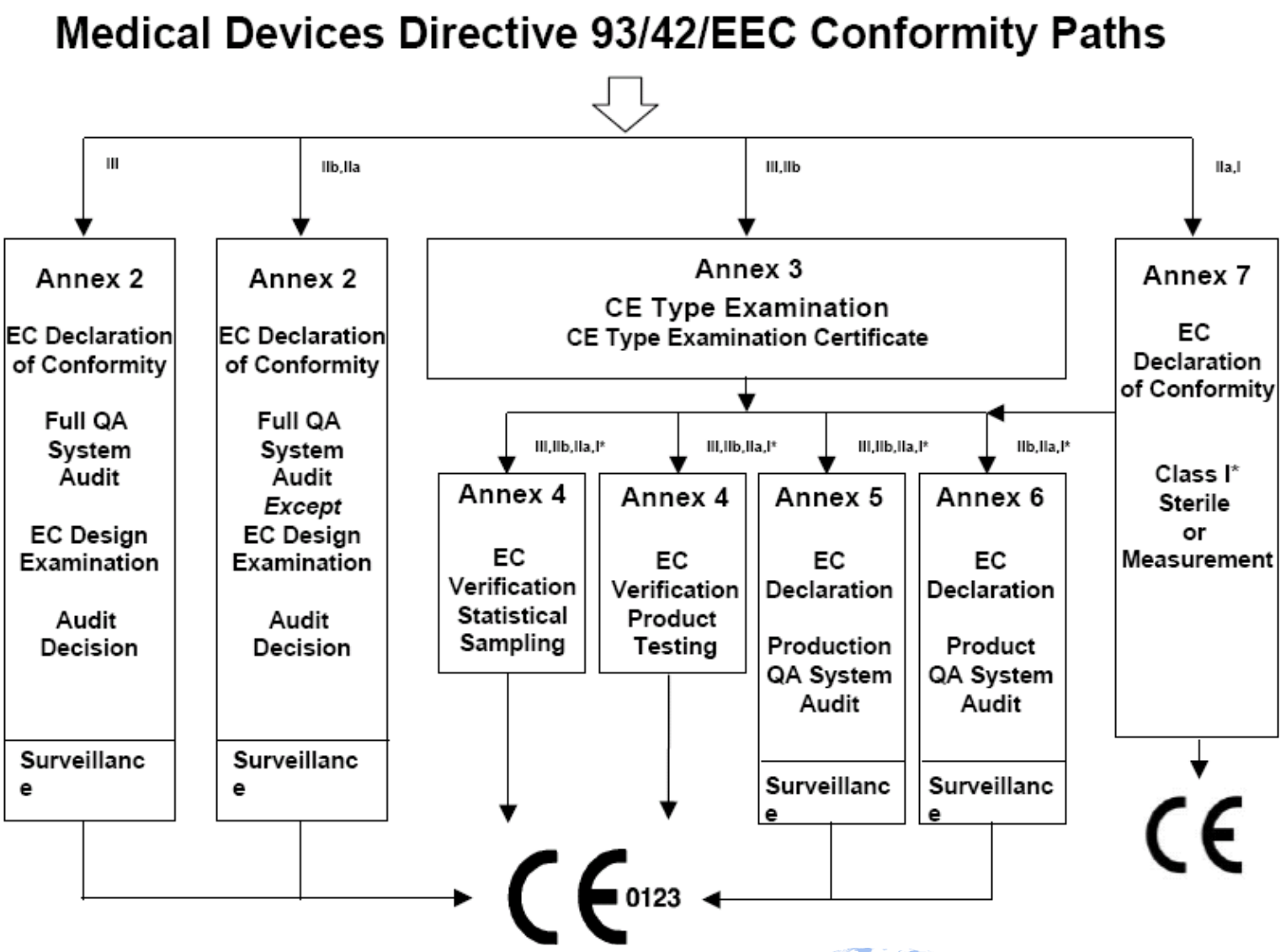
Preparation of Technical Documentation

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

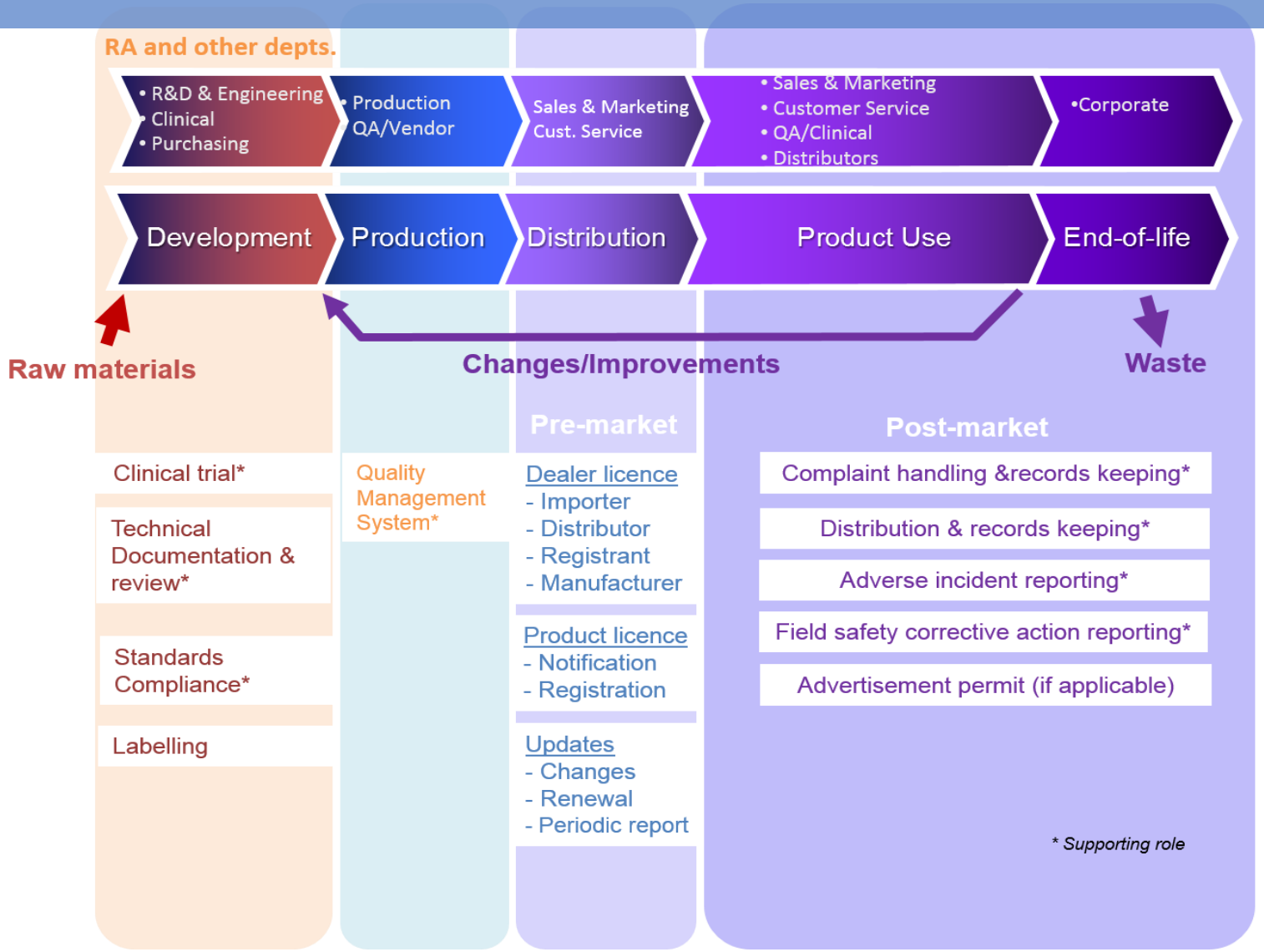
Product registration by Local Authorised Representative – Some countries require conformity assessment on manufacturers' product and/or manufacturers' QMS

Product Approval

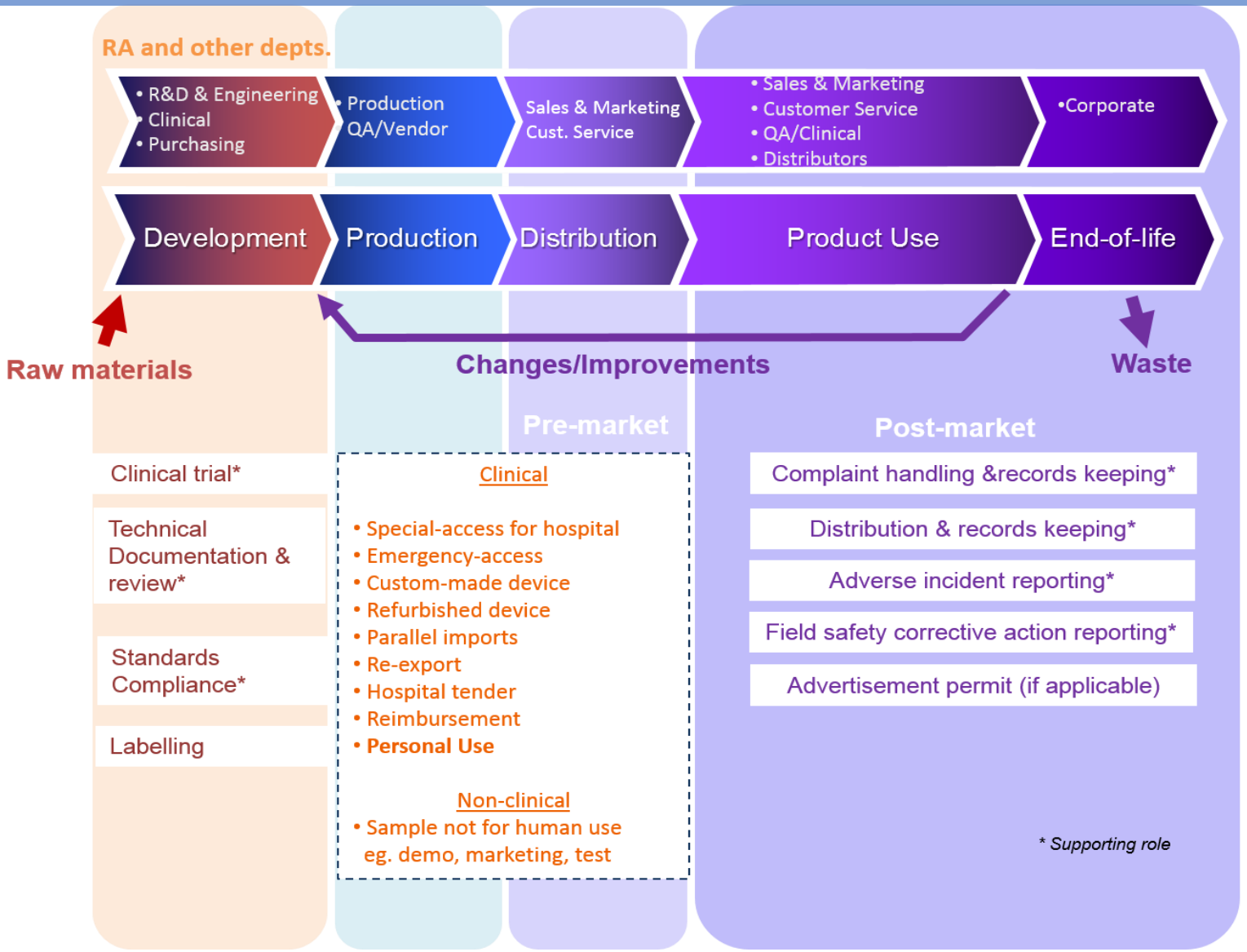
Global Product registration – CE MDD



Global regulatory control – product lifecycle



Global regulatory control – product lifecycle



PUBLIC ENQUIRY - SINGAPORE MEDICAL DEVICE REGISTER (SMDR)

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

1. Abbott Ireland Diagnostics Division [Abbott] Finisklin Business Park, Sligo, IRELAND

Registrant

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

Imported By

No records found

Models

No.	Model Name	Identifier
1	Reagent Pack	LN 7K54-20
2	Master Calibrators	LN 7K54-30
3	Controls	LN 7K89-10
4	Calibrators	LN 7K89-01

Take Home Message & Challenges to Penetrate ASEAN/Asia

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**

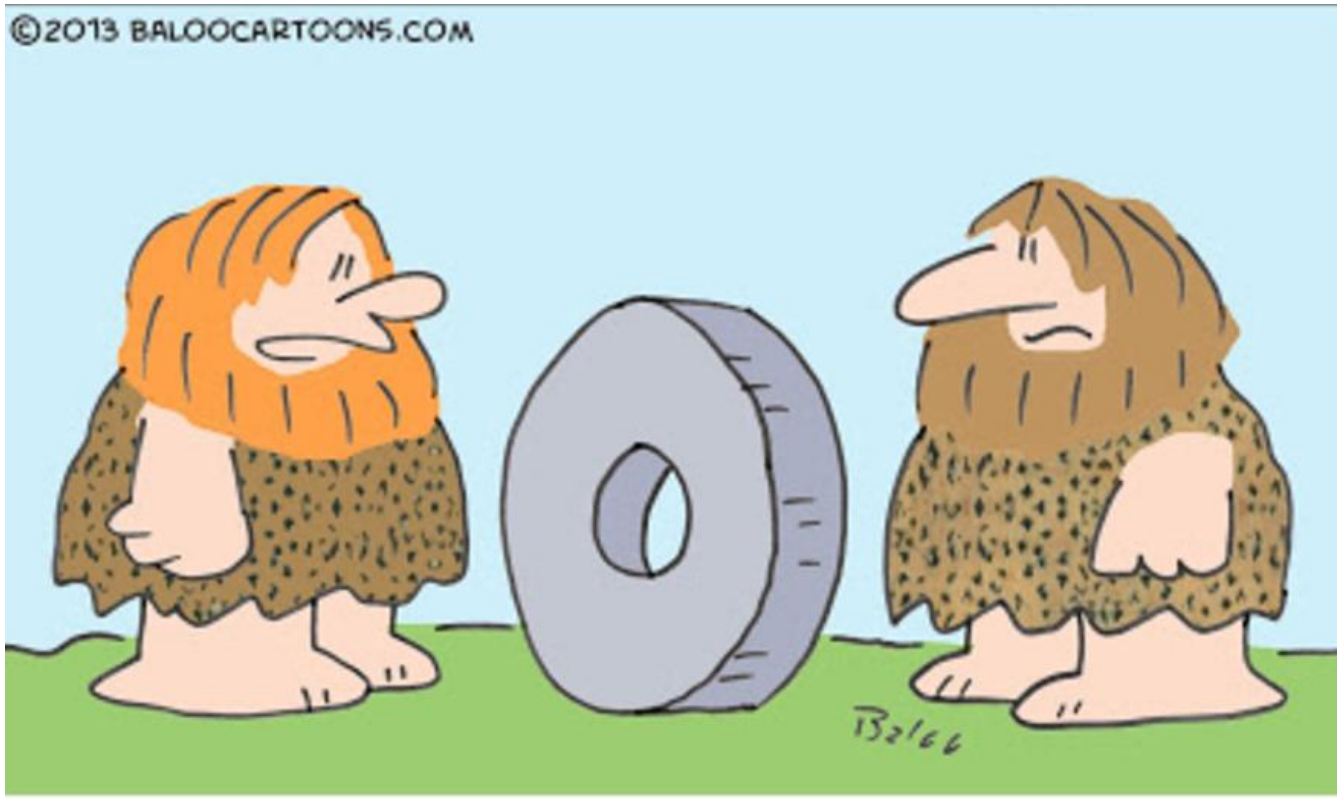
10. Reimbursement assessment

- 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

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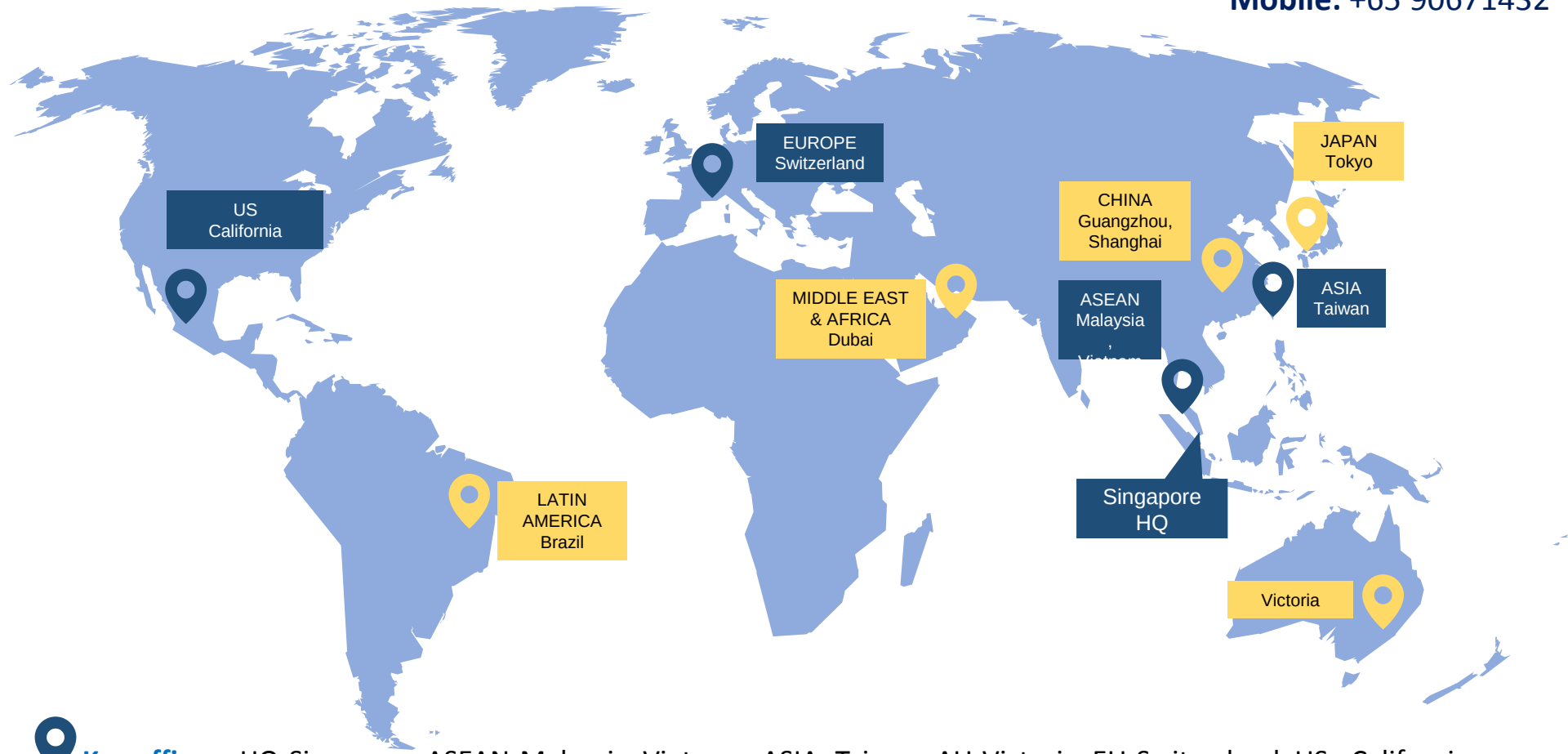
Mobile: +65 90671432



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