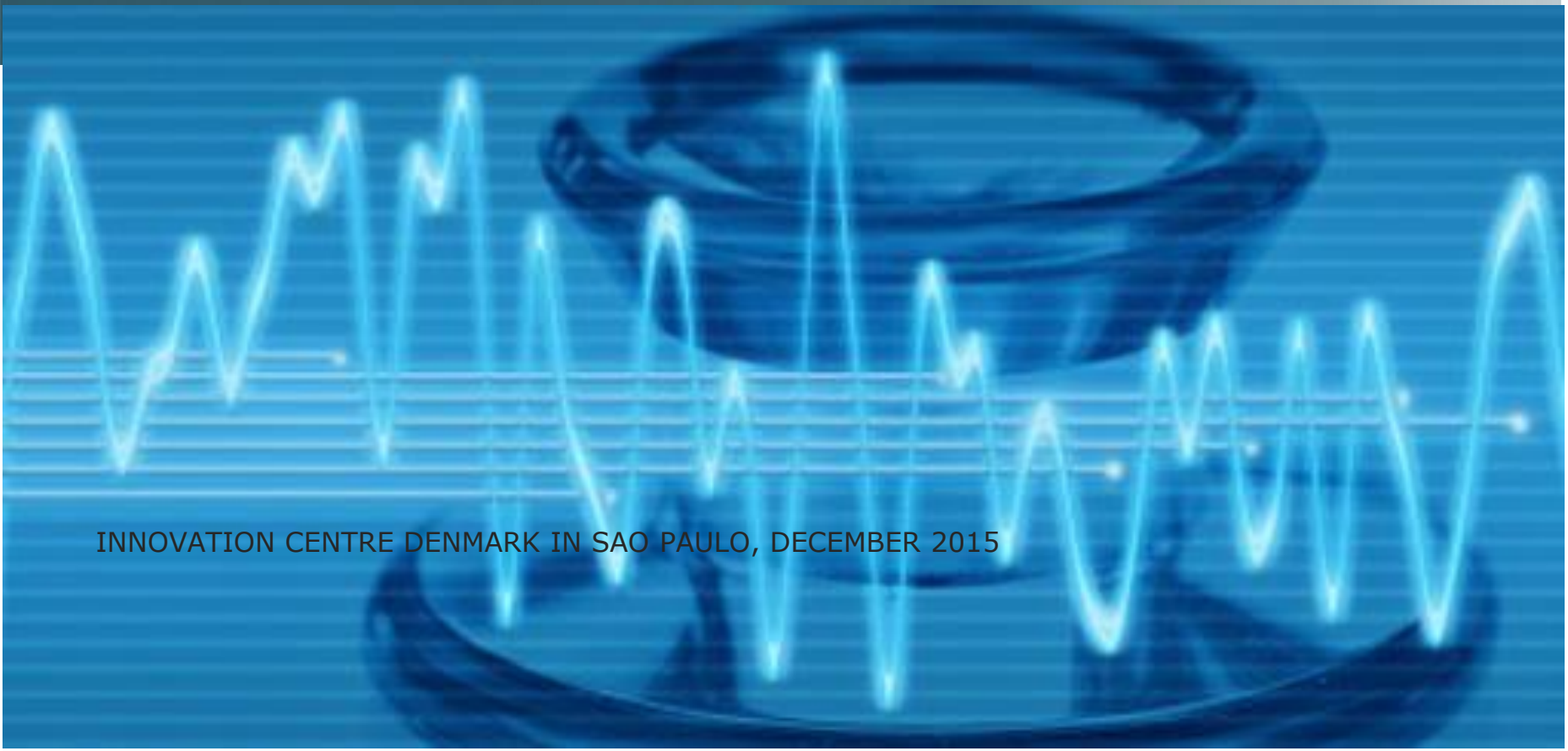
REGULATION AND BUSINESS MODEL STRATEGIES FOR MEDICAL DEVICES CLASS I + II IN BRAZIL



INNOVATION CENTRE DENMARK IN SAO PAULO, DECEMBER 2015

A PARTNERSHIP BETWEEN
THE MINISTRY OF HIGHER EDUCATION AND SCIENCE
AND THE MINISTRY OF FOREIGN AFFAIRS OF DENMARK

CONTENT

1: BRAZILIAN MEDICAL DEVICE CLASSIFICATION

- Is similar to the European CE, but NOT equivalent, meaning that CE marking does not give authorization to enter Brazil
- Requirements are changing on a frequent basis, so what was true one year ago may not any longer be applicable – make sure to understand the process, time lines and costs before you work deeper with the Brazilian market

2: KEY CONCEPTS IN THE REGISTRATION PROCESS OF MEDICAL DEVICES IN BRAZIL

- **ANVISA**: the Brazilian National Health Surveillance Agency that evaluates applications of drugs and medical devices for the Brazilian market

- **INMETRO CERTIFICATE**: Necessary for electro-medical products. Tests performed outside Brazil by an ILAT-certified lab is usually accepted (CB Scheme not). Tests cannot be more than 2 years old. Certificate valid for five years, annual audits and fees necessary

- **Brazilian Good Manufacturer Practice (B-GMP)**: similar to ISO13485, inspection needed for Class 3 + 4 medical devices, compliance needed for Class 1 + 2

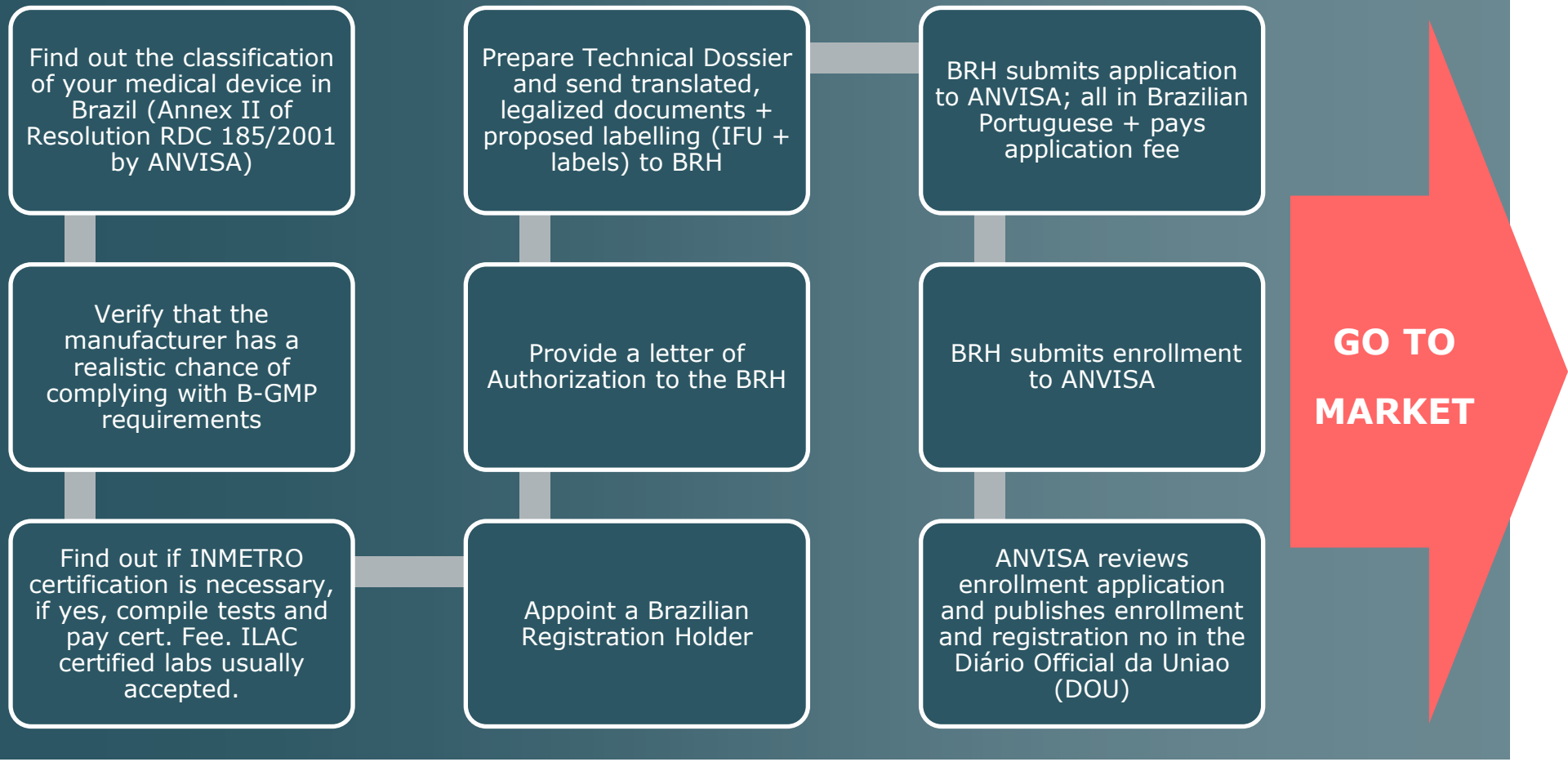
- **BRH, Brazilian Registration Holder**: the responsible company vis-a-vis ANVISA of your product and the ”owner” of the registration in Brazil. Choosing BRH partner in Brazil is an important strategic decision

3: BRAZILIAN MEDICAL DEVICES - OVERVIEW OF TIME LINES AND FEES

	Time to register *	ANVISA fee**	Fees for inspection of compliance with Brazilian Good Manufacturing Practices (B-GMP)	INMETRO fee***	Expiration of registration	List of requirements for enrolment/registration
Class I + II	2 – 6 months	BRL 90 - 1,800	N/A. According to regulation of 2014, Class I and II devices must comply with Brazilian Good Manufacturing Practices, but inspection is not conducted. Brazilian GMP resembles ISO 13845, and the manufacturer must be able to present GMP certificate or similar from local authority	BRL 14,000 – 43,000	Does not expire. Changes in BRH cannot be made for commercial reasons	- Form containing the manufacturer or importer data, according to resolution RDC no. 185/2001 - Proof of payment of Health Inspection Fee (BRH) - Information on the product (identifcation, specification, origin) - Graphic images of product - Labeling template - Instruction for Use - Technical Report (detailed description of the medical product: principle of operation and its action, its content/composition, list of accessories intended to be part of the product, indication, purpose of use, precautions, restrictions, warnings, special care, storage, transport, dosage forms, brief description of each step of the manufacturing process, description of efficacy and safety - Comparative chart containing the similarities and differences - INMETRO Certificate of Compliance (if applicable) Especially for class 3 + 4 - Letter of authorization of the manufacturer for the applicant for the registration of the product in Brazil (for class II and IV products) - Certificate of Free Sale – CFS - Good Manufacturing Practies Certificate – GMPC
Class III + IV	6 – 8 months (but the line for inspections can make registration considerably longer!)	BRL 600 – 20,000	Manufacturers must be audited for B-GMP, resembling ISO 13485 Audits in Brazil or Mercosur: BRL 2,200 – 44,000*. Audits in other countries: BRL 109,000.		Expires after five years. Registration renewals must be initiated 12 months before expiration, min 6 months ahead. Expiration is an opportunity to change BRH if desired and contractually possible	

* Estimates, may take longer if documentation is considered insufficient by ANVISA, or owing to backlog at ANVISA
**The price depends on the size of the Brazilian Register Holder, that is the company that registers/enrol the medical device. Prices are from 2015 and are

4: BRAZILIAN MEDICAL DEVICES REGISTRATION: PROCESS OVERVIEW, CLASS I + II MEDICAL DEVICES



5: KEY ROLES: BRAZILIAN REGISTRATION HOLDER

- The registration holder/owner is legally responsible for the product registered in Brazil, and is the company who should respond to the Health Authorities about any occurence related to the product in Brazil
- The BRH needs to be a Brazilian company that:
  - …is registered as a such at ANVISA (takes up to 2 years to get a BRH)
  - …has a technical responsible, and posseses an Operation Permit (AFE) as well as a Operating Permit (LF)

→ See next slides for further information of each of these requirements

5: KEY ROLES: BRAZILIAN REGISTRATION HOLDER

- According to the legislation, a BRH cannot be changed randomly, only every five years, or if a BRH is no longer able to perform its duties as BRH
- A BRH needs to approve every import into Brazil of the product, and thus has an important and strategically powerful position. If a distributor is the BRH, the distributor may theoretically prevent other distributors access and/or can impose a BRH fee towards other distributors, increasing the costs signficantly
- A number of consultancy companies are available on the market offering to be BRH against an annual fee + a fee per import. This allows for a flexible, multiple distributor strategy, but also comes with extra costs

→ Choose your Brazilian Registration Holder with great care!

5: KEY ROLES: BRAZILIAN REGISTRATION HOLDER *- 3 DIFFERENT STRATEGIES*

Strate -gy	Using your importer as BRH	Using an agent or distributor as BRH	Using an independent consultant as BRH
PROS	An importer with a BRH-structure will help avoid costs of using independent consultants to register the products and pay annual BRH fees. If the importer is different from your distributor(s), the company does not have any advantage of preventing distributors to market your products in Brazil	An agent or distributor with a BRH-structure will help avoid costs of using independent consultants to register the products and pay annual BRH fees. Helps build trust vis-a-vis the distributor: with the BRH license of your product, the agent/distributor holds an important key to the market, which may help the company invest more in the partnership	With an independent consultant, you create a flexible distribution strategy, allowing you to use multiple distributors/agents as none of them have the BRH license for your product. This is recommendable if you are looking to create a multiple agent/distributor strategy If you use a well-renowned consultant, you will also benefit from the consultants regulatory knowledge for the registration + regulatory market updates
CONS	May charge indirect high fees for being the BRH, typically paid by the distributors If the importer also serves as distributor, the company may want to exclude competing distributors of getting access to your products May lack regulatory insights and thus not be aware of important changes that affects your product If the importer suddenly stops business, and you need to find a new BRH, this can stop importing meanwhile. Therefore it will be important to choose a financial sound importer as BRH in case you choose this strategy	You are dependent on the distributor being succesful and/or open to letting other distributors marketing your products Distributors with BRH-license will typically ask for a fee (flat or a percentage) to let other distributors market the products in Brazil May lack regulatory insights and thus not be aware of important changes that affects your product If the distributor suddenly stops business, and you need to find a new BRH, this can stop importing meanwhile. Therefore it will be important to choose a financial sound importer as BRH in case you choose this strategy	Independent consultant typically charges three fees: 1) A fee for registrering the product at ANVISA 2) An annual BRH fee (Emergo Group, as an example charged around EUR 2,400 in 2014 for this service per registred product) 3) A fee per import With multiple products (or products not belonging to what ANVISA would classify as a product family), using an independent consultant becomes an expensive solution

6: KEY ROLES: THE TECHNICAL RESPONSIBLE
- THE PERSON AT THE BRH COMPANY RESPONSIBLE VIS-A-VIS ANVISA

- This is the employee that is responsible in Brazil for the product and for its compliance with ANVISA's rules
- A technical responsible is needed for the BRH company
- Depending on the medical device, ANVISA has different requests related to the professional competencies. Typically a technical responsible is a pharmacist, a dentist or another health care professional
- To assume the technical responsibility, the professional should be regularly enrolled in the corresponding Regional Board of Professional Class and prove employment relationship with the company by means of Employment Agreement or registration in the Labor and Social Security ID Card (CTPS)
- A team in the Department of Inspection of Regional Board of Professional Class will analyze the application and issue a certificate of tecnical suitability for the year in force
- A technical responsible receives a minimum fee established by law. Pharmacists receives around BRL 2,800 per month for being a technical responsible, but this is independent of the number of products. When BRH companies/consultants requests a fee for its service, it is also a reflection of the costs of having to pay a technical responsible. It may be relevant, in negotiations with a BRH, to understand how many products besides the ones of your company the technical responsible cater.

7: KEY LICENSES NEEDED FOR BRH, IMPORTERS AND DISTRIBUTORS TO HANDLE MEDICAL DEVICES IN BRAZIL

- As Danish exporter, you should make sure that your Brazilian cooperation partners

- …have an Operation License (LF) and Operating Permit (AFE) enabling them to handle medical devices in Brazil, and that the permits also covers the handling of the type of medical devices that you wish to market in Brazil

7: KEY LICENSES NEEDED FOR BRH, IMPORTERS AND DISTRIBUTORS TO HANDLE MEDICAL DEVICES IN BRAZIL

If you wish to invest in your own operation in Brazil handling (part of) the distribution process, here is an overview of the process to obtain the main licenses:

1. You need to assign a technical responsible, and need to apply to the relevant board of professionals (eg. Pharmacists) for their approval of the person
2. You can now apply for an initial **Operating Licence (LF)** and petition of plant verification with the State Department of Health Surveilance
3. The State Department of Health Surveilance issues an inspection report in which the evaluate the technical criteria related with the activies requested and suitability of the physical area. If the facilities are approved, the Company's **Operating Permit (AFE)** – will be published in the Brazilian Official Gazette (DOU)
4. With the publication granting the AFE, you may now apply for the State Center of Health Surveillance to publish the companies **Operation License (LF).** With the LF and the AFE, you are able to start handling the given medical devices and, if you will be the BRH, to enrol the product with ANVISA (that requires proof of payment of the Health Inspection Fee

THE ABOVE PROCESS MAY TAKE UP TO TWO YEARS IN TOTAL, BUT MAY BE FASTER

8: HOW THE INNOVATION CENTRE IN SAO PAULO MAY HELP YOU

- Help verifying the classification of your medical device + need of Inmetro certification
- Help finding suitable partners (BRH, Importers, Distributors, Investors)
- Help evaluating the fit of your product with the Brazilian market, connecting you with market experts and key opinion leaders in the specific area of use
- Help engaging relevant private and public stakeholders

Contact our sector specialist, Elisangela Zeoli, pharm.: elizeo@um.dk