‘Comparative Analysis of Market Authorization Approval Processes for Medical Devices in USA and Brazil’

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Abstract:

This review article provides a comparative analysis of the market authorization approval processes for medical devices in Brazil and the United States. The regulatory frameworks and pathways for obtaining market approval in both countries are explored, focusing on key aspects such as regulatory agencies, submission requirements, premarket assessments, clinical data requirements, and post-market surveillance.

In Brazil, the National Health Surveillance Agency (ANVISA) oversees the regulatory approval process for medical devices, which includes classification, technical documentation submission, Good Manufacturing Practices (GMP) compliance, and product registration. The article discusses ANVISA's requirements and timelines for market authorization, highlighting challenges and opportunities for manufacturers entering the Brazilian market.

In contrast, the United States Food and Drug Administration (FDA) regulates medical devices through a multifaceted approach, including classification (Class I, II, or III), premarket notification (510(k)), premarket approval (PMA), and de novo pathways. The review outlines the FDA's rigorous evaluation criteria, including clinical trials, performance data, labelling requirements, and post-market surveillance obligations.

By comparing these regulatory frameworks, the article aims to provide insights into the complexities and nuances of obtaining market authorization for medical devices in Brazil and the USA. Understanding these processes is crucial for industry stakeholders, regulatory professionals, and healthcare providers navigating the global medical device landscape.

Introduction: UNITED STATES

Country	United States
Capital	Washington, DC
Currency	United States dollar
Language	English
Regulatory authority	Food and Drug Administration (FDA)
Regulation	Title 21 Code of Federal Regulations (21 CFR) Parts 800 – 1299
Regulatory pathway	Pre-Market Notification or Pre-Market Approval or De-Novo Classification
Authorized representative	U.S. Agent
QMS requirement	Quality System Regulation (QSR) (21 CFR part 820)
Assessment of technical data	Centre for Devices and Radiological Health
Validity of license	Unlimited
Labeling requirement	21 CFR Part 801
Flag	

Medical Devices as per US FDA

Section 201(h) of the Federal Food, Drug, and Cosmetic Act. It is a very broad definition. It basically says a medical device is “any instrument, machine, contrivance, implant, in vitro reagent that's intended to treat, cure, prevent, mitigate, diagnose disease in man” This includes component parts or accessories that meet the following criteria:

The device must fulfil one or more of the following conditions:

(A) Recognized in the official National Formulary or the United States Pharmacopoeia, or any supplement to them.

(B) Intended for use in the diagnosis of disease or other conditions, or in the cure**,** mitigation**,** treatment**,** or prevention of disease in humans or animals.

(C) Intended to affect the structure or function of the body of humans or animals.

It should not achieve its primary intended purposes through chemical action within or on the body and must not be dependent upon being metabolized for its primary intended purposes.

Note that the term “device” excludes software functions excluded pursuant to section 520 (o) .

Determining if Your Product Is a Medical Device:
To ascertain whether your product falls under the medical device category, follow these steps:
Step 1:
Define the intended use and indications for use of your product.
Intended Use: The general purpose or function of the device.
Indications for Use: Describes the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including details about the patient population for which the device is intended.

Step 2:
Search for existing product classifications that may apply to your product. These classifications help determine if your product is regulated as a medical device

Submission Format:

I. **510(k) Submissions**:
   a. The 510(k) process is used for premarket notification of medical devices. It allows manufacturers to demonstrate that their device is substantially equivalent to a legally marketed device (predicate device) and does not pose any significant differences in safety and effectiveness.
   b. The FDA provides an Electronic Submission Template for 510(k) submissions. This template ensures consistency and efficiency in the review process.
   c. You can find detailed information in the FDA's guidance document titled "Electronic Submission Template for Medical Device 510(k) Submissions"
   d. . It covers standards for electronic submission, establishment timelines, and criteria for waivers and exemptions.
   e. The FDA intends to require electronic submissions for 510(k) submissions starting from October 1, 2023**.**
   f. However, they will accept submissions saved to electronic storage media and mailed if received before that date .

II. **Electronic Common Technical Document (eCTD)**:
   a. While the eCTD format is primarily used for drug submissions, it's essential to be aware of it. The eCTD is the standard format for submitting applications, amendments, supplements, and reports to the FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) .

III. **PMA Application Contents**:
   a. If you are submitting a Premarket Approval (PMA) application, ensure it includes all the following:
      i. The name and address of the applicant.
      ii. A table of contents specifying the volume and page number for each item referred to in the table

Classification:

Class	Risk	Level of regulatory Control
Class I	Minimal	General control
Class II	Medium	General control and Special control(510k)
Class III	High	General control and PMA

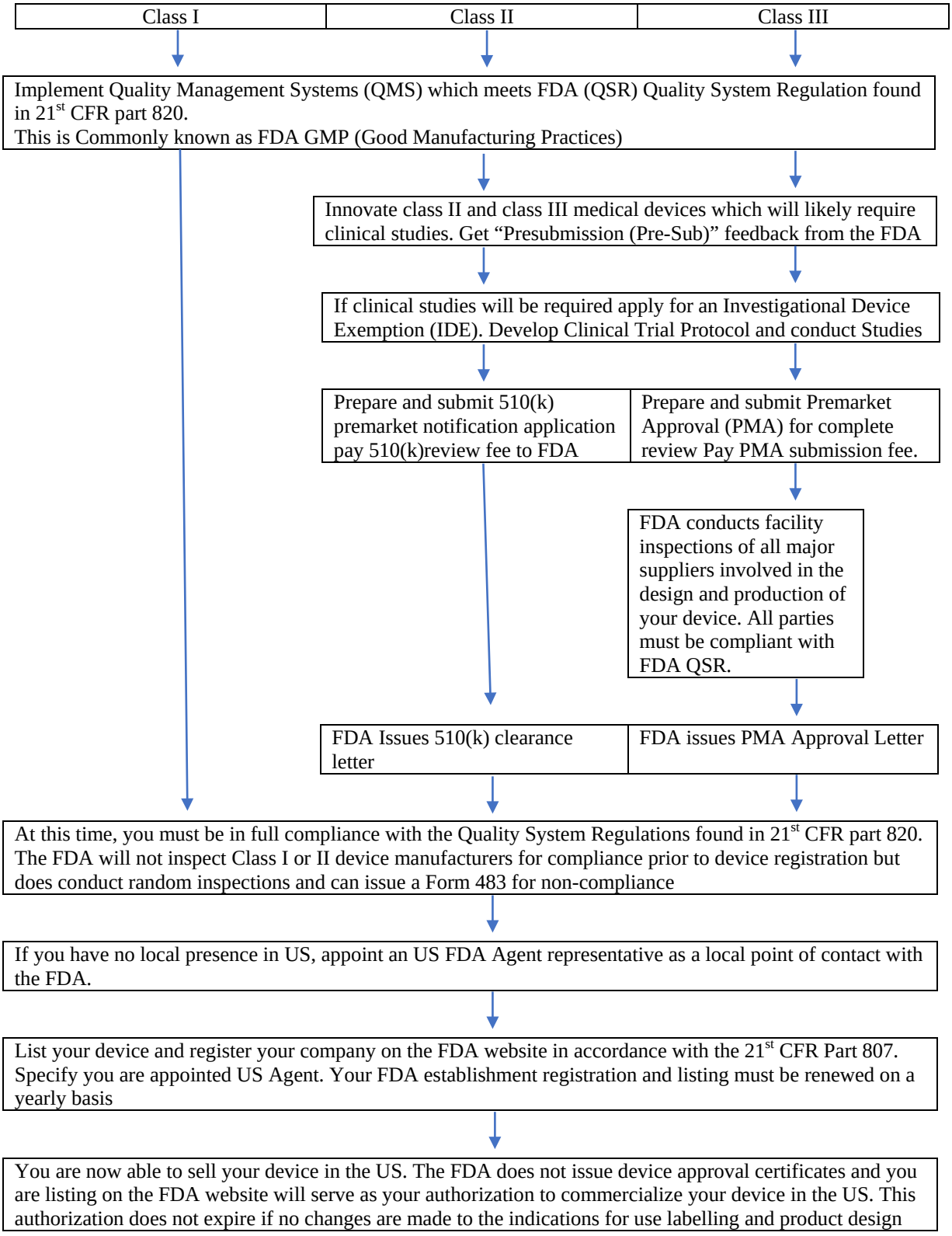
Regulations:

Sr.No.	Categorizes	Regulations
01.	Medical Equipment	Title 21 part 807
02.	Material for Health use	ICH Q7 GMP Guidance
03.	Orthopedic implants	Title 21 sub chapter H part 888
04.	In vitro Diagnostics	Title 21 sub chapter H part 809

Timeline:

Class	Timeline	Validation
Class I	1 month	With Exemptions
Class II	3-6 month	With Exemptions
Class III	18-30 months	Months to several years

Using the FDA Classification database determine the classification of your device by searching predicate devices already registered in US market. Pay special attention to three letter product code and seven-digit regulation number associated with the predicate devices you identify. If no predicate found then use (513) g or De Novo Process.



Introduction: BRAZIL

Country	Brazil
Capital	Brasília
Currency	Brazilian real
Language	Portuguese
Regulatory authority	The National Health Surveillance Agency or ANVISA (Agência Nacional de Vigilância Sanitária)
Regulation	RDC 751/2022
Regulatory pathway	Notification (*Notificação*) and Registration (Registro)
Authorized representative	Brazil Registration Holder (BRH) Required
QMS requirement	Brazilian GMP/MDSAP
Assessment of technical data	ANVISA
Validity of license	Ten years
Labeling requirement	Chapter VI of RDC 751/2022
Flag	

Medical devices as per Brazil:

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 purposes 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

ANVISA categorizes Medical Devices into four types:

- medical equipment's,
- materials for health use,
- orthopaedic implants and
- in vitro diagnostics

Submission format:

Classification of Medical Devices:

- The Brazilian risk-based classification system categorizes medical devices into four classes: I (low risk), II (medium risk), III (high risk), and IV (maximum risk)**.**
- To determine the correct classification, follow the 22 classification rules outlined in RDC 751/2022.
- Specific rules exist for Software as a Medical Device (SaMD) (rule 11) and nanomaterials (rule 19).

Submission Routes:

- Class I/II devices are submitted to ANVISA using the Notification process ("Notificação")**.** This route requires fewer documents and does not need revalidation.

- Class III/IV devices follow the Registration process ("Registro")**.** The complete technical dossier undergoes expert assessment, including rounds of questions and answers. These devices must be revalidated every ten years

Electronic Submission:

- All submissions must be performed in electronic format through the ANVISA's Electronic Petitioning System.

Market Access Considerations:

- Brazil is the largest medical device market in Latin America.
- Understanding the pros and cons of various pathways for market access is crucial for informed decision-making.

Classification:

Class	Risk	Level of regulatory control
Class I	Low risk	Notification process ("Notificação")
Class II	Low-moderate risk	Notification process ("Notificação")
Class III	Moderate-high risk	Registration process ("Registro")
Class IV	High risk	Registration process ("Registro")

Regulations:

Sr.No.	Categories	Regulations
1	Medical equipment	Resolution RDC 185/2001 and RDC 211/2018
2	Materials for health use	Resolution RDC 185/2001 and RDC 211/2018
3	Orthopedic implants	Resolution RDC 185/2001 and RDC 211/2018
4	In vitro diagnostics	Resolution RDC 185/2001 and RDC 211/2018

Timeline:

Class	Timeline	Validation
Class I	1-3 months	Does not expire
Class II	1-3 months	Does not expire
Class III	8-15 months	10 years
Class IV	8-15 months	10 years

Determine classification of your device using rules found in Annex II of Resolution RDC 185/2001 published by ANVISA. The cadastro registration is for lower risk devices, has a simplified application, and typically takes less time than registro reviews.

Class I	Class II	Class III	Class IV

↓

Appoint a company that holds a company working allowance permit from ANVISA as your brazil registration holder (BRH).

↓

Provide letter of authorization to your BRH, who will submit registration application to ANVISA. Your BRH maintains control of your device registration and Brazil Good Manufacturing Practice (BGMP) certification, if applicable.

↓

Certain devices* require INMETRO certification. Testing for electro medical products performed outside Brazil is Usually accepted, if performed by an ILAC-certified lab (CB scheme is not accepted). ** compile tests and pay fee to INMETRO certifier. INMETRO certification is valid for 5 years, and annual audits and fees are required.

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Class I and II device manufacturers must comply with BGMP requirements. However, ANVISA will not conduct an audit.	Class III and IV manufacturers must be audited for BGMP compliance by ANVISA as outlined in RDC 16/2013. BGMP fees are due every two years.

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Prepare technical dossier and cadastro application. Send legal documents, as well as proposed RDC 185/2001-compliant labeling (IFU and labels) to BRH. These files are maintained by your BRH in case of ANVISA on-site inspections.	Prepare technical file, including clinical data, clinical studies (if applicable), information on your device in accordance with annex III, part A, B, C in RDC 185/2001, and proposed labeling (IFU and labels) per Annex III part B.

↓

BRH prepares and submits the application to ANVISA. All documents must be submitted in Brazilian Portuguese. Pay application fee.

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ANVISA reviews registration application. Upon approval, ANVISA will publish registration number in the Diario official da Uniao (DOU)

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Class I and II registrations do not expire	Class III and IV registrations are valid for 5 years. Registration renewals must be initiated one year, and no later than six months, prior to expiration.

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Appoint a qualified importer/distributor to bring your device into brazil. You may now begin marketing your device.

Conclusion:

There are significant distinctions between the stringent marketing authorization approval procedures for medical devices in the US and Brazil. Brazil's ANVISA has rigorous testing and paperwork requirements, which frequently cause clearance delays. On the other hand, the US FDA's procedure places more emphasis on post-market surveillance and pre-market filings, with an emphasis on efficacy and safety. Gaining an understanding of these differences is essential for entering both countries' markets successfully.

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