

Pathway for Marketing Authorisation Approval of Medical Device in US

The process of developing a revolutionary medical device from the proof-of-concept stage to the marketing stage is expensive and complicated. The creation of a new product is a costly and time-consuming endeavour. Demonstrating the safety and efficacy of the technology is just as crucial as the innovation itself. These requirements can assist you update your development operations and create a product that fulfils the regulatory standards of your targeted authority, i.e., a safe and effective product for its intended application. Although information on the regulatory requirements (e.g., laws, guidance documents, international standards) for the creation of healthcare products is readily available, navigating the regulatory system is not easy, and it becomes even more complicated when working with various countries. To assist healthcare product developers who are entrepreneurs or regulators.

The major objective is to facilitate the knowledge of the regulatory framework that controls medical devices and to ensure compliance with regulatory frameworks. It is possible to make use of it as a launching point for the development of your device. The purpose of the guidance is not to serve as a collection of regulations; rather, it focuses on discussing the underlying ideas and principles involved in regulatory affairs. It lays out a plan of action for entrepreneurs to follow.

Key words: Marketing Authorisation Approval, Medical Devices, Regulatory Information Management, Food Drug Administration, Navigation, Guidance's, Entrepreneurs, Healthcare Products.

The process of producing an innovative healthcare product (a drug, a biologic, or a medical device) from the proof-of-concept stage (idea to demonstrate) to the commercialisation stage is expensive and complex. It needs a substantial investment of time and effort in research and development over many years.¹

In order to reduce the amount of time and money spent on bringing products to market, product development processes ought to be carried out in accordance with the pertinent regulatory standards. By adhering to these requirements, you may be able to speed up the development operations and produce a product that satisfies the regulatory standards of your target authority(s), which means that the product will be of high quality and will be both safe and effective for the use to which it is put.²

The drug regulatory bodies are being set up in different countries all over the world. The regulatory body makes sure that a drug meets all of the rules and laws that apply to it. In every country, there is a regulatory body that enforces the rules and regulations and sets guidelines for how drugs are made, licenced, registered, sold, and labelled. The regulatory body also makes sure that the rules and regulations are being followed.³

In order to assure the safety, efficacy, and quality of pharmaceuticals, as well as the accuracy and appropriateness of drug information available to the general public, regulatory authorities and organisations are responsible for effective drug regulation.⁴

In order to have access to information regarding drugs, one must first gain an understanding of the locations on regulatory websites where the regulated material, such as acts, regulations, and guidance, is kept. After that, in order to acquire the correct information, one needs to be aware of the correct information that is stored on particular regulatory websites. To gain access to this, you will need to follow a "navigation pathway" that has been established by a particular agency in order to get regulatory approval. To commercialise a product, we must first submit an application to the appropriate regulatory agency, which then ensures that the product is both safe and effective for people all over the world. As a result, we require a specific navigation method for specific applications or pharmaceutical items.⁵ It is quite simple to implement a comprehensive regulatory information management (RIM) solution, which can be used to a wide range of difficult situations. Regulatory agencies becoming



more safety conscious and demanding more data, regulatory information management (RIM) which leads to increase in demand of navigation pathway. Global regulatory authorities and organisations face a number of significant challenges, the most significant of which are: ensuring the safety, quality, and efficacy of medicines and medical devices; harmonising legal procedures related to drug development; and monitoring and ensuring compliance with statutory obligations.⁶

Discussion: United States

- The United States is a founding member of numerous international organisations, including the United Nations, the World Bank, the International Monetary Fund, and the Organization of American States (OAS).
- The US is either the third or fourth largest country in terms of total area, and it has the third-highest population.
- Capital: Washington D.C.
- Area: 3.8 million square miles (9.8 million km²)
- Population: 325 million people
- National language: English
- Currency: American Dollar (1 dollar = 64 Indian Rupee)
- The US is a highly developed country which is provided in Table 1 It has the largest economy in the world when measured by nominal GDP and the second largest economy when measured by PPP (Public-Private Partnerships).⁷

Parameters	US
Population	321,368,864
Primary language(s)	English
Total healthcare spending	\$3 trillion
Healthcare expenditures total (% of GDP)	17.1%
Healthcare expenditures per capita	\$9403 (USD)
Expenditures on healthcare	Government: 48% Private: 52%
Size of medical device market (USD)	\$147.7 billion (USD)
Currency	US dollar (\$)

Table 1: General Information about USA⁷

1. IDE
2. Regulations set down in accordance with 21 CFR 812 are referred to as IDE. The sponsor's research application has been approved by the IRB (and FDA for major risk devices) and all conditions under 21 CFR 812 have been met with an approved IDE.
3. Guidance documents required for the IDE provided in Table 3.
4. An IDE application must be submitted by the sponsor of a major risk device study to the FDA.
5. Discussion about the regulatory process about Medical Device as provided in Table 2.
6. Submission and the navigation pathway required for the Medical Device according to the IDE guidance documents has provided in the Figure 1 & Figure 2.
7. A 510K is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR 807.92(a)(3)) that is not subject to PMA, Exemptions and the waivers has to be followed by the applicant as mentioned in the Table 4. Person who wants to market in the U.S., as to follow the guidance documents which is provided in the Table 5 a class I, II and III devices intended for human use, for which a Premarket Approval (PMA)

Regulatory factsheet	
Product	Medical device
Country	USA
Type of application	IDE
Lifecycle phase	R&D

Regulatory department	Department of Health and Human Services
Regulatory agency	US Food & Drugs administration (FDA)
Regulatory classification	Medical device

KEY RESOURCES		
Regulations: Code of Federal Regulation		
No.	CFR Part	Application Type
1	21 CFR 812	Investigational Device Exemptions
2	21 CFR 56	Institutional Review Boards
3	21 CFR 58	Good Laboratory Practice for Nonclinical Laboratory Studies

Table 2: Regulatory Factsheet about Medical Device in US⁸

Sl. No.	Title	Links
1	Guidance for Sponsors, Investigators, and Institutional Review Boards – Questions and Answers on Informed Consent Elements 21 CFR 50.25(c)	http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM291085.pdf
2	Centre for Devices and Radiological Health's Investigational Device Exemption (IDE) Refuse to Accept Policy	http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM081312.pdf
3	Continued Access to Investigational Devices During PMA Preparation and Review July 15, 1996 (Blue Book Memo)	http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080260.htm
4	Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies – Guidance for Industry and Food and Drug Administration Staff	http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279103.pdf
5	FDA Decisions for Investigational Device Exemption Clinical Investigations – Guidance for Sponsors, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff	http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279107.pdf

Table 3: USFDA IDE Guidance Documents⁹

is not required, must submit a 510(k) to FDA unless the device is exempt from 510(k) requirements of the Federal Food, Drug and Cosmetics Act.

8. Navigation and the submission pathway which is required for the 510k approval has to be followed by the applicant is mentioned below in the Figure 3 & Figure 4.

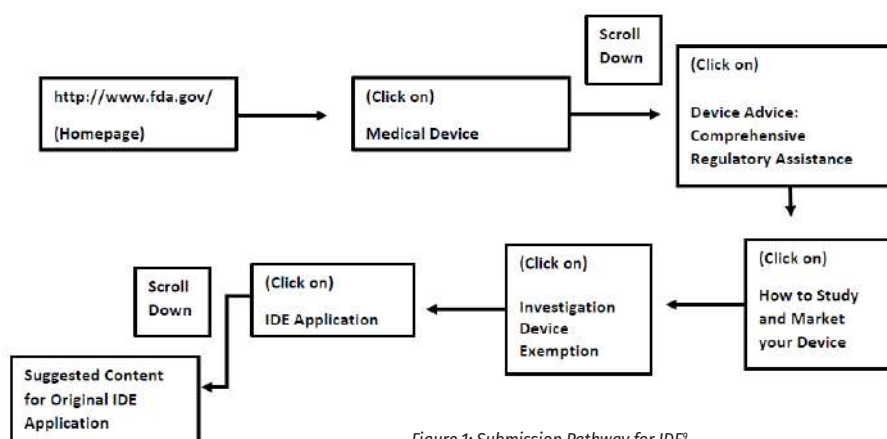


Figure 1: Submission Pathway for IDE⁹

Regulatory factsheet	
Product	Medical device
Country	USA
Type of application	510K

Regulatory department	Department of Health and Human Services
Regulatory agency	US Food & Drugs administration (FDA)
Regulatory classification	Medical device

Fees: MDUFA III Fee page lists 510(k) fees.

Exemptions and waivers:

Category	Exemption or Waiver
Third-party 510(k)	Exempt from any FDA fee; however, the third-party does charge a fee for its review
Any application for a device intended solely for paediatric use	Exempt from user fee. Please note that changing the intended use from paediatric use to adult use requires the submission of a new 510(k). The new 510(k) is subject to the 510(k)-review fee at the time of submission
Any application from a State or Federal Government entity	Exempt from any fee unless the device is to be distributed commercially

Table 4: Key Resources¹⁰

Sl. No.	Title	Links
1	Guidance for Industry and FDA Staff: Bundling Multiple Devices or Multiple Indications in a Single Submission	http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089731.htm
2	Guidance for Industry and Food and Drug Administration Staff – User Fees and Refunds for Premarket Notification Submissions (510(k)s)	http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm345277.ht

Table 5: USFDA 510K Guidance Documents¹¹

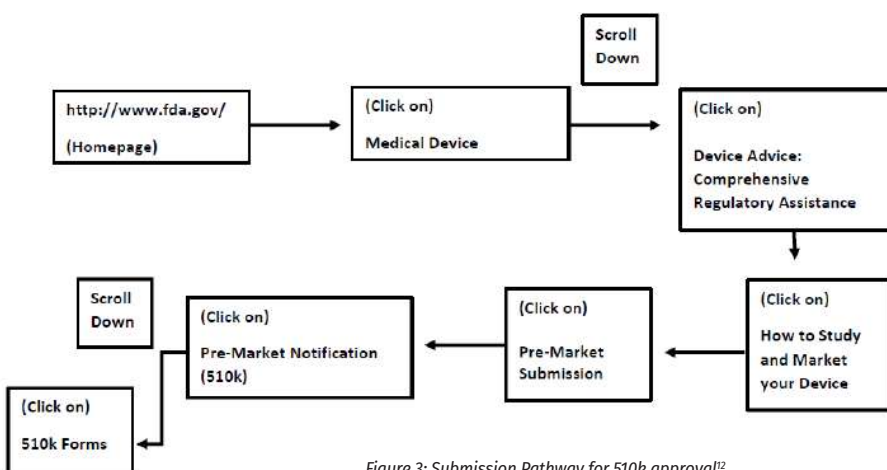


Figure 3: Submission Pathway for 510k approval¹²

9. Premarket Approval (PMA): It is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. PMA is the most stringent type of device marketing application required by FDA is provided in the Table 6. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).
10. Title 21 Code of Federal Regulations (CFR) Part 814 governs premarket approval. The PMA application procedure necessitates a copy of the relevant federal regulation code as been provided in Table 7.
11. Submission & Navigation pathway which is required for the Premarket approval in US as been provided in the Figure 5 & 6.

12. Post Approval Changes (PAC)
FDA must be notified of any changes to a product, manufacturing process, quality controls, equipment facilities, or the employees responsible for them: A supplement requiring approval prior to distribution
 - A supplement at least 30 days prior to distribution of the product made using the change, all the documents related to changes has to be followed the guidelines which is given from the FDA is provided in Table 8.

U.S. Department of Health and Human Services

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Medical Devices

Home > Medical Devices > Device Advice: Comprehensive Regulatory Assistance > How to Study and Market Your Device > Premarket Submissions > Premarket Notification (510k)

Premarket Notification (510k)

510(k) Submission Process

510(k) Forms

510(k) Submission Methods

How To Prepare A Special 510(k)

How to Find and Effectively Use Predicate Devices

How to Prepare a Traditional 510(k)

Premarket Notification [510(k)] Review Fees

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

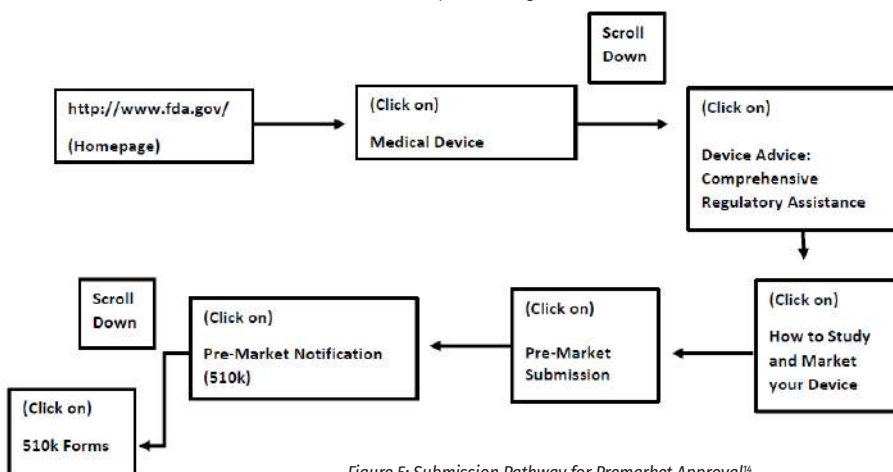
- Overview
- Fees
- Exemptions and Waivers
- When to Pay
- How to Prepare Your Payment
- Complete the Medical Device User Fee Cover Sheet
- Submit Your Payment

Figure 4: USFDA 510K Navigation Pathway¹³

Product	Medical device	Regulatory department	Department of Health and Human Services
Country	USA	Regulatory agency	US Food & Drugs administration (FDA)
Type of application	PMA Approval	Regulatory classification	Medical device
Lifecycle phase	MMA		

Table 6: Regulatory Factsheet of PMA¹⁴

No.	CFR Part	Application Type
1	21 CFR 814	Premarket Approval of Medical Devices
2	21 CFR 54	Financial Disclosure by Clinical Investigators
3	21 CFR 201	Labelling
4	21 CFR 820	Quality System Regulation

Table 7: US Code of Federal Regulations¹⁴Figure 5: Submission Pathway for Premarket Approval¹⁴

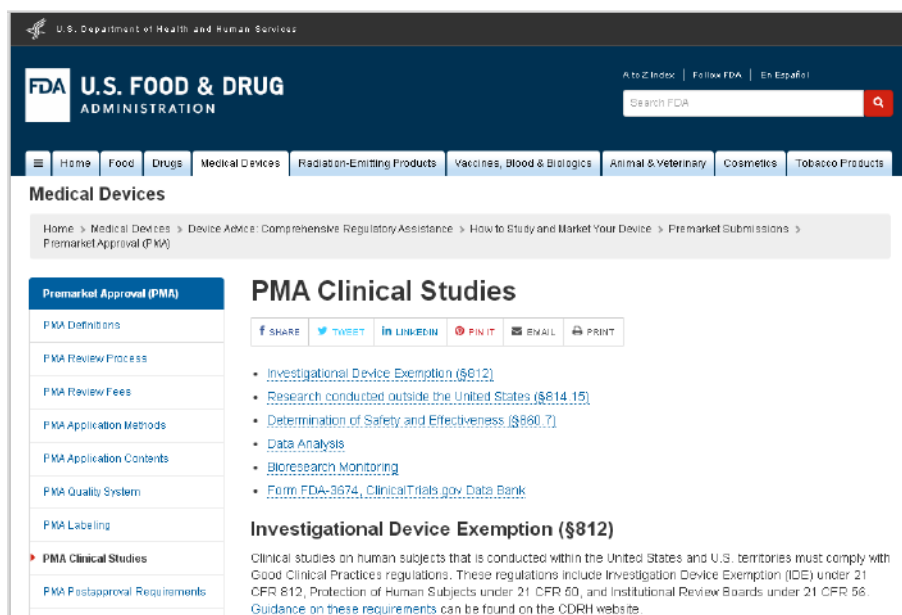


Figure 6: USFDA PMA Navigation Pathway¹⁵

Regulatory factsheet	
Product	Drugs, Biologics & Medical Devices
Country	USA
Lifecycle phase	PAC

Regulatory department	Department of Health and Human Services
Regulatory agency	US Food & Drugs administration (FDA)
Regulatory classification	Drugs, Biologics & Medical Devices

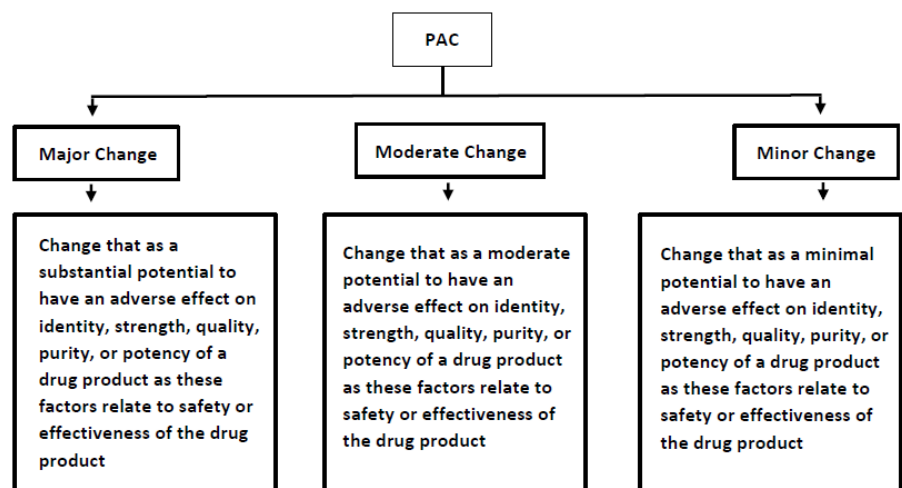


Figure 7: Types of Changes in Post Approval Changes¹⁶

- On the basis of its potential to affect the biological product's identity, strength, quality and purity as they may relate to the product's safety or effectiveness, an annual report may be required.
- Changes which is required during the post approval changes in FDA is mentioned below in Figure 7.

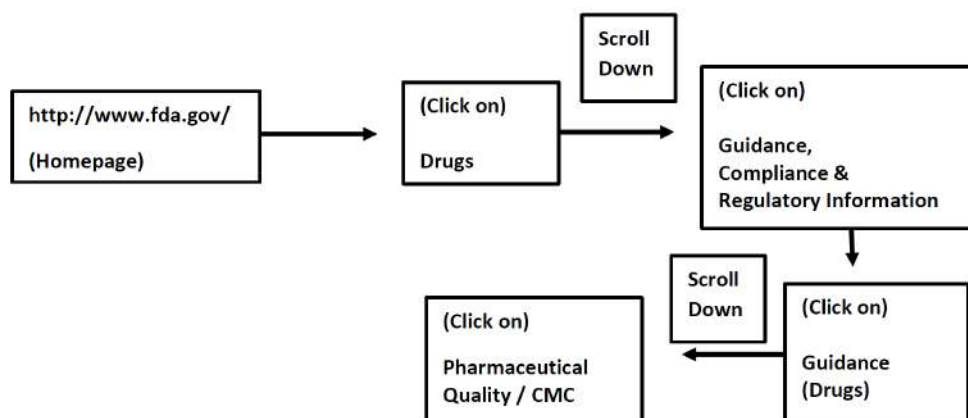
Pharmaceutical Quality related issues has to be followed a particular Submission and Navigation Pathway is provided below in Figure 8 & Figure 9.

Applications for FDA approval to market a new drug in USA as to be followed a particular code of federal regulations is mentioned below in Figure 10.

Resource		
Reporting Category	Type of Changes	Supplement Application
	Major Change	Prior Approval Supplement
	Moderate Change	Change Being Affected in 30 days/
	Minor Change	Annual Report
List of Changes	- Component and Composition - Manufacturing Sites - Manufacturing Process - Specifications - Container closure system - Labelling - Miscellaneous Changes and - Multiple related Changes	

Sl. No.	Guidance	Issued Date
1	SUPAC: Manufacturing Equipment Addendum	12/01/14
2	SUPAC-IR: Immediate-release Solid Oral Dosage Forms: Scale-UP and Post-Approval Changes: Chemistry, Manufacturing and Controls, <i>In Vitro</i> Dissolution Testing, and <i>In Vivo</i> Bioequivalence Documentation	11/01/95
3	SUPAC-MR: Modified Release Solid Oral Dosage Forms: Scale-UP and Post-approval Changes: Chemistry, Manufacturing and Controls, <i>In Vitro</i> Dissolution Testing, and <i>In Vivo</i> Bioequivalence Documentation	10/06/97
4	SUPAC-SS: Nonsterile Semisolid Dosage Forms; Scale-Up and Post-approval Changes: Chemistry, Manufacturing and Controls, <i>In Vitro</i> Release Testing, and <i>In Vivo</i> Bioequivalence Documentation	05/01/97

Table 8: USFDA PAC Guidance Documents¹⁶

Figure 8: Submission Pathway for Pharmaceutical Quality¹⁶

U.S. Department of Health and Human Services
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Drugs

Home > Drugs > Guidance, Compliance & Regulatory Information > Guidances (Drugs)

Guidances (Drugs)

- Advertising
- Animal Rule
- Biopharmaceutics
- Biosimilars
- Clinical / Antimicrobial
- Clinical / Medical
- Clinical Pharmacology
- Combination Products

Pharmaceutical Quality/CMC

Below is a sortable table of Pharmaceutical Quality/CMC Guidances:

*Note: The category "Chemistry, Manufacturing, and Controls (CMC)" is renamed to Pharmaceutical Quality/CMC

New! Note: Once finalized, the Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information Guidance for Industry will supersede the Comparability Protocols -- Chemistry, Manufacturing, and Controls Information draft guidance from 2003.

The guidance document entitled "[Submitting Documentation for the Manufacturing of and Controls for Drug Products](#)" was withdrawn 4/14/2015. This guidance was withdrawn because many of the recommendations were obsolete and have been more recently addressed in FDA and ICH guidance documents, including, but not limited to:

INDs for Phase 2 and Phase 3 Studies: Chemistry, Manufacturing, and Controls Information

Figure 9: USFDA PAC Navigation Pathway¹⁵

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?CFRPart=314

FDA Protecting and Promoting Your Health

Home > Food > Drugs > Medical Devices > Radiation-Emitting Products > Vaccines, Blood & Biologics > Animal & Veterinary > Cosmetics > Tobacco Products

CFR - Code of Federal Regulations Title 21

FDA Home > Medical Devices > Databases

The information on this page is current as of April 1 2015.
 For the most up-to-date version of CFR Title 21, go to the [Electronic Code of Federal Regulations \(eCFR\)](#).

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 CHAPTER I--FOOD AND DRUG ADMINISTRATION
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 SUBCHAPTER D--DRUGS FOR HUMAN USE
 PART 314 APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

Subpart A--General Provisions

- § 314.1 - Scope of this part
- § 314.2 - Purpose
- § 314.3 - Definitions

Subpart B--Applications

- § 314.50 - Content and format of an application
- § 314.52 - Notice of certification of invalidity or noninfringement of a patent
- § 314.53 - Submission of patent information
- § 314.54 - Procedure for submission of an application requiring investigations for approval of a new indication for, or other change from, a listed drug
- § 314.55 - Pediatric use information
- § 314.56 - Amendments to an unapproved application, supplement, or resubmission
- § 314.57 - Withdrawal by the applicant of an unapproved application
- § 314.70 - Supplements and other changes to an approved application
- § 314.71 - Procedure for submission of a supplement to an approved application
- § 314.72 - Change in ownership of an application
- § 314.80 - Postmarketing reporting of adverse drug experiences
- § 314.81 - Other postmarketing reports

Figure 10: USFDA 21 CFR Part 314¹⁵

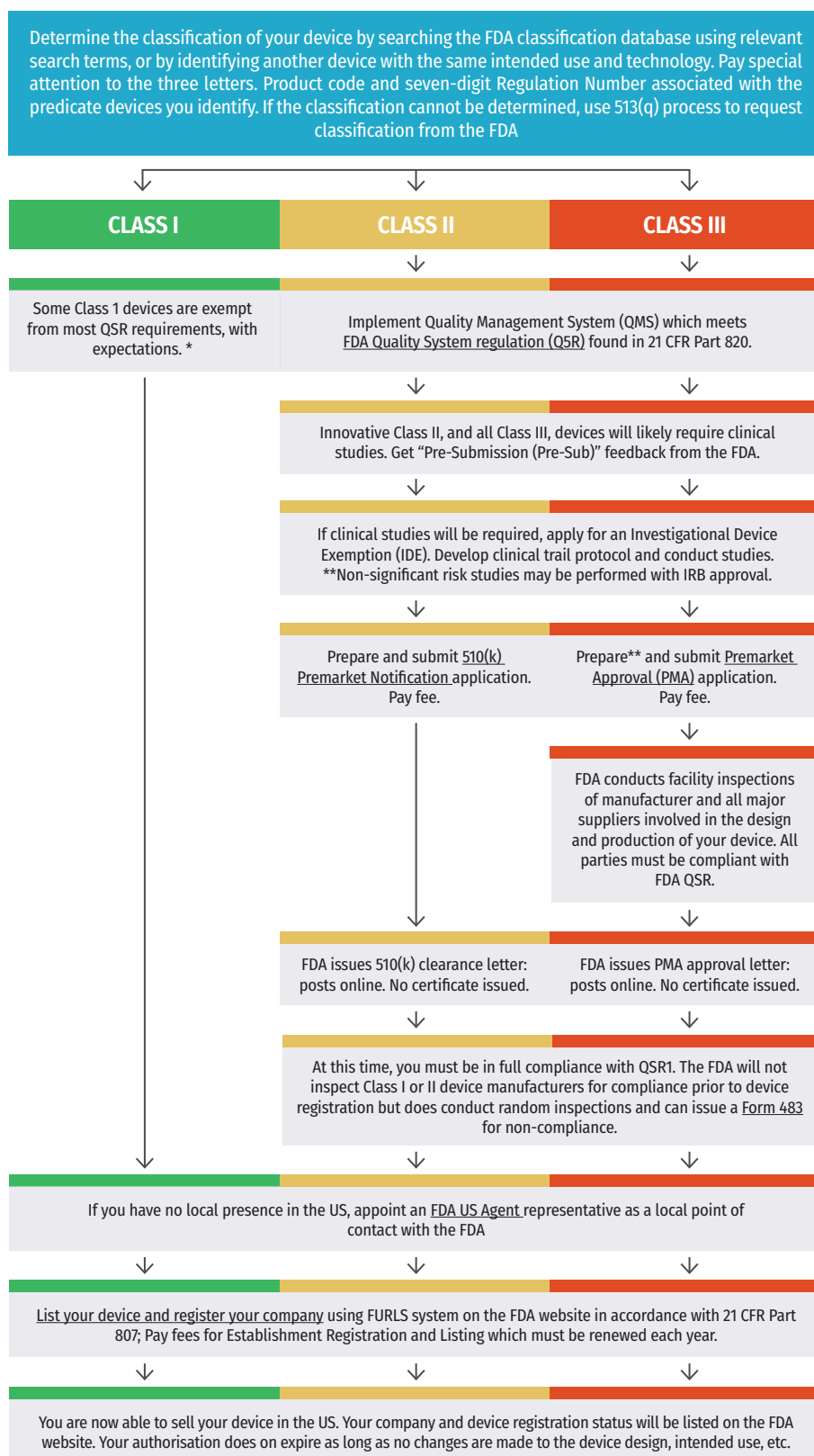


Figure 11: Registration Procedure for Medical Device in US¹⁶

Registration procedure has to be followed by the applicant for the manufacturing of medical device in USA according to the classes which is classified is provided below in the Figure 11.

Requirements related to the Medical Device regulatory pathway has to be

followed according to the guidelines and is mentioned in Table 9.

Conclusion

- To understand the regulatory pathway for Medical device in US
- A detailed Factsheet & checklist has

been prepared based on the guidelines issued by the USFDA

- Collation of compliance requirements for navigation pathway.
- Hence, US regulatory authority has their own regulation and guidelines for navigation pathway for the drug improvements and for the patient's safety.

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Conflict of Interest

There are no conflicts of interest. It has been mentioned by authors.

Authors Contribution

All the authors are contributed in preparing the manuscript and designing the information pertaining to the article.

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Device classification in the United States	Class I	Class II	Class III
How long you should expect to wait after submission until approval is granted	1 month	6–9 months	18–30 months
Validity period for device registrations	Does not expire	Does not expire	Does not expire
Registration renewal should be started this far in advance	Not applicable	Not applicable	Not applicable
Complexity of the registration process for this classification	Simple 2	Simple 4	Simple 5
Overall cost of gaining regulatory approval	Low 1 High	Low 3 High	Low 5 High

Table 9: Requirements for medical device registration in the US¹⁶

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