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Pathway for Marketing Authorization Approval of Drug Product in US

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Abstract

Developing a promising drug molecule is the main aim of the pharmaceutical company and it takes approximately fifteen years to develop one new medicine from the earliest stages of discovery to the time it is available for treating patients. To fasten the process in bringing products to market, product development activities should be conducted in accordance with the related regulatory requirements. These requirements assist in manufacture a product that meets the regulatory standards of targeted authority. Even though information on the regulatory requirements (e.g. laws, guidance documents, international standards) for healthcare product development is readily accessible, navigating the regulatory system is not simple, and it gets even more complex when dealing with multiple authorities. To aid the drug manufacturers and to simplify the regulatory understanding that governs the product development and ensures regulatory compliance. It can be used as a starting point to assist in developing the product. Rather than serving as a compilation of regulations, the guide discusses the fundamental concepts and principles in regulatory affairs. It gives entrepreneurs a road map to follow.

Keywords: Drug Development; Marketing Authorization; Road map; Regulations; Regulatory requirement; USFDA

Introduction

Developing a promising drug molecule is the main aim of the pharmaceutical company and it takes approximately fifteen years to develop one new medicine from the earliest stages of discovery to the time it is available for treating patients. To fasten the process in bringing products to market, product development activities should be conducted in accordance with the related regulatory requirements. These requirements assist in manufacture products that meet the regulatory standards of targeted authority. In order to control and regulate medicinal products, Drug regulatory authorities are being established in various countries across the globe. The regulatory body ensures in various legal and regulatory aspects of a drug.

Regulatory authorities are in charge for enforcing the rules and regulations issuing the guidelines to regulate the drug development process, licensing, registration, manufacturing, marketing and labeling of pharmaceutical products. They also responsible to ensure safety, efficacy and quality of drugs and also provide drug information available to the public Even though information on the regulatory requirements (e.g. laws, guidance documents, international standards) for healthcare product development is readily accessible, navigating the regulatory system is not simple, and it gets even more complex when dealing with multiple authorities.

In order to fasten the process of bringing the product into the market, there is a need to know where the regulatory information (Acts / Regulations / Guidance) are located on the regulatory websites. This can be obtained by the help of a "Navigation pathway" to get a regulatory approval from a targeted authority and to market the drug products that are safe and effective to provide healthcare to individuals around the world.

Steps in the Product development life cycle

Step 1: Classify the healthcare product

Step 2: Identify the healthcare claim and/or product label

Step 3: Step 3: Determine the healthcare market

Step 4: Develop the regulatory strategy

Step 5: Establish the product development plan

Step 6: Execute the product development plan

Step 7: Execute the clinical plan

Step 7a: Prepare for a pre-submission meeting to support the CTA

Step 8: Collect the data for regulatory submission

Step 8a: Prepare for a pre-submission meeting to support licensing application

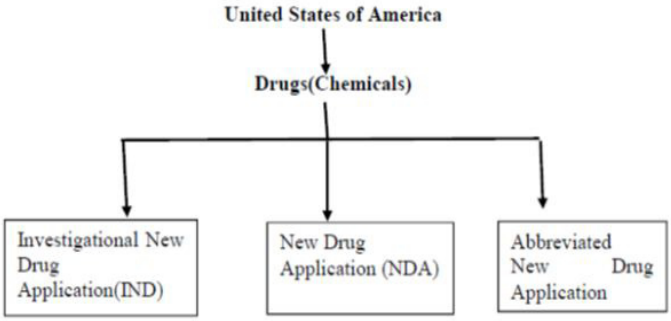
Step 9: Collate the data for regulatory submission

Step 10: Ensure post-marketing surveillance

Advantages of Navigation Pathway

- Providing an applicant / regulatory expert on the website with the most descriptive path to application / regulatory information is one of the easiest ways to ensure they don't get confused while preparing a regulatory application / dossier.
- If websites are to attract application/application services, they need easy browsing experience, and then the path of navigation of the website will be the main factor in the website design and development process.
- The navigation pathway not only benefits the applicant but also benefits the agency stakeholders, i.e. industry and agency.

Discussion



United States of America Factsheets

• **Chemicals: IND-US**	
• **Regulatory Factsheet**	
• Product	• Drugs
• Country	• USA
• Type of Application	• IND
• Life Cycle Phase	• R&D
• Regulatory Department	• Department of Health and Human Services
• Regulatory Agency	• US Food and Drug Administration(FDA)
• Division	• Center for Drug Evaluation & Research (CDER)
• Regulatory Classification	• Chemicals

Introduction

The IND is the means through which the sponsor technically obtains this exemption from the FDA. The sponsor's primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies commercial development.

Resources for Ind Submissions

The following resources include the legal requirements of an IND application, assistance from CDER to help you meet those requirements, and internal IND review principles, policies and procedures.

Guidance Documents for IND

These documents are prepared for FDA review staff and applicants/sponsors to provide guidelines to the processing, content, and evaluation/approval of applications and also to the design, production, manufacturing, and testing of regulated products.

Laws, Regulations, Policies and Procedures

The Federal Food, Drug, and Cosmetic Act is the basic food and drug law of the U.S. With numerous amendments, it is the most extensive law of its kind in the world. The law is intended to assure consumers that foods are pure and wholesome, safe to eat, and produced under sanitary conditions; that drugs and devices are safe and effective for their intended uses; that cosmetics are safe

and made from appropriate ingredients; and that all labelling and packaging is truthful, informative, and not deceptive.

Code of Federal Regulations (CFR)

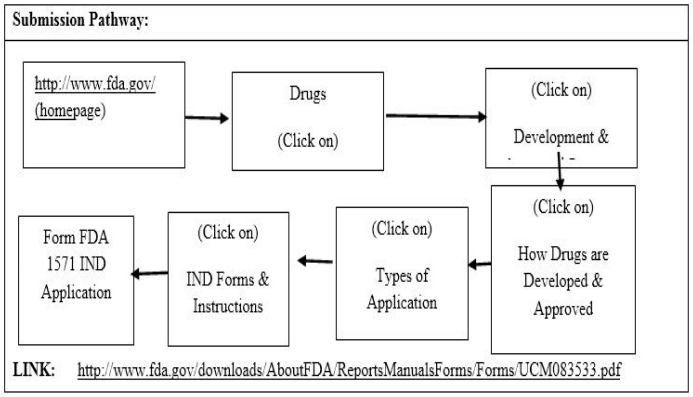
The FDA's portion of the CFR interprets The Federal Food, Drug, and Cosmetic Act and related statutes. The CFR is divided into 50 titles that represent broad areas subject to Federal regulations. The following regulations apply to the IND application process:

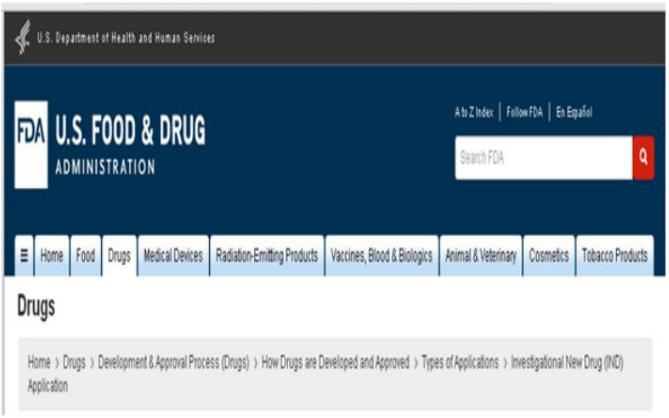
Sl No.	CFR Part	Type of Application
01	21CFR Part 312	Investigational New Drug Application
02	21CFR Part 314	INDA and NDA Applications for FDA Approval to Market a New Drug (New Drug Approval)
03	21CFR Part 58	Good Lab Practice for Nonclinical Laboratory [Animal] Studies

CDER's Manual of Policies and Procedures (Ma PPs)

These documents are approved instructions for internal practices and procedures followed by CDER staff to help standardize the new drug review process and other activities

Guidance Documents - Ind		
Sl No	**Title**	**Issued Date**
1	Safety Reporting Requirements for INDs (Investigational New Drug Applications) and BA/BE (Bioavailability/Bioequivalence) Studies Safety Reporting Requirements for INDs (Investigational New Drug Applications) and BA/BE (Bioavailability/Bioequivalence) Studies	12/19/12
2	Current Good Manufacturing Practice for Phase 1 Investigational Drugs	07/14/08
3	Exploratory IND Studies	01/12/06
4	Content and Format of INDs for Phase 1 Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-Derived Products. Questions and Answers	10/01/00
5	Bioavailability and Bioequivalence Studies Submitted in NDAs or INDs - General Considerations	03/17/14
6	IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer	01/15/04
7	Drug Master Files: Guidelines	09/01/89
8	FDA IND, NDA, ANDA, or Drug Master File Binders	
9	Immunotoxicological Evaluation of Investigational New Drugs	10/01/02
10	Content and Format of Investigational New Drug Applications (INDs) for Phase 1 Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-derived Products	11/01/95
11	Safety Assessment for IND Safety Reporting Guidance for Industry	12/16/15





Checklist
http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/UCM368873.pdf [2]
Reference Link
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm [3]

Chemicals: NDA-US	
Regulatory Factsheet	
Product	Drugs
Country	USA
Type of Application	NDA
Lifecycle Phase	R&D
Regulatory Department	Department of Health and Human Services
Regulatory Agency	US Food & Drugs Administration (FDA)
Division	Center for Drug Evaluation & Research (CDER)
Regulatory Classification	Drugs

Introduction

The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S. The data gathered during the animal studies and human clinical trials of an Investigational New Drug (IND) become part of the NDA.

Resources for Ind Submissions

The following resources are provided in the website for understand the legal requirements of a new drug application, assistance from CDER to meet those requirements, and internal NDA review principles, policies and procedures.

Guidance Documents for NDAs:

These documents are prepared for FDA review staff and applicants/sponsors to provide guidelines to the processing, content, and evaluation/approval of applications and also to the design, production, manufacturing, and testing of regulated products.

Laws, Regulations, Policies and Procedures:

The Federal Food, Drug, and Cosmetic Act is the basic food and drug law of the U.S. With numerous amendments, it is the most extensive law of its kind in the world. The law is intended to assure consumers that foods are pure and wholesome, safe to eat, and produced under sanitary conditions; that drugs and devices are safe and effective for their intended uses; that cosmetics are safe and made from appropriate ingredients; and that all labelling and packaging is truthful, informative, and not deceptive.

CDER's Manual of Policies and Procedures (MaPPs):

These documents are approved instructions for internal practices and procedures followed by CDER staff to help standardize the new drug review process and other activities.

Prescription Drug User Fee Act (PDUFA):

This legislation includes authorization for FDA to continue to collect three types of user fees from applicants who submit certain new drug applications.

NDA Forms and Electronic Submissions:

This section provides information on various application forms required for submission of NDA application.

Advisory Committees:

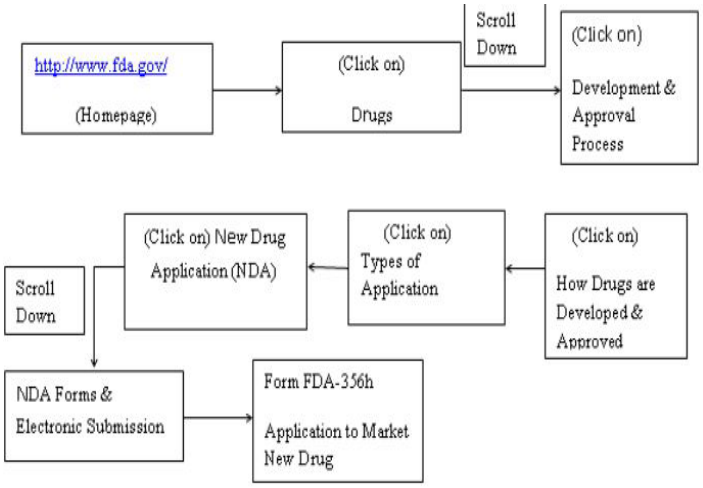
Advisory committees provide independent advice and recommendations to the FDA on scientific and technical matters related to the development and evaluation of products regulated by the Agency. CDER requests advice from advisory committees on a variety of matters, including various aspects of clinical investigations and applications for marketing approval of drug products.

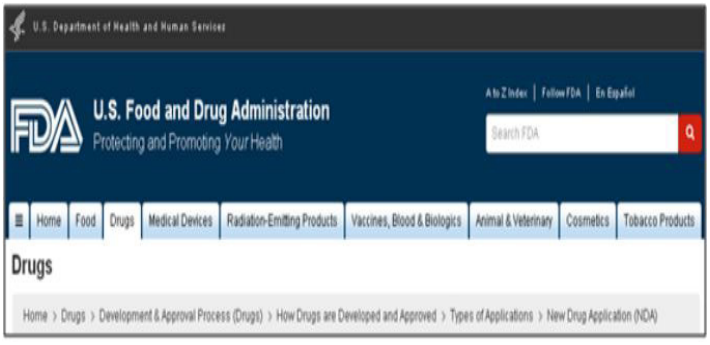
Guidance Documents-NDA

Sl No	Title	Issued Date
01	Bioavailability and Bioequivalence Studies Submitted in NDAs or INDs - General Considerations	03/17/14
02	Changes to an Approved NDA or ANDA	04/01/04
03	Changes to an Approved NDA or ANDA: Questions and Answers	01/01/01
04	Container Closure Systems for Packaging Human Drugs and Biologics	05/01/99
05	Format and Content of the Microbiology Section of an Application	01/01/90
06	Format and Content of the Clinical and Statistical Sections of an Application	07/01/88
07	Summary for New Drug and Antibiotic Applications--Format and Content of the Summary for New Drug and Antibiotic Applications	02/01/87
08	Formatting, Assembling and Submitting New Drug and Antibiotic Applications	02/01/87

09	Guideline for Submitting Supporting Documentation in Drug Applications for the Manufacture of Drug Products	
10	NDAs: Impurities in Drug Substances	02/01/87
11	Format and Content of the Human Pharmacokinetics and Bioavailability Section of an Application	02/01/87
12	Format and Content of the Nonclinical Pharmacology/Toxicology Section of an Application	02/01/87
13	Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products	
14	Drug Master Files: Guidelines	09/01/89
15	FDA IND, NDA, ANDA, or Drug Master File Binders	
16	PET Drug Applications - Content and Format for NDAs and ANDAs_2011	08/31/11

Submission Pathway





Checklist
http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM315023.pdf [5]

Reference Link: Quality Accreditation	
Type of Certificate	**URL website**
GMP	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=211
GLP	http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=58&showFR=1
GCP	http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm219433.htm
Reference Link	
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.ht [6]	

Chemicals: ANDA-US	
Regulatory Factsheet	
Product	Drugs
Country	USA
Type of Application	ANDA
Lifecycle Phase	MAA
Regulatory Department	Department of Health and Human Services
Regulatory Agency	US Food & Drugs Administration (FDA)
Division	Center for Drug Evaluation & Research (CDER)
Regulatory Classification	Chemicals

Introduction

An Abbreviated New Drug Application (ANDA) contains data which when submitted to FDA's Centre for Drug Evaluation and Research, Office of Generic Drugs, provides for the review and ultimate approval of a generic drug product. All approved products, both innovator and generic, are listed in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)

Generic drug applications are termed "abbreviated" because they are generally not required to include preclinical (animal) and

clinical (human) data to establish safety and effectiveness. Using bioequivalence as the basis for approving generic copies of drug products was established by the "Drug Price Competition and Patent Term Restoration Act of 1984," also known as the Waxman-Hatch Act

Resources For And a Submissions

The following resources have been gathered to provide you with the legal requirements of an ANDA application, assistance from CDER to help you meet those requirements, and internal ANDA review principles, policies and procedures.

Guidance Documents for ANDAs:

These documents are prepared for FDA review staff and applicants/sponsors to provide guidelines to the processing, content, and evaluation/approval of applications and also to the design, production, manufacturing, and testing of regulated products.

Laws, Regulations, Policies and Procedures:

The Federal Food, Drug, And Cosmetic Act is the basic food and drug law of the U.S. With numerous amendments, it is the most extensive law of its kind in the world. The law is intended to assure consumers that foods are pure and wholesome, safe to eat, and produced under sanitary conditions; that drugs and devices are safe and effective for their intended uses; that cosmetics are safe and made from appropriate ingredients; and that all labelling and packaging is truthful, informative, and not deceptive.

CDER's Manual of Policies and Procedures (MaPPs):

These documents are approved instructions for internal practices and procedures followed by CDER staff to help standardize the drug review process and other activities.

ANDA Forms and Electronic Submissions:

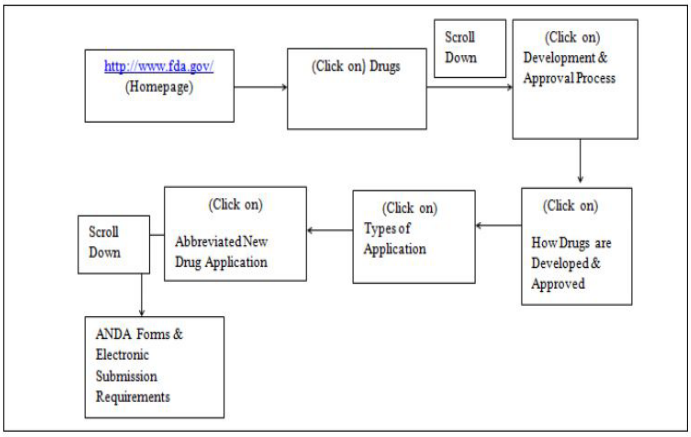
This section provides information on various application forms required for submission of ANDA application

Guidance Documents - ANDA

Sl No	Title	Issued Date
01	Microbiological Data for Systemic Antibacterial Drug Products - Development, Analysis, and Presentation	08/25/16
02	ANDA Submissions - Refuse to Receive for Lack of Justification of Impurity Limits	08/24/16
03	Regulatory Classification of Pharmaceutical Co-Crystals	08/16/16
04	Ulcerative Colitis: Clinical Trial Endpoints Guidance for Industry	08/05/16
05	Insanitary Conditions at Compounding Facilities Guidance for Industry	08/03/16
06	E2C(R2) Periodic Benefit-Risk Evaluation Report (PBRER)	07/18/16
07	E2C(R2) Periodic Benefit-Risk Evaluation Report - Questions and Answers	07/18/16
08	Bacterial Vaginosis: Developing Drugs for Treatment Guidance for Industry	07/13/16
09	Updating ANDA Labeling After the Marketing Application for the Reference Listed Drug Has Been Withdrawn Guidance for Industry	07/08/16
10	Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance for Industry	07/07/16
11	Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry	07/07/16
12	Elemental Impurities in Drug Products	06/30/16
13	Vulvovaginal Candidiasis: Developing Drugs for Treatment	06/30/16
14	Recurrent Herpes Labials: Developing Drugs for Treatment and Prevention	06/30/16
15	Technical Specifications Document: "Quality Metrics Technical Conformance Guide, Version 1.0" has published	06/24/16
16	Quality Attribute Considerations for Chewable Tablets Guidance for Industry	06/16/16
17	Osteoporosis: Nonclinical Evaluation of Drugs Intended for Treatment Guidance for Industry	06/13/16
18	Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance for Industry	06/09/16
19	Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Ac	06/09/16
20	Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance	06/09/16
21	Charging for Investigational Drugs Under an IND - Qs & As	06/02/16
22	Expanded Access to Investigational Drugs for Treatment Use - Qs & As	06/02/16

23	Individual Patient Expanded Access Applications: Form FDA 3926	06/02/16
24	E18 Genomic Sampling and Management of Genomic Data	06/02/16
25	Assessing Adhesion with Transdermal Delivery Systems and Topical Patches for ANDAs Draft Guidance for Industry	05/31/16
26	Chronic Obstructive Pulmonary Disease: Developing Drugs for Treatment	05/19/16
27	Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry	05/16/16

Submission Pathway



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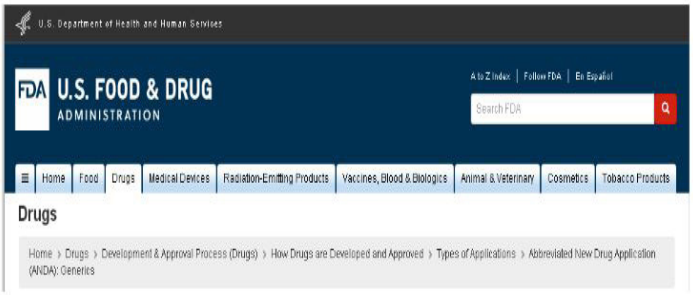

Checklist
http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM320405.pdf [8]
Reference Link
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm [9]

References

1. http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf
2. http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/UCM368873.pdf
3. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm
4. http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf
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