Early Drug Development Package

Welcome and congratulations on developing your pharmaceutical drug or concept for a new drug. Compliance Insight has put together information to assist with navigation of the FDA website and determining how to move forward with your new invention. The information and attachments center around FDA regulations related to pharmaceuticals for human use.

FDA Website Links

1. The link to FDA's webpage on "How Drugs are Developed and Approved", "How Drugs are Developed and Approved"
2. The link to FDA Good Manufacturing Practices, 21 CFR Part 210/211. These are the minimum manufacturing requirements for drug manufacturing,
   CFR – Code of Regulations Title 21Part 210
   CFR – Code of Federal Regulations Title 21 Part 211
3. Link to the FDA Pre-IND Consultation Program,
   Pre-IND Consultation Program
4. Link to the FDA Types of Applications: IND, NDA, ANDA, OTC and Entire Drug Development process,
   New Drug Development and Review Process
   The Drug Development Process

What is included?

1. FDA Drug Approval pathways
2. FDA Drug Approval Process and Timeline
3. Abbreviated New Drug Application (ANDA) Timeline
4. OTC Drug Monograph Process
5. FDA Pre-IND Contact List
6. FY 2023 GDUFA & PDUFA User Fees
7. Minimum Required Documents for Phases 1-3 (3 pages)
8. Common issues with filing an ANDA or NDA
9. A basic list of SOPs recommended for Virtual and Start UP companies. This list will be modified based upon the drug manufacturing process

For additional questions/concerns please set up an initial consultation by calling 513-860-3512 or email info@compliance-insight.com

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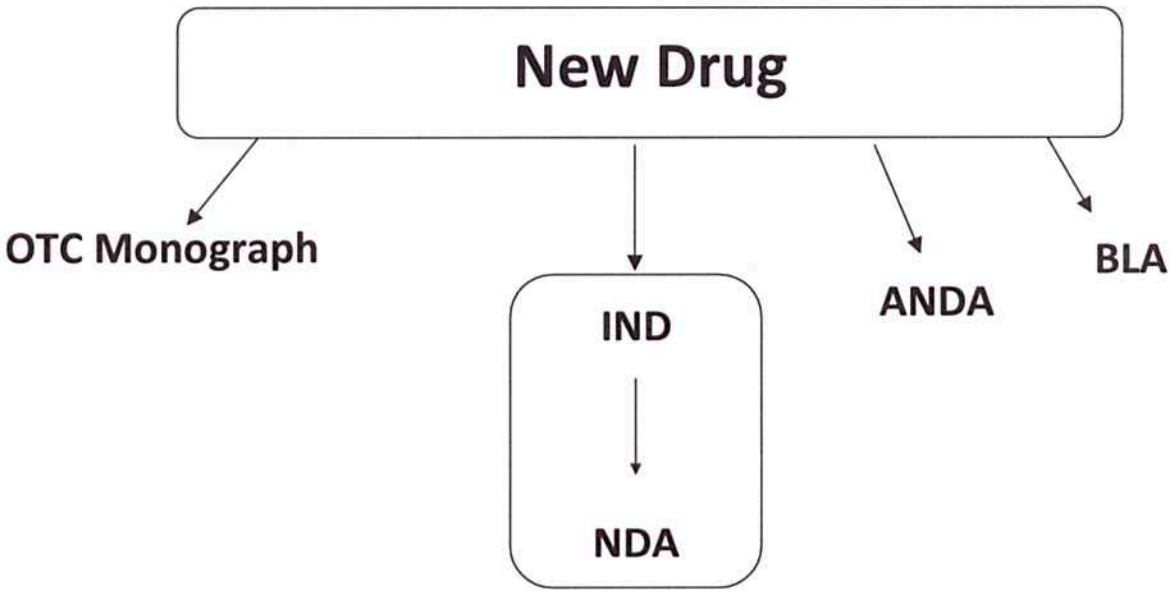
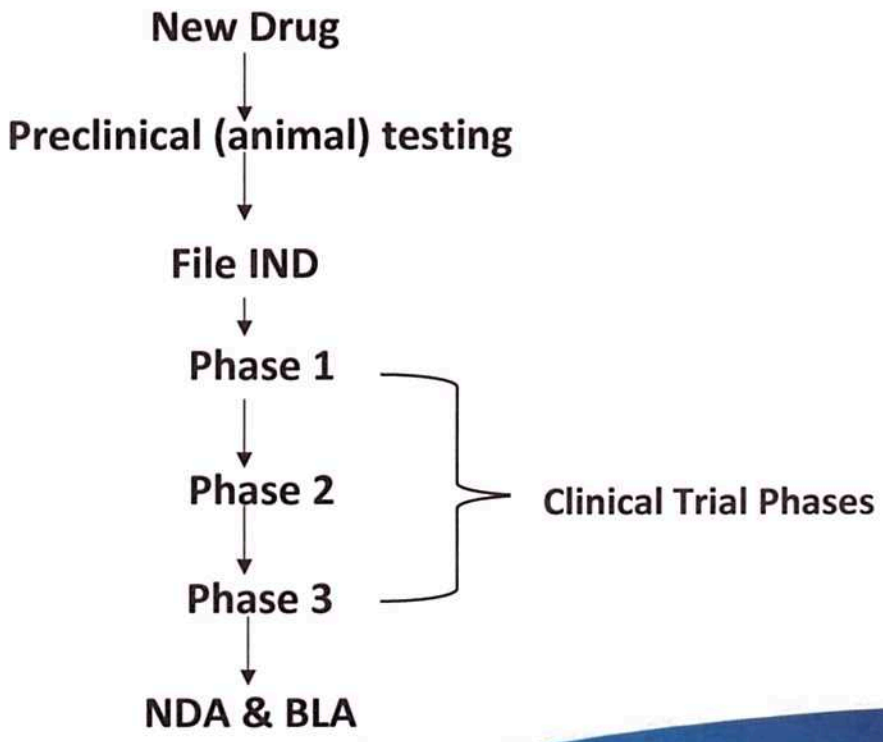
FDA Drug Approval Pathways



NDA Process; Shown in more detail



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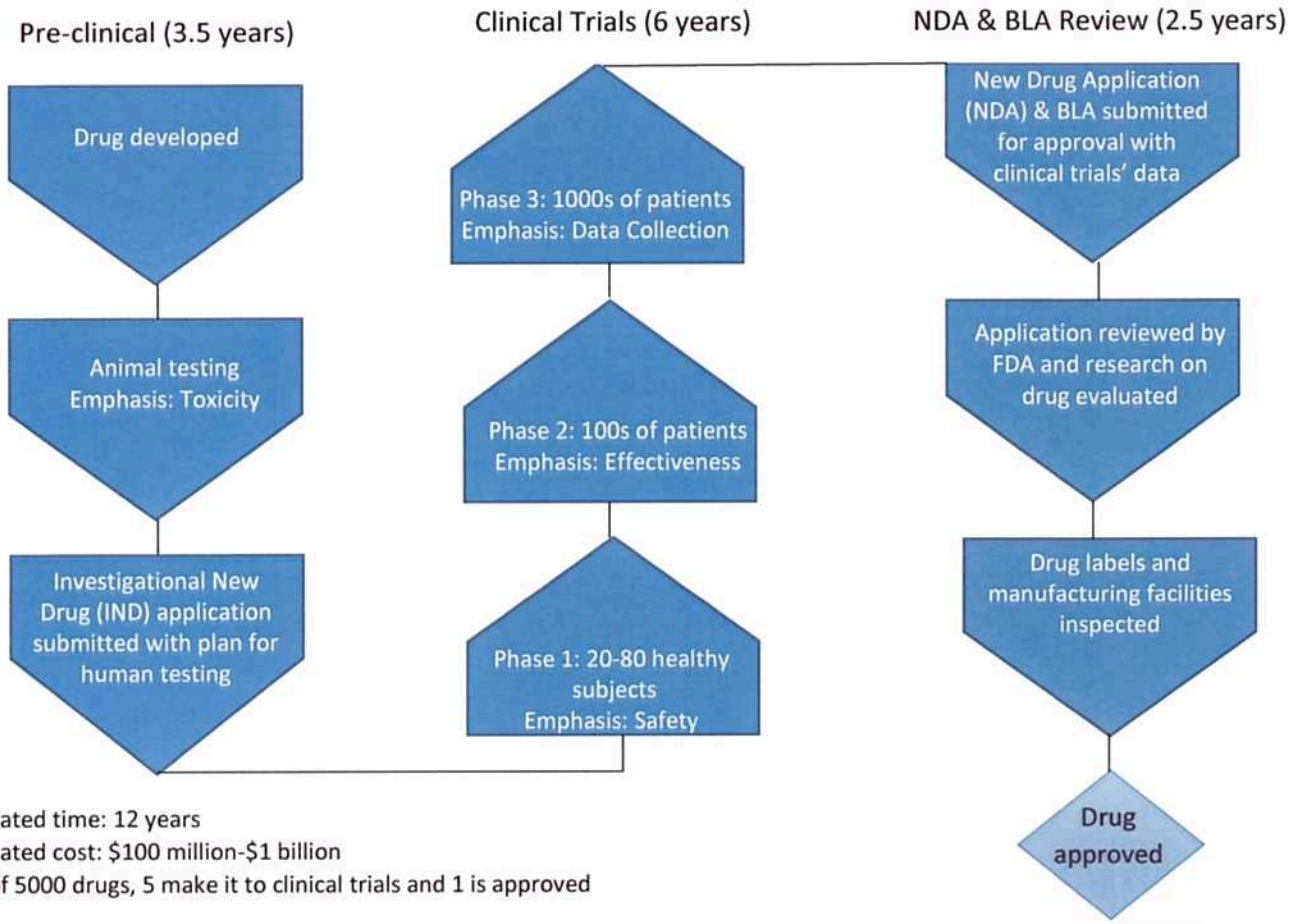
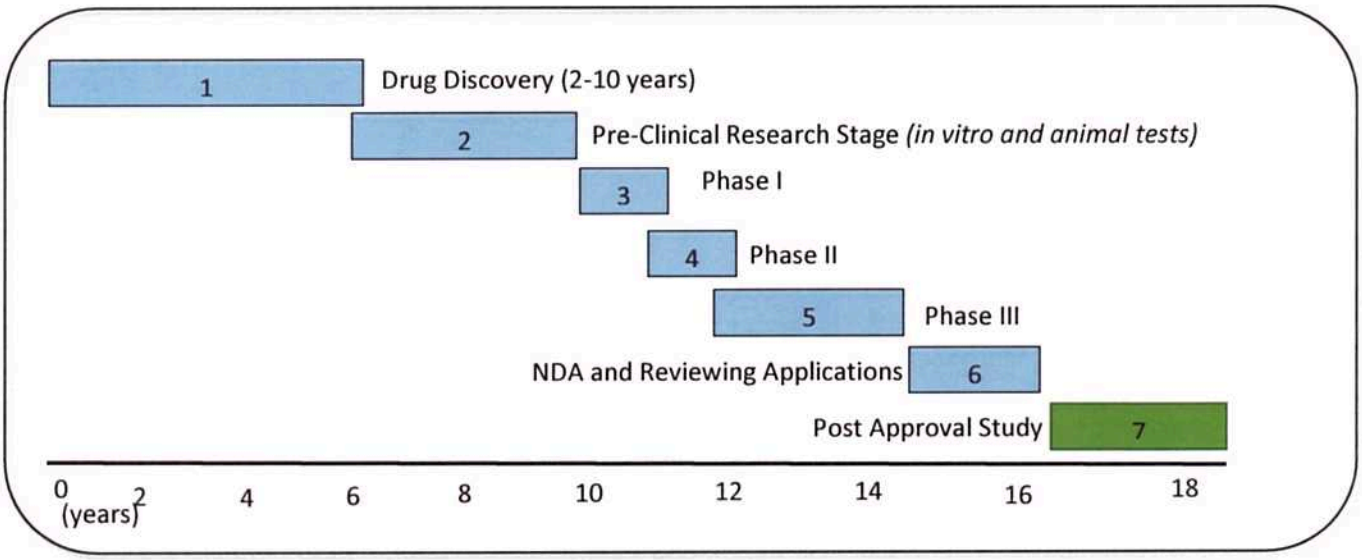
FDA Drug Approval Process and Timeline



- Estimated time: 12 years
- Estimated cost: $100 million-$1 billion
- Out of 5000 drugs, 5 make it to clinical trials and 1 is approved



www.nationaljournal.com
www.justforecast.com

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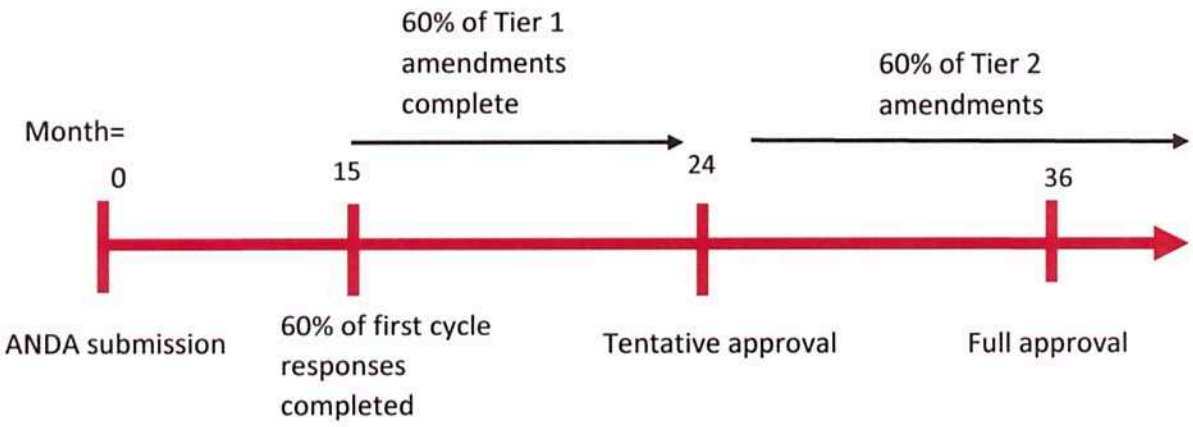
ANDA Timeline



Source: FDA, statnews.com

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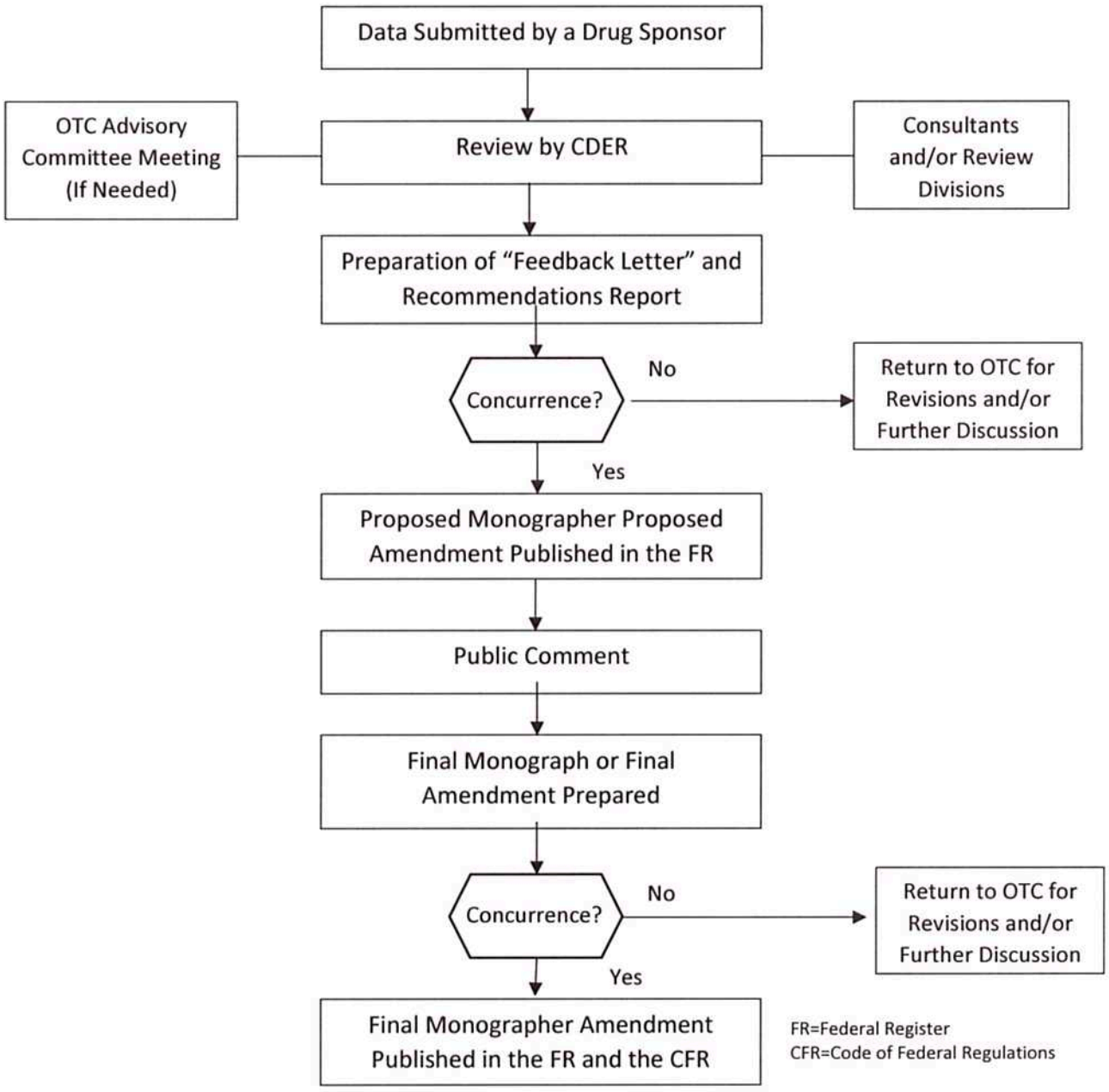
OTC Drug Monograph Process



FR=Federal Register
CFR=Code of Federal Regulations

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CENTER FOR DRUG EVALUATION AND RESEARCH
PRE-IND Consultation Contacts

Office of Drug Evaluation I

Division of Cardiovascular & Renal Products
Edward Fromm
301-796-2240
Fax: 301-796-9841

Division of Neurology Products
Jacqueline Ware
301-796-1160
Fax: 301-796-9842

Division of Psychiatry Products
Steven Hardeman
301-796-1081
Fax: 301-796-9838

Office of Drug Evaluation II

Division of Anesthesia, Analgesia & Addiction Products
Parinda Jani
301-796-1232
Matt Sullivan
301-796-1245
Fax: 301-796-9722

Division of Metabolism & Endocrinology Products
Julie Van der Waag
301-796-1280
Pamela Lucarelli
310-796-3961
Fax: 301-796-9712

Division of Pulmonary, Allergy and Rheumatology Products
Sandy Barnes
301-796-1174
Fax: 301-796-9728

Office of Drug Evaluation III

Division of Gastroenterology & Inborn Error Products
Richard (Wes) Ishihara
Brian Strongin
301-796-2120
Fax: 301-796-9906

Division of Dermatology & Dental Products
Barbara Gould
301-796-4224
Fax: 301-796-9895

Division of Reproductive & Urologic Products
Jennifer Mercier
301-796-0934
Margie Kober
301-796-0937
Fax: 301-796-9897

Office of Drug Evaluation IV

Division of Nonprescription Clinical Evaluation
Dan Brum
301-796-0578
Fax: 301-796-9899

Division of Medical Imaging Products
Kyong Kang
301-796-2050
Fax: 301-796-9848

Division of Non-Prescription Regulation Development
Dan Brum
301-796-0578
Fax: 301-796-9899

Botanical Review Team
Jagit Grewal
301-796-0846
Fax: 301-595-7865

Office of Antimicrobial Products: PRE-IND Consultation Program

Division of Anti-Infective Products
Carrmen DeBellas
301-796-1203
Maureen Dillion-Parker
301-796-0706
Fax: 301-796-9881

Division of Transplant & Ophthalmology Products
Diana Williard
301-796-1600
Fax: 301-796-9880

Division Anti-Viral Products
Nina Mani
Karen Winestock
301-796-1500
Fax: 301-796-9883

Office of Hematology and Oncology Drug Products

Division of Oncology Products (1)
Christy Cottrell
301-796-4256
Alice Kacuba
301-796-1381
Fax: 301-796-9899

Division of Oncology Products (2)
Monica Hughes
301-796-9225
Melanie Pierce
301-796-1273
Fax: 301-796-9849

Division of Hematology Products
Theresa A. Carioti
301-796-2848
Amy Baird
301-796-4969
Fax: 301-796-9848

Division of Hematology
Division of Oncology
(Please reference any of the point of contacts listed above.)

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https://www.fda.gov/media/77025/download

Updated on 4/12/2017

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2023 GDUFA User Fees

Application	Standard Fee
Abbreviated New Drug Application (ANDA)	$240,582
Drug Master File	$78,293
Facilities	**Standard Fee**
Active Pharmaceutical Ingredient (API)-Domestic	$37,544
Active Pharmaceutical Ingredient (API)-Foreign	$52,544
Finished Dosage Form (FDF)-Domestic	$213,134
Finished Dosage Form (FDF)-Foreign	$228,134
Contract Manufacturing Organization (CMO)	$51,152
Contract Manufacturing Organization (CMO)-Foreign	$66,152
GDUFA Program	**Standard Fee**
Large size operation generic drug applicant	$1,620,556
Medium size operation generic drug applicant	$648,222
Small size operation generic drug applicant	$162,056

https://www.federalregister.gov/documents/2022/10/12/2022-22099/generic-drug-user-fee-rates-for-fiscal-year-2023

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Minimum Required Documents for Phases 1-3

Phase 1 Required Documents

Investigator brochure	API Certificate Of Analysis
Phase 1 Clinical study protocol outline	API test method description and specifications (if available)
API manufacturing process flow diagram	API stability data to support Phase 1 studies
FP Quantitative Composition	FP manufacturing process flow diagram
FP test method description and specifications (if available)	FP stability data to support Phase 1 studies
FP Labeling mock up	Pharmacology and Distribution
Toxicology summary	Toxicology tabulation data
Environmental assessment information	

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/Overview/UCM166356.pdf

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Phase 2 Required Documents

Data from first Phase Clinical trial plus any updates and safety concerns	Updated API manufacturing process flow diagram with added details
Phase 2 clinical study protocol outline	API stability data to support Phase 1 and 2 studies
API characterization	API impurity profile
Reference/Working standard	API container/closure system
API test method description and specifications (if available)	Updated FP manufacturing process flow diagram with details
Specs for each excipient with test methods. Test method validation summary should be available	Updated specs for FP and test methods. Test method validation summary should be available
FP Labeling mock up	FP stability data to support Phase 1 and 2 studies
Environmental assessment updates	Updated FP Quantitative Composition

Also see Phase 1 required documents

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/Overview/UCM166356.pdf

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Phase 3 Required Documents

Clinical data from Phase 2 study	Clinical study protocol for Phase 3
API detailed characterization	New API impurities update with limits
Clinical trial API batch test data, specs, test methods, and validation data summary	Updated manufacturing flow chart and detailed step by step description
Updated API reference standard and/or working standard characterization	Stress study data for API
FP test method description and specifications (if available)	API stability data to support Phase 1, 2, 3 studies and stability protocol
Updated batch formula	Degradation profile and limits
Updated excipient controls	Updated FP labeling
Updated FP container closure system	Composition and control of Placebo
FP stability data to support Phase 1, 2, 3 studies and stress testing data	Updated test methods and specifications with validation data available
Environmental assessment updates	x

Also see Phases 1 & 2 required documents

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/Overview/UCM166356.pdf

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Common issues filing an ANDA or NDA

1. Unexpected safety issues
2. Failure to demonstrate drug effectiveness
3. Added clinical studies required for more people, different types of people, or for a longer time period
4. Manufacturing issues noted prior to or during the Pre-Approval Inspection (PAI) related to failure to meet GMPs
5. Manufacturing scale up issues
6. Supplier issues

The drug application requires significant times and resources. If preparing these submissions becomes an overwhelming hurdle, we can help.

www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm289601.htm

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SOP Index for Virtual/Startup Companies

SOP Number	Title
QA-XXX	**Quality Assurance**
001	General Requirements for SOPs
002	Quality Assurance
003	SOP Numbering System
004	Change Control
005	Documentation Practices
006	Personnel Training
007	Customer Complaints
008	Returned Goods
009	Product Recall, Field Alerts and Market Withdrawal
010	Records Retention
011	Document Storage Guidelines
012	Internal Quality Audits
013	Qualification of Raw Material Vendors
014	Conducting Investigations
015	Deviation/Investigation Reports
016	CAPA Program
017	Annual Product Review
018	Master Batch Records Preparation Guidelines
019	Retention & Retrievability of Executed Batch Records
020	Qualification Management of 3rd Party Vendors
021	Vendor Audits
022	Quality Agreements
023	Hosting a GMP Audit
024	Labeling Specifications
025	Labeling Reconciliation
026	Trend Analysis
027	Management Notification
028	Quality Roles & Responsibilities
029	Annual Report & Supplements
030	Process Risk Analysis
031	Part 11 Compliance-Change Control
032	Part 11 Compliance-General Requirements
033	Security Controls
034	Electronic Records
035	Electronic Signatures

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SOP Number	Title
VA-XXX	**Validation**
001	Validation
002	Validation of Manufacturing Processes
003	Software Validation
004	Equipment Qualification
005	Method validation
QC-XXX	**Quality Control**
001	Specifications for Raw materials & Finished Product
002	Retention Samples
003	Certificate of Analysis
004	Handling of Out of Specification (OOS) Results
005	Stability Program
006	Impurity Profile
SD-XXX	**Packaging, Storage and Distribution**
001	Shipping Specifications for Product
002	Warehousing and Distribution of GMP manufactured Products
003	Product Distribution Records
004	Inventory Control of Finished Products