Module 6: New Drug Application Documents

Topic 6.1 FDA Review Process

Welcome. This module will focus on the the final stage of drug approval. When the clinical studies are complete, it is time to submit final documents to the FDA. The application documents you submit are very specific depending on whether you are submitting a drug, a biologic, or a medical device. Regardless of the the type of product you are submitting for approval, the format and content are rigorously determined by the regulations of the FDA and ICH. In this module we will look at the FDA Review Process and the History of the FDA rules and regulations in order to fully understand what goes into a new application for a product (drug, biologic, or device) and why.

In our first topic we will discuss the FDA Review Process.

Submission to the FDA

The FDA review and approval process is centered around the submission of appropriate applications.

The IND, Investigational New Drug Application you have already learned about. It is a milestone or gatekeeper for the beginning of Phase 1 trials.

The IND is a living document that is updated throughout the trial process. It is the foundation of the final applications and approvals.

Investigational New Drug (IND)

Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA

New Drug Application (NDA)

When the sponsor of a new drug believes that enough evidence on the drug's safety and effectiveness has been obtained to meet FDA's requirements for marketing approval, the sponsor submits to FDA a new drug application (NDA). The application must contain data from specific technical viewpoints for review, including chemistry, pharmacology, medical, biopharmaceutics, and statistics. If the NDA is approved, the product may be marketed in the United States. For internal tracking purposes, all NDA's are.

Abbreviated New Drug Application (ANDA)

An Abbreviated New Drug Application (ANDA) contains data that, when submitted to FDA's Center for Drug Evaluation and Research, Office of Generic Drugs, provides for the review and ultimate approval of a generic drug product. Generic drug applications are called "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and effectiveness. Instead, a generic applicant must scientifically demonstrate that its product is bioequivalent (i.e., performs in the same manner as the innovator drug). Once approved, an applicant may manufacture and market the generic drug product to provide a safe, effective, low cost alternative to the American public.

Biologic License Application (BLA)

Biological products are approved for marketing under the provisions of the Public Health Service (PHS) Act. The Act requires a firm who manufactures a biologic for sale in interstate commerce to hold a license for the product. A biologics license application is a submission that contains specific information on the manufacturing processes, chemistry, pharmacology, clinical pharmacology and the medical affects of the biologic product. If the information provided meets FDA requirements, the application is approved and a license is issued allowing the firm to market the product.

Label and Approval

Approved labeling language for the product is the ultimate goal of the process.

Common Technical Documents

ICH established a common format and content requirements for most applications worldwide.

Technical information can be prepared once for worldwide use.

We will cover the modules of the Common Technical Document later in Topic 6.3 Marketing Application Documents.

International Council on Harmonisation

International Council on Harmonisation (ICH Guidelines) (Coordination of US, EU and Japan requirements) EMA Changes (2006 - 2007) Japan moving towards harmonization.

FDA Major Concerns

It is important to understand the main concerns of the FDA.

- IDENTITY
- PURITY
- SAFETY
- EFFICACY
- QUALITY
- INTELLECTUAL PROPERTY RIGHTS (only from a listing perspective)

Comparative efficacy and Pricing is not a concern of FDA, but is an element of the review and registration process for EU countries

FDA Divisions

There are numerous divisions in the FDA. These are the ones that concern the approval of new medical products.

- Office of Regulatory Affairs
- Center for Biologics Evaluation and Research (BLA)
- Center for Drug Evaluation and Research (NDA)
- Center for Devices and Radiological Health (PMA)

Prescription Drug Fee User Acts

Fees (can be waived for small businesses)	Federal FY 1998	Federal FY 2016
Applications with Clinical Data	$ 256,846	$ 2,374,200
Applications without Clinical Data	$ 128,423	$ 1,187,100
Supplements with Clinical Data	$ 128,423	$ 1,187,100
Annual Establishment Fees	$ 141,966	$ 585,2000
Annual Product Fees	$ 18,591	$ 114,450

All but one of the novel drugs approved in 2014 met the PDUFA goal Almost three-quarters of the novel drugs approved in 2014 were approved in first cycle review

More than half of the novel drugs approved in 2014 were Priority Review More than on-third of novel drugs approved in 2014 received Fast Track designation

Summary

In this topic we began to describe the purpose of FDA review and approval.

- Built from first FDA correspondence (IND)
    - Living document
    - Built from all data submissions
- Proof of safety and efficacy
- Quality compliance
- Contents support labeling