

14.3. ABBREVIATED NEW DRUG APPLICATION (ANDA)

14.3.1. Introduction

An Abbreviated New Drug Application (ANDA) includes data which is submitted to FDA for the review and potential approval of a generic drug product. An applicant may manufacture and market the generic drug product once approved to offer a safe, effective, lower cost alternative to the brand-name drug. Generic drug applications are normally not required to include preclinical (animal) and clinical (human) data to establish safety and effectiveness that is why they are termed as "abbreviated".

14.3.2. Objectives

- 1) To check whether the benefits of the drug outweigh the risks and whether the drug is safe and effective in its proposed use.
- 2) To check whether the drugs' proposed labelling (package insert) is appropriate and the matter in its content.
- 3) To check whether the controls used to preserve the drug's quality and the methods used in developing the drug are adequate to preserve the drug's identity, strength, quality, and purity.
- 4) To reduce the price of the drug.
- 5) To reduce the time development.
- 6) To increase the bioavailability of the drug in comparison to reference listed drug.

14.3.3. Content and Format

- 1) **Application Form:** A complete and signed application form should be submitted.
- 2) **Table of Contents:** The archival copy must contain a table of contents that shows the volume number and page number of the contents of the submission.
- 3) **Basis for Abbreviated New Drug Application Submission:** The name of the reference listed drug, including its dosage form and strength. For ANDA, a reference to FDA-assigned docket number for the petition and a copy of FDA's correspondence approving the petition.
- 4) **Conditions of Use:** A statement that the conditions of use prescribed, recommended, or suggested in the labelling proposed for the drug product have been previously approved for the reference listed drug.
- 5) **Active Ingredients:** It is observed that the active ingredients of the suggested drug are the same as those of the reference listed drugs.
- 6) **Administration Route, Dosage Form, and Strength:** Route of administration, dosage form, and strength of the proposed drug product are the same as those of the reference listed drug that are included in the statement.
- 7) **Bioequivalence:** The applicant relies on the information that the drug is bioequivalent to the reference listed drug. The results of any bioavailability of bioequivalence testing are required by the agency if the abbreviated new drug application is submitted.
- 8) **Labelling:**
 - i) **Listed Drug Labelling:** A copy of the currently approved labelling for the listed drug referred to in the abbreviated new drug application, if the abbreviated new drug application relies on a reference listed drug.
 - ii) **Copies of Proposed Labelling:** All labelling for the drug product and copies of the label.

- iii) **Statement on Proposed Labelling:** If applicable a statement that as the same as the labelling of the reference listed drug.
- iv) **Comparison of Approved and Proposed Labelling:** There may be difference in labelling revisions made to comply with current FDA labelling guidelines or other guidance, omission of an indication or other aspect of labelling protected by patent or accorded distinctiveness, bioavailability, or pharmacokinetics, expiration date and formulation for the applicants proposed labelling and labelling approved for the reference listed drug.
- 9) **Chemistry, Manufacturing, and Controls:** A description of the equipment, to be used for the manufacture of a commercial lot of the drug product, the proposed or actual master production record are to be included in the information provided.
- 10) **Samples:** Until requested by FAD samples are not required to be submitted.
- 11) **Patent Certification:** The generic manufacturer is required to file one of the four listed possible certifications on the subject of the reference brand name patent listed in the Orange Book while filling an ANDA.
 - i) **Para I Certification:** For the drug listed in this book there is no patent.
 - ii) **Para II Certification:** The listed patent has expired.
 - iii) **Para III Certification:** The patent is valid and listed but generic wants the permit to market the drug once the pertinent patent expires.
 - iv) **Para IV Certification:** The generic manufacturer either defines the validity of the brand name listed patent declaring it to be invalid or fake, or it confirms not to cross the fringe of the brand name patent claims.

14.3.4. Approval of ANDA

Procedure for ANDA approval:

- 1) Under section 505(j) Application for ANDA is made to FDA.
- 2) To determine whether the application is sufficiently complete to permit a substantive review a filing review is conducted.
- 3) Based on the completeness of the Abbreviated New Drug Application Acceptance/Refuse to Receive Letter is issued.
- 4) The OGD of CDER issue market is approved if all the information submitted by the applicant is accepted.

14.4. NEW DRUG APPLICATION (NDA)

14.4.1. Introduction

The basis for the control and regulation of new drug in the US for decades is the **New Drug Application (NDA)**. 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.

An NDA requires the following documents to provide the information about the drug:

- 1) Procedure of clinical tests
- 2) Ingredients of the drug
- 3) Results of the animal studies
- 4) Pharmacokinetics
- 5) Manufacturing, processing and packaging of drug

14.4.2. Objectives

The objective of NDA is to offer sufficient information to permit FDA reviewer to reach the following key decisions:

- 1) Whether the benefits of the drug outweigh the risks, whether the drug is safe and effective in its proposed use.
- 2) Whether the drugs' proposed labelling (package insert) is appropriate and it's content.
- 3) Whether the controls used to preserve the drug's quality and the methods used in manufacturing the drug are adequate to preserve the drug's identity, strength, quality, and purity.

14.4.3. Content and Format

It requires submitting the application in CTD format with different sections as following:

- 1) FDA form 356h,
- 2) User Fee Cover Sheet (FDA form 3397),
- 3) Cover letter,
- 4) Summary,
- 5) Chemistry, manufacturing and control,
- 6) Samples, method validation package and labeling,
- 7) Non-clinical pharmacology and toxicology,
- 8) Human pharmacokinetics and bioavailability,
- 9) Microbiology (For antimicrobial drugs only),
- 10) Statistical methods and analysis of clinical data,
- 11) Safety update report i.e., usually submitted 120 days after NDA submission,
- 12) Statement regarding compliance to IRB and Informed Consent Requirements,
- 13) Case report tabulations,
- 14) Case report forms,
- 15) Patent information and certification, and
- 16) Other information.

14.4.4. Approval Process for NDA

- 1) The process starts with a Pre-NDA meeting and addresses the submission of NDA including issues such as format and content.
- 2) The NDA submission and review is next to Pre-NDA meeting.

- 3) The time duration for deciding whether to accept the files to review FDA has 60 days.
- 4) FDA forwards this file to CDER for review and CDER will evaluate the eligibility for filing. If drug is found eligible accepts the application and forwards it to the FDA reviewer team.
- 5) The Food and Drug Administration (FDA) conducts inspections of regulated facilities to determine a firm's submission with applicable laws and regulations, like the Food, Drug, and Cosmetic Act and acts related to it.
- 6) The reviewer team submits the report to CDER within 180 days.
- 7) FDA issues marketing authorisation to the sponsor if the review result is positive.

14.5. NEW DRUG DEVELOPMENT