FORMATTING, ASSEMBLING & SUBMISSION OF ABBREVIATED NEW DRUG APPLICATION

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CHIPS

ANDA

- An Abbreviated New Drug Application (ANDA) contains data which when submitted to FDA's CDER, Office of Generic Drugs, provides for the review and ultimate approval of a generic drug product.

- Once approved, an applicant may manufacture and market the generic drug product to provide a safe, effective, low cost alternative to the public.

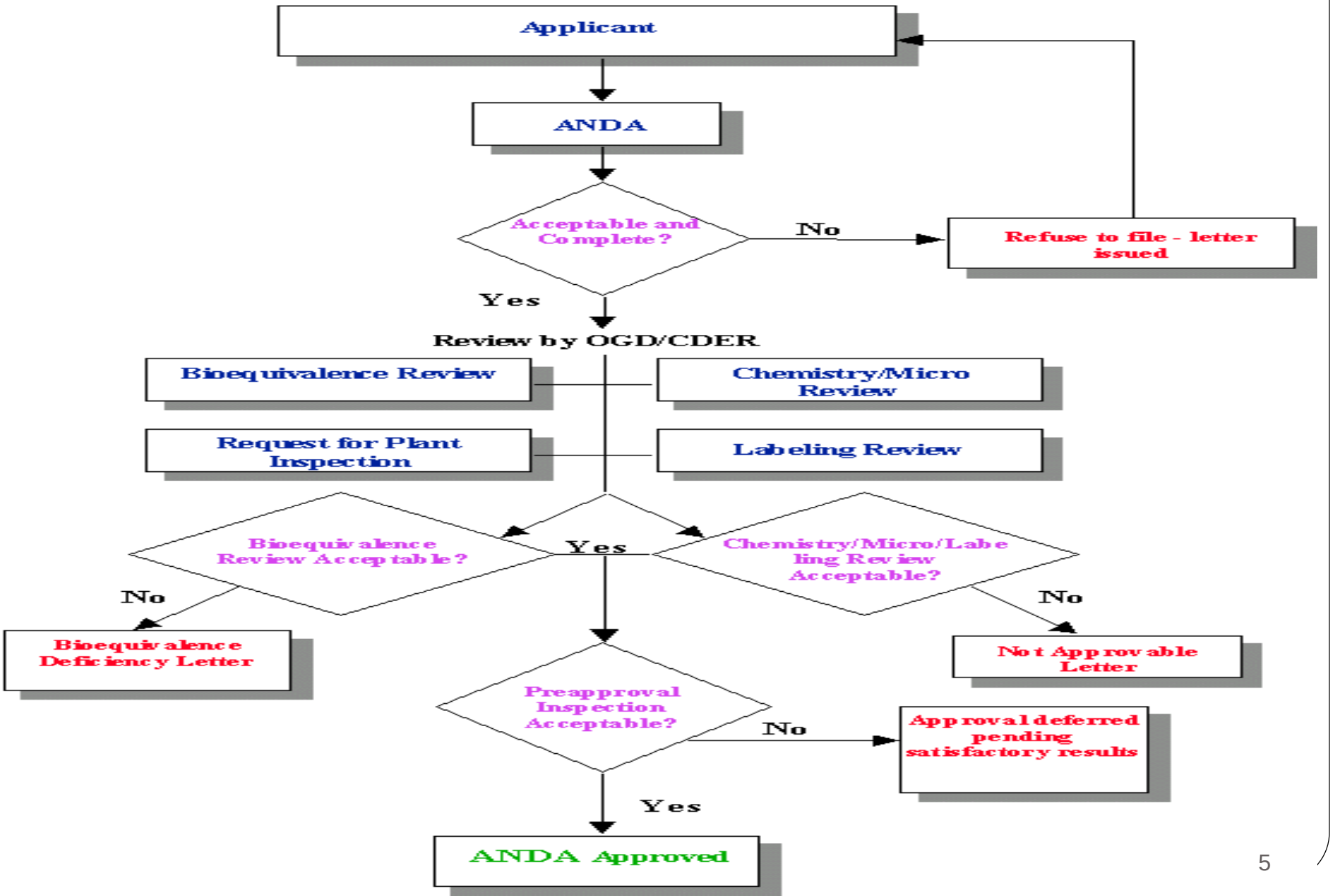
- All approved products, both innovator and generic, are listed in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (*Orange Book*).

- Use of bioequivalence as the base for approving generic drug products was established by the "*Drug Price Competition and Patent Term Restoration Act of 1984*," also known as the WAXMAN-HATCH ACT.
- A generic drug product is one that is comparable to an innovator drug product (also known as the reference listed drug (RLD) product as identified in the FDA's list of ***Approved Drug Products with Therapeutic Equivalence Evaluations***) in dosage form, strength, route of administration, quality, performance characteristics and intended use.

Goal of ANDA

- To reduce the price of the drug.
- To reduce the time development.
- Increase the bioavailability of the drug in comparison to references list drug.

ANDA Review process



NDA vs. ANDA Review Process

NDA Requirement	ANDA Requirement
1. Labeling	1. *Labeling*
2. Pharm/Tox	2. Pharm/Tox
3. Chemistry	3. Chemistry
4. Manufacturing	4. Manufacturing
5. Controls	5. Controls
6. Microbiology	6. Microbiology
7. Inspection	7. Inspection
8. Testing	8. Testing
9. Animal Studies	
10. Clinical Studies	9. Bioequivalence
11. Bioavailability	

ANDA Requirement

1) **Signed FDA form 356h**. Provides information regarding the applicants name & address, name of the drug product, the product strength & route of administration, indication of drug master files cited, proposed indications, a statement regarding whether the product is for prescription or over the counter.

2) **An index** should specify volume & page number for each complete & detailed item.

3) **Information on the basis for which the ANDA is being submitted**.

a) Name of the reference drug, its dosage form & strength.

b) Information on exclusively for the listed drug.

c) If a suitability petition is approved a reference to the FDA number that was assigned to that suitability petition.

4) **Condition for use, including**

a) A statement regarding the condition for which the drug will be used.

b) b) A reference to the annoted labeling for the product & the currently approved labeling for the listed drug product.

5) **A statement that active ingredient** is the same as for that of the reference drug. For the combination product this must be shown for both active ingredient.

6) **Route of administration**, dosage form & strength. This should include a statement that the route of administration, dosage form & strength are same as the reference drug. Bioequivalence. This should include information to demonstrate that the proposed drug is bioequivalent to the listed drug product.

7.Index:

- It is a comprehensive table of contents that enables reviewers to find specific information in this massive document.

8.Labeling:

- This section must include all the draft labeling that is intended for use on product container, packings including the proposed package insert.
- NDA must have four copies of graft labeling.

9.Chemistry, Manufacturing & Controls

This section includes description of drug substance

- Generic name
- Chemical name
- Molecular structure & formula
- Molecular weight
- Appearance, M.P. & B.P.
- Refractive index, viscosity & specific gravity.
- Polymorphs
- Solubility
- Synthesis scheme & description.

10.Microbiology.

- This section is required only for anti infective drug products.
- This section requires following technical information
- Complete description of biochemical basis of drug action on microbial physiology.
- The drugs anti microbial spectrum
- Clinical microbiology laboratory methods.

11.Human Pharmacokinetics & Bioavailability.

- This include information concerning
- The Design
- The Dosing procedure
- The number & frequency of blood & urine collection & Methodology for the assay.

12.Samples

- The sample of the Drug substance & finished product should be provided four individuals units with sufficient quantities in each unit to permit the FDA to perform all the tests included in the specifications at least three times

13.**Analytical method for drug substance & drug product.**

- This section should consists of the specifications, analytical method, certificates of analysis, method of analysis, method validation & stability indicating data as contained in the chemistry, manufacturing & control part of the application.

Refuse to file letter issued

- If the application is missing one or more essential components, a “Refuse to File” letter is sent to the applicant.
- No further review of the application occurs until the applicant provides the requested data & the application is found acceptable & complete.

Bioequivalence Review:

- The Bioequivalence Review process established that the proposed generic drug is bioequivalent to the reference listed drug, based upon a demonstration that both the rate & extent of absorption of the active ingredient of the generic drug fall within established parameters when compared to that of the reference listed drug.
- Applicants may request a waiver from performing in vivo (testing done in humans) bioequivalence studies for certain drug products where bioavailability may be demonstrated by submitting data such as

1) a formulation comparison for products whose bioavailability is self evident, for example, oral solutions, injectables, or ophthalmic solutions where the formulations are identical.

2) comparative dissolution.

ANDA Approved

- After all components of the application are found to be acceptable an approval or tentative approval letter is issued to the applicant.
- If the approval occurs prior to the expiration of any patents or exclusivities accorded to the reference listed drug product, a tentative approval letter is issued to the applicant which details the circumstances associated with the tentative approval of the generic drug product & delays approval until all patent/exclusivity issues have expired.
- A tentative approval does not allow the applicant to market the generic drug product.