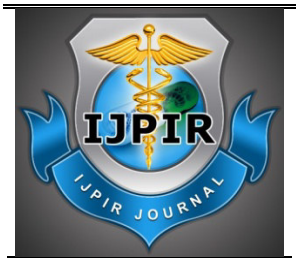
Research Article



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Regulatory strategy for filing NDA /ANDA

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ABSTRACT

In Pharmaceutical Industry, Regulatory Affairs Department makes an interface between the regulatory authorities and pharmaceutical industry. The Regulatory Affairs department is an important part of the organizational structure of pharmaceutical companies. Internally it liaises at the inter phase of drug development, manufacturing, marketing and clinical research. Externally it is the key interface between the company and the regulatory authorities. Regulatory Affairs is involved in the development of new medicinal products from early on, by integrating regulatory principles and by preparing and submitting the relevant regulatory dossiers to health authorities. Regulatory Affairs is actively involved in every stage of development of a new medicine and in the post-marketing activities with authorized medicinal products. This professional can play a key role in guiding drug development strategy in an increasingly global environment and has an important role for submitting the newly discovered drug products approval documents to the US FDA regulatory authorities and to carry out all the practices required for obtaining the drug products approval. This article mainly focuses on the US FDA drug approval strategies. These strategies playing core job in the pharmaceutical industry. These strategies having all the guidelines which are indispensable part of the IND, NDA and ANDA drug approval applications. It plays a significant role in sequence for registration of newly exposed products and also providing the guidelines which is helpful preparing the registration documents to regulatory authorities.

Keywords: Food and Drugs Administration, Pharmaceutical Industry, Regulatory Affairs, IND, NDA, ANDA and CDER.

INTRODUCTION[1]

The mission of FDA's Center for Drug Evaluation and Research (CDER) is to ensure that drugs marketed in this country are safe and effective. CDER does not test drugs, although the Center's Office of Testing and Research does conduct limited research in the areas of drug quality, safety, and effectiveness. It has responsibility for both prescription and nonprescription or over-the-counter (OTC) drugs.

Some companies submit a new drug application (NDA) to introduce a new drug product into the U.S. Market. It is the responsibility of the company seeking to market a drug to test it and submit evidence that it is safe and effective. A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the sponsor's NDA containing the data and proposed labeling.

Types of Applications[2]

- Investigational New Drug (IND)
- New Drug Application (NDA)
- Abbreviated New Drug Application (ANDA)
- Over-the-Counter Drugs (OTC)
- Biologic License Application (BLA)

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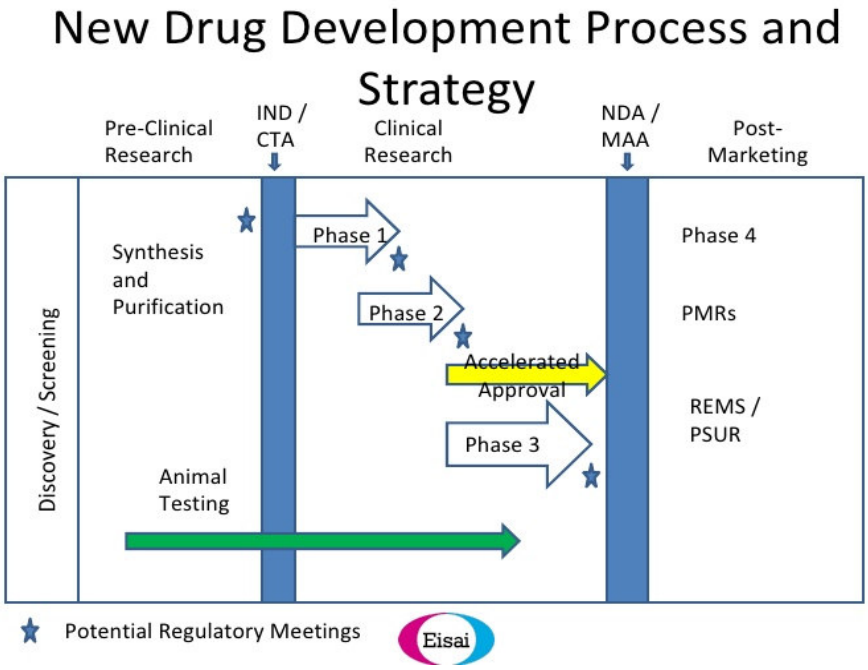

Figure 1: New drug development process and strategy

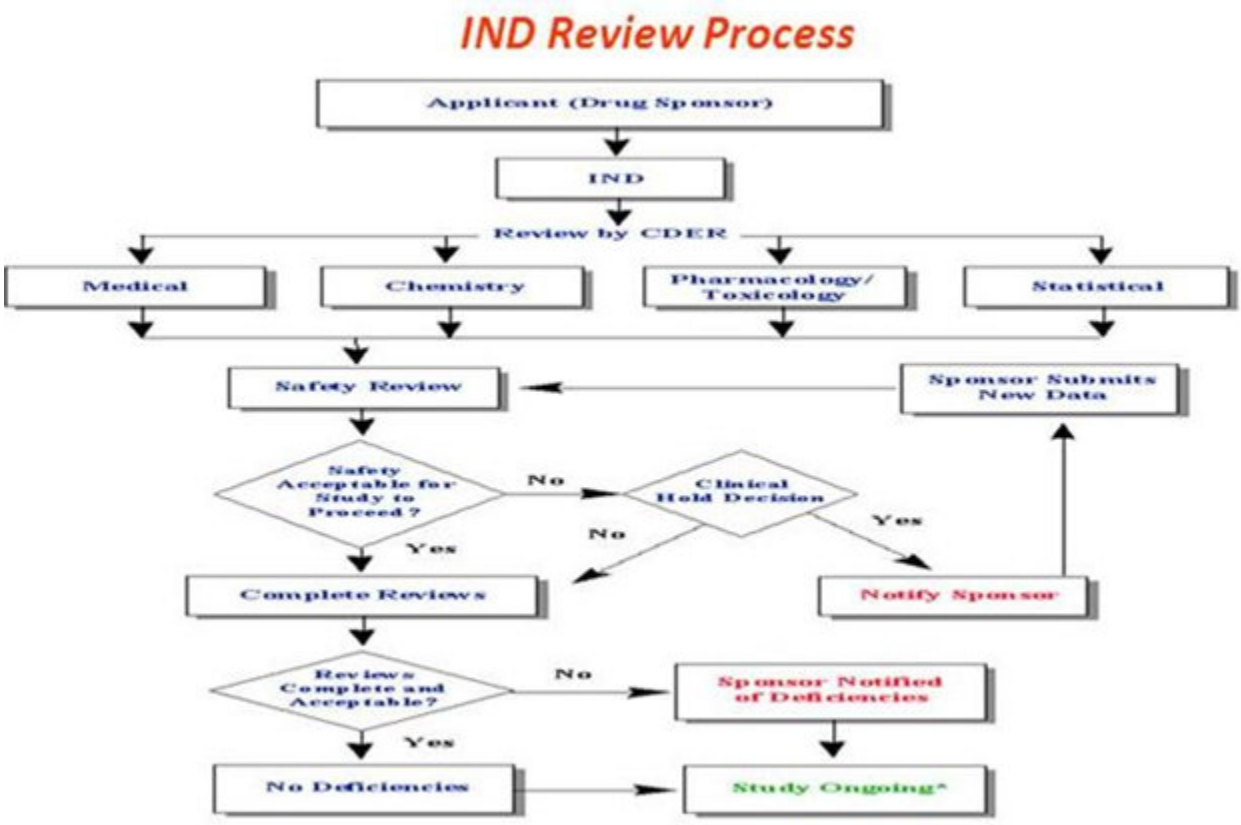

Figure 2: IND Review process

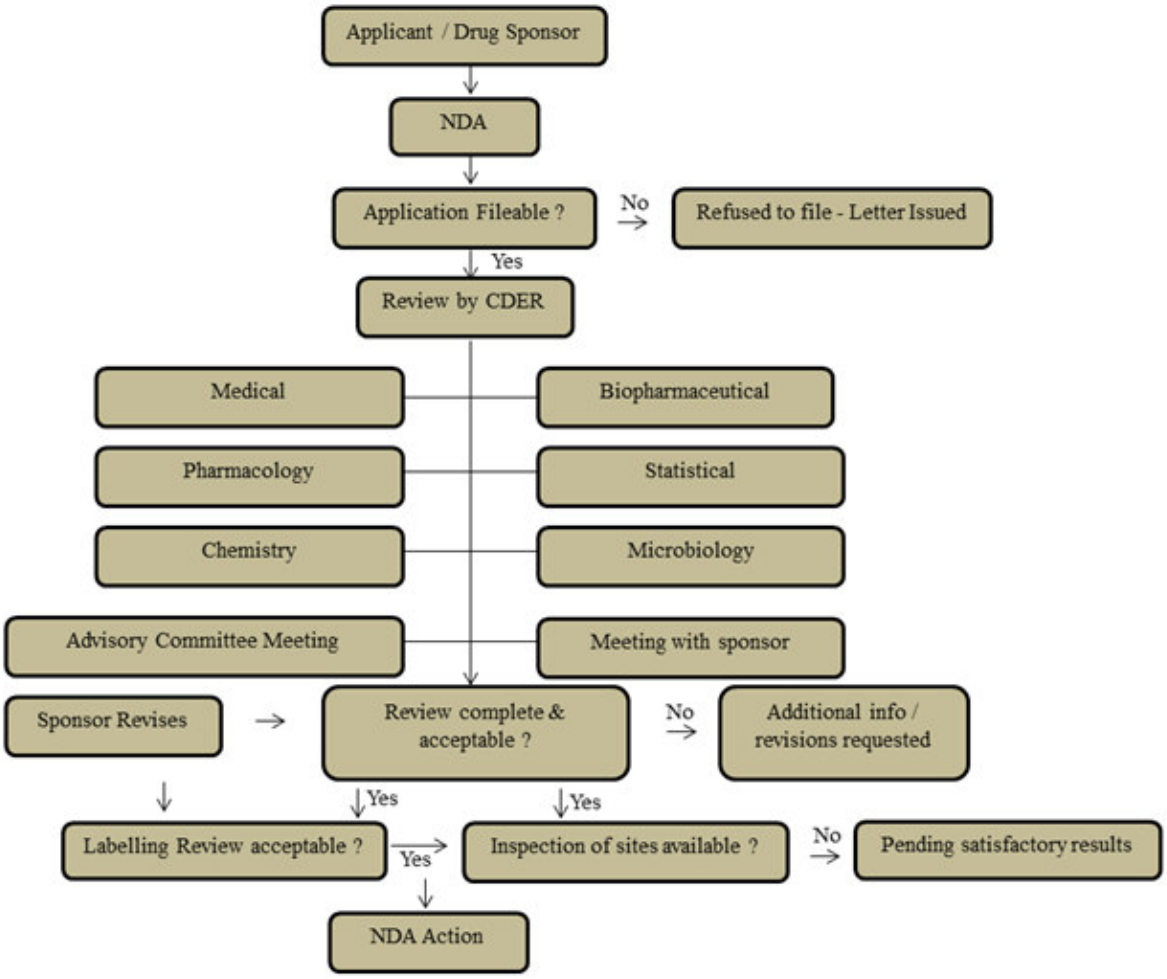

Figure 3: NDA review process

- Form FDA-3331. New Drug Application Field Report.

NDA REGULATIONS

- Review Time Frames (21 CFR 314.100)
- This time frame includes:
- Within 180 days of receipt of an application, the FDA will review and issue an approval, approvable, or not approvable letter. This 180- day period is called the „review-clock"
- During the review period an applicant may withdraw an application (21 CFR 314-65) and later resubmit it.
- The time period may be extended by mutual agreement between the FDA and the applicant or as the result of submission of a major amendment (21 CFR 314.60**)**

Filing Time Frames (21 CFR 314.101)

- , the sponsor will be given the opportunity to meet with FDA to discuss the reasons why the application is not file able.

NDA Pre-Approval and Post- Approval Safety Reports

- These safety reports must be submitted as follows:
- Four months after the initial submission
- Following receipt of an approvable letter
- At other times as requested by FDA

Computer Assisted New Drug Application (CANDA)

- Concept: it is designed to shorten FDA review time by submitting data to FDA in a form ready for manipulation by a computer.
- Importance is given on the clinical sections of the NDA, as they require the maximum time to review and often require manipulation of the data by FDA.

In a September 15, 1988 Federal Register Notice, FDA stated to increase the use of computers in field of improving efficiency of the drug review process. FDA had not provided exact blue print on how to best organize / submit a CANDA, but two basis computer systems have been developed so far:

- Involves keeping the data on a mainframe computer that is operated either by the sponsor / by the computer company assisting it with FDA able to access the information via a telephone connection.
- Putting the data on a floppy disk, laser disc, etc. for use by FDA via desktop computers that are provided by the sponsor.
- One possible concern of CANDAs is the possibility o data dredging by FDA reviewers that is pursuing

tangential rather than central issues because the computer makes it easy to do so, but this has not been observed routinely.

Abbreviated new drug application (anda) [4, 5]

An Abbreviated New Drug Application (ANDA) contains data submitted to FDA's Center for Drug Evaluation and Research, Office of Generic Drugs, for review and ultimate approval of a generic drug product. Once ANDA is approved; an applicant may manufacture and market the generic drug product to provide a safe, effective, low cost alternative to the public. (Figure 4)

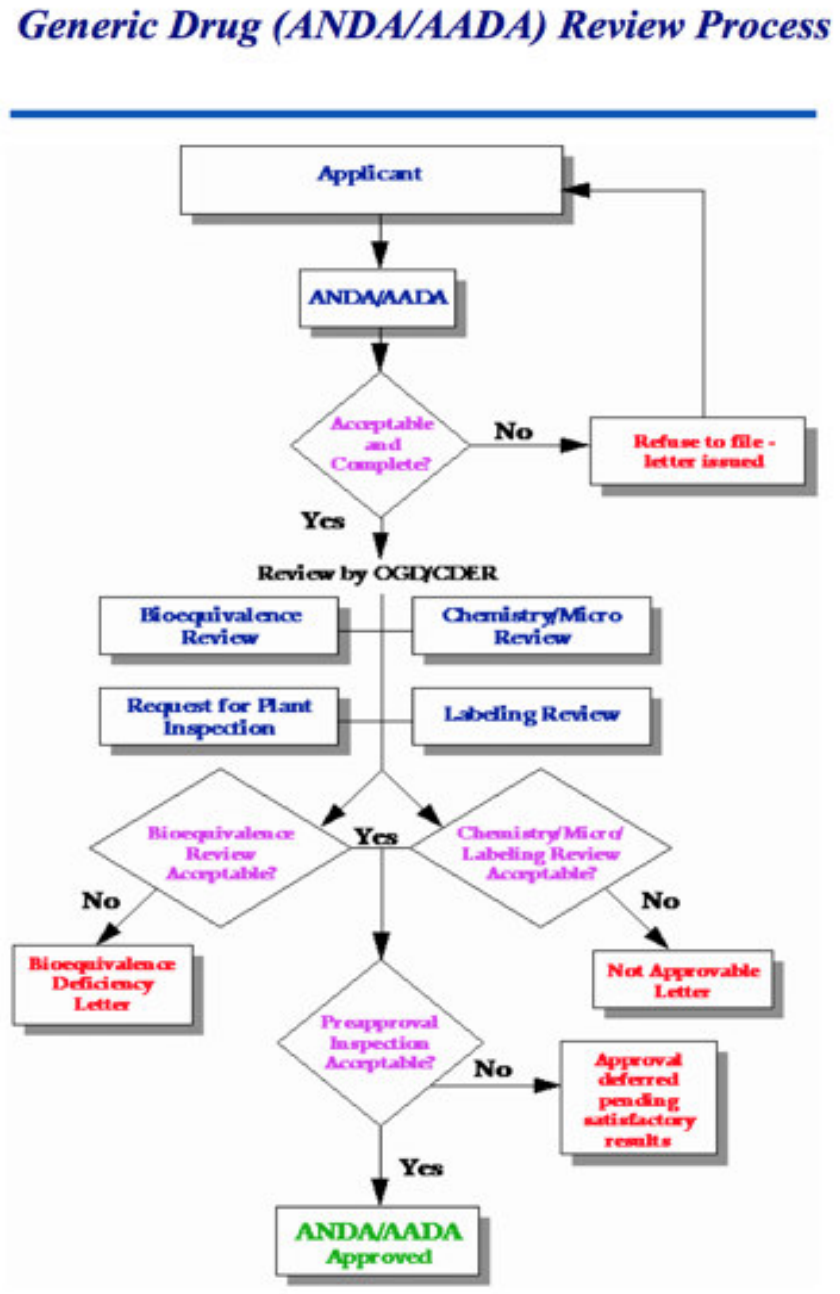

Figure 4: ANDA Review process

Aim and objectives

Filing review is conducted to determine whether the application is sufficiently complete to permit a substantive review and these strategies plays a significant role in sequence for registration of newly exposed products and also providing the guidelines which is helpful preparing the registration documents to regulatory authorities

List of New Drug Applications[14]

Information is arranged in alphabetical order by the name of the applicant.

- New Drug Applications with Supporting Documents
- Complete List of Currently Approved NDA and ANDA Application Submissions (B)

The final step formally taken by a drug sponsor, wherein it applies to the Food and Drug Administration (FDA) for the approval required to market a new drug in the U.S. An NDA

is a comprehensive document with 15 sections that includes data and analyses on animal and human studies, the drug's pharmacology, toxicology and dosage, and the process to manufacture it. When an NDA is submitted, the FDA has 60 days to decide whether to file it for review, or reject it because some required information is missing. The goal of the FDA's Center for Drug Evaluation and Research (CDER) is to review and act on at least 90% of NDAs for standard drugs within 10 months after the applications are received, and six months for priority drugs.

Breaking down 'new drug application (NDA)'

The NDA has formed the basis for regulating and controlling new drugs in the U.S. since 1938, and has evolved significantly since then. Under the Food, Drug and Cosmetic Act (FD&C) passed in 1938; NDAs were only required to contain information relating to the proposed new drug's safety. In 1962, amendments to the FD&C Act required NDAs to also include evidence on the new drug's effectiveness for its intended use, and confirm that its established benefits outweighed its known risks. In 1985, the FDA completed a review of NDA regulations and in order to expedite the review process, restructured the organization and presentation of information and data contained in the NDA. (Figure 5)

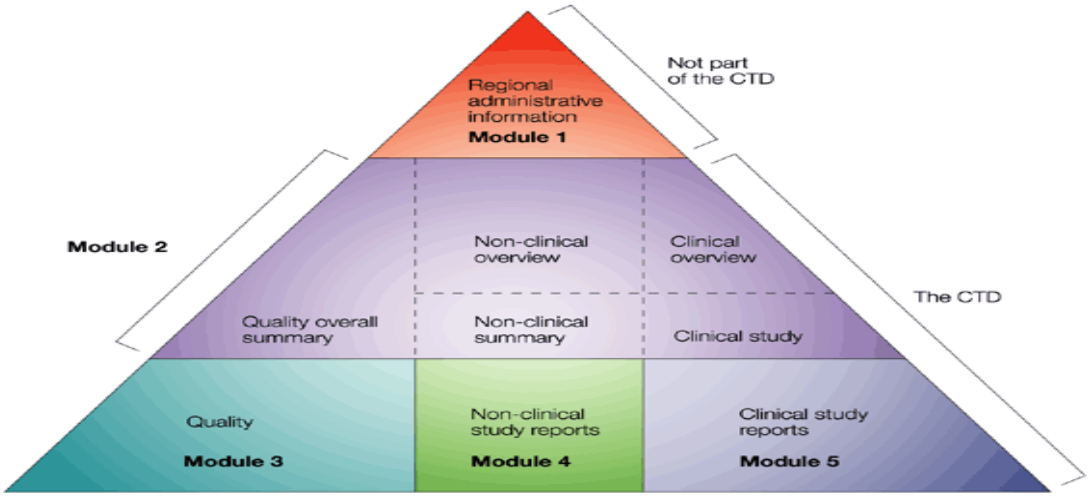

Figure 5: CTD Triangle

Documents in each Module

Table 1

Module	Information
1	Administrative and prescribing information (region specific): a. FDA form 356h b. Comprehensive table of contents (as per 21 CFR 314.50) c. Administrative documents: d. Prescribing information e. Annotated labeling text:

2	Summaries and overview a. Common technical document table of contents (Modules 2–5) b. CTD introduction c. Quality overall summary d. Nonclinical overview e. Clinical overview f. Nonclinical written and tabulated summaries Pharmacology, Pharmacokinetics, Toxicology g. Clinical summary Biopharmaceutics studies and associated analytical methods, Clinical pharmacology studies, Clinical efficacy, Literature references
3	Information on product quality a. Table of contents b. Body of data c. Literature References
4	Nonclinical study reports a. Table of contents b. Study reports and related information c. Literature References
5	Clinical study reports a. Table of contents b. Study reports and related information c. Literature References

Filing a generic drug application

When a dossier is ready as per the regulatory requirement of the respective country, it is submitted to the regulatory agency of that country. Various regulatory agencies worldwide are
Food and Drug Administration(FDA), European Medicines Agency (EMA), Pharmaceutical and Medical Devices Agency (PMDA), Therapeutic Goods Administration (TGA), Medicines Control Council (MCC), Tanzania Food and Drugs Authority (TFDA), Agência Nacional De VigilânciaSanitária (National Health Surveillance Agency) (ANVISA), Commonwealth Independent States (CIS), Department of Health (DOH), The Gulf Co-Operation Council (GCC).

ANDA Approval

All review disciplines find the ANDA acceptable and all facilities are in satisfactory standing as
reviewed and inspected.

- Full Approval - all valid patents and exclusivities for the RLD are expired or any legal issues that may block approval of the ANDA are settled.
- Tentative Approval – there exist unexpired patents and exclusivities for the RLD.

Challenges in Generic Drug Review

- Complex products and dosage forms
- Growing workload
- Receipt of applications continue to be greater than approvals
- Increasing complexity of review process
- GDUFA review performance commitments

Signature

CONCLUSION

Regulatory Strategies describes how the pharmaceutical companies communicate about the approval for drug products. It is necessary to understand the various steps for drug approval. Deciding on a suitable regulatory strategy plays a vital role in gaining time on the market authorization of a drug product.

REFERENCES

1. Available from: http://globalresearchonline.net/journalcontents/v25-1/24.pdf [cited 31/3/2021].
2. Drug Development Approval Process Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/default.htm [cited 31/3/2021].
3. Hand Book CDER" http://CDER Guidance: IND Application Process (interactive session).
4. IND, NDA, ANDA, concept of Para I to IV. Exclusivity: content, format & application. Available from: http://pharmaquest.weebly.com/uploads/9/9/4/2/9942916/3.pdf [cited 31/3/2021].

5. Availablefrom:http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm [cited 31/3/2021].
6. Kaur Jaspreet. US FDA drug approval strategies for pharmaceutical industry. Int J Pharm Sci. Mar–Apr 2014:137-46: Article No. 24.
7. Handoo Shweta, Arora Vandana, Khera Deepak, Nandi Prafulla Kumar, Sahu Susanta Kumar. A comprehensive study on regulatory requirements for development and filing of generic drugs globally. Int J Pharm Investig. 2012 Jul–Sep; 2(3):99-105. doi: 10.4103/2230-973X.104392, PMID 23373001.
8. Chunilal Patel Ruchi, Dr. Dilip Maheshwari. An eCTD filing for generic drug application in United States of America (USA). J Pharm Sci Bioscientific Res. 2014; 4(4) :(228-36).
9. Mistry Ravi, Maheshwari Dilip. Regulatory exclusivity strategies: further protection for pharmaceuticals in US, Europe and Canada. J Glob Trends Pharm Sci: 6(1)-(2015) 2300 – 2310.
10. Available from: http://www.jpsbr.org/index_htm_files/JPSBR14RS4027.pdf [cited 31/3/2021].
11. Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA [cited 31/3/2021].
12. Available from: https://en.wikipedia.org/wiki/New_drug_application [cited 31/3/2021].
13. Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/ [cited 31/3/2021].
14. Available from: http://www.fda.gov/biologicsbloodvaccines/bloodbloodproducts/approvedproducts/newdrugapplicationsndas/default.htm [cited 31/3/2021].
15. Available from: http://www.investopedia.com/terms/n/new-drug-application-nda.asp [cited 31/3/2021].
16. Available from: http://www.jpsbr.org/index_htm_files/JPSBR14RS4027.pdf [cited 31/3/2021].
17. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3555014/ [cited 31/3/2021].
18. Available from: http://www.asq509.org/ht/a/GetDocumentAction/i/86200 [cited 31/3/2021].
19. Available from: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformatin/guidances/ucm400630.pdf [cited 31/3/2021].
20. New Drug Application Introduction. Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/ [cited 31/3/2021].
21. Available from: http://www.fda.gov/cber/gdlns/m4ctd.pdf [cited 31/3/2021].
22. Available from: http://www.slidesshare.net/Rajashriojha/anda-2011-ppt-raajgprac [cited 31/3/2021].
23. Authorized Generics: Anti trust Issues and the Hatch Waxman Act. Available from: http://www.fenwick.com/fenwickdocuments/authorized_generics.pdf [cited 31/3/2021].
24. ANDAitigationbasic.pdf. Available from: http://crobcp.thelawlinks.com/crbcp/docs/ANDA_Litiaon_Basic.pdf [cited 31/3/2021].
25. Abbreviated New Drug Application AND Generics. Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ [cited 31/3/2021].
26. Drug Applications forOver-the-Counter (OTC) Drugs. Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/Over-the-CounterDrugs/default.htm [cited 31/3/2021].
27. Over-the-counter medications: use in general and special populations, therapeutic errors, misuse, Storage And disposal. Available from: http://c.ymcdn.com/sites/www.acpm.org/resource/resmgr/timetools-files/otcmedsclinicalreference.pdf [cited 31/3/2021].
28. Biologics License Applications (BLA) process (CBER). Available from: http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess [cited 31/3/2021].
29. FDA IND, NDA, ANDA, or drug master file binders. Available from: http://www.fda.gov/drugs/.../drug master files dmfs/ucm073080.htm [cited 31/3/2021].
30. Rick NG. Drugs from discovery to approval. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc. p. 201.
31. Rick NG. Drugs from discovery to approval. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc. p. 202.
32. Berry IRA R, Martin Robert P, editors. The pharmaceutical regulatory process. 2nd ed. Informa healthcare. p. 45.
33. Rick NG. Drugs from discovery to approval. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc. p. 203-4.
34. Berry IRA R, Martin Robert P, editors. The pharmaceutical regulatory process. 2nd ed. Informa healthcare. p. 51.
35. Rick NG. Drugs from discovery to approval. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc. p. 218-20.