International Journal of Pharmaceuticals and Health care Research (IJPHR)

IJPHR |Vol.13 | Issue 4 | Oct - Dec -2025

www.ijphr.com

ISSN: 2306-6091

DOI : https://doi.org/10.61096/ijphr.v13.iss4.2025.516-526

Review

Comparative Study of New Drug Application Procedure in US, EU and India

Vadthya Priyanka*, Dr. Vishnupriya, Dr. D. Varun

Department of Pharmaceutical A Regulatory Affairs, Sri Indu Institute of Pharmacy, Sheriguda (V), Ibrahimpatnam, Telangana, 501510

*Author for Correspondence: Vadthya Priyanka
Email: priyanka.vadthya46@gmail.com

Published on: 27 Oct 2025

Published by:
Futuristic Publications

Abstract

This topic aims at reviewing the drug filing and different aspects of obtaining United States Food & Drug Administration (USFDA) and European Medicines Agency (EMA) approval for a drug in order to get a Marketing Authorization in US & Europe and their effective role in improving the standards laid down by them. All new / generic drug products must be approved by the respective regulatory agency governing the respective market before a particular product can be introduced into the market. By law, all new drugs must first be shown to be safe and effective before they can be approved by the respective regulatory agency for marketing. USFDA is the regulatory agency which is responsible for safety regulation of the food and drug products in US. EMA is the regulatory agency decentralized body which is responsible for safety regulation of the food and drug products in Europe. Drug approval process in USFDA involves submitting of an Investigational New Drug Application, followed by submission of New Drug Application. The applications are reviewed and agency officials examine the drug's safety and efficacy data and the drug is approved. EU establishes 4 different drug approval processes: 1) Centralized Procedure 2) Decentralized Procedure 3) National Procedure 4) Mutual Recognition Procedure.

Keywords: Drug Approval, EMA, USFDA.

INTRODUCTION

The United States of America & Europe are the two main regulatory agencies in the world apart from Japan. US is a single country but EU is a union of countries. Therefore the Drug approval process in both the regulatory agencies has been summarized for easy understanding.

Drug Approval in United States

The United States has perhaps the world's most stringent standards for approving new drugs. Drug approval standards in the United States are considered by many to be the most demanding in the world.[1-3]

Investigational New Drug (IND)

Application It's an application filed to the FDA in order to start clinical trials in humans if the drug was found to be safe from the reports of Preclinical trials. A firm or institution, called a Sponsor, is responsible for submitting the IND application.[4]

A pre - IND meeting can be arranged with the FDA to discuss a number of issues:

♣ The design of animal research, which is required to lend support to the clinical studies

♣ The intended protocol for conducting the clinical trial

♣ The chemistry, manufacturing, and control of the investigational drug

Such a meeting will help the Sponsor to organize animal research, gather data, and design the clinical protocol based on suggestions by the FDA.

Abbreviated New Drug Application (ANDA)

It's an application made for approval of Generic Drugs. The sponsor is not required to reproduce the clinical studies that were done for the original, brand name product. Instead, generic drug manufacturers must demonstrate that their product is the same as, and bioequivalent to, a previously approved brand name product.[7]

Drug Approval in Europe

Similar to the US requirements, there are two regulatory steps to go through before a drug is approved to be marketed in the European Union. These two steps are clinical trial application and marketing authorization application. There are 27 member states in the European Union (as of August 2007); Clinical Trial Applications are approved at the member state level, whereas marketing authorization applications are approved at both the member state or centralized levels.[8]

Centralized procedure

The centralized procedure is one which allows applicants to obtain a marketing authorization that is valid throughout the EU.[9]

♣ Results in a single authorization valid in EU, Norway, Iceland and Liechtenstein.

♣ Application evaluated by an assigned Rapporteur.

♣ Timeline: EMA opinion issued within 210 days, and submitted to European Commission for final approval.

Centralized process is compulsory for:

♣ Those medicines which are derived from any biotechnology processes, such as genetic engineering.

♣ Those medicines which are intended for the treatment of Cancer, HIV/Aids, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions.

♣ Medicines officially designated 'orphan medicines' (medicines used for rare diseases).

Mutual Recognition Procedure

The Mutual Recognition procedure allows applicants to obtain a marketing authorization in the member states (Concerned Member State) other than the member state (Reference Member State) where the drug is previously approved.[10]

♣ Applicant submits identical dossier to all EU member states in which it wants authorization, including required information.

♣ As soon as one Member State decides to evaluate the medicinal product (at which point it becomes the "RMS"), it notifies this decision to other Member States (which then become the "CMS"), to whom applications have also been submitted.

♣RMS issues a report to other states on its own findings.

♣ Generic industry is the major user of this type of drug approval procedure.

♣ This process may consume a time period of 390 days.

♣ Nationalized Procedure

The Nationalized procedure is one which allows applicants to obtain a marketing authorization in one member state only.[11,12]

♣ In order to obtain a national marketing authorization, an application must be submitted to the competent authority of the Member State.

♣ New active substances which are not mandatory under Centralized procedure can obtain marketing authorization under this procedure.

♣ Timeline for this procedure is 210 Days.
Decentralized procedure

AIM AND OBJECTIVE

The drug filing and different aspects of obtaining United States Food & Drug Administration (USFDA) and European Medicines Agency (EMA) approval for a drug in order to get a Marketing Authorization in US & Europe and their effective role in improving the standards laid down by them. All new / generic drug products must be approved by the respective regulatory agency governing the respective market before a particular product can be introduced into the market. By law, all new drugs must first be shown to be safe and effective before they can be approved by the respective regulatory agency for marketing.

DISCUSSIONS

POST APPROVAL CHANGES – EUROPEAN UNION
TYPES OF VARIATION

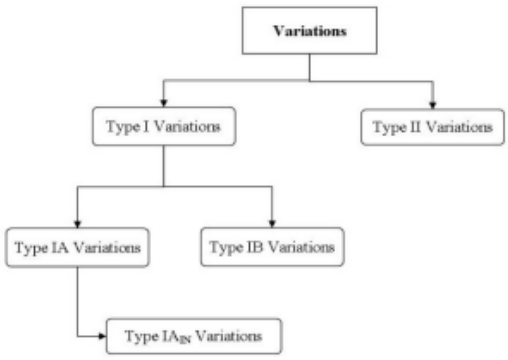

Fig 1: Classification of Variation

Type IA Variations
Do not require immediate notification. May be submitted by the marketing authorization holder (MAH) within 12 months after implementation, or may be submitted earlier should this facilitate dossier life-cycle maintenance. The 12 months deadline to notify minor variations of Type IA allows for an 'annual reporting' for these variations
Type IAIN Variations
Type IAIN variations must be notified (submitted) immediately to the National Competent Authorities/European Medicines Agency ('the Agency') following implementation.
Type IB Variations:
Variation which is neither a Type IA variation nor a Type II variation nor an Extension; such minor variations must be notified to the National Competent Authority/European Medicines Agency ('the Agency') by the Marketing Authorization Holder (MAH) before implementation. MAH must wait a period of 30 days to ensure that the notification is deemed acceptable by the National Competent Authority/the Agency before implementing the change
Type II Variations
Any change which may have a significant impact on the quality, safety or efficacy of the medicinal product must be submitted as a Type II variation.
Type II Extension
Change which may have a significant impact on the quality, safety or efficacy of the medicinal product must be submitted as a Type II variation.
Changes requiring an extension application
Changes to the active substance(s)
Changes to strength, pharmaceutical form and route of administration

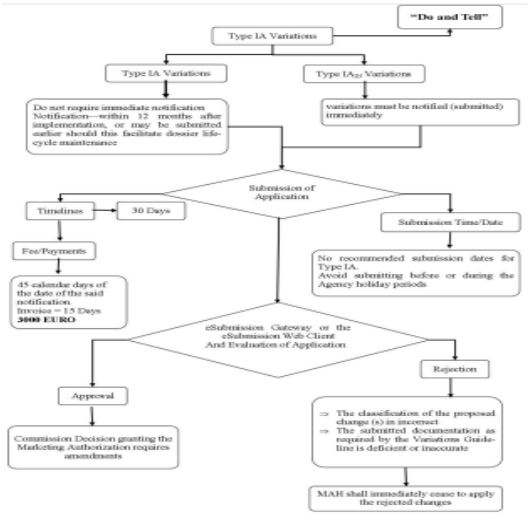

Fig 2: Process of Approval of Type IA Variation

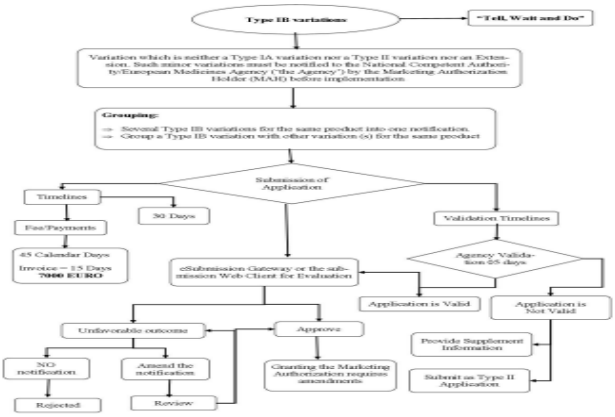

Fig 3: Process of Approval of Type IB Variations

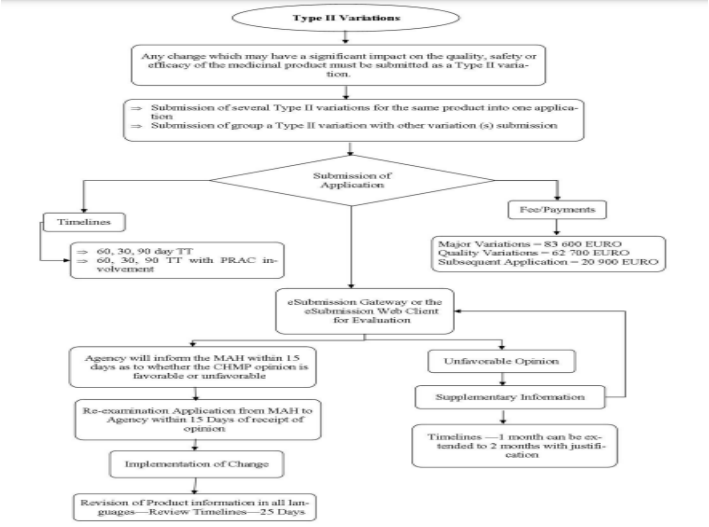

Fig 4: Process of Approval of Type II Variations

Post Approval Changes – US

In US post approval changes are designated as Scale Up and Post Approval Changes, the changes are categorized into three level:

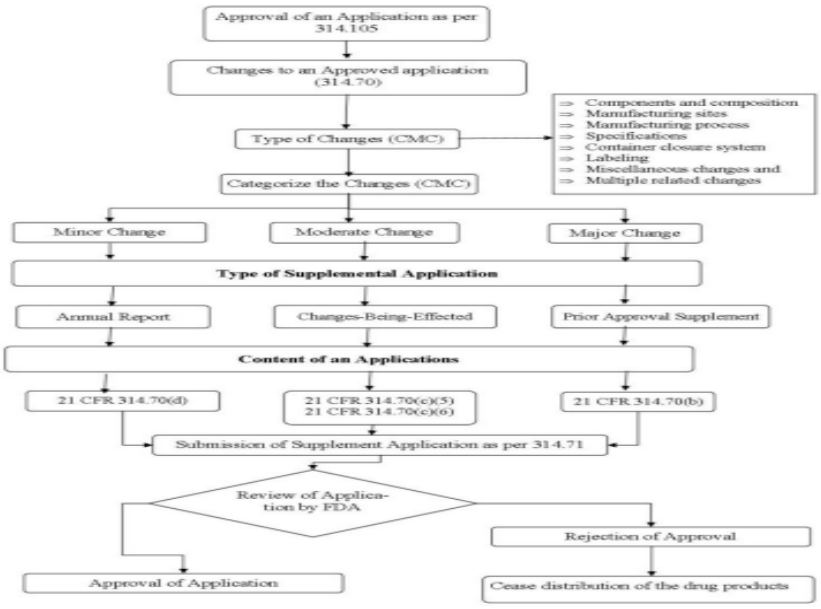

Fig 5: Process of Approval

Post Approval Changes: India

Classification of Changes

Level I: Changes that have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a biological product as these factors may relate to the safety or effectiveness of the product.

Level II: Changes that have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the biological product as these factors may relate to the safety or effectiveness of the product.

Level III: Changes that have minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the biological

PATENT LITIGATIONS

Patents are the property rights for a branded company "to exclude others from making, using, offering for sale and import" for a limited period. It is a primary tool for the branded company to market its products without competition. Usually, the patents will be issued for 20 years. if the patent expires, it leads to an immediate fall of income by generic entrants, and this quick fall of income is called a "Patent cliff". If any violation occurs from the competitors without permission from the patent holder it is called patent infringement. The patent holder can file the legal petition in court and can request an immediate injunction. In addition to a primary patent if there are other patents on crystalline forms of the active molecule, different formulations, and new uses, are known as secondary patents. Some of the developing countries have restrictions on secondary patents. If a pharmaceutical company files multiple patents to protect their product it is called a patent cluster. Which prevents the entry of generic drugs immediately after patent expiration? Generic entrants can launch their products by challenging the validity of the patent in court. In some situations, both the companies can settle their patent litigation by out-of-court agreement to avoid court expenses these are patent term settlements. Exclusivity protects the innovator drug from generic competition for a certain period after patent expiry. It is designed to promote a balance between branded and generic drug competition. Exclusivity is granted when statutory requirements are met and it is not added to the patent life. In our study we found that every primary patent is protected by more than 2 to 3 secondary patents the patent infringement cases filed against generic companies showed that every infringement case is associated with one or more product-related patents. As most of the secondary patents are invalid the generic companies are challenging these patents. Since there is a more chance of winning secondary patents in recent years the number of patent cases was increased drastically. For successful marketing, the companies should maintain strong legal and intellectual teams because if any mistake in filing leads to huge penalties by the courts,

it is very difficult for the generic companies to pay such huge fines. So, the generic companies should be cautious while challenging the patents.

New Formulations

Developing new formulations from existing drugs is one of the most important aspects of LCM, which accounts for more than 60% of newly approved drugs. New technologies in formulation development were implemented including transdermal patches, inhalation products. In oral formulations, the variation between normal tablets to extended-release tablets will show an impact on patents. The reformulation drugs are more convenient for patients especially children, old aged persons. These have significant business in the market and are generally considered as safer.

Fixed-Dose Combinations

These became prominent in areas of cardiovascular, lung, and immune disorders, where multiple FDCs have been developed and launched. The main aim behind the development is to improve the critical condition of a patient. This is advantageous for certain targeted populations such as elderly patients with chronic disease conditions. In some infectious diseases, two or more drugs have to be administered simultaneously at this instance the fixed doses will give more advantages compared to individual compounds.

New clinical Investigations

These are next-generation products that build on the mode of action and pharmacology of first-generation products and have significantly improved chemical properties. The drug profiles must be compared in a broad variety of tests and their potential strengths have to be demonstrated. The indication expansion will extend the patent tenure. The timing of investigating new clinical uses and market introduction plays a major role in the success of second-generation drugs.

Switch Rx to OTC

To grant the OTC status safety and efficacy must be demonstrated in a wide manner with proper labelling. It involves high scrutiny from regulatory authorities. The OTC products are characterized by low price levels and heavy advertising with one or more brand names. Some of the companies will develop secondary fighter brands gives tough competition.

Importance

Lifecycle management is a stage-wise succession from the product development to its withdrawal from the market. In every stage, it will maintain certain predetermined standards which will reduce the loss of revenue and time. The stages are classified as development, approval, market introduction, growth, maturity, and decline. In the development stage, the new molecular entities are to be identified and synthesized in proper dosage forms so that they should give a targeted clinical benefit. Most of the drugs will fail in the developmental stage. Proper LCM strategies have to be implemented from the developmental stage itself for quick approval from the regulatory authority. In the approval phase, there will be a rigorous collection of clinical data and sending for regulatory approval, it requires vast communication between the regulatory authority and company personnel. In the market introduction, the company has to follow the current business trends on how to introduce a product in the highly competitive market, what are the strategies to be followed in product launch, brand advertising, and price fixing. In the growth phase, there is no competition for the products and the product is patent protected then the sales will grow very high for certain patented periods. The maturity phase involves finding the causes for the stop in growth rate, listing the competitive brands, pricing the products available in the market, and changing the advertising modes. The decline phase involved strategic alliances with other generic firms, license selling, brand merging with other companies, and price reduction are some of the strategies. The generic companies should follow these stages properly for successful marketing.

The ANDA-EFFECT trial aims to test the effects of systematic development and implementation of theory and evidence-informed changes to the audit feedback delivered to diabetes centres participating in an established national clinical diabetes audit. Tis feedback will be directly influenced by our prior qualitative work which elucidated some of the barriers to the use of the audit feedback currently provided and contemporary audit and feedback literature. Potential benefits of improved audit feedback include more optimal engagement with the feedback by clinicians and diabetes centres which, ultimately, may lead to improvements in care for people living with diabetes.

ICH Recommendations

a. ICH has revised BCS-based bio waivers (M9) and bio analytical method validation (M10) guidelines and constructed guidelines for demonstrating equivalence. The new M9 guidelines recommend supporting the waiver of bioequivalence studies for highly soluble drugs belonging to BCS class I and class III. The M10

guidelines try to harmonize the bio analytical method validation during product development. Continuing attempts of harmonizing every part of drug product development may be essential for an effective harmonization of global regulations.

b. For non-complex generic dosage forms, ICH builds a series of guidelines for validating bioequivalence studies. ICH working group plans to consider the feasibility of harmonizing the bioequivalence testing across the markets and aligning them into a uniform guideline. These new guidelines will demonstrate equivalences that are to be submitted to the multiple regions for products of immediate-release oral dosage forms. ICH also aims to build a committee to validate these studies and narrow the therapeutic drugs and other variable drugs that need provide special consideration.
c. Series of guidelines contain the developed harmonization for oral and parenteral dosage forms and even strengthen the product line of bio-waivers. The nature of this bioequivalence analysis intends to allow for more than one reference drug to be used for bridging purposes. A three-way crossover analysis, for example, could allow generic drug details to be submitted for approval by using one test trial product in multiple regions d. ICH guidelines also focus on pharmaceutical equivalence and bioequivalence standards for complex API formulation, topical products, oral dosage forms and complex drug-device combinations. This harmonization may reduce the requirement of clinical bioequivalence studies. Creation of a generic drug dialogue forum and connecting it to other international generics initiatives.

ICH established a discussion committee to further consider certain areas and opportunities for harmonized guidelines. The responsibility of these committees is to suggest for revisions that is required in a specific condition or for certain generic drug, by reviewing the existing guidelines(17).This committee must order the work areas carefully and they should communicate via mail, or by conducting an online meeting or by face-to-face meetings or by telecommunication. Responsibilities of discussion committee are as follows:

- Amending the reflection paper Based on multi-regional input
- Advancement of generic standard harmonization by identifying novel topics
- Examining current ICH recommendations as well as applicable WHO guidelines for generic drug requirements to find any missing area in generic drug guidance.
- Together with the ICH implementation subcommittee to determine regional ICH recommendations for generic drug implementation accuracy.
- To recommend the ICH management committee areas must prioritize for harmonization
- the committee must discuss collaboration activities internationally. About current problems related to generic drugs.
- Publish international guidelines for bioequivalence studies for oral generic dosage form drugs.
- To assure that medicines which international buying agencies supply meets appropriate standards of safety, quality, and efficacy as prescribed by WHO.
- Avoid duplicating science that is already being discussed in other international forums.

The creation of this discussion committee would recognize the need for science and technological intervention as well as cooperation between experts to produce generic drug standards that are harmonized.

REMEDIES TO PREVENT THE IMPURITIES INPHARMACEUTICAL PRODUCTS

Some of the remedies to help the contaminations in pharmaceutical products are listed below:

- Control of critical factors during the manufacturing of any product; which affect the product.
- Extreme functional care should be taken while handling the outfit’s, ministries, reactors and other tools that by any mean due to the functional exertion, contamination shouldn't be entered into the product.
- The wet cutlet should be completely washed to remove all unwanted chemical including the residual detergents.
- In the specification, maximum possible contaminations should be specified with strict limits for the better- quality products.
- Time to time the specifications of medicine substances and medicine products should be studied and revised for specific contamination profiling and should be made strict for contamination acceptance criteria.
- During logical system development and confirmation study of any medicine substance and medicine product, the system parameters should be optimized in such a way that the system can resolve maximum number of contaminations which will help the synthetic druggist to ameliorate the synthetic process.
- Stability study should be carried out methodically and strictly for the identification of declination products and to fix the shelf life of medicine substances and medicine products.
- Stress study should be performed for any medicine substance or medicine product to handle the transportation related issues duly.
- Packaging care should be taken for the humidity/ light/ terrain/ stress sensitive accoutrements.

- Regulatory authorities should come stricter before giving any license or authorization for any product to be vended in any regulated request.
- Before giving any blessing related to FDA, for any pharmaceutical product to any company, the authorities should ensure the total compliance of the manufacturing point and product, as this is the matter related to mortal health and it cannot be taken in veritably casual way. However, also the medicinal diligence can get relieve of this burning issue of contaminations at major extent, if some of the listed remedies are enforced seriously and rigorously.

Eventually, ICH looks to the future. It has established a structure to maintain the guidelines, and at the same time is looking to make available information on the ICH process and guidelines to non-ICH regions with the establishment of the Global Cooperation Group. As well as making information available, the group will act as a resource in the understanding, and indeed acceptance, of numerous of the guidelines. From an assiduity perspective globalization is arguably the most important issue it faces, and the capability of these guidelines to effect intra-company globalization is a hand of ICH that cannot be ignored. This is formerly passing within companies. Its value has not been quantified; still, the companies suitable to embrace these principles moment will be the world leader's hereafter. Companies who fail to see the value of harmonisation — the value that's formerly being felt by the scientists carrying out the development, and the value that's yet to be realized in the full medicine development cycle will be left at the starting line of the assiduity's globalization race.

As noted above in the case studies, in the recent past, numerous applicants have included MARS data in IND, NDA, and ANDA submissions to predict retest date and/or shelf-life at various stages of the drug development program. MARS refer to using stability data collected over a much shorter time span of 3–6 weeks and at elevated temperatures and humidity beyond what are commonly employed with conventional ICH Q1A (R2) stability protocols. MARS are called by various names in the literature: Accelerated Stability Assessment Program (ASAP), Accelerated Stability Modelling (ASM), Risk-Based Predictive Stability (RBPS), and Accelerated Predictive Stability (APS). MARS approaches rely on certain select critical quality attributes such as assay and purity of DS/DP to be modelled using the Arrhenius equation, i.e., using the data collected at elevated temperatures to estimate retest date and shelf life at the proposed long-term storage conditions. While the temperature dependence of degrading formation and assay loss can be readily derived from the Arrhenius equation, degrading formation and assay loss as a function of relative humidity is not possible using the original Arrhenius equation. Modifications to the Arrhenius equation to include the effect of relative humidity on degrading formation and assay loss have been developed. Is conversion time, which is the time taken to reach the specification limit as a function of temperature and relative humidity appears to be a predominant underlying principle in developing MARS. Statistical principles and available tools described herein are incorporated in the predictive models. An underlying assumption in using MARS is that there are no physical changes such as API melting or polymorph inters conversions. Although MARS has been used to model changes in the dissolution of a solid oral dosage form, the current modified Arrhenius equation-based models do not appear to be broadly applicable for predicting dissolution or other physical changes.

It should be noted that the case studies presented herein are representative of MARS studies observed to date containing a significant amount of ICH data that confirm the shelf-life predicted by the model, suggesting the potential utility of MARS in setting tentative retest periods or expiration dates for NDAs with an expedited review designation. However, the MARS data packages in the regulatory submissions often lack details of the model including kinetic study specific's, and the assumptions made in the statistical methods for deriving the shelf-life of products under normal stability conditions. Our experience has shown that enhanced communication early on during development through CMC specific meetings can be critical for NDAs with an expedited review designation, and such early communications can be helpful in resolving the following MARS-related statistical questions:

To the author's knowledge, while the scholarly literature on the general question of regulatory influences in innovation in the US medical product is large5, it is amorphous with certain efforts concentrated: on a certain type of medical product – either medical devices medicines, on the faults of a specific implemented regulation (or guideline or on requests for additional regulatory clarity on simply sharing regulatory knowledge to a select audience. Importantly, this is a first research inquiry into the impact of regulation onto innovation that considers a clear statistically testable hypothesis that treats the industry holistically. The approach uses two direct (surrogates) metrics of innovation and regulation directly applicable to medical products and which recapitulates the evolution of the FDA as well as the medical product industry, as it integrates temporal data (from 1976 to 2020).

This work finds that regulation and innovation are:

- Complex entities (like other econometrics or scientometrics variables): metrics that ebb and flow in time in a non-stationary, non-linear, non-contiguous, and with a long memory manner
- Interdependent: correlatively and bidirectional (symmetrically) co-influencing and co-moving variables concomitantly reacting with (likely the same or similar) extrinsic forces

- Time dependence: Steep linear in construct early in lifecycle but then reaching an inverted (exponentially negatively square or cubic) structure after a period of stability.

If the results of this analysis hold after further scrutiny, it suggests that in its early stages regulations supported, if not accelerated, innovation, over time, however, regime change led to the current state in which regulatory complexity may be now hindering innovation.

The data was collected from the publicly accessible FDA website. To the author's knowledge, there is no public presentation of the processes (e.g., auditing) used to collect the data. The number of and accompanied metadata are large; manual culling was required to isolate the variables of interest to prepare for this analysis. Thus, while every effort was taken to minimally process the data, and while relying on the FDA 'system of record,' there is residual uncertainty in the integrity of the final datasets.

From an analysis perspective, it is critical for the reader to understand that the author has constructed a cumulative medical product data record for both registrations and guidelines, for which the key results rest on a statistical approach (viz., determining the statistical characteristics of the data, estimating interdependency and thus regression). The cumulative medical product data assumes that the FDA and sponsor continue their prosecution of the medical product and guideline from its inception onward; that is, the individual metrics accumulate over time. Should the number of guidelines (or registrations) materially decrease, then the ratio of registrations to guidelines would change and such the curve may or may not invert. Confirmation of the database is outstanding and may also comprise corollary investigations. Also, the collection method did not take into number of withdrawn records for either registrations or guidelines. The FDA or the sponsor may have withdrawn / rescinded / retired a registration or guideline. It may be possible (but challenging) to estimate through sensitivity analyses (partly informed by FDA or sponsor media communications) superannuated records, with caveat. For example, a sponsor may withdraw a registration without informing the market (e.g., for patent expired assets with minimal to no commercial value), creating a difficult to ascertain degree of difference between a relative truth and its estimate in the analysis.

Lastly, the causality assessment using VLTE is relatively new and as such additional testing using different economic/ scent-metrics may be appreciated to better understand the algorithm's limitations. Potentially other algorithms may also be used to cross-check the analysis; however, to the author's knowledge, none thus far take into regards both the variable lag as well as structural complexities of such data.

FDA has issued guidelines to ANDA sponsors who intend to change components or composition, manufacturing site, scale-up=scale-down of manufacturing, and=or manufacturing process and equipment for immediate release (IR) 1 and modi¢ed release (MR) solid oral dosage forms during the post-approval period.

An Abbreviated New Drug Application (ANDA) is an application for a U.S. generic drug approval for an existing licensed medication or approved drug. The ANDA contains data which when submitted to FDA's Centre for Drug Evaluation and Research, 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 American public.

The European Medicines Agency (EMA) is a European agency for the evaluation of medicinal products. The EMA operates as a decentralized scientific agency of the European Union and is responsible for the protection and promotion of human and animal health, specifically through the coordination of evaluation and monitoring of centrally authorized products and national referrals, developing technical guidance and providing scientific advice. The application dossier for marketing authorization is called New Drug Application (NDA) in the USA or Marketing Authorization Application (MAA) in the European Union and other countries, or simply registration dossier.

The ICH CTD is divided into 5 modules whereas the ACTD contains of 4 parts. The reason for doing this is the fact that the ASEAN countries normally receive a reference application, which is a dossier which was already approved in other countries in the world (mostly EU and USA) and make the evaluation of the parts mainly based on the overviews and summaries.

The Module 1 of the CTD containing the regional registration and administrative information is still presented as Part 1 of the ACTD. The Module 2 of the CTD does not exist itself for the ACTD. The Quality Overall Summary (QOS) and the overview and summaries of the nonclinical and clinical documentation (similar like the documents in ICH Module 2) are included at the beginning of these Parts. Part II of the ACTD contains the pharmaceutical chemical-biological documentation (the quality information), which corresponds to the ICH Module 3. The nonclinical information is presented as Part III of the ACTD (equivalent to ICH Module 4) and the clinical documentation are contained in Part IV of the ACTD (to be consistent with ICH Module 5).

Bioequivalence studies should be conducted for the comparison of two medicinal products containing the same active substance. The studies should provide an objective means of critically assessing the possibility of alternative use of them. Two products marketed by different licensees, containing same active ingredient(s), must be shown to be therapeutically equivalent to one another in order to be considered interchangeable. Several test methods are available to assess equivalence, including:

i comparative bioavailability (bioequivalence) studies, in which the active drug substance or one or more metabolites is measured in an accessible Biological fluid such as plasma, blood or urine

ii comparative pharmacodynamics studies in humans

iii comparative clinical trials

iv in-vitro dissolution tests

The guidelines describe when bioavailability or bioequivalence studies are necessary and describe requirements for their design, conduct, and evaluation. The possibility of using *in vitro* instead of *in vivo* studies with pharmacokinetic end points is also envisaged.

For classes of products, including many biological such as vaccines, animal sera, and products derived from human blood and plasma, and product manufactured by biotechnology, the concept of interchange ability raises complex which may be addressed by the applicant on the basis of contemporary scientific rationale.

In vivo bioequivalence/bioavailability studies recommended for approval of Modified release products should be designed to ensure that

i the product meets the modified release label claims

ii the product does not release the active drug substance at a rate and extent Leading to dose dumping

iii there is no significant difference between the performance of the modified Release product and the reference product, when given in dosage regimes to arrive at the steady state.

iv there must be a significant difference between the performance of modified Release product and the conventional release product when used as reference product.

It is appreciated that pharmacokinetic studies can be conducted during any phase of a clinical trial for New Chemical Entities (NCEs). While these guidelines deal with pharmacokinetic / pharmacodynamics studies vis-à-vis bioavailability or bioequivalence studies for a generic drug, the principles described herein, are applicable for any pharmacokinetic / pharmacodynamics study.

REFERENCE PRODUCT

For purpose of these guidelines, the reference product is a pharmaceutical product which is identified by the Licensing Authority as "Designated Reference Product" and contains the same active ingredient(s) as the new drug. The Designated Reference Product will normally be the global innovator's product. An applicant seeking approval to market a generic equivalent must refer to the Designated Reference Product to which all generic versions must be shown to be bioequivalent. For subsequent new drug applications in India the Licensing Authority may, however, approve another Indian product as Designated Reference Product.

CONCLUSION

The Drug approvals in the United States & Europe are the most demanding in the world. The primary purpose of the rules governing medicinal products in US & Europe is to safeguard public health. It is the role of public regulatory authorities to ensure that pharmaceutical companies comply with regulations. There are legislations that require drugs to be developed, tested, trialed, and manufactured in accordance to the guidelines so that they are safe and patient's well - being is protected.

ACKNOWLEDGEMENT

The Authors are thankful to the Management and Principal, Sri Indu Institute of Pharmacy, Sheriguda (V), Ibrahimpatnam, Telangana, for extending support to carry out the research work. Finally, the authors express their gratitude to the Sura Pharma Labs, Dilsukhnagar, Hyderabad, for providing research equipment and facilities.

REFRENCES

1. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 201
2. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 202
3. IRA R Berry, Robert P Martin, editors. The Pharmaceutical Regulatory Process. 2nd ed. Informa healthcare. p. 45
4. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 203-4
5. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 205-7
6. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 208-10

7. IRA R Berry, Robert P Martin, editors. The Pharmaceutical Regulatory Process. 2nd ed. Informa healthcare. p. 46
8. IRA R Berry, Robert P Martin, editors. The Pharmaceutical Regulatory Process. 2nd ed. Informa healthcare. p. 48
9. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 212-14
10. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 215-17
11. Rick NG. Drugs from discovery to approval. 2nd ed. John Wiley & Sons, Inc., (Hoboken, New Jersey). p. 218-20
12. IRA R Berry, Robert P Martin, editors. The Pharmaceutical Regulatory Process. 2nd ed. Informa healthcare. p. 49
13. IRA R Berry, Robert P Martin, editors. The Pharmaceutical Regulatory Process. 2nd ed. Informa healthcare. p. 50
14. IRA R Berry, Robert P Martin, editors. The Pharmaceutical Regulatory Process. 2nd ed. Informa healthcare. p. 51
15. Ministry of Chemicals and Fertilizers (2015) Drai National Medical Device Policy.
16. http://www.skpgroup.com/data/resource/skp_the_medical_device_industry_in_india_.pdf 3. U.S. Food and Drug Administration (2014) Classify Your Medical Device. Department of Health and Human Services.
17. http://www.qrasupport.com/FDA_MED_DEVICE.html
18. Ministry of Health and Family Welfare (2013) Guidance Document on Common Submission Format for Import License of Non Notiٹed Diagnostic kits in India. Central Drugs Standard Control Organization.
19. https://www.emergogroup.com/resources/regulations-india
20. http://companiesinindia.net/top-10-medical-device-companies-inindia.html