ISSN: 2349-5448

Intercontinental Journal of Pharmaceutical Investigations and Research (ICJPIR)

ICJPIR |Vol.11 | Issue 2 | Apr - Jun -2024

www.icjpir.com

DOI : https://doi.org/10.61096/icjpir.v11.iss2.2024.45-50

Review

A New Current Regulations For Clinical Trials

B.Kavya*[1], B.Thejovathi[1], L.Harikiran[1]

Department Of Regulatory Affairs, Princeton College Of Pharmacy In Narapally, Ghatkesar, Telangana

*Author for Correspondence: B. Kavya
Email: surapharmalabs@gmail.com

Published on: 25 Apr 2024

Published by:
DrSriram Publications

Abstract

Regulatory process, by which a person/organization/sponsor/innovator gets authorization to launch a drug in the market, is known as drug approval process. In general, a drug approval process comprises of various stages: application to conduct clinical trials, conducting clinical trials, application to marketing authorization of drug and post-marketing studies. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs. This work focuses on the drug approval process in India and USA.

Keywords: Drug approval process, Clinical trials, marketing.

INTRODUCTION

Introduction to regulatory affairs in pharmaceutical industry
Introduction to regulatory affairs:

Regulatory affairs (ra), also called government affairs, is a profession within regulated industries, such as pharmaceuticals, medical devices, energy, and banking. Regulatory affairs also has a very specific meaning within the healthcare industries (pharmaceuticals, medical devices, biologics and functional foods). Most companies, whether they are major multinational pharmaceutical corporations or small, innovative biotechnology companies, have specialist departments of regulatory affairs professionals. The success of regulatory strategy is less dependent on the regulations than on how they are interpreted, applied, and communicated within companies and to outside constituents.

This department is responsible for knowing the regulatory requirements for getting new products approved. They know what commitments the company has made to the regulatory agencies where the product has been approved. They also submit annual reports and supplements to the agencies. Regulatory affairs typically communicates with one of the centers (e.g., center for drug evaluation and research) at the fda headquarters, rather

than the fda local district offices. Gimps do not directly apply to regulatory affairs; however, they must understand and evaluate changes to drug manufacturing and testing activities to determine if and when the fda must be notified.

Importance of regulatory affairs

In today's competitive environment the reduction of the time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its regulatory affairs activities is therefore of considerable economic importance for the company.

Inadequate reporting of data may prevent a timely positive evaluation of marketing application. A new drug may have cost many millions of pounds, euros or dollars to develop and even a three-month delay in bringing it to the market has considerable financial considerations. Even worse1 failures to fully report all the available data or the release of product bearing incorrect labeling, may easily result in the need for a product recall. Either occurrence may lead to the loss of several millions of units of sales, not to mention the resulting reduction in confidence of the investors, health professionals and patients.

A good regulatory affairs professional will have a 'right first time' approach and will play a very important part in coordinating scientific endeavor with regulatory demands throughout the life of the product, helping to maximize the cost-effective use of the company's resources.

The regulatory affairs department is very often the first point of contact between the government authorities and the company. The attitudes and actions of the regulatory affairs professionals will condition the perceptions of the government officials to the company for better, or worse officials respond much better to a company whose representatives are scientifically accurate and knowledgeable than to one in which these qualities are absent.

The importance of the regulatory affairs function is such that senior regulatory affairs professionals are increasingly being appointed to boardroom positions, where they can advise upon and further influence the strategic decisions of their companies.

Responsibility of regulatory affairs professional's

The regulatory affairs professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products. They also advise on the legal and scientific restraints and requirements, and collect, collate, and evaluate the scientific data that their research and development colleagues are generating. They are responsible for the presentation of registration documents to regulatory agencies, and carry out all the subsequent negotiations necessary to obtain and maintain marketing authorization for the products concerned. They give strategic and technical advice at the highest level in their companies, right from the beginning of the development of a product, making an important contribution both commercially and scientifically to the success of a development program and the company as a whole.

It may take anything up to 15 years to develop and launch a new pharmaceutical product and problems may arise in the process of scientific development and because of a changing regulatory environment. Regulatory affairs professionals help the company avoid problems caused by badly kept records, in appropriate scientific thinking or poor presentation of data. In most product areas where regulatory requirements are imposed, restrictions are also placed upon the claims which can be made for the product on labeling or in advertising.

Need of regulatory affairs in the pharmaceutical industry

Regulatory affairs professionals are the link between pharmaceutical industries and worldwide regulatory agencies. They are required to be well versed in the laws, regulations, guidelines and guidance of the regulatory agencies. There is a growing need to incorporate the current requirements of pharmaceutical industries in the standard curriculum of pharmacy colleges to prepare the students with the latest developments to serve the industries.

As the pharmaceutical industries throughout the world are moving ahead towards becoming more and more competitive, these are realizing that the real battle of survival lies in executing the work by understanding the guidelines related to various activities carried out to give an assurance that the process is under regulation. Pharmaceutical industry, being one of the highly regulated industries in immense need of people than ever before who are capable of handling issues related to regulatory affairs in a comprehensive manner.

In India import, manufacturing, sale and distribution of drug is regulated under drugs and cosmetics act 1940 and drugs and cosmetic rules 1945 (hereinafter refer as act) made there under. At present, bulk drug (active pharmaceutical ingredients) and finished formulations are regulated under the said act. Any substance falling within the definition of drug (section 3b of the act) required to be registered before import into the country. Not only drug but the manufacturing site needs to be registered for import. If the drugs, fall within the definition of new drug (rule 122 e of the act), the new drug approval is the pre-requisite for submission of application for registration and or import of drug. The application for registration and import can be made to the licensing authority under the act i.e. To the drugs controller general (i) at cdsco, fda bhawan, kotla road, near bal bhawan,

new delhi by the local authorized agent of the foreign manufacturer having either manufacturing or sale license or by the foreign manufacturers‘ having a whole sale license in the country

A regulatory process by which a person/organization/sponsor/innovator gets authorization to launch a drug in the market, is known as drug approval process.

In general, a drug approval process comprises of various stages: application to conduct clinical trials, conducting clinical trials, application to marketing authorization of drug and post-marketing studies.

Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs.

The new drug approval is of two phase process - the first phase for clinical trials and second phase for marketing authorization of drug. Firstly, non-clinical studies of a drug are completed to ensure efficacy and safety, and then application for conduct of clinical trials is submitted to the competent authority of the concerned country. Thereafter, the clinical trials can be conducted (phase i to phase iv). These studies are performed to ensure the efficacy, safety and optimizing the dose of drug in human beings. After the completion of clinical studies of the drug, then an application to the competent authority of the concerned country for the approval of drug for marketing is submitted. The competent authority review the application and approve the drug for marketing only if the drug is found to be safe and effective in human being or the drug have more desirable effect as compare to the adverse effect

Even after the approval of new drug, government should monitor its safety due to appearance of some side effects, when it is used in larger population. The interactions with other drugs, which were not assessed in a pre-marketing research trial and its adverse effects (in particular populations) should also be monitored.

Major bodies regulating drugs and pharmaceuticals

The principal regulatory bodies entrusted with the responsibility of ensuring the approval, production and marketing of quality drugs in india at reasonable prices are:

The central drug standards and control organization (cdsco), located under the aegis of the ministry of health and family welfare. The cdsco prescribes standards and measures for ensuring the safety, efficacy and quality of drugs, cosmetics, diagnostics and devices in the country; regulates the market authorization of new drugs and clinical trials standards; supervises drug imports and approves licences to manufacture the above-mentioned products;

The national pharmaceutical pricing authority (nppa), which was instituted in 1997 under the department of chemicals and petrochemicals, which fixes or revises the prices of decontrolled bulk drugs and formulations at judicious intervals; periodically updates the list under price control through inclusion and exclusion of drugs in accordance with established guidelines; maintains data on production, exports and imports and market share of pharmaceutical firms; and enforces and monitors the availability of medicines in addition to imparting inputs to parliament in issues pertaining to drug pricing.

The department of chemicals and petrochemicals also oversees policy, planning, development and regulatory activities pertaining to the chemicals, petrochemicals and pharmaceutical sector. The responsibilities assumed by this body are relatively broader and varied in comparison to the other two bodies. The main aspects of pharmaceutical regulation are thus divided between the above two ministries. The ministry of health and family welfare examines pharmaceutical issues within the larger context of public health while the focus of the ministry of chemicals and fertilizers is on industrial policy. However, other ministries also play a role in the regulation process. These include the ministry of environment and forests, ministry of finance, ministry of commerce and industry and the ministry of science and technology. The process for drug approval entails the coordination of different departments, in addition to the dcgi, depending on whether the application in question is for a biological drug or one based on recombinant dna technology. Issues related to industrial policy such as the regulation of patents, drug exports and government support to the industry are governed by the department of industrial policy and promotion and directorate general of foreign trade, both under the aegis of ministry of commerce and industry and the ministry of chemicals and fertilizers. With respect to licencing and quality control issues, market authorization is regulated by the central drug controller, ministry of health and family welfare, department of biotechnology, ministry of science and technology (dst) and department of environment, ministry of environment and forests. State drug controllers have the authority to issue licences for the manufacture of approved drugs and monitor quality control, along with the central drug standards control organization (cdsco).

Prevailing mechanisms

This sub-section primarily focuses on major regulatory policies and mechanisms in relation to drug pricing and development of standards for ensuring safety and efficacy.

In india, drug manufacturing, quality and marketing is regulated in accordance with the drugs and cosmetics act of 1940 and rules 1945. This act has witnessed several amendments over the last few decades. The drugs controller general of india (dcgi), who heads the central drugs standards control organization (cdsco), assumes responsibility for the amendments to the acts and rules. Other major related acts and rules include the

pharmacy act of 1948, the drugs and magic remedies act of 1954 and drug prices control order (dpco) 1995 and various other policies instituted by the department of chemicals and petrochemicals.

Some of the important schedules of the drugs and cosmetic actsi include: schedule d: dealing with exemption in drug imports, schedule m: which, deals with good manufacturing practices involving premises and plants and schedule y: which, specifies guidelines for clinical trials, import and manufacture of new drugs

In accordance with the act of 1940, there exists a system of dual regulatory control or control at both central and state government levels. The central regulatory authority undertakes approval of new drugs, clinical trials, standards setting, control over imported drugs and coordination of state bodies' activities. State authorities assume responsibility for issuing licenses and monitoring manufacture, distribution and sale of drugs and other related products.

Temporal progression of drug policies & acts

The patents act of 1970, drug price control order 1970 and foreign exchange regulation act 1973 played a significant role in terms of the building of indigenous capability with regard to manufacture of drugs. The new drug policy of 1978 provided an added thrust to indigenous self-reliance and availability of quality drugs at low prices. dpco 1987 heralded the increasing liberalization in the industry. One of the important features of this act was the reduction of the number of drugs under price control to 143.

The major objective of dpco 1995 was to decrease monopoly in any given market segment, further decrease the number of drugs under price control to 74 and the inclusion of products manufactured by small scale producers under price control list.

In 1997, the national pharmaceutical pricing authority was constituted in order to administer dpco and deal with issues related to price revision.

The pharmaceutical policy 2002 carried forward earlier governmental initiatives in terms of ensuring quality drugs at reasonable prices, strengthening of indigenous capability for cost-effective production, reducing trade barriers and providing active encouragement to in-house r&d efforts of domestic firms.

In 2003, the mashelkar committee undertook a comprehensive examination of the problem of spurious and sub-standard drugs in the country and recommended a series of stringent measures at central and state levels. The regulatory body came in for censure with the committee noting that there were only 17 quality-testing laboratories, of which only seven laboratories were fully functional.

The national pharmaceuticals policy 2006, among other initiatives, has proposed a slew of measures such as increasing the number of bulk drugs under regulation from 74 to 354, regulating trade margins and instituting a new framework for drug price negotiations in a move to make drugs more affordable for the indian masses.

Drug pricing

As mentioned earlier, pricing policy and industry regulation constitutes one of the key responsibilities of the nppa. Price control on medicines was first introduced in india in 1962 and has subsequently persisted through the drug price control order (dpco). As per the directive of nppa, the criterion for price regulation is based on the nature of the drug in terms of whether it enjoys mass consumption and in terms of whether there is lack of adequate competition for the drug. The year 1978 witnessed selective price controls based on disease burden and prevalence. The list of prices under dpco subsequently witnessed a gradual decrease over a period of time. Around 80% of the market, with 342 drugs, was under price control in 1979. The number of drugs under dpco decreased from 142 drugs in 1987 to 74 in 1995.

Drugs with high sales and a market share of more than 50% are subjected to price regulation. These drugs are referred to as scheduled drugs. The nppa also regulates the prices of bulk drugs. The mrp excise on medicines was levied by the finance ministry in 2005. The objective was to increase revenue and lower prices of medicines by using fiscal deterrent on mrp. This change may have had some impact in terms of magnifying the advantage to industries located in the excise free zones. This also succeeded in attracting some small pharmaceutical firms to these zones. (gehl sampath 2008, srivastava 2008).

As the report by niper, submitted to the ministry of chemicals and fertilizers in 2007 points out, this may have led to tax disparities among firms located in tax exempt zones and tax non exempt areas. This has also led to small firms in non exempt areas requesting for tax subsidies from the government.

For drugs not under price control, firms can set the minimum retail price (mrp). The nppa only intervenes in cases where drugs have significant sales and where the annual price increases by 10%. This is a recent development, which came into effect in 2007, as in the past the nppa would intervene only if the annual price increases were more than 20%. This development indicates the heightened sensitivity of the government towards consumer access to medicines at reasonable prices and keeping a check on profit mongering by the industry. (ibid)

Fixed dose combinations and prevalence of counterfeit and spurious drugs

Recently, 294 fixed dose combinations were withdrawn by the central drug control authority on grounds that these drugs were therapeutically irrational. The order was subsequently stayed by the madras high court. The

issue of the definition of counterfeit drugs is relevant in the context of different drug quality standards prevailing in the indian market. While exported drugs were of a higher quality (who/fda/emea/tga), to meet the required standards in the country of export, in the case of the domestic market, adherence to local quality standards, fixed by the regulatory body was sufficient. Also absence of transparency in licensing procedures has resulted in the market being flooded with counterfeit and substandard drugs. In this context, the mashelkar committee report has referred to a who study, which declared that nearly 30% of the indian market was flooded with spurious, substandard or counterfeit drugs. The government's own estimates have been in the range of 8-10% for substandard drugs and 0.2-0.5% for spurious drugs.

Patents and data protection related issues

The indian patent act, 1970 was amended through the patents amendment act (2005). A technical expert group was constituted under the chairmanship of dr r.a. Mashelkar, then director general of the csir. The committee decision was that it would be trips incompatible to exclude microorganisms from patents and to limit the grant of the patent for pharmaceutical substance to a new chemical entity or a new medical entity involving one or more inventive steps. The committee also opposed the granting of frivolous patents and evergreening and recommended the formulation of detailed guidelines to ensure that only those patents proving 'substantial human intervention' and 'utility' were granted.

As per the provisions of article 39(3) of the trips agreement, member countries have to provide protection to regulatory data submitted for market approval of pharmaceutical products under specific circumstances. The government of india constituted an expert committee under the chairmanship of mr satwant reddy to formulate adequate steps to deal with the issue of data protection. The reddy committee report, brought out in 2007, stated that in the context of pharmaceuticals, the present legal regime was inadequate to address the issues related to data protection with respect to article 39(3) provisions. It also underscored the need for more clear and stringent mechanisms within the drugs and cosmetics act to ensure that undisclosed test data was not put to unfair commercial use in india.

Good manufacturing practices

Good manufacturing practices (gmp) constitute an international set of guidelines for the manufacture of drugs and medical devices in order to ensure the production of quality products. In recent years, gmp protocols are being adopted and followed in over 100 countries, either in the form of regulations (japan, korea and united states), or directives (european union) or guides (united kingdom) or codes (australia).

The objective of gmps is to minimize risks with reference to the manufacturing, packaging, testing, labeling, distributing and importing of drugs, cosmetics, medical devices, blood and blood products, food items etc. These protocols are largely concerned with parameters such as drug quality, safety, efficacy and potency.

Who gmp protocols

World health organization gmp guidelines were instituted in 1975 in order to assist regulatory authorities in different countries to ensure consistency in quality, safety and efficacy standards while importing and exporting drugs and related products. India is one of the signatories to the certification scheme. The who-gmp certification, which possesses two-year validity, may be granted both by cdsco and state regulatory authorities after a thorough inspection of the manufacturing premises.

CONCLUSION

Any medicinal agent to be marketed in the United Kingdom has to follow the guidelines and regulations framed by MHRA, a regulatory authority which approves the drug products. The objective of this review article is to highlight information regarding the requirements, the different types of submissions for the registration of a medicinal product in a market in the UK. It also includes all the details about the fee for the application and the time period for the approval of the application after the submission of the application. By knowing the requirements of the MHRA guidelines and regulations, it is easy for a product to get into the UK market.

Generally, the drug approval process comprised mainly the two steps, application to conduct clinical trial and application to the regulatory authority for marketing authorization of drug. The new drug approval process of various countries is similar in some of the aspects whereas it differs in some aspects. In most of the counties, sponsor firstly files an application to conduct clinical trial, and only after the approval by the regulatory authority, the applicant conducts the clinical studies and further submits an application to the regulatory authority for marketing authorization of drug. In all countries, information submitted to regulatory authorities regarding the quality, safety and efficacy of drug is similar; however, the time, fee and review process of clinical trials and marketing authorization application differs. For the purpose of harmonisation, the International Conference on Harmonisation (ICH) has taken major steps for recommendations in the uniform interpretation and application of

technical guidelines and requirements. This step will ultimately reduce the need to duplicate work carried out during the research and development of new drugs. Therefore, harmonization of drug approval processes either by ICH or WHO may be initiated at global level.

ACKNOWLEDGEMENT

The Authors are thankful to Sura Labs, Dilshukhnagar, Hyderabad for providing the necessary facilities for the research work.

REFERENCES

1. Planning commission of india. 2006. Report of the working group for drugs and pharmaceuticals for eleventh five-year plan (website: www.planningcommission.nic.in)
2. Schuchman, miriam. 2007. 'commercializing clinical trials: risks and benefits of the cro boom'. New england journal of medicine. October 4.
3. Pacific bridge. 2007. 'medical device marketing situation in india.'
4. Gehl sampath, padmashree. 2008. 'india's pharmaceutical sector in 2008. Emerging strategies and global and local implications for access to medicines'.
5. Oppi. 2008. Indian pharmaceutical industry: vision 2015.
6. Singh, seema. 2007. 'indian pharma enters the global arena'. Cell. 128 march 9. Elsevier.
7. Das, anjan & kumar, subodh. 2008. 'innovation, ipr and public good'. Express pharma pulse. 16-31 december, 2008.
8. Ficci. 2005. White paper on 'clinical trials in india'.
9. Srivastava, d. 2008. 'a country level report on the pharmaceutical sector in india'. Report commissioned by dfid, uk
10. Central drugs standards control organization. (website: www.cdsco.nic.in).
11. Horner a., comparison of a global submission of new biological entity and a new chemical entity - strategic decisions and criteria for implementation (2005) http://www.dra.uni-bonn.de/hoerner. (assessed on march 09th 2010).