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PHARMACEUTICALS REGULATIONS IN INDIA

BY SHARJEEL AHMAD

INTRODUCTION

Indian is a socialist country. The Constitution of India establishes the socialistic fabric of state by way of fundamental rights and directive principle of state policy. The socialist state is a state which lays emphasis on the welfare of the its citizen. Whereby India follows the mixed economy pattern wherein there is engagement of public and private sector in affairs of trade and business. Thedevelopment of a country largely depends on the health condition of the citizen. The health condition of a country depends upon the nutrition and hygiene of the citizens. India spends 1.62% of its GDP in health care and allocated 1,84,220 crore in the food subsidy of the budget of 2018-19. Therefore, with a population of 121 crore the funds and GDP spent doesn't meet the requirement of the country's marginalized population. The other health indicator is the role of pharmaceuticals as it attained an important aspect in the international fora with regard to country's development. The economic and legal issues which revolves pharmaceuticalshave become more complex and politicized due to the rise in the global trade.

Need of laws and regulations for Pharmaceuticals

The usage of ineffective, substandard quality or harmful medicines may result in therapeutic failure, aggravation of disease, resistance to drugs, and death. It also affects the confidence in the heath care infrastructure whichcomprises of heath professionals, pharmaceutical manufacturers and distributors. In order to protect public health, government of the all the countries needs to establish a mechanism wherein the laws and regulations are made which would ensure that the manufacture, sale and usage of medicines are regulated and accurate information pertaining to medicines are in hands of public.

Relations between pharmaceutical laws, regulations and guidelines

In the recent times the laws are generally written taking into account the current situation of the functioning of a commodity and its future prospects. The laws basically give the structure for the function and enables the government to issue regulations under it. The legislation of laws generally requires more time as it need to be passed in the central assemblies of the country. Regulations are passed in a simpler way than the laws, it involves approval of a specific ministryon the recommendation of theexperts. The regulations are altered easily as the process is simple. The regulations stand at the samefooting as the law after the grant of the approval. Guidelines are the line of orders which do not carry any force of law, which is easily amended and updated as per the government's will in order to have implementation of the regulation.

Pharmaceuticals involves plethora of parties consisting of manufacturers, workers, sales people, heath workers, doctors, patient. The field of pharmaceuticals involves high risk ; people may suffer from other disease or die not only from lack of drugs but also from substandard drug intake, wrongly prescribed medicines and etc.

The Regulatory Process of India

The growth of pharmaceutical market in India has been very eye-popping during the last two decades.The growth of pharmaceutical market depends upon the various factors among one is drug regulatory system and regulatory legislations. The Present scenario of drug regulatory system in India is on the path of constant improvement and under transition stage viz.,inception of gazette notifications,beefing up of Central licensing agency and amendment, formation of committees (NDAC /SEC, technical, expert, and apex).

The antiquity of drug regulatory dates back from colonial era, which time pharmaceuticals wereimported from other countries. Subsequent to World War I, this scenario has changed, and notonly were pharmaceutical products importedin aggravated volume, However, the demand forindigenouslybloomed products also grew. Butmany unprincipled oversea manufacturers flooded the Indian domestic market with bogus and adulterated drugs which led to a rapid growth ofpharmaceutical production throughout the earlypart of the centennial, Thus, it became coherent thatcomprehensive legislation was required. Hence, Central Government, then, constituted a Drug inquiry committee under supervision of Sir Ram Nath Chopra also known as 'Chopra Committee' whose recommendations later on introduced amidst growing protest in

legislative assembly as 'The Drug Bill' later on amended to the Drugs and Cosmetic Act 1940 (D and C Act) and Drugs and Cosmetic rules of 1945[1]. This would be the central legislation that regulates India's drug and cosmetic manufacture, import, sale and distribution. This also constituted the Central Drugs Standard Control Organization (CDSCO)[2]. The CDSCO toils in the Directorate General of Health services, is a subset in Ministry of Health and Family welfare, Government of India, administeredby Drug Controller General of India (DCGI). Currently CDSCO has 6 zonal offices, 4 sub-zonal offices, eleven port offices and sixlaboratories under its jurisdiction. It has 4 zonal, 3 sub-zonal and 7 port/airport offices and 6 laboratories to execute its activities[3].

The different committees constituted to facilitate the regulatory process and decision making of DCGI, a committee and a statutory boardhave been constituted called Drugs Technical Advisory Board (DTAB) and Drug Consultative Committee (DCC) separately for Modern Scientific System of Medicine and Indian traditional system of Medicine and a provision of Central Drug Laboratory at Central Research Institute, Kasauli (HP) for testing of drugs/medicines. DTAB consists of technical experts who advises state and central governments on technical issues of Drug regulation. Amendment, if any, to Drug and Cosmetic are done after consulting this board. Drug Consultative Committee, which has state and central Drug Control officials as its members, warrant drug control measures in all over India. It is an advisory body for the Central Government, the State Government and DTAB.

Different committees set up by MoH& FW

S. No.	Committees	Roles and Responsibilities
1.	DCC	Drug Consultative Committee, which has state and central Drug Control officials as its representative, warrants drug control measures in all over India. It is an advisory body for the Central Government, the State Government and DTAB.
2	DTAB	DTAB consists of technical experts who advises central

[1] Singh H. Sir Ram Nath Chopra: A profile. J Young Pharm. 2009;1:192–4.
[2] http://www.cdsco.nic.in/Drugs&CosmeticAct.pdf.
[3] . http://www.cdsco.nic.in/forms/contentpage1.aspx?lid=1853.

		and state governments on technical issues of Drug regulation. Amendment, if any, to Drug and Cosmetic are done after consulting this board.
3	IND	The committee renderadvises DCGI in issues to undertake in-depth evaluation of non-clinical data together with pharmacological toxicological data, clinical trial data (if any) tendered by the applicant for approval of IND substances of biological and chemical origin.
4.	SEC and MDAC	Each of the panels constituted to advise in matters related to review and regulatory approval of new drugs and clinical trials, except for Investigational New Drugs (INDs), relating to different (12)therapeutic sphere for Subject Expert Committee (SEC) erstwhile called as NDAC and 07 MDAC. "The committee will advise DCGI in issues to undertake in-depth evaluation of non-clinical data incorporates pharmacological toxicological data, clinical trial data (stage I, II, III, and IV) tender by the applicant for approval of new drug substances of biological and chemical origin to be advanced first time in the country including r-DNA and vaccines derived products. MDAC for Medical Devices.
	TRC	Technical Review committee (TRC) shall assess the recommendations provided by SEC on requisitions of clinical trials and new drugs/medicines after thorough evaluation. DCGI will grant approval of clinical trial and new drugs/medicines based on recommendations of TRC.
5.	Technical committee	Clinical trial protocol will be mentions for review by Technical experts after the same has been approved by NDAC. Technical Committee and Apex Committee

		meet once every month in a year.
6.	Apex committee	Apex committee will convey their opinions/ recommendations after review of proposition conveyed by Technical committee for clinical trial application which have been formerly approved by TRC.
7.	Expert committee	Professor Ranjit Roy Chaudhury expert committee to Formulate policy and guidelines for approval of banning of drugs, new drugs and clinical trials. The Professor CK Kokate expert committee to draw guidelines and policy for approval of new drugs, clinical trials and banning of FDCs.

The government of India, perceiving thelatent of clinical research for new therapies, has amended and modified Schedule Y to the Drug and Cosmetics Rules of 1945. Schedule Y[4] establishes a set of guidelines and essentials for clinical trials. Notwithstanding, Schedule Y was drawn with the generics industry in loop but widen entry of foreign pharmaceutical companies subsequent to the introduction of firm patent rules in the domain of clinical research led the authorities to introduce many changes. The government authorities recognized the significance of their regulation and consequently developed Regulatory and Ethical Guidelines. The Indian Council of Medical Research (ICMR) framed he Ethical Guidelines for Biomedical Research on Human Subjects in the year 2000[5] and CDSCO issued Indian Good Clinical Practice (GCP) guidelines in the year 2001[6].

Without a regulatory necessary condition for GCP compliance, however, most companies abstained to invest in clinical trials. Low quality data upshot in degrading India's reputation. Also, India's stringent bureaucratic setup made it tough to manage simple tasks for say getting customs clearance for the equipment's consequence of regulation in a phase lag, granting companies to conduct a Phase II trial in India only if a Phase III study was going on somewhere else [20]. However, in the year 2005, CDSCO has come up with extreme revisions to Schedule Y

[4] http://www.cdsco.nic.in/html/scheduleY%20(Amended%20Version2005)%20original.htm.
[5]http://cdsco.nic.in/html/GCP1.html.
[6].Nundy S, Gulhati CM. A new colonialism – Conducting clinical trials in India. N Engl J Med. 2005;352:1633–6.

to strive to bring at par with globally accepted definitions and procedures. The amendments which took place are as follows:

1. Definitions of Phase 1-4 trials, which eliminated the Phase lag[7].

2. Coherent responsibilities for investigators; and sponsors.

3. Condition for notifying changes in protocol.

TheGovernment of Indiarendered another advancement to the drug-development industry by revoking the twelve percent service tax on clinical trials in the year of 2007. However, in the Union budget presented on 12 Jul 2014 and prefer to withdraw the service tax exemption given on technical screening of new drugs, including herbal remedies and vaccines[8]. In the month of February 2009, the industry praised recent regulations on exporting samples. Earlier, an export license was required to obtain samples from abroad which has been removed now saving the time.

Thus, to further strengthen the scientific scrutiny and approval of novel drugs/devices and the ministry has specified twelve New Drug Advisory Committee's (NDAC) and seven Medical Device Advisory Committee's (MDAC) to suggest the CDSCO in forming their decisions on grant of global clinical trials and new drugs, the NDAC expert committees have started assessing the global clinical trial documents, bythe middle of 2011[9].

As per the directions of supreme court, Ministry of Health and Family Welfare (MoHFW) off-lately came up with robust confidence building programme to safeguard the rights of the subjects engaged in clinical trials (CTs), by notifying 3rdconsecutive amendments to drugs and cosmetic rules i.e. Rule 122 DAB (1st amendment)[10], Rule 122 DAC (2nd amendment)[11] and Rule 122 DD (3rd amendment)[12]. Although the aforementioned steps have been in the right path, concurrently these steps have raised hurdles for the device/academic investigators/ regulators /biotech industry/Contract Research Organizations (CROs) and pharma themselves, all of whom have had

[7]Thatte UM, Bavdeka SB. Clinical Research in India: Great expectations. J Postgrad Med. 2008;54:318–23.
[8]Ghooi RB. Trials and tribulations of clinical research teaching and training. PerspectClin Res. 2010;1:139–42.
[9]http://acplgroupindia.co.in/pdf/45.pdf.
[10] http://www.cdsco.nic.in/forms/list.aspx?lid=1833&Id=31.
[11] . http://www.cdsco.nic.in/forms/list.aspx?lid=1833&Id=31.
[12] . http://www.cdsco.nic.in/forms/list.aspx?lid=1833&Id=31.

to reallocate themselves with the conditions, that are now mandated. The Investigators and their crew, the sites ethics committees (ECs) and the site/institutional heads/chairman all of them have got subsidiary responsibilities as part of their purview. While, ECs have initiated applying and making themselves registered. The unregistered ECs can't legally accord& review their grant for CT protocols which has led to delays in study initiation at those crippled and sites recruitment projections for granted CT(s) from the licensing authority (LA). Moving forward, it would be suggested for CROs/sponsors to select sites, which are linked to registered ECs, rather than jeopardizing unregistered sites as segment of the study.The issuanceof grants for CT protocols have a binding on the applicant to follow the new rules. This has stimulated amendments to informed consent documents & their submission to LA and ECs. Changes in inauspicious event reporting conditions have forced ECs &investigators apart from the sponsors/CROs to be more vigilant and sensitive to the issue. They need to disburseextra time on each specific case than what generally they used to do erstwhile & report the event as per the defined process within the given timelines. With time bound measures to be taken for serious inimical events (SAE) leading to CT related death or injury[including compensation around issues], all collaborator needs to have to bona fide systems in place to warrant compliance. There have been some disputable issues in Rule 122 DAB i.e. provisions of compensation is to be given in case of failure of an investigational product to provide an intended therapeutic effect [lack of efficacy]; administration of inactive drug providing no therapeutic benefits or unpropitious effects due to concomitant medications, which need further elucidation. Comprehensive risk assessment evaluation plans require to be chalked out by sponsors to element compensation related risks. There is a high possibility that people may get lured by economic incentives to participate as subjects in CTs. The insurance and sponsors providers are reexploring the type and level of indemnity andinsurance cover needed or which can be given for the underway and future CTs. The scope of documentation to be perpetuated at EC, sponsor, site, CRO and at LA end has fatten multi-fold with these said rulings.

Rule 122DAB which enables the DCGI to regulate the quantum of compensation which is to be paid to the family/ nominees of the subject in case of a SAE in clinical trial. The said amendment was introduced to enable a case by case assessment of the circumstancesand facts that led to the SAE and accordingly regulate the extent of negligence by each of the involved parties. However, the CDSCO has now envisaged a system to prescreening of all "SAE reports"which are to be

considered by the DCGI. The prescreening would be taken placeby CDSCO officers formed on a specified checklist for determining the acceptability of an SAE report in order to ensure that it contains all required technical and administrative information necessary for comprehending the nature and cause of the SAE, thereby allowing prudent determination of the quantum of compensation.

The expert committees formed by the MoHFW in the month of Feb 2013 for developing guidelines, standard operating procedures (SOP) and approval procedures have been tendered recommendations upon receipt of advice from stakeholders by holding meetings in order to come forward with an efficacious policy document. The six-member Prof. Ranjit Roy Chaudhury Expert Committee gave Recommendations, itsuggested to set up a council to oversee the accreditation of institutions, institute ethics committees for clinical trials, clinical investigators in the country. It also stated that clinical trials only be carried out at accredited centers. Both the principal investigator of the trial, and the ethics committee of the institute should be accredited.it further statedthat only those trials conducted at such centers should be accepted by the Drugs Controller General of India (DCGI).

India: Liberalization and competition

India has two main pieces of legislation that pertain to retail pharmacy which are the Drugs and Cosmetics Act of 1940 and the Pharmacy Act of 1948. The said Act requires all the States to create Pharmacy Councils which is responsible for keeping a register of pharmacists and information pertaining to their place of practice and qualification. An extensive revision of the Pharmacy Act, 1948 was initiated by the Pharmacy Council in 2005[13].

Pharmacy licensing is regulated by the Food and Drug Administration of India which issues license only to qualified pharmacist to operate. hence, many pharmacies set up by non-pharmacist businessmen are able to hire a signature pharmacist who works part time and fulfills the regulatory requirements. The said pharmacies are commonly employed by pharmacy assistants or less trained staff [14].

[13] India Amending Pharmacy Act to raise professional standards. Pharmabiz.com, New Delhi. 27 October 2005. http://www. pharmabiz.com/article/detnews.asp?articleid=30394&sectionid =50 accessed 28 June 2008.
[14]Adikwu MU. Sales practices of patent medicine sellers in Nigeria. Health Policy Plan 1996;11(2):202-5.

In the mid-1990s hospital chains began to include pharmacies into their facilities, thus, establishing de-facto pharmacy chains. Their success, combined with a growing urban middle-class market &larger access to financing as India's economy liberalized which led to the creation of independent pharmacy chains, the first of such chain started around1997 and expanded rapidly after 2000. Wherein South Africa, most of these chains have been placed in general merchandise stores and grocery, but chains of standalone pharmacies are also developing. There are estimated to be approximately 1500-2500 pharmacies assembled in retail chains. Though this number is still very less when compared to the estimated 550,000 drug andpharmacies sellers nationally, it is growing rapidly[15].

Retail prices for many medicines in India are set by the government. Resulting, competition by chains has successfully emphasized delivery and discounting. From 1997 onwards, a company, Subhiksha, has opened over 1000 stores in 90 cities and sells all medicines at 10% discount from the government set-prices.

Despite the marvelous interest in this filed in the last five years, there is fewevidences that expansion has reduced due to the increasing cost of retail real estate, an overall fall of qualified pharmacists and rising salaries. A comparison analysis of the projections of five of the biggest groups with the real situation shows that by early 2008 none of them had come close to opening the number of stores initially projected[16]. Despite challenges, in the year of 2007, around a dozen of other healthcare firms had plans for large-scale extension into retail pharmacy[17].

The development of retail chains has initiated friction with individually owned pharmacies, Encouraging the latter to organize against the perceived threat from large retailers. In the month of June 2007, the All India Organization of Chemists and Druggists (AIOCD) set in motion an initiative to bring together many of the country's 500,000 drug and pharmacies sellers into a single corporate entity, the All Indian Origin Chemists and Distributors Limited. The goal of creating such corporation is to lay emphasis and coordinating direct purchasing from drug

[15] "Legislation in the retail pharmacy sector in low-income countries" Southern Med Review Vol 2 Issue 2 Sep 2009.
[16] Jayakumar PB. Pharmacy chains on oxygen. Business Standard, Mumbai. April 28, 2008. http://www.business-standard.com/ search/storypage_new.php?leftnm=1&leftindx=1&subLeft=1&a utono=321351 accessed 2 July 2008.
[17] Retail pharmacies: the next big battle ground. IndiaRetailBiz. http://www.indiaretailbiz.com/blog/2007/02/16/retailpharmacies-the-next-big-battle-ground/ accessed 2 June 2008.

companies, share logistics and standardize, and to obtain supplies through a common system at lower costs. The new organization is to be formed in collaboration with State Chemist and Druggist Associations and planned to raise Rs 250 million ($5 million USD) through issuance of shares to members[18].

At the same time a smaller organization, the Retail and Dispensing Chemists Association (RDCA), is organizing 5000 individual pharmacies and drug sellers to adopt shared management practices, including customer loyalty schemes, and modernize stores with computerized dispensing records and air conditioning[19]. The organization is also working with wholesalers to prevent stock-outs in member pharmacies[20].

CONCLUSION

The law governing healthcare and Medicare includes pharmacy laws and the pharmacy sector is an important source of healthcare in any country. This paper shows that the legislation and regulations in India pertaining to pharmacy is inadequate, unenforceable and many times appears to work against the larger goals of the Health infrastructure which assures easy and affordable access to the quality of drugs and medicines.

The amendments in legislation and where change in the paradigm becomes successful the market forces will lead to growth in both franchise and chain operations for retail pharmacies. The scope is very limited and contradictory, evidence pertaining to this consolidation towards pricing, quality, enforcement of regulation and responsiveness to patient needs.

[18] Jayakumar PB. Drug retailers plan cooperatives. Rediff News, Mumbai. 20 June 2007. http://in.rediff.com/money/2007/ jun/20drug.htm accessed 2 June 2008.
[19] Roy S. Chemist Sena' takes retail chains head on. livemint. com, Mumbai, 11 May 2007. http://www.livemint.com/ Articles/2007/05/11235108/Chemist-Sena-takes-retail-ch.html accessed 2 July 2008..
[20] Khanna RM. Association cuts medicine supply to Subhiksha. The Chandigarh Tribune, 21 March 2007. http://www.tribuneindia. com/2007/20070322/cth1.htm accessed 2 July 2008.