

## FEEBLE REGULATORY AFFAIRS WEAKEN THE BACKBONE OF INDIAN DRUG INDUSTRIES

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### REVIEW ARTICLE

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#### ABSTRACT

India is emerging as a global outsourcing power house in almost all fields including Drugs and Pharmaceutical sector. Now it becomes a hub to conduct clinical trials and contract researches. Pharmaceutical industry currently opts for total quality management as primary criteria to prevent sub-standard products which do not fall under official specifications. However, there are many areas where immediate regulatory measures are desired. Central Drugs Standard Control organization (CDSCO) is the prime regulatory authority for the purpose of enforcement according to the Drugs and Cosmetic Act 1940 and Rules 1945, with its amendments. There is no established system for monitoring the Physician's samples as it generally moves from medical representatives to patients via medical professionals. Fixed dose combinations are approved by Drug Controller General of India without proper dose schedule and indications. Metered dose inhaler is presented without dose counter, so that user cannot read how many doses remain. The capacity of CDSCO/the licensing authority/ controlling authority at both national and state level need to be matched with Pharmaceutical Industry in term of man power, infrastructure and training to provide safe and effective drugs to the patients. In the present review, those areas have been highlighted along with some possible solutions such as more stringency and uniformity in drug regulatory policies, use of software to identify duplicate and misbranded medicines, speedy functioning of drug regulatory authorities etc.

**Keywords:** Indian pharmaceutical industry, Patent, Clinical trials, Inhaler, Fixed dose combinations.

#### INTRODUCTION

Over the last few decades, the Indian pharmaceutical sector has experienced phenomenal growth and transformation. The implementation of several important policies such as implementation of product patent in 2005, foreign directive investment (FDI) etc. of the Government of India has played a potential role in the growth and development of the Indian pharmaceutical industry. Broadly, the evolution of Indian pharmaceutical industry has been divided into two distinct phases; namely, phases at pre - and post independence scenario. The allopathic form of medicine was introduced into Indian market after the advent of the British rule but drug production in the country was far below the need and met only 13% of total medicinal requirement of the country. India started her journey of pharmaceutical industry by establishing Bengal Chemicals in Kolkata, the first Indian pharmaceutical company established by Acharya Prafulla Chandra Roy.

Eventually, many Indian companies such as Unichem, Chemo Pharma, Zandu Pharmaceutical Works, Calcutta Chemicals, Standard Chemicals, Chemical Industrial and Pharmaceutical Laboratories (now known as Cipla), East India Pharmaceutical Works were established at different parts of India. With these establishments, the pace of drug manufacturing had increased dramatically and was able to satisfy 70% of requirement. The pharmaceutical industries have experienced therapeutic revolution at post independent era. The Government of India took a sincere effort to establish two public sector units (PSUs) such as Hindustan Antibiotics Ltd. (HAL) in 1951 and Indian drug and Pharmaceutical Company Ltd (IDPL) in 1961 to start the production of drugs from its basic stage. Apart from PSUs, the public funded research institutes have also been found to play key roles in the growth of the sector. (1, 2)

The growth impetus that the sector has received earlier, now reaches to new heights after the implementation of product patent in 2005. (3, 4) The licensing requirement for entry and expansion of firms has been removed by Government of India. Apart from that the Government has allowed 100% inward foreign direct investment under the automatic approval of Reserve Bank of India (RBI) and the automatic approval for technological collaboration is allowed. (5) Further, the Government has implemented certain rules in New Drug Policy for strict maintenance of good manufacturing practices to produce quality products. Therefore, regulatory authorities have an enormous responsibility to maintain the standard and quality of the products by preventing the adulterated, spurious and fake drug production. Pharmaceutical sectors of India is rising day by day, therefore, regulatory authorities should adopt necessary steps for the better therapeutic outcome and patient compliance. In spite of such huge growth of Indian pharmaceutical industries and a continuous monitoring of them by drug regulatory authorities, there are many lacunae and queries, bringing a serious threat for these industries and of the end products of these industries. Some of them are going to be highlighted in this article.

### Indian market with respect to drug

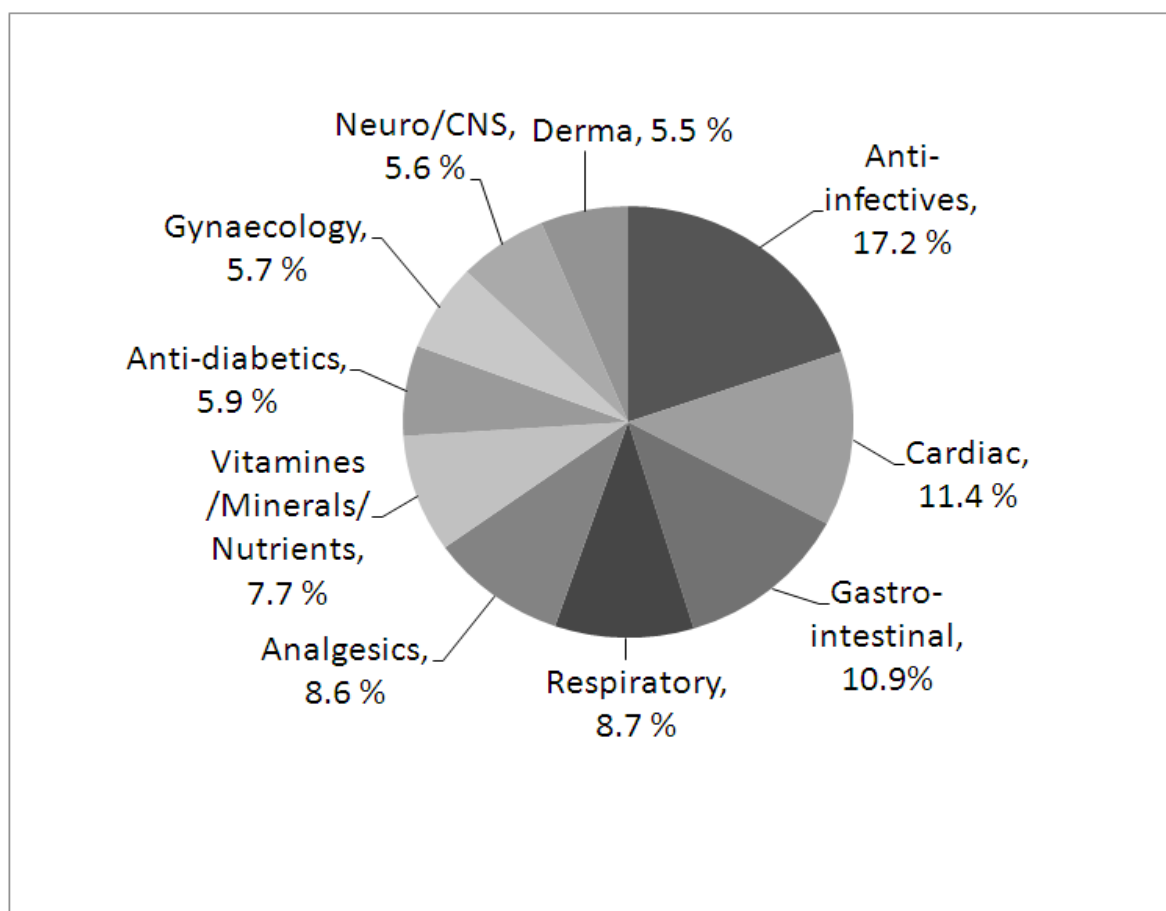
Indian Pharmaceutical companies are fast emerging and fighting neck to neck with its established global counterparts. It is globally the 3<sup>rd</sup> largest (Table 1) in terms of volume and 13<sup>th</sup> largest in terms of value (3,6,7). The total market size of rupees 1,233 billion includes domestic consumption market of rupees 600 billion (contributing approximately 48.6%) and the export market of rupees 633 billion (contributing approximately 51.4%). The industry has grown at a Compounded Annual

Growth Rate (CAGR) of 12.5% during the past five years and is expected to growth at a robust CAGR of 15.1% during Financial Year 2012-17 showing huge export potential coupled with steady growth in the domestic formulation market.(6) Indian pharmaceutical sector will touch rupees 45 billion by 2020, according to a major study by global management and consulting firm, McKinsey & Company. (8) In terms of the global market, India currently holds a modest 1–2% share, but it has been growing at approximately 10% per year. India gained its foothold on the global scene with its innovatively engineered generic drugs and active pharmaceutical ingredients (API), and it is now seeking to become a major player in outsourced clinical research as well as contract manufacturing and research. There are 150 United States Food and Drug Administration (US FDA) approved manufacturing facilities in India including multinational companies (MNCs) which are more than in numbers in any other country outside the US. Since the beginning of 2013, the US Food and Drug Administration (FDA) have approved nearly 290 abbreviated new drug application allowing pharmaceutical firms to manufacture and sell generic drugs as a safe, effective and low-cost alternative to the Americans. FDA data showed at least 110 of these approved applications are from the Indian companies, or entities owned or controlled by an Indian firm. The US market is home to generic drug spending of about USD 300 billion every year and India produces nearly 40 per cent of generic and over-the-counter products, while its share in the finished dosage medicine segment is about 10 per cent. India shipped pharmaceutical products worth over USD 4 billion to the United States in 2012, with a growth rate of around 30 per cent from the previous year. (8, 9). Some of the data summarizing the distribution and classification of pharmaceutical industries in the country are given in Figure 1.

**Table: 1 Distribution of Pharmaceutical Companies state-wise (7)**

Sl. No.	State	No. of manufacturing units		Total
		Formulation	Bulk drugs	
1	Maharashtra	1928	1211	3139
2	Gujarat	1129	397	1526
3	West Bengal	649	62	756

4	Andhra Pradesh	528	199	727
5	Tamil Nadu	472	98	570
6	Others	3423	422	3845
7	Total	8174	2389	10563



**Figure 1:** Market turnover of major therapeutic segment (9)

### Challenges faced by Pharmaceutical Industries

Even though the pharmaceutical market figures show a healthy picture but there are many challenges faced by the industries, specifically with respect to their relation with the regulatory authorities, are enormous. Earlier, the lack of extensive patent protection specifically made the Indian market less attractive to the multinational companies, particularly those dominating the global field. While these giants streamed out, Indian companies have been carving a niche in both the Indian and world markets with their expertise in reverse-engineering new processes for manufacturing drugs at low costs. Some of

the larger companies have taken steps towards drug innovation; however they are mostly at their infancy. But with the changing times, the industry was forced to adapt its business model to recent changes in the operating environment. The first and most significant change was on 1<sup>st</sup> January 2005, the enactment of an amendment to India's patent law that reinstated product patents for the first time since 1972. (9) Under this new law, India has been forced to recognize not only new patents but also any patents filed after 1<sup>st</sup> January 1995. Indian companies, had previously achieved their status and fortune in the Indian market, were estimated a loss of \$650 million in the local generics market because of the deal. Bigger companies which could afford

the loss have set their sights on an even higher goal: new molecule discovery. The initial investment in research and development (R&D) was huge as the companies were being lured by the promise of hefty profit margins and presence of the need to outdo the legitimate competitors in the global industry. But even after the increased investment, market leaders such as Ranbaxy and Dr. Reddy's Laboratories spent only 5–10% of their revenues on R&D, lagging far behind Western Pharmaceuticals Houses such as Pfizer, whose research budget at that year was greater than the combined revenues of the entire Indian pharmaceutical industry. The drug discovery process is further hindered by a dearth of properly trained scientists. Due to the discrepancies between academic curriculum and industry requirements, pharma industries in India also lack the academic collaboration that is crucial to drug development in Western developed countries.(8-10) Apart from that, certain lacunae of regulatory authorities also impair the growth of Indian pharmaceutical industry as discussed here. Manpower of regulatory authorities should be sufficiently increased to perform their responsibilities as quick as possible. More importantly, serious attentions should be paid in order to avoid unnecessary delaying on testing of drug samples procured by the inspectors due to the infrastructure for testing. Moreover, state and central authorities should try to bridge the gap between them and should work in tandem to design unique policies while keeping eye on the objectives and vulnerability of policies. Furthermore, they should sit together to design standardized guidelines for banning and revocation of drugs as applicable. Another important sector that requires the attention of regulatory authorities is clinical research industry. India becomes the hub of clinical trials because of genetic diversity, prevalence of different types of disease, availability of skilled professionals at low cost and clinical infrastructure. However, certain issues such as unethical practices in clinical trials, approval of drugs without clinical trials and the payment of compensation or kin in the event of adverse events in clinical trials require serious attention from Indian government. Numerous steps have been taken already by government of India in order to provide stringent control over the clinical trials. However it is recommended that

regulatory authorities should strictly monitor these on a regular basis in order to exploit the benefits of numerous clinical trials for development of newer and smarter tools for mankind. Apart from that pharmaceutical industries as a whole have come across against number of hurdles such as delays in clinical trial approvals, uncertainties over the Foreign Directive Investment (FDI) policy, the new pharmaceutical pricing policy, a uniform code for sales and marketing practices as well as compulsory licensing. These ultimately affect the growth and development of pharmaceutical industries. Therefore regulatory authorities have enormous task in their hand to frame the policies that become commercially viable. For example, FDI is important for the growth of pharmaceutical sector in India, however FDI policies should be flexible enough to encourage more investments.

### **Role of the Regulatory Authorities: structure and function**

The Indian pharmaceutical companies are focusing on the generic drug market which has also caught the eye of the Indian wings of various multinational companies. Hence, in this environment of cut-throat competition, the regulatory authorities and their laid out requirements play a key role in maintaining the appropriate standards of pharmaceutical manufacturing practices. Acquisitions, alliances and product fillings weave the main theme in the sector. Some Indian Pharmaceutical companies are scouting for acquisitions in regulated markets like US and Europe. The international drug companies are preparing to open up their global product portfolio to Indian consumers. In this light, at least some forms of compliance between the Indian and global regulatory requirements should exist. But that is far from the reality because there are huge discrepancies, ambiguities and irrationalities in the Indian regulatory systems.

To delve deeper into this subject, we have to understand the basic framework of the regulatory authorities in the country. Under the Drug and Cosmetics Act of India, the regulation of manufacture, sale and distribution of drugs are primarily the concern of the State authorities while the Central Authorities are responsible for approval of new drugs, clinical trials in the

country, laying down the standards for drugs, control over the quality of imported drugs, coordination of the activities of the State Drug Control Organisations and providing expert advice with a view of bringing about the uniformity in the enforcement of the Drugs and Cosmetics Act. The Drug Controller General of India (DCGI) is responsible for approval of licenses of specified categories of drugs such as blood and blood products, intravenous (I.V.) fluids, vaccine and sera. Within the Central Drug Standard Control Organisation (CDSCO), the DCGI regulates pharmaceutical and medical devices, under the gamut of Ministry. The DCGI is advised by the Drug Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC). It is divided into zonal offices which are engaged in pre-licensing and post-licensing inspections, post-market surveillance, and recalling when needed. New drugs and fixed dose combined drugs are approved and some of the marketed drugs are banned as and when required by the CDSCO. (11)

The major function of the manpower employed in any regulatory agency is the duty of enforcement and inspection of the following aspects:

- Retail Pharmacy premises both for allopath and homeopath.
- Whole sale Pharmacy premises both for allopath and homeopath.
- Pharmaceutical manufacturing unit: allopath, homeopath and Indian system of medicine
- Blood banks
- Testing laboratories
- Approval of new drugs and fixed dose combination drugs etc.

The FDA's job is to make sure that medical treatments are safe and effective for people to use. However, FDA does not develop new therapies or conduct the clinical trials to demonstrate safety and effectiveness. FDA personnel /staff members meet with researchers and perform inspection of clinical trial study sites to protect the rights of participants and to verify the total quality and integrity of the data.

From the perspective of conductance of proper clinical trials, the regulatory agencies are also conferred with certain of responsibilities which are to inspect that the clinical trial:

- Confirms strict adherence to the principles of good clinical practices (GCP),
- Has adequate human subject protection (HSP) which is universally recognised as a critical requirement to conduct research involving human subjects.

The major regulatory activities from the purview of clinical trials are:

(a) To collect the list of clinical investigators by the centre for biologics and evaluation research and containing names and addresses; and to collect other information gathered from inspections of clinical investigators who have conducted studies with investigational new drugs.

(b) Bioresearch Monitoring Information System files (BMIS). BMIS contains information submitted to FDA identifying clinical investigators (CIs), Contract Research Organisation (CROs), and Institutional Review Boards (IRBs) involved in the conduct of Investigational New Drugs (IND) studies with human investigational drugs.

(c) Investigational Human Drugs Clinical Investigator Inspection list: FDA inspection

(d) Warning letters

(e) Clinical Investigator–Disqualification Proceedings

(f) Application Integrity Policy (AIP)

(g) Notice of opportunity for Hearing (NOOH)- Proposal to debar

(h) FDA Debarment list.

The organizational structure and man power available of Central Drugs Standard Control Organization are depicted in Table 2.

Table 2 Manpower and working area of CDSCO (11)

Sl. No.	Working area	Man power Employed
1	Throughout India	<b>Drugs Controller General (India), one</b>
2	Throughout India	Joint Drugs Controller (India), one
3	Throughout India	Deputy Drugs Controller (India) , 7 numbers
4	Throughout India	Deputy Director Administrator, one
5	Throughout India	Assistant Drugs Controller (India), 16 numbers
6	Throughout India	Drugs Inspectors, 29 numbers
7	East Zone: Andaman & Nicobar Island, Arunachal Pradesh, Bihar, Jharkhand, Manipur, Meghalaya, Mizoram, Nagaland, Orissa, Sikkim, Tripura & West Bengal	Deputy Drugs Controller (India)
		Drugs Inspector 1
		Drugs Inspector 2
		Drugs Inspector 3
		Drugs Inspector 4
		Drugs Inspector 5
		Drugs Inspector 6
		Drugs Inspector 7
8	West Zone: Chhattisgarh, Goa, Daman & Diu, Gujarat, Madhya Pradesh, Maharashtra,	Joint Drugs Controller (India)
		Drugs Inspector 1
		Drugs Inspector 2
		Drugs Inspector 3
		Drugs Inspector 4
		Drugs Inspector 5
		Drugs Inspector 6
		Drugs Inspector 7
		Drugs Inspector 8
		Drugs Inspector 9
		Drugs Inspector 10
9	Ahmadabad, Zonal Office	Assistant Drugs Controller (India)
		Drugs Inspector 1
		Drugs Inspector 2
		Drugs Inspector 3
		Drugs Inspector 4
		Drugs Inspector 5
		Drugs Inspector 6
		Drugs Inspector 7
		Drugs Inspector 8
10	North Zone: Haryana, Himachal Pradesh, Jammu & Kashmir, Punjab, Rajasthan, Uttaranchal, Utter Pradesh, NCT of Delhi & Union Territory of Chandigarh	Deputy Drugs Controller (India)
		Assistant Drugs Controller (India)
		Drugs Inspector 1
		Drugs Inspector 2
		Drugs Inspector 3
		Drugs Inspector 4
		Drugs Inspector 5
		Drugs Inspector 6
		Drugs Inspector 7
		Drugs Inspector 8
Drugs Inspector 9		
11	Sub-Zonal Office , Chandigarh	Assistant Drugs Controller (India)
		Drugs Inspector 1
12	Sub-Zonal Office, Jammu	Assistant Drugs Controller (India)
		Drugs Inspector 1

13	South Zone: Andhra Pradesh, Karnataka, Kerala, Puducherry & Tamil Nadu	Deputy Drugs Controller (India)								
		Drugs Inspector 1	Drugs Inspector 2	Drugs Inspector 3	Drugs Inspector 4	Drugs Inspector 5	Drugs Inspector 6	Drugs Inspector 7	Drugs Inspector 8	
14	Sub-Zonal Office: Bangalore	Deputy Drugs Controller (India)								
		Drugs Inspector 1	Drugs Inspector 2	Drugs Inspector 3	Drugs Inspector 4	Drugs Inspector 5	Drugs Inspector 6	Drugs Inspector 7		
15	Hyderabad, Zonal Office	Deputy Drugs Controller (India)								
16	Port Office Hyderabad	Assistant Drugs Controller (India)								
		Drugs Inspector 1	Drugs Inspector 2	Drugs Inspector 3	Drugs Inspector 4	Drugs Inspector 5	Drugs Inspector 6	Drugs Inspector 7	Drugs Inspector 8	Drugs Inspector 9
17	Chennai, Zonal Office	Deputy Drugs Controller (India)								
18	Cochin, Zonal Office	Deputy Drugs Controller (India)								
19	Delhi, Zonal office	Assistant Drugs Controller (India)								
		Drugs Inspector								
20	Kolkata, Zonal Office	Deputy Drugs Controller (India)								
		Assistant Drugs Controller (India)								
21	Mumbai	Deputy Drugs Controller (India)								
		Assistant Drugs Controller (India) 1				Assistant Drugs Controller (India) 2				

The manpower of Central Drugs Standard Control Organisation are utilised for following purposes:

- To control manufacturing drugs of standard quality
- To supply the working standard to manufacturing units
- To issue manufacturing licence
- To order the manufacturing unit to recall that the drugs are not of standard quality available in the market
- To publish the gazette notification regarding banning of drugs and or revoke order

- To publish the new Pharmacopoeia along with the addendums
- To issue approval of fixed dose combination of drugs with dose and indications
- To issue the license for import of new drugs
- To control blood banks
- To issue the approval for starting the clinical trial
- To issue the approval for marketing of new drugs
- To perform inspection of clinical trial study sites to protect the rights of participants and to verify the quality and integrity of the data
- To regulate the manufacturing quality medical device
- To issue the license for export etc.

Evaluating the safety and effectiveness of new drugs is very important. Evaluation of data from the design stage through product commercialization establishes scientific evidence that a process is constantly capable of delivering quality product. Continual verification should be performed using a product lifecycle approach to keep a process in validated state as product profile.

### Problems

So far we have focused on providing an understanding of the structure and function of the major regulatory agencies of the country. In spite of having such a strong network, certain major decisions taken by the regulatory authorities, which raise serious questions. Some of them are listed below. These decisions have overlooked the awareness of huge Indian population as well as their socioeconomic status. Most of Indian people favours to buy medicines from retail shops before visit to doctors for common ailments like diarrhoea, fever, acidity. Most of the retailers are not registered pharmacists and they do not have any knowledge regarding side-effects of most of the medicaments. Another serious concern is that some of the registered medical practioners are prescribing combination of drugs especially antibiotics of different class for their own benefit while ignoring their detrimental effects. Most of the Indian people do not complete a full course of antibiotics which results in evolution of resistant strain of microbes. Moreover, literature inserts given by

pharmaceutical companies are not sufficient enough to circulate among the larger number of populations. Therefore, it is recommended that drug regulatory bodies should take some formidable measures so that people remain aware enough of side-effects as well as indiscriminate and improper usage of medicines.

Pioglitazone an anti-Diabetic drug was suspended by CDSCO [the powers conferred by section 26A of Drugs and Cosmetic Act 1940(23 of 1940)] in terms of gazette notification no. GSR 379(E) dated 18<sup>th</sup> June 2013 as it has serious detrimental effects on bladder cancer patients. Again the suspension has been revoked on recommendations of Drugs Technical Advisory Board (DTAB) placing "Inserts/promotional literature" of the drug inside the package by gazette notification no. GSR 520(E) dated from the 31<sup>st</sup> July 2013. Drugs are prescribed by the doctor and are purchased from retail Pharmacy outlets on producing the relevant prescription. It has been observed that only one "insert/promotional literature" of the drug is placed in a box having 5/10 strips. Hence a patient buying less than an entire strip of Pioglitazone (which generally happens) or one or two strips is deprived of the information booklet and hence the requisite information that patients remain aware of any complications related to the consumption of the drug. Moreover the hazards also remain to diabetic patients to whom the bladder cancer has not yet been detected. Therefore, without ensuring all the drawbacks related to Pioglitazone, its ban should have been revoked or not is an extremely debatable issue.

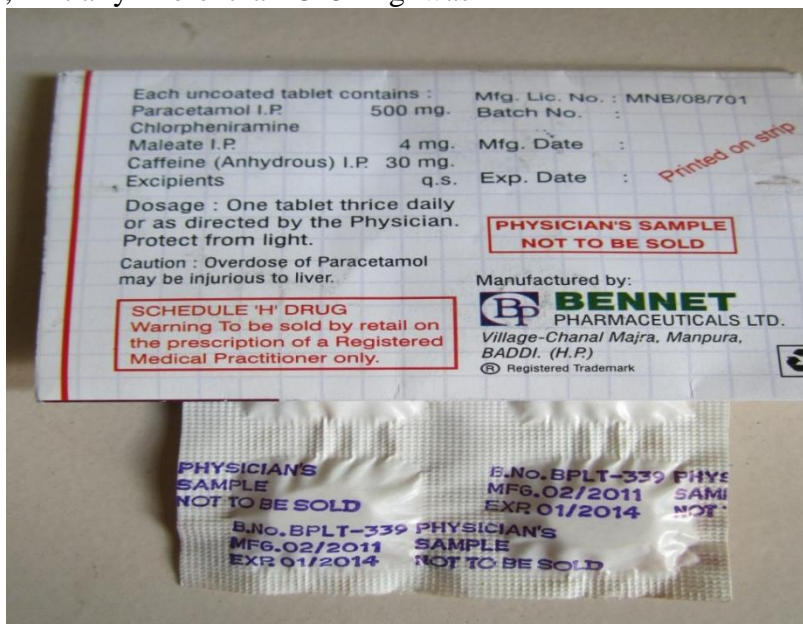
Some similar questions can be raised on the revoke of the ban on Nimesulide. Nimesulide formulations for human use in children below 12years of age were prohibited under section 26A of Drugs and Cosmetic Act 1940 vide Gazette notification no. GSR 82(E) dated 10.02.2011. After a lapse of about eight month, DTAB has recommended that a box warning "Use of Nimesulide should ordinarily be restricted to 10 days. If longer clinical use is warranted, liver function test should be assessed periodically" should be printed in the secondary packing cartons of Nimesulide strips and the previous notification was hence revoked on 10.10.2011. (12,13) However, in a country like



India where illiteracy is the biggest social menace, these methods of using printed information as a strategy to combat the serious detrimental effects of Nimesulide on liver can be considered to be an extremely impractical proposition.

Likewise, for fixed dose combinations of Paracetamol, initially more than 325 mg was

prohibited. Later it was allowed by placing a box with a warning “Taking more than daily dose may cause serious liver damage or allergic reactions (e.g. swelling of the face, mouth and throat, difficulty in breathing, itching or rash)” dated 4<sup>th</sup> April 2012, which again clearly seems like an extremely ambiguous strategy (Figure 2).



**Figure 2:** Physician’s sample: a fixed dose combination of paracetamol which contains 500 mg of paracetamol, but not 325 mg as permitted.



**Figure 3:** Inhaler with dose counter

Coming to the example of Metered dose inhaler medication, these inhalers consist of a

pressurized canister containing medication that fits into a boot shaped plastic mouthpiece. With

most of the metered dose inhalers, medication is released by pushing the canister into the boot. A type of metered dose inhaler releases medication automatically when one user inhales. Some metered dose inhalers have counters so that user can read how many doses remain. If there is no counter, user will need to track the number of doses used to understand when the inhaler is low on medication (by writing the number of puff taken after every use, which is difficult for many patients).



**Figure 4** Inhaler without dose counter

In case of such types of inhalers where counters are not provided, it may be very difficult for a patient to keep track of the amount of medication remaining and it may so happen that the inhaler may be low on medication at the time of emergency when the patient is suddenly suffering from serious breathing trouble. The regulatory authorities should lay stress on the proper designing of such products to make them more compliant to patients.

It was also observed that anti-allergic, antibiotic and anti-parasitic drugs all sold under the brand name AZ by three drug manufacturing companies namely (i) Sienna formulations (ii) Cure Quick Pharma and (iii) Eugenics. However, the products were recalled by the order of the DCGI from the market. Medicines sold under the same brand name but used to treat different ailments should be disbanded as it leads to confusion and could harm the consumers for taking a wrong drug. Streamlined remedies have not been developed yet to address

For example

(i) Seroflo inhaler 250 Batch no. D12886; Mfg. date: Dec'11 Exp. Date: Nov'14, Mfg. by: CIPLA LTD; Medicament: Salmeterol xinafoate IP, and Fluticasone propionate IP 250 mcg (Figure 3)

(ii) Asthalin inhaler Batch no. A30334; Mfg. date: Feb'13 Exp. Date: Jan'16, Mfg. by: CIPLA LTD; Medicament: Salbutamol IP, 100mcg /dose, 200 metered doses (Figure 4).

these problems. (14) Therefore it is necessary to develop a strict controlling system between DCGI and each state drugs administration so that 'Brand' problem can be avoided.

There is no established system for monitoring the physician's samples as it generally moves from medical representative to patient via medical professional. For example in case of Numol-A (combination of Aceclofenec and Paracetamol), the label is present on the box but not on the blister package (Figure 5).

If we observe the number of DCGI approved clinical trial registered in Clinical Trial Registry-India (CTRI) website it shows that the number of expert personnel required to verify data of clinical trials is less than the existing numbers to provide authenticity of data (Table 3).

Another major point of concern is the authenticity of the exhibited clinical data as there have been incidents of major discrepancy

in the recent past. The chief Swiss 'Pharma Giant' Novartis apologized to Japanese Health Minister Norihisa Tamura for alleged

manipulation of data in the clinical trial of a drug produced by the company for high blood pressure patients. (15)



**Figure 5** Physician's sample: a blister pack of fixed dose combination strip.

**Table 3** DCGI approved clinical trials registered with CTRI (11)

Year	No of DCGI approved clinical trials
2007	3
2008	65
2009	391
2010	500
2011	321
2012	262
23 <sup>rd</sup> January, 2013	6
Total	1548

### Data required for new drugs and existing quarries

CDSCO and DTAB formulated GCP under schedule Y in the year 2005. Schedule Y specifies the special studies of post marketing products under clinical trial studies such as bioavailability and bioequivalence studies.

Data required to be submitted with an application for permission to manufacture and market a new drug are given below

- A brief description of drug and the category to which it belongs

- Chemical and Pharmaceutical information including stability data
- Animal Pharmacology: special pharmacological actions, general pharmacological actions, pharmacokinetics; absorption; distribution; metabolism; excretion etc.
- Animal toxicity: acute toxicity, long term toxicity, reproduction studies, local toxicity, mutagenicity and carcinogenicity study
- Human clinical pharmacology (Phase I): specific pharmacological effects, general pharmacological effects, pharmacokinetics; absorption, distribution, metabolism, excretion, safety and tolerability etc.

- Exploratory clinical trials (Phase II): Investigator-wise reports. To evaluate the effectiveness of a drug for particular indicators
- Confirmatory clinical trials (Phase III): investigator-wise reports, demonstration of therapeutic benefit, drug safety and effectiveness for use
- Post marketing Trials (Phase IV) : drug-drug interaction, dose-response or safety studies, mortality/morbidity studies
- Special studies: bioavailability and bioequivalence studies, investigator-wise reports
- Studies in special population: geriatrics, paediatrics, pregnant or nursing women
- Evaluation of the effect of food on absorption following oral administration
- Regulatory status in other countries:
  - (a) Countries where marketed, approved, under trial with phase or withdrawn for any reasons
  - (b) Restrictions on use, if any, in countries where approved/marketed
  - (c) Free sale certificate from country of origin
- Marketing information:
  - (a) Product monograph (proposed)
  - (b) Draft cartoons and label
  - (c) Testing protocol with sample of pure drug substances

But several doubts that float in the mind are:

- Is there relevance between the supplied data and the literature data, which is obviously not supplied by the applicant?
- Is it possible to check and authenticate such intricate data by the insufficient man power that is employed?
- Are the employed manpower provided with sufficient infrastructure to validate the data?
- Twenty two new drugs have been approved by CDSCO during the period 01.01.2013 to 11.06.2013. Inspection of statutory and regulatory activity in such a short period with insufficient manpower to validate data could be specific.

### Measures to be taken

Some important steps should be taken by regulatory authorities in order to provide strong guidelines regarding the usage of medicaments for different ailments as follows

[i] National authority is to be established for nomenclature, checking and verifying the brand names of drugs and pharmaceuticals. Technological innovations such as usage of software would be useful to make the system more vibrant as well as equipped for identifying duplicate, misbranded medicines.

[ii] Inhaler devices with dose counter should be mandatory.

[iii] Regulatory authorities should come up with definitive plans regarding clinical trials in order to avoid unnecessary delay as well as uncertainty. This is very much essential to support the innovations as well as to exploit opportunity of India as a destination for clinical trials.

[iv] Another area which requires strong intervention of regulatory authorities is the usage of fixed dose combination of drugs. It should be closely monitored and guidelines should be strong enough in order to avoid the detrimental effects of drugs

[v] Moreover, guidelines should be framed in such a way in order to avoid the prospects and growth of pharmaceutical companies.

[vi] Functioning of regulatory authorities should be speeded up and in this case usage of automated systems as much as possible with vibrant software is extremely vital.

[vii] More stringent regulations should be imposed on the labeling of physician samples as well as on the general products for sale

### CONCLUSION

Qualms are far and many. Answers are few and vague. As per Drugs and Cosmetics Act, drugs, cosmetics as well as medical devices should be safe for human consumption and free from serious adverse effects. Moreover, the National Human Rights Commission (NHRC) described 'the manufacture, distribution and sale of unsafe drugs and medical devices as a violation of human rights'. Steps are to be taken by the regulatory authority so that drugs, cosmetics and medical devices should be safe and effective for patients. As clinical trial requires the study of effect of drugs on geriatrics, paediatrics, pregnant or nursing women and for other tests, it

should be time framed on the basis of methodology specified in standard method of practice. FDA should be more stringent on inspections of clinical trial in case of new drug.

The FDA/regulatory authority should find out the short-comings both in the manpower and infrastructures to overcome the loopholes and to become confident for providing the best health care facilities and services to the patients and strengthening the health-care provisions and thus the well-being of the nation. The need of the hour is to go beyond the trivial interests of individuals and work towards making the country one of the pioneers of the pharmaceutical industry. India has enormous advantages, including a large, well-educated, skilled and English-speaking workforce, low operational costs, improving regulatory infrastructure etc. India has the potential to become the region's hub for pharmaceutical and biotechnology discovery research, manufacturing, exporting and health care services. The only important aspect is that the regulatory authorities should work in tandem to make policies that will help the growth of pharmaceutical industry as well as to provide mankind with a quality medicament to avoid any unnecessary risks. Thus India may be 'truly shining' in the pharmaceutical sector in the international arena.

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## CONFLICT OF INTEREST

Authors have no conflict of interest.

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