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REVIEW ARTICLE

Regulatory Aspect for OTC and Cosmetics products in India and Overseas

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ABSTRACT

With the heady optimism surrounding the potentially massive growth of the consumer healthcare segment, much of it justified, come real difficulties. When the pharmaceutical industry cuts out the middle man and sells straight to the customer, the dangers of counterfeiting and the challenges of keeping an eye on a more complicated supply chain arise. Number of drugs going off-patent, and will be free for competitors to replicate. Switching from prescription-only treatments to OTC can be seen as a way for pharmaceutical companies to protect revenues from brands that are soon to lose their patent protection, with the profits from selling a widely recognized product OTC, offsetting the losses caused by losing exclusive rights to produce the drug. The 1938 Food, Drug, and Cosmetic Act brought the cosmetic industry under the regulatory jurisdiction of the FDA. However, the confluence of federal administrative budgetary constraints, historical conditions of the cosmetic industry's development, and pragmatic policy considerations has fostered a unique regulatory regime. The FDA has come to rely heavily on the cosmetic industry to regulate itself in order to ensure consumer safety. The current regulations of cosmetics are stringent.

KEYWORDS

OTC Market, Cosmetics, European Market, Switch to OTC drugs, Prescription

INTRODUCTION

The manufacture and sale of cosmetic products are regulated by different governmental entities around the world. There may be different specific regulatory systems; they have a common goal of ensuring that cosmetic products are safe and properly labeled. In the industrialized countries these regulations have evolved to the point where they are rather extensive and, largely because the United States and European Union are the two largest markets in the world for cosmetic products. The cosmetics market in India is growing at 15- 20% annually, twice as fast as that of the United States and European market.

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Indian cosmetic industry is matured enough and responsible to ensure the quality and safety of its products. The cosmetic regulations in India are complex and time consuming for pre marketing approval. It is therefore important for a cosmetic manufacture to understand the difference in regulatory system in India when compare to USA and EU. The aim of the present article is to compare the cosmetic regulations in USA, EU and India which impact directly on the manufacture and sale of cosmetic products include the following aspects. Legal authority and manufacture of cosmetics for sale. Most citizens likely believe, probably vaguely but with conviction, which the FDA engages in expansive direct regulation of the detailed workings of the cosmetic industry. In fact, the first Food and Drug Act in 1906 did not even include cosmetics

within its purview – it was not until the 1938 Act that cosmetics came under FDA regulatory authority. Contrary to popular belief, FDA regulation under the 1938 Act has primarily been limited to regulation of cosmetic products after their release into the marketplace; in other words, despite popular understanding of "the mighty FDA [as] a powerful organization," "neither products nor ingredients are reviewed or approved before they are sold to the public." This ex post regulation of cosmetics involves a process by which the FDA "functions like a highway patrolman" – "its inspectors look out for products that are dangerous to health, about which it can, like a highway patrol man, do something.... manufacturers routinely do [pre-market] testing, but that is not because FDA demands it." In place of extensive pre-marketplace regulation, the FDA has a long history of reliance on the cosmetic industry's engagement in voluntary self-regulation[3].

All too often around the world, regulation of nonprescription medicines is not clearly distinguished from that of prescription medicines. This lack of distinction places limits on achieving an optimal level of public health (through appropriate patient and consumer usage) and negatively impacts the international competitiveness of the nonprescription industry. Nonprescription medicines are in fact different from prescription medicines in some significant and under-appreciated ways. Better regulation is a big issue in developed countries at the moment. The challenge for all countries is to recognize and reconcile the different objectives of regulation, and to avoid unintended consequences of the inappropriate application of prescription drug regulation to the nonprescription sector. Public health and consumer safety will not be compromised by more appropriate and proportionate regulation of nonprescription medicines. In fact, it is possible to promote responsible usage of these medicines while diminishing 'self-prescription,' the inadvertent and irrational use of prescription drugs without the intervention and supervision of a medical doctor – an all-too common practice in developing countries. Nonprescription products are medicines with usually many years – often decades – of experience of safe usage. Many nonprescription medicines are in use in a large number of countries around the world, and this experience should be taken into account in regulatory regimes. Furthermore, and to an increasing extent today, certain medicines that previously have been treated as prescription only are being examined now for potential 'switching' to nonprescription status[2]. The substantial knowledge built up under prescription conditions of a medicine's quality, safety and efficacy profile can be carried over to nonprescription use. Overall, this means that nonprescription products do not need to be subject to the same extent of regulation as new prescription medicines at the point of registration (marketing authorization) or in ongoing usage. Nonprescription medicines' chemical entities are commonly not protected by intellectual property patents on the basic molecule. Innovation and competition between manufacturers, which benefits patients, is based upon the development of new therapeutic claims for established products[2]. This innovation is costly, not least to small companies, leading to the need for data protection and marketing exclusivity for innovation rather than patent protection on a new chemical entity. Doctors can play a very important part in encouraging and supporting self-care activities. But the fundamental difference between prescription medicines and nonprescription products is that the latter can be purchased and used by the consumer of the medicine without the necessary intervention of a medical doctor. In today's information age, where the public is increasingly interested in healthcare matters and willing to play a more active role in its own healthcare, nonprescription medicines provide a tool for patients to practice 'self-care' (see Section II). Developing self-care also allows governments to move towards more patient-oriented and disease-preventive health services (see Section II), leading to improved public health standards. It is therefore in the interest of all that public health policies explicitly recognize and support self-care. Opportunities to encourage wider appropriate access to self-care

products should also be considered, on a country-by country basis.

Improving Public Health

Around the world, in developing as well as developed countries, the emergence of chronic diseases – cancer, cardiovascular problems, diabetes etc – is being recorded. From a projected total of 58 million deaths from all causes worldwide in 2005, the WHO estimated that chronic diseases accounted for 35 million, which is double the number of deaths from all infectious diseases (including HIV/AIDS, tuberculosis and malaria)[3]. Importantly, the contributing factors of these diseases are now well understood – obesity, insufficient exercise and tobacco smoking. Even more significantly, these factors are preventable, and the better use of nonprescription products can make a significant contribution. In most countries however, the focus of healthcare systems is on treating a disease after it appears, rather than on preventing it in the first place. A major future challenge therefore is to encourage people to take more care of themselves through self-care, improving individual lives and, collectively, public health.

The cosmetic registration process requires meticulous planning and review of the ingredients and labeling for registration in India. Any company intending to import and market cosmetic products has to go through this tedious process. The cosmetic application should clearly define the products in respective categories. The Government of India through the Drug and Cosmetic act 1940 and rules 1945 has made stringent provisions regarding import, Manufacturing, Sale and Distribution of Cosmetics. These provisions mainly cover the licensing for the import, manufacturing of cosmetics and also the GMPs for the manufacturing of cosmetics. Also these guidelines have covered certain categories of cosmetics whose import and sale is prohibited by the Law. These guidelines have also listed the 28 cosmetics whose import is allowed only on to the conformance to the Indian standards. These guidelines have also covered the offences and penalties in case of contravention of the provisions of the Drug and Cosmetic Act 1940. Under the Drug and Cosmetic Act Cosmetic has been defined as "Any article intended to be rubbed, poured, sprinkled or sprayed on, or introduced into or otherwise applied to, the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance and includes any article intended for use as a component of cosmetic".

Regulatory Provisions on Import of Cosmetics in India

Chapter III of Drug and Cosmetic Act deals with import of Drug and Cosmetic. Now import of certain cosmetic is prohibited under section 10 of the Act and rules 134A, 135, 135A of Drug and Cosmetic Rules 1945 they are:

- Any cosmetic this is not of Standard Quality.
- Any cosmetic this is misbranded or spurious.
- A cosmetic containing ingredient which render it injurious or harmful or unsafe to use.
- A cosmetic whose import is prohibited by rule.
- Any cosmetic containing hexachlorophene.
- Any cosmetic in which lead or arsenic compound used for coloring purpose.
- Any cosmetic which contains mercury compounds.

The Government of India In Fed 2007, the Ministry of Health and Family Welfare has bring amendment in Drug and Cosmetic Rule, 1945 according to which a cosmetic to be imported into the India has to be get registered under Rule 129D by licensing authority appointed by Central Government under Rule 21. Usually Drug controller General of India is the Licensing Authority. There should be a single Application made for one or more cosmetic which are manufactured by same manufacturer. And the registration Certificate which is provided is valid for 3 years if it is not cancelled. And the application for the registration should be made either by manufacturer or his agent or importer in

India. Cosmetic can be imported in India only through following ports as per the **rule 43A**[3].

Indian Pharmaceutical: An Overview

The Pharmaceutical industry represents one of the India's strength. The regulation of pharmaceuticals in India is generally seen to be in need of reform, and has been the subject of many official commissions since 1995. Most commentators agree that the state should intervene to prevent untrammeled market forces leading to citizens' suffering, because adequate information about the costs and benefits of different pharmaceuticals is inaccessible to most users. But in India, a wide range of stakeholders must be considered before changes can be made to the regulatory framework. The Indian pharmaceutical sector has come a long way, being almost non-existent before 1970 to a prominent provider of healthcare products, meeting almost 95 per cent of the Country's pharmaceuticals needs. The Industry today is in the front rank of India's science-based industries with wide ranging Capabilities in the complex field of drug manufacture and technology. It ranks very high in the third world, in terms of technology, quality and range of medicines manufactured.

The Indian pharmaceutical industry is the world's second-largest by volume and is likely to lead the manufacturing sector of India. The number of purely Indian pharma companies is fairly low. Indian pharma industry is mainly operated as well as controlled by dominant foreign companies having subsidiaries in India due to availability of cheap labor in India at lowest cost. In 2002, over 20,000 registered drug manufacturers in India sold $9 billion worth of formulations and bulk drugs. 85% of these formulations were sold in India while over 60% of the bulk drugs were exported, mostly to the United States and Russia. Most of the players in the market are small-to-medium enterprises; 250 of the largest companies control 70% of the Indian market· The government started to encourage the growth of drug manufacturing by Indian companies in the early 1960s, and with the Patents Act in 1970. Thus, the objective of regulatory control is a question of achieving a 'balance' between protecting and promoting public health and facilitating the industry vis-à-vis compliance with regulatory standards. Consequently, although the regulatory objectives seem clear, the actual quantum of regulatory oversight, the mechanism for achieving regulatory compliance and the actions needed to deal with non-compliance have to be designed in a manner that is sensitive to the characteristics of the regulatory space, 4 and specifically, the actors operating in that space. Many point out that a historical pattern of tragedy and its attendant publicity provided the political impetus and momentum for legislative change in the form of increased federal regulation of cosmetic products. For example, one writer argues that "some well-publicized incidents caused by unregulated products, particularly cosmetics, spurred consumer activism in the years from 1900 to 1945. It was grassroots political activism, combined with the power of personal tragic stories, I argue, that ultimately challenged, and changed, national law culminating in the 1938 Food, Drug, and Cosmetic Act." A notable player in this consumer activism was M.C. Phillips and her 1934 report *Skin Deep* – an "expose of the beauty industry that did much to whip up the demand for cosmetics regulation"; through this expose, Phillips "denounced the 'cosmetics racket' for selling illusions, and she claimed women's right, as voters and taxpayers, to safe, honest cosmetics."

MATERIALS AND METHOD

Generic Market

According to our new report, "Booming Generics Drug Market in India", the Indian generic drugs market has posted an impressive growth pattern over the last few years. Currently, the Indian pharmaceutical market is fully dominated by generic drugs and in the near future, this scenario is likely to remain the same. In FY 2010, the share of generic drugs in the overall pharmaceutical market was estimated to be around 79.2% and by FY 2013, the share is likely to escalate to around 80.5%

We have found that generic drugs developed by India are now distributed and sold in several parts of the globe that, in turn, has augmented the demand for Indian generic drugs. With the key drugs going off-patents in the coming future, which also include blockbusters, there is an immense opportunity for Indian generics manufacturers to strengthen their market share in countries, such as the US, Europe, and Japan.

Broadly Indian Pharmaceuticals sector is classified into Bulk drugs, Formulation and Contract Research and Manufacturing Services (CRAMS). The drug and pharmaceuticals industry in India meets around 70% of the country's demand for bulk drugs, drug intermediates and formulations. There are about 500 corporate players with more than 20000 players in general and thus fragmented Indian pharmaceutical industry. The bulk drugs and pharmaceuticals manufacturers produce complete range of pharmaceutical formulation and about 350 bulk drugs.

Mapping the Administrative Structure

The central and the state governments are both identified as regulators under the DCA. Regulatory functions are clearly separated between these two primary regulators. The table below provides a detailed mapping of regulatory responsibilities distributed between the national government (CDSCO) and the state government (SDRAs). The main functions of the central government include approval of new drugs; registration and control of imported drugs; approvals for clinical trials; laying down standards for drugs, cosmetics, diagnostics and devices; approval of licenses for high risk products (large volume parenterals, vaccines and biotechnology products and operation of blood banks); coordinating activities of the states and advising them on matters of uniformity in regulatory administration in the implementation of the DCA. The state governments are responsible for licensing of manufacturing establishments and sale premises, undertaking inspections of such premises to ensure compliance with license conditions, drawing samples for testing and monitoring of quality of drugs, taking actions like suspension/cancellation of licenses, surveillance over sale of spurious and adulterated drugs, instituting legal prosecution when required and monitoring of objectionable advertisements for drugs[4].

Regulatory Overview of Other Jurisdictions

As a part of our research, we reviewed the drug regulatory system in four jurisdictions, namely, USA, EU, Indonesia and China. The jurisdictions were chosen based on their similarity to India and regulatory leadership so that we can learn from their experiences. The Food, Drug and Cosmetics (FDC) Act, 1938, forms the basis for drug regulation in the USA. The corresponding law in the EU is Article 55 of Regulation (EC) No 726/2004; in Indonesia, it is the Decree of the Head of the National Agency of Drug and Food Control, 2011, and for China, it is the Drug Administration Law of the People's Republic of China. With the exception of the EU, all the other three jurisdictions have a singularly centralized system of drug regulation where the central drug regulatory system is empowered to provide licenses for marketing and manufacturing. This body takes the form of an agency in the USA and Indonesia (the Food and Drug Administration (USFDA) in the case of the USA and Badan POM or the National Agency of Drug and Food Control (NA-DFC) for Indonesia). In China, the China Food and Drug Administration (CFDA) is a ministry-level agency responsible for drug regulation and provide policy guidance at the provincial level FDA.

DISCUSSION

Drug Regulatory Affair Department is the cornerstone of Pharmaceutical industry with motto being protection of public health. It plays a crucial role both internally in pharmaceutical company as well as externally with regulatory agencies. Internally the department works in coordination and liaison with other department like drug development, manufacturing, marketing and clinical research. Externally, it is the key interface between the regulatory authorities and the company.

The department is involved right from the initiation of research activities till after the shelf life of the products. Interestingly, the scope of regulatory affairs activities has seen widening over the years. The requirement and importance of regulatory affairs was highlighted after global mishaps with drugs were experienced. Some of key ones are highlighted below.

Medicines upholds the great role in human life and their regulations incorporates several mutually reinforcing activities all aimed at promoting and protecting public health. They basically concentrate on Quality, Safety and Efficacy. To fulfill these requirements companies undergo discover, manufacturing, and marketing of the product. Drug development to commercialization is highly regulated. These activities vary from country to country in scope and implementation[5].

Hence, every drug before getting marketed must undergo scrutiny to ensure safety. These standards and guidance is set by the regulatory authorities of their respective countries such as- FDA of United States, DCA of India etc. some incidents have ended up in tragedy which made the development of regulatory authorities which can be explained from the history of medicines regulation like:

History of Medicine Regulation

Major Incidences made us to understand that rules and regulations are required to prove safety along with efficacy of drug. Regulation for the modern medicine started in late 19th century after the breakthrough process especially in chemistry, physiology etc. In 1937, over 100 people in U.S died of Diethylene Glycol poisoning following the incident of sulphanilamide elixir in 1938 used as a solvent in medications without any safety testing, considering this, introduction to Federal Food Drug &Cosmetic Act with Pre-market notification requirement for new drugs came in to force.

- UK regulatory system was introduced due to Thalidomide Incident happened in 1956 and hence law was made in 1963 which included the NDAs and GMP.
- Europe was affected with this tragedy and therefore they introduced their **Directive-65/65/EEC** which aimed at harmonizing Standards for the approval of medicines within the **E**uropean **E**conomic **C**ommunity. Regulation of the medicines also includes customs inspection and verification which further includes import/export of the drug products.
- The Mexican-American war at Mexico during **1846-1848** led to the introduction and development of Custom Laboratory which made the Inspection of the imported drug products a mandatory aspect, hence the first law for customs was passed in **1848.** Regulation affects all aspects of the pharmaceutical world, from independent innovators and pharmaceutical companies to regulatory and administrative bodies and patients also. Regulatory Affairs takes care of Development plan, supervising-writing[6].

Drug Regulatory Bodies-Key Role Players in Different Regions

Regulation of pharmaceutical products has been expanding since early 20th century. Regulatory agencies are being established in an ever increasing number of countries on the globe.In the past, drug regulation has been one of the major concern for the governments of many nations, particularly the developed nations and has been limited to the national boundaries. Regulatory affairs professional personnel work closely associated with marketing and research to develop the innovative products that take advantage. The principal regulatory bodies entrusted with the authority of ensuring the drug approval, production and marketing in India.

- Developing a new drug requires great amount of research work in chemistry manufacturing, preclinical tests, and clinical trials. Therefore, drug reviewers in regulatory agencies around the world bears the responsibility of evaluating whether data supports the safety and efficacy or not. For this to work

efficiently, ICH came in action which has issued a number of guidelines to harmonize the amount of data a company needs to submit for the approval. An effective drug regulation broadly explains the method to examine the regulatory framework between different countries.

Hence, it describes the qualifications and standards required to create the administrative bodies necessary for implementing drug regulation and also the structural and functional relationships. They further help in establishing the administrative and legal sanctions that will be applied if the drug provisions are violated, also states the terms and conditions for suspending or cancelling the licenses to import, export, manufacture, sell/supply or promote the drugs. Single regulatory approach to various countries is usually a difficult task, and therefore, different countries are following different regulations for approval, marketing authorization for a new drug.

- Generally, two phenomenon are found in the structural design of the regulatory authority which can present the problem related to regulatory effectiveness, i.e. Fragmentation and Uncoordinated Delegation. Fragmentation is when drug laws assign different responsibilities to the different drug regulatory authorities. Hence, it is a tedious task to overlook whether the desired objective has been achieved or not.

Whereas, uncoordinated delegation results in the disturbed working pattern of the authorities. Drug regulatory structure should be designed in such a way that there is central coordinating body within overall responsibility and accountability.

In addition, Standard Operating Procedure should be set up with the ultimate goals of safety, quality and efficacy. Resources for the proper drug regulation are very important which includes the financial sustainability of the drug regulatory authority (DRAs). In only a few countries the DRA is self-financed namely Sweden, France & U.K. Moreover, implementation of these regulations is a major aspect which includes three sectors:

1. Informal sector
2. Post-Marketing Surveillance sector
3. Drug information centre. Drug regulatory authority also has the review committees like
    - Self- Review
    - Peer Review

Supervisory Body review which helps in evaluations[7].

Regulation Followed for OTC products in India

- **Over-the-counter** (**OTC**) **drugs** are medicines sold directly to a consumer without a prescription from a healthcare professional, as compared to prescription **drugs**, which may be sold only to consumers possessing a valid prescription.

Generally, Non-prescription drugs usually have these characteristics:

- The benefits of these drugs outweigh their risks.
- There are low chances for misuse and abuse.
- Consumer can use them for self-diagnosed health conditions.
- These drugs can be adequately labelled.
- There is no requirement of health professionals for the safe and effective use of the product.

Key categories of medicines with high OTC potential:

1. Vitamins and Minerals
2. Cough & Cold
3. Gastrointestinal
4. Analgesics

There are basic rules and regulations which should be followed while manufacturing an OTC formulation, they can be explained as:

Facility

a) Well established water system

b) Air Flow

c) Cleaning of the facility

d) Proper maintained SOPs

e) Pest Control

f) Glass sterilization

g) Restricted notes on entry of prohibition

h) Area qualification according to **ISO 8**

Equipment

a) Equipment must be accompanied by Performance Qualification

b) Data should be present with DQ, IQ, OQ

c) Calibration cleaning

d) Validation

e) SOPs

Production

a) Well maintained Batch Manufacturing Record

Quality Assurance

a) Batch Record review

b) Validation protocol

c) Product complaint record

d) Master validation plans

e) Record of inspections and Audits conducted[9]

Differences between OTC Drugs & Prescription Drugs[8]

Role	Prescription	OTC
Price regulations	Governed by NPPA (DPCO)	Governed by the competitive scenario (increase in competition reduces in healthcare costs)
Legal Recognition & Acceptance	All prescription drugs fall under schedule-H , X and C/C1 Accepts stability data of 3 validation batches of GMP certified manufacturing plant.	No legal recognition in India & Accepts stability data for 3 validation batches of GMP certified plant.

Procedure for Drug Approval in India

Drug Controller General of India

Clinical Research is regulated in India by DCGI. The office of DCGI runs under CDSCO.

CDSCO- the Central Drugs Standard Control Organization (CDSCO) headed by the Drugs Controller General **(India**) (DCGI) discharges the functions allocated to Central Government. The CDSCO is attached to the office of the Director General of Health Services in the Ministry of Health and Family Welfare. The DCGI is a statutory authority under the Drugs Act and has port offices, zonal offices and drug testing laboratories functioning under him. The State Governments are responsible for licensing of manufacturing establishments and sales premises, carrying out inspections of licensed premises for ensuring compliance to conditions of licenses, drawing samples for test and monitoring the quality of drugs and cosmetics moving in the State. The State Drug Controllers exercise these functions through **State Drugs Inspectors.**

Some of the rules and regulations to be followed for regulation of the drug product are as:

- Drugs & Cosmetics Act 1940 & its rules 1945
- Narcotic drugs and Psychotropic substances- 1985
- Drugs Price Control Order- 1995

- Schedule Y guidelines
- Factories Act
- ICH GCP Guidelines
- ICMR guidelines

Compulsory licensing of patents, government price control and narrow standards for patentability. Currently different countries have to follow different regulatory requirements for approval of new drug. For Marketing Authorization Application (**MAA**) a single regulatory approach is applicable to various countries is almost a difficult task. The new drug approval process consists of two stages (phases) - first phase is for Clinical trials and second is for Marketing Authorization of the drug.

- Clinical studies- ensure safety and efficacy.
- Studies from phase1 –phase 4.

The application for marketing of drug is carried out by the Competent Authority.

New Drug Application- NDA is an application submitted to FDA for permission to market a new drug. To obtain this permission a sponsor submits the Preclinical and Clinical test data to NDA for analyzing the drug information and their mechanisms.

After NDA receives then it undergoes the Technical Screening. This evaluation ensures the sufficient data and information have been submitted in each area justifying the **filing** procedure.

At the conclusion of the FDA review on NDA there are three possible actions that can be sending to the applicant:

a) Not Approvable- list of deficiencies

b) Approvable- minor deficiencies that can be corrected

c) Approval- states that drug is completely approved

If the action taken is either an approvable or non-approvable then FDA provides applicant with an opportunity to meet the agency and discuss the deficiencies.

Stages of Approval

- Submission of clinical trial application for evaluating safety and efficacy.
- Requirements for permission of the new drugs.
- Post approval changes in biological products: quality, safety and efficacy.
- Preparation of the quality information for drug submission for new drug approval.

Application for Approval to Manufacture New Drug Other Than Drugs Classifiable Under Schedule C and C1 (Rule 122 A)

- No new drug shall be manufactured for sale unless it is approved by the Licensing Authority as defined in clause (b) of rule 21.
- An application for grant of approval or to manufacture new drugs for its approval and new formulations shall be made in Form 44 to the licensing authority as defined in clause (b) of rule 21 and shall be accompanied by fifteen thousand fees.
- The manufacturer of the new drug under sub-rule 1 when applying for approval to the licensing authority shall submit the data as mentioned in Appendix 1 of schedule 1 including the results of the clinical trials.

The licensing authority as prescribed in clause (b) of rule 21 after being satisfied that the drug if approved to be manufactured as raw material or as the finished formulation shall be effective and safe for the use in country, shall issue the approval in Form 46 or 46A, as the subject may be.

Hence, wherever the data is found to be inadequate applicant should be informed in writing and he should clear the all the doubts and mistakes before the approval period.

Appeal (122 C)

- Any person aggrieved by an order passed by the Licensing authority under this part, within sixty days from the day of order, appeal to the Central Government.

Therefore, above discussion can be concluded as in:

- All clinical studies reports and related information regarding the approval of new drug in India should provide necessary requirements along with NDA to FDA. Generally, the drug approval process comprised mainly of 2 steps: a) Application to conduct Clinical trial b) Application to the regulatory authority for marketing authorization of the drug[10].

Deficiencies and Limitations of the Current Regulatory Regime

- Dual licensing mechanism
- Lack of transparency in licencing procedures
- Inadequate regulatory expertise and testing facilities to implement uniform standards.
- Need for greater clarity on patentability of pharmaceutical substances and conditions under which firms can apply for compulsory licences to prevent legal battles.
- Need for greater coordination, accountability and transparency in functioning.

Recent Regulatory Initiatives

- Establish an integrated regulatory system through the constitution of a National Drug Authority so that quality regulation and price control is performed.
- Establishment of pharmacovigilance centres at national, zonal and regional levels to monitor **adverse drug reactions**.
- Strengthening to monitor clinical trials, including the setting up of the Clinical Trials Registry of India **(CTRI).**
- Bought nearly 374 bulk drugs under price control[11].

Regulatory Approval Procedure for Cosmetics in India

Cosmetics- it can be defined as any article intended to be rubbed, poured, sprinkled or sprayed on or introduced into or applied to any part of the human body, for cleaning, beautifying, promoting attractiveness or altering the appearance and includes any articles intended for use as a component of cosmetics.

e.g., Cosmetic products include:

Creams, Lotions, Gels, Oils for skin hand, feet, etc.

Classification of Cosmetics

They can be classified according to their use:

a) Skin-Creams, Powders, lotions

b) Nail- Nail Polish

c) Teeth- Dentifrices

Cosmetic according to their function:

a) Decorative- Face Powder

b) Protective- Face Powder

Cosmetics according to their Physical Nature

a) Cakes- Makeup compact

b) Paste- Toothpaste

Central Regulatory Authority & Address	Drug Controller General of India (DCGI) FDA Bhawan, ITO, Kotla Road, New Delhi-110002 Phone-91-23236965 E-mail- dci@nb.nic.in
Governing Regulations	Drug & Cosmetic Act (1940) and Rules, 1945
Pre-Market Approval	• Manufacture of cosmetics for sale or distribution, manufacturer should build the premises as per Sch-M. • Information reviewed by (Local State Licensing Authority) **List of equipments** • Manufacturing

	facility details with minimum area of 15 sq. Metres. • Technical component personal details • Relevant SOPs are required. Specifications should comply with BIS standards if applicable or else acceptable international standards		
License required **Form-31**	Fee **Rs 2500/-**	Inspection Fee **Rs1000/-**	Approval Form-32 **(30 days)**

Application Form-42

- Covering Letter-Purpose should be clearly mentioned with page number and Index.
- Duly filled, signed and stamped original application by the Indian Agent/Importer/Manufacturer.
- Name of the Cosmetic Product, Pack sizes, variants (if along) with actual manufacturer of the product to be registered. The categorization of the product should be as per Column 3 of the guidelines.
- Name & Address of the Authorized Agent/Importer in India.
- Name & Address of Manufacturer and its Factory Premises[12].

Regulatory Certificates

- Authenticated copy of manufacturing licenses/registration/marketing authorization in respect of applied products issued by the regulatory Authority from country of origin.
- Original Free Sale Certificate issued by the National Regulatory Authority of Country of origin for the applied products.
- In case, if not issued by the National Regulatory Authority from the country of origin then from other Competent Associations/organizations duly authenticated from Indian embassy of country of origin need to be submitted.
- The products shall not contain prohibited items (such as mercury, lead, arsenic) and should comply with the standards of either BIS or any International Cosmetic Standards.
- Government Fee by TR challan as applicable.

Chemical Information of Cosmetics

- Test protocol for testing of cosmetics
- Specifications'
- Test report including result of Pb, As, Hg and microbiological test (Wherever applicable)

Technical Documents

Labels and Inserts

- Product labels should show the address of the manufacturer, manufacturing and expiry date.
- Importer name and address
- Import License number, indications and cautions or contra-indications
- Products inserts should describe the brief description of the product and its intended use.
- Company Profile
- Products specifications and testing protocol
- List of ingredients with details of each ingredients used in the products to be registered.

Legal Documents for Registration

Documents by Indian Agent

- Form-42 (it should be signed and stamped by Indian Agent)

Documents by Manufacturer

- POA- Power of Attorney by Indian Embassy of the country of origin, and should be co-jointly signed by the both parties (manufacturer and Indian agent in given format)

- Schedule- DIII- they should be signed and stamped by Manufacturers in the given format.

Assessment of Fee and Timeline for Registration of Cosmetics

- Government fees as TR challan of USD 250 or its equivalent Indian rupees is required for each brand.
- Registration procedure takes 2-3months by the Technical data Associates of CDSCO.
- Registration Certificate (RC) is given in **Form -43**.

Labeling Requirements

- Original label for proposed products along with their volumes as per Drugs and Cosmetics rules, 1945 includes:
  a) Name of the Cosmetics
  b) Name of the manufacturer and complete address of premises where the cosmetic is manufactured
  c) Shelf life
  d) Direction for safe use/caution
  e) Batch no
  f) Manufacturing License no
  g) Registration Number and Importer address and name
  h) Other information (if any)

Note-List of ingredients with details of concentration of each ingredient used in the product composition duly signed by the Competent QC person from the manufacturer.

Chemical Information of Cosmetics

- Test protocol for testing of cosmetics
- Specifications
- Test report including result of Pb, As. Hg and microbiological tests wherever possible[13]

Import & Sale in India

Import of Cosmetics	Import and Sale in India
Licensing Authority	Rule 21 of Drugs & Cosmetics Rules, 1945 Form-42
Application	The manufacturer himself having registered office in India The Authorized Agent of the manufacturer The subsidiary of the manufacturer Any other importer
Requirement for registration of import of cosmetics/ who can be importer?	• Each application will be accompanied by a fee of USD 250 or its equivalent Indian rupees for each Brand. • Executed and authenticated either in India before First Class Magistrate or in the country of origin of the manufacturer. ✓ While submitting the Power of Attorney • It should be conjointly signed and stamped by the manufacturer as well as the Authorized agent indicating the name and designation of the authorized signatories.
Brand Registration Fees	It should clearly list the names of all cosmetic

	products along with their trade names, Brand names, and variants. Further, the name of the cosmetics should correlate with those mentioned in the Form-42
Labels & Changes	The label of imported cosmetics will bear the registration certificate number of the brand and address of the registration certificate holder.
From Manufacture	
Documents needed for Registration	Power of Attorney Original or a copy of a label Free Sale certificate Product specifications/testing protocols Soft copies of the information about brands, products
	From Indian importer/Authorized Agent/Exclusive Distributor in India Covering Letter Form-42 Treasury Challan Schedule-DIII[14]

Benefits and Risks of Switching From Prescription Only to O.T.C.

* ***Possible Benefits***

1. Increased access
2. Decreased frequency of visits to physicians, leading to lower healthcare costs
3. Improved education of consumers
4. Increased autonomy of patients
5. Decreased cost to third party players

****Possible Risks***

1. Inaccurate diagnosis
2. Delay in obtaining needed therapy
3. Use of suboptimal therapy
4. Drug resistance
5. Increased costs to patients
6. Failure to follow label instructions (Adverse effects, Drug interactions)
7. Perceived loss of control by physicians

Distribution

There is at present no system of national chains of supermarkets or drugstores / pharmacies, and small independent shops dominate retailing. However, a few chains such as Apollo Pharmacy, Medicine Shoppe, and Good Health etc. are entering the market, which will make inroads all over India in the near future. Typically however, less than 5% of sales of FMCG manufacturers currently (in 2006) go through organized retailers[9].

Pricing

Price controls are carried out on certain drugs by virtue of the Drugs (Prices Control) Order 1995 (DPCO), under the Essential Commodities Act (ECA). The DPCO is the responsibility of the Ministry of Chemicals and Fertilizers and is supervised by the National Pharmaceutical Pricing Authority (NPPA). It outlines the classification of price-controlled products and methods of price fixation and revision. The NPPA monitors the prices by fixing and revising prices of drugs. Only a few OTC actives, e.g. acetylsalicylic acid and ephedrine & its salts, fall under current DPCO price control[15].

CONCLUSION

Microencapsulation means packaging an active ingredient inside a capsule ranging in size from one micron to several millimeters. The capsule protects the active ingredient from its surrounding environment until an appropriate

time. Then, the material escapes through the capsule wall by various means, including rupture, dissolution, melting or diffusion. Microencapsulation is both an art and a science. The microencapsulation technique offers a variety of opportunities such as protection and masking, reduced dissolution rate, facilitation of handling, and spatial targeting of the active ingredient. This approach facilitates accurate delivery of small quantities of potent drugs. In future by combining various other approaches, microencapsulation technique will find the vital place in novel drug delivery system. And they are characterised by using the methods which are in the evaluation part.

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