

DRUGS REGULATIONS AND PLANT BASED PHARMACEUTICALS IN POST WTO ERA

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Drugs are the greatest weapons of mankind to fight diseases and deaths. Drug control is the only tool to ensure highest quality and purity of drugs. In the beginning of the 20th century, the Drugs Industry was non-existent in India and drugs were imported from abroad. Demand for drugs increased during and after the First World War and cheap drugs were imported in large volume. Increasing demand of drugs resulted in production of cheaper and inferior drugs by some Indian companies to compete with imported drugs. To control the situation, the government passed the **Poison Act** in 1919 and **Dangerous Drugs Act** in 1930 respectively. But to have comprehensive legislation, the Indian Government appointed a Drug Enquiry Committee under the Chairmanship of **Lt-Col. R. N. Chopra** in **1931** to make recommendations about the ways and means to control production and sale of Drugs and Pharmaceuticals in the interest of public health. The Committee submitted a voluminous report to the Government suggesting the creation of a Drug control machinery at the center with branches in all provinces. The committee also recommended the establishment of a well-equipped Central Drugs Laboratory with competent staff and experts. Creation of Central Pharmacy Council and Provincial Council to train young men and women was also suggested by the Chopra Committee.

As a result, the **Drugs Act** was passed in **1940**, partly implementing the Chopra Committee's recommendations to regulate the import, manufacture, distribution and sale of drugs in India. In 1985 repealing the Dangerous Act, 1930, and **Opium Act, 1878**, enacted the **Narcotic Drugs and Psychotropic Substances Act**. The Drugs Rules were framed in 1945 to give effect to the provisions of the Act. At present, the following Acts and Rules regulate manufacture, export and Clinical research of Drugs and Cosmetics in India:

- (i) Drugs and Cosmetics Act, 1940
- (ii) Drugs and Cosmetics Rules, 1945
- (iii) Pharmacy Act, 1948
- (iv) Drugs and Magic Remedies (Objectionable advertisements) Act, 1954
- (v) Narcotic Drugs and Psychotropic Substances Act, 1985
- (vi) Medicinal and Toilet Preparations (Excise Duties) Act, 1955
- (vii) Drugs (Price Control) Order, 1955

Drug include

- All medicines for internal or external use of human beings or animals and all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in

human beings or animals, including preparations applied on human body for the purpose of repelling insects like mosquitoes

- Substances (other than food) intended to affect the structure or any function of the human body or intended to be used for the destruction of or insects, which cause disease in human beings or animals
- All substances intended for use as components of a drug including empty gelatin capsules
- Such devices intended for internal or external use in diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals

Drugs and Cosmetics Act, 1940

The Indian Legislature passed the Drugs and Cosmetics Act in 1940 with the object to regulate the import, manufacture, distribution and sale of drugs. **It is applicable on Allopathic, Homeopathic, Unani and Siddha drugs as well as on contraceptives, mosquito repellents, creams, lotions, cosmetics and devices used for internal and external use for diagnosis.**

Under the Drugs and Cosmetics Act, the regulation of manufacture, sale and distribution of Drugs is 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 standards for Drugs, control over the quality of imported Drugs, coordination of the activities of State Drug Control organizations and providing expert advice with a view of bringing about uniformity in the enforcement of the Drugs and cosmetics Act.

Drugs Controller-General of India [DCG(I)] is responsible for approval of licenses of specified categories of Drugs such as blood and blood products, IV fluids, vaccine, and sera.

Central Drugs Standard Control Organization (CDSCO) is located at Nirman Bhawan, New Delhi and functions under the Directorate-General of Health services. There are four zonal offices of CDSCO:

East Zone: Andaman and Nicobar Island, Arunachal Pradesh, Assam, Bihar, Manipur, Meghalaya, Mizoram, Nagaland, Orissa, Sikkim, Tripura & West Bengal

West Zone: Chattisgarh, Goa, Daman & Diu, Gujarat, Madhya Pradesh and Maharashtra

North Zone: Haryana, Himachal Pradesh, Jammu & Kashmir, Punjab, Rajasthan, Uttaranchal, Uttar Pradesh, National Capital Territory of Delhi & Union Territory of Chandigarh

South Zone: Andhra Pradesh, Karnataka, Kerala, Pondicherry and Tamil Nadu

Central Drugs Laboratory (CDL)

The CDL is the oldest national statutory laboratory of the Govt for quality control of Drugs and Cosmetics and functions under the administrative control of the Director-General of Health Services in the Ministry of Health and Family Welfare.

(1) The functions of the Laboratory in respect of following drugs or classes shall be carried out at the Central Research Institute (CRI), Kasauli.

- (1) Sera
- (2) Solution of serum proteins intended for injection
- (3) Vaccines
- (4) Toxins
- (5) Antigens
- (6) Anti-toxins
- (7) Sterilized surgical ligature and sterilized surgical suture
- (8) Bacteriophages

1-A The functions of the Laboratory in respect of oral Polio vaccine shall be carried out by the following institutes:

- (a) Pasteur Institute of India, Conoor
- (b) Enterovirus Research Centre (ICMR), Haffkine Institute Compound, Parel, Bombay
- (c) The National Institute of Biologicals, Noida

2. The functions of the laboratory in respect of the following drugs or class of drugs shall be carried out at the Indian Veterinary Research Institute, Izatnagar/Mukteswar

- (1) Anti-sera for veterinary use
- (2) Vaccines for veterinary use
- (3) Toxoids for veterinary use
- (4) Diagnostic antigens for veterinary use

Central Drug Testing Laboratory (CDTL), Chennai

The CDTL is statutory laboratory engaged in research and analysis of Drugs and Cosmetics as per Drugs and Cosmetics Act, 1940

Central Drugs Testing Laboratory (CDTL), Mumbai

The CDTL is statutory laboratory functions under the administrative control of DCG(I). The laboratory tests bulk drugs and formulations referred by Assistant Drugs Controller (I). The laboratory is notified as an Appellate Laboratory for Copper T Intra-Uterine Contraceptive Device and Tubal Rings under the Drugs and Cosmetics Rules.

Central Drugs Testing Laboratory (CDL), Guwahati

The statutory laboratory functions under the administrative control of DCG(I) and takes care off entire North-Eastern State including Sikkim.

Central Indian Pharmacopoeia Laboratory (CIPL), Ghaziabad

The CIPL is a national statutory laboratory functions under the administrative control of Director-General, Health Services in the Ministry of Health & Family Welfare. It undertakes work related to standards and analytical specifications of monographs to be incorporated in the Pharmacopoeia, acts as government analyst for such States who do not have their own testing facilities, act as Nodal center of regular condom testing, research & training of other Condom Testing Laboratories.

Central India Pharmacopoeia Commission

Indian Pharmacopoeia Commission under the capacity building project for Food Safety and Quality Control of Drugs, has been set up as a Registered Society under the Societies Act, No.21, 1860. The Pharmacopoeia Commission will consist of General Body, Governing body

New Drugs Regulatory System in India

The Ministry of Health and Family Welfare, Gol constituted an Expert Committee of **Dr. R. A. Mashelkar**, Director General of CSIR to undertake a comprehensive examination of drug regulatory issues on January 27, 2003. The committee noted that the Drugs and Cosmetics Act, 1940 has been in force for the past 56 years, the level of enforcement in many States has been far from satisfactory. The non-uniformity in the interpretation of the provisions of laws and their implementation and the varying levels of competence of regulatory officials were the main reasons for this less than satisfactory performance. The committee recommended that the Central Drugs Administration (CDA) should be made into an independent office under the Ministry of Health and Family Welfare.

Plant based Pharmaceuticals

Bio-pharming

The emerging manifestation of recombinant DNA technology is plant based pharmaceuticals product, also known as "**Bio-pharming**". This technique allows for plants such as corn, tobacco, rice and others to generate proteins that have pharmaceutical and industrial application and in this process save cost too. The manufacturing resources required for biopharming are negligible when compared with the complex and labor intensive mammalian cell culture methods. Energy for this purpose is derived from the sun, and its primary raw materials are water, Co₂ and soil nutrients. Plant based proteins are free from harmful prions.

Molecular farming

Transgenic plant production of pharmaceuticals involves the genetic modification of plants such as corn, tobacco, alfalfa and lemma to produce the proteins of interest. Insertion of gene of interest through common soil bacterium called *Agrobacterium tumefactions* method or gene method gene of interest is inserted into the plant cells allowed to grow in laboratory and then grown on a large scale in field. After harvest, the protein of interest is extracted and purified. According to industry

source, more than 130 area of land in the United States of America are currently being used for the cultivation of plant-based pharmaceuticals. Two different types of plant expression systems:

Vegetative: uses plants such as tobacco, lemna, alfalfa; advantage: quantum and quality of yield of proteins

Grain based system: uses corn, rice and others; advantages: ability to store at normal room temperature or even warmer than room temperature without affecting the activity of proteins.

“**Molecular farming**” is the production of pharmaceutical proteins in transgenic plants and has great potential for the production of therapeutic anti-cancer antibodies and recombinant therapeutic proteins. Plants make fully functional recombinant human or animal antibodies. Cultivating transgenic plants on an agricultural scale will produce almost unlimited supplies of recombinant proteins for uses in medicine. Combinatorial library technology is a key tool for the generation and optimization of therapeutic antibodies ahead of their expression in plants.

PLANT BASED DRUGS AND MEDICINES

Today there are at least 120 distinct chemical substances derived from plants that are considered as important drugs currently in use in one or more countries in the world.

Indian System of Medicine (ISM) and Herbal Products

All traditional medicines like Ayurvedic, Unani and Siddha products containing primarily one or more medicinal plant ingredients are governed under Chapter IV A of Drugs and Cosmetics Act which was introduced in 1969. Before this amendment, definition of products containing herbs or herbal ingredients was non-existent in the Indian Drug Laws. However, plant based products are also regulated under Chapter IV where adequate scientific data on safety, efficacy and quality are available. A few such plant based medicines, which were well standardized and clinically tested, have been licensed by DCG(I).

Regulation of Plant based Pharmaceuticals

The basic federal guidance for regulating all biotech products, including plant based pharmaceuticals is the “Coordinated Framework of Regulation of Biotech” published in 1986 by the White House Office of Science & Technology Policy. The framework provides a regulatory approach intended to ensure the safety of biotech research and products using statutory authority and previous agency experience with traditional breeding technique.

The three lead agencies are USDA’s

Animal and Plant Health Inspection Service (APHIS), which regulates the importation, interstate movement and field testing of genomically engineered plants and organisms

Plant Protection Act

Food and Drugs Administration (FDA)

The Environmental Protection Agency which approve the use of all pesticides including those genetically engineered into plants

INDIA

All traditional medicines (like Ayurvedic, Unani and Siddha products) containing primarily one or more medicinal plant ingredients are governed under Chapter IV A of Drugs and Cosmetics Act, which was introduced in 1969. Before this amendment, definition of products containing herbs or herbal ingredients was non-existent in the Indian Drug Laws. Plant based products are also regulated under Chapter IV where adequate scientific data on safety, efficacy and quality are available. As a part of this amendment, the definition for Ayurveda, Siddha and Unani medicines as well as Patent or Proprietary Medicines was incorporated in the Drugs & Cosmetics Act under Section 3 (a) and 3 (h). For the purpose of these two definitions, Schedule 1 was introduced in the Act, which listed some books as official textbooks of Ayurveda, Siddha and Unani. These official books formed the basis for recognition of recipes of herbs, minerals and other ingredients and the processing methods, which became mandatory requirements for the manufacture of drugs.

There is a separate Department of ISM and H under the Ministry of Health and Family Welfare. The provisions of the Drugs and cosmetics Act have been in existence for more than 3 decades. The licenses are issued at State level for both classical and Patent or Proprietary medicines. In some states Drug Controller, issues license whereas in several States, licenses are issued by Director of Ayurveda on the advise of an Ayurvedic Technical Officer. The conditionalities laid down for the issue of licenses do not provide for detailed mandatory requirements with regard to documentary evidence of safety, efficacy, standardization and quality control methods. Generation of scientific data on these aspects of ISM products or their raw materials is not required under the current law. Dr. Mashelkar's Committee (2003) felt that science based considerations in respect of standards; GMPs, Safety, Evaluation and Quality Control should be similar for all drugs, irrespective of the system to which they may belong. Some of the recommendations say:

1. Schedule I of the Drugs and Cosmetics Act should be revised
2. The definition given under 3 (h) of the Drugs and cosmetics Act uses the term "Patent or Proprietary (P&P) Medicine". The meaning of the term "Patent" in the present day context is totally different and has other legal implications. Hence, this definition should be amended to drop the word "Patent or".
3. The legal aspects of Patent or Proprietary Medicines is not very clearly understood by the consumer and there is an ambiguity with regards to terms like Ayurvedic medicine, Ayurvedic product, Herbal product, Ayurvedic ingredients, Herbal cosmetics, Ayurvedic Cosmetics etc.

4. The Current Indian Law permits new combination of ingredients from different recipes from one or more authoritative books recognized in Schedule I, without need for any data on their safety and efficacy. The mere mention of these ingredients in the authoritative books is taken to provide enough rationale, while issuing P&P license. There is an urgent need for emphasis on **safety and efficacy**.

5. The law should be tightened up to address safety and efficacy of new combinations

Ayurvedic Cosmetics

A large number of herbal products are currently licensed as Patent or Proprietary Medicines but are primarily designed and meant to be used as Cosmetics for skin, hair, nail etc. For lack of provisions in the Drugs and Cosmetics Act, they are licensed as Patent or Proprietary Medicines. It would be appropriate if such products are classified as a New category of cosmetics.

Drugs of Natural Origin

In addition to the medicinal plants, minerals, metals and animal based products, recognized and used in ISM drugs, the western herbs and ingredients also play an important role in the health care. Suitable legislation and criteria for their evaluation and approval for marketing be introduced.

Several regulatory authorities of the world like US FDA, Australian TGA have proposed guidelines for evaluation of Botanical drugs to be licensed as Over The Counter (OTC) drug or prescription drugs. As per the Drugs and Cosmetics Act Rules, there is no separate category of drugs called OTC drugs. Currently, those drugs, which, are not covered under Schedule H or G and their formulations (except their products for external applications) can be called OTC drugs. However, all these need to be stocked, distributed and sold through premises licensed for sale, except for those, which have been specifically exempted by inclusion in Schedule K of D&C Rules.

If herbs from outside India are adequately researched using research methodology of ISM and characteristics are evaluated on ISM guidelines, adoption of such herbs in ISM may be permitted. Provisions do not exist clearly in the Indian laws pertaining to import and marketing of herbal products and cosmetics from other countries.

It is recommended that standard monographs of important and most commonly used medicinal plants and their standardized extracts be prepared and published which will help in monitoring of the quality. It is pertinent to mention that United States Pharmacopoeia and British Pharmacopoeia have included monographs on several medicinal plants in their recent editions. A number of countries including Canada, China, France, Germany, USA etc are registering standardized plant extracts of proven clinical efficacy and safety obtained from natural sources as herbal drugs or dietary supplements. In spite of the fact that India has a vast resource of drugs of natural origin, we are unable to exploit the vast world market because we have an unsatisfactory system of their quality control and registration.

Post WTO & Pharmaceuticals Policy, 2002

The Drugs Policy of 1986, which was titled “**Measures for Rationalization, Quality Control and Growth of Drugs and Pharmaceuticals Industry in India**” was evolved under the dynamic guidance and leadership of **late Shri Rajiv Gandhi**. The main objectives of the Drugs Policy, 1986 were:

- (a) ensuring abundant availability, at reasonable prices, of essential and life saving and prophylactic medicines of good quality;
- (b) strengthening the system of quality control over drug production and promoting the rational use of drugs in the country;
- (c) creating an environment conducive to channeling new investment into the pharmaceuticals industry to encouraging cost effective production with economic sizes and to introducing new technologies and new drugs; and
- (d) strengthening the indigenous capability for production of drugs

The drug and pharmaceutical industry in the country today faces new challenges on account of liberalization of the Indian economy, the globalization of the world economy and on account of new obligations undertaken by India under the WTO Agreements. These challenges require a change in emphasis in the current pharmaceutical policy and the need of new initiatives beyond those enumerated in the Drugs Policy, 1986, as modified in 1994, so that policy inputs are directed towards making it more internationally competitive. The Prime Minister's Advisory Council on Trade and Industry has identified the pharmaceuticals industry as one of the most important knowledge based industry in India. The process of liberalization set in motion in 1991, has considerably reduced the scope of industrial licensing and demolished many non-tariff barriers to imports.