Semester- 6th

Subject: Herbal Drug Technology

Subject code: BP603

Module - 5

General Introduction to Herbal Industry

Objectives: upon compilation of this module the student should be able to:

1. Know about the present scope and future prospects of herbal drug industry
2. Know about the various plant based industries and institutions
3. Know about the various industries involved in work on medicinal and aromatic plants in India
4. Know about the Schedule-T and its objectives
5. Know about the components of GMP and various infrastructural requirements of working space

Learning outcomes: the student will be able to:

1. Learn about the present and future aspects of Herbal drug industry
2. Learn about the various industries involved in work on medicinal and aromatic plants
3. Learn about the components of GMP
4. Learn about the Schedule-T drugs
5. Learn about the working space, storage area and other conditions for herbal drugs

Introduction: Herbs are those remedial agents which are created by nature for curing human illness. Herbal extracts have been used since ancient times in traditional medicine. This system of medicine (Ayurveda, Unani and Siddha) is 5000 year old recommends a combination of lifestyle management and treatment with specific herbs and minerals to cure various diseases. Approximately 1250 Indian medicinal plants are being used to formulate beneficial measures according to Ayurveda. WHO define Traditional herbal medicines as naturally occurring, plant derived substances with minimal or no industrial processing that have been used to treat illness within local or regional healing practices. Traditional herbal medicine and their preparations have been widely used for the thousands of years in developing and developed countries due to its natural origin and lesser side effects. These medicines initially used in the form of crude drugs such as tinctures, teas, poultices, powders, and other herbal formulations. The use of plants for healing purposes predates human history and forms the origin of much modern medicine. Clinical, pharmacological, and chemical studies of these traditional medicines, which were derived predominantly from plants, were the basis of most early medicines such as aspirin

(Willow bark), digitoxin (Foxglove leaves), morphine (Opium poppy), quinine (Cinchona bark), and pilocarpine (Jaborandi). Herbal medicine is still the mainstay of about 75-80% of the world population, mainly in the developing countries, for primary health care. This is primarily because of the general belief that herbal drugs are without any side effects besides being cheap and locally available. According to the WHO, the use of herbal remedies throughout the world exceeds that of the conventional drugs by two to three times.

Recently WHO classified herbal medicines into four different classes according to their origin, evolution and forms of current usage.

- Indigenous herbal medicines
- Herbal medicines in systems
- Modified herbal medicines
- Imported products with a herbal medicine base

Indigenous herbal medicines are those which historically used in a local community or region and are very well known through long usage by the local population in terms of its composition, treatment and dosage. It can be used freely by the local community or in the local region. However, if the medicines in this category enter the market or go away from the local community or region, they have to meet the requirements of safety and efficacy as per the national regulations for herbal medicines. Herbal medicines in systems have been used for a long time and are documented with their special theories and concepts, and accepted by the countries such as Ayurveda, Unani and Siddha. Modified herbal medicines have been modified in shape, or form including dose, dosage form, mode of administration, herbal medicinal ingredients, methods of preparation and medical indications. They have to meet the national regulatory requirements of safety and efficacy of herbal medicines. Imported products with herbal medicine base covers all imported herbal medicines including raw materials and products. Imported herbal medicines must be registered and marketed in the countries of origin. The safety and efficacy data have to be submitted to the national authority of the importing country and need to meet the requirements of safety and efficacy of regulation in the recipient country.

Past and Present Status of Herbal Medicines: Plants and natural products were used by humankind over the years as food and medicines to cure and prevent diseases. It is very difficult to point out an exact time when the use of plants was started as medicine, the carbon dating from ancient Babylon (Iraq) records that plants were cultivated as medicines 60,000 years ago. Written materia medica of medicinal herbs go back approximately 5,000 years in India, China and Egypt and at least 2,500 years in Greece and Asia Minor. Neanderthal remains have been found to contain the remnants of medicinal herbs. Ancient Ayurveda was meant essentially to promote health, however, rather than fight disease. Charak Samhita (1000 BC) and Sushrut Samhita (100 AD) are the main text available. Ayurveda materia medica gives detailed descriptions of over 1500 herbs and 10,000 formulations.

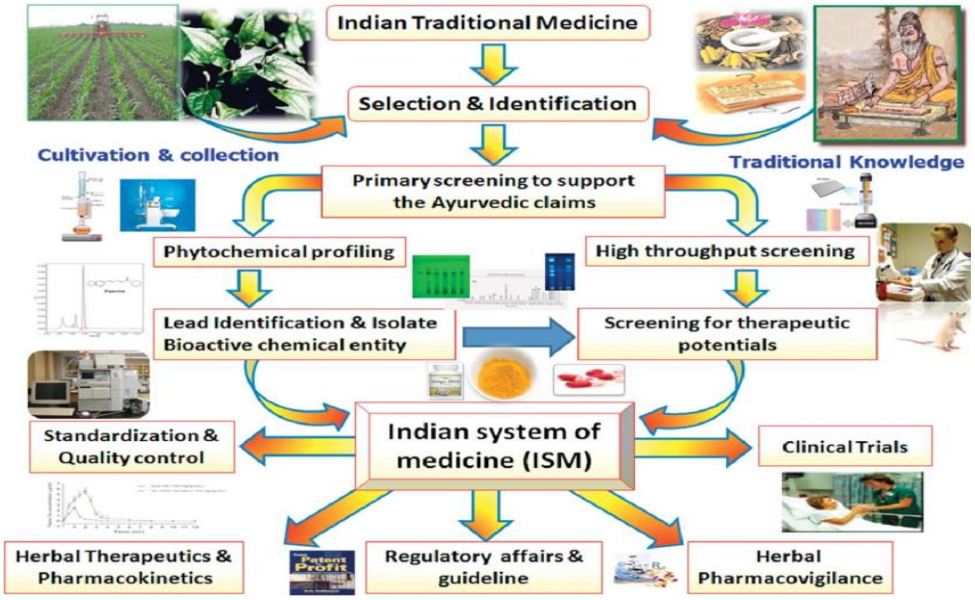
Currently more than 80% of the world population depends on traditional and plant derived medicine because plants are important sources of medicines and presently about 25% of pharmaceutical prescriptions in the United States contain at least one plant derived ingredient. In the last century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various sources. In fact, it is now believed that nature contributes up to 90% to the new drug molecule. Nature has provided many of the effective agent such as dactinomycin, bleomycin, and doxorubicin, vinblastine, irinotecan, topotecan, etoposide, and paclitaxel (anticancer), efloquine, chloroquine, amodiaquine, artemisinin, artemether, and arteether (anti-malarial), metformin and eventually the other biguanide, harunganin, cryptolepine, maprouneacin (anti-diabetic), calanolide A, cucrcumin, phenoxidiol (anti-HIV drugs) etc. India has around 25,000 effective plant based formulations used traditionally with over 1.5 million practitioners of traditional medicinal system and 7800 medicinal drug manufacturing units in India, which consume about 2000 tones of herbs annually.

Traditional medicine in most regions of the world takes place after WHO Traditional Medicine Strategy 2002-2005, state member also developed their own documentation and safety concern. The diversity of regulations and regulatory categories for Traditional medicinal products makes it difficult to assess the size of the market for products across member states accurately. However, available data suggests that the Traditional medicine have significant market in member states. Indian herbal market is nearly 50 billion rupees with 14% annual growth. One billion rupees worth of herbal product are being exported. The demand for medicinal plants is increasing everyday and WHO has projected that global herbal market will grow up to $ 5 trillion in 2050 from the current level of $ 62 billion. India and China produce more than 70% of the global diversity. The significant global herbal export market include EU, USA, Canada, Australia, Singapore, and Japan while Brazil, Argentina, Mexico, China and Indonesia are new emerging market.

Future Prospects of Herbal Medicine: It is estimated that there are about 350,000 species of existing plants (including seed plants, bryophytes, and ferns), among which 287,655 species have been identified as of 2004. Relatively small percentages (1 to 10%) of these are used as foods by both humans and other animal species. It is possible that even more are used for medicinal purposes. WHO has shown great interest in documenting the use of medicinal plants used by tribes from different parts of the world. Many developing countries have intensified their efforts in documenting the ethno-medicinal data on medicinal plants. Research to find out scientific evidence for claims by tribal healers on Indian herbs has been intensified. Once these local ethno-medicinal preparations are scientifically evaluated and disseminated properly, people will be better informed regarding efficacious drug treatment and improved health status. The traditional knowledge system needs to be studied, documented, preserved and used for the benefit of humankind, before it is lost forever. This will require a holistic approach, and involvement and participation of local inhabitants. The Associated Chambers of Commerce and Industry of India (ASSOCHAM) has projected that the market size of herbal industry which is

currently estimated at Rs. 7,500 crores (Rs.75 billion) will double to levels at Rs.15,000 crores by 2015 since this industry would be growing at a compounded annual growth rate of over 20% hence forth. In a study brought out by ASSOCHAM on herbal industry and global market 2015, it is pointed out that India's rich resource of medicinal plants and traditional treasure of knowledge in this area, its share at present is considered very meager. A quick estimate of the potential reveals that India can generate raw stock of around Rs. 300 billion and easily achieve around Rs.150 billion value added products**.** Thus India is hardly able to exploit less than 50% of its potential. Interestingly both raw materials (herbs) and herbal products have ready market globally.

Global Overview of Medicinal Plants: The current and recent trends all over the world have clearly shown that for one reason or the othe rpeople are not only willing to try natural medicine especially those of plant origin but alternatively are seeking nonconventional remedies. As a result of this situation there is a global resurgence in the trade of herbal medicines. International market for medicinal plants is reported to be over 62 billion US dollars per year during 2000-2001, which is growing steadily at the rate of 7% annually. The botanical retail market, inclusive of herbs and medicinal plants, in USA, is estimated to be approximately 1.6 billion US dollars annually. It is estimated that countries in Europe annually imports about 400,000 tonnes of medicinal plant material with an average market value of 1 billion US dollars from countries in Africa and Asia. A growing awareness of this new and recent contributor to the foreign exchange reserves of several national treasuries is beginning to emerge globally. To satisfy the growing market demands for medicinal plants, surveys worldwide are being conducted by the pharmaceutical industries and research organization to unearth and unveil new medicinal plant sources as herbal remedies, medicines, and bio-molecules.



Trade of Medicinal plants/ Indian Scenario: India is one of the richest regions as far as the diversity of plant species is concerned. India is the largest exporter, next to China., accounting for about 13% of the global exports. If we look at the socio-economic scenario of Asian and African countries, modern medicine is neither affordable nor within the reach of many villagers and tribes inhabiting remote areas and deep forests. There are certain pockets in a country like India where the tribal people have no access to modern amenities like roads, telecommunications or electricity, and therefore, these communities rely only on their traditional knowledge of medicine for day-today requirements. It is well established that industrialisation has many direct and indirect effects on the human population. Increased stress is the most evident, although this is offset by increased health awareness among the people and better medical facilities. Nevertheless, increases in the incidence of diseases (mostly in urban populations) such as coronary heart disease, diabetes, hyperlipidaemia, AIDS and cancer cannot be denied. There are many examples where medicines have been obtained from plants known to traditional healers. With the development of modern analytical tools, interest in natural product chemistry has led to the isolation by Serturner of morphine alkaloid from opium, a mixture of plentiful alkaloids. This in turn was obtained from the opium poppy (Papaver somniferum) by processes that have been used for over 5000 years. Quinine isolated from the Cinchona tree had its origin in the Royal household of South American Incas. Long before the first European explorers arrived, the native people of South America had developed medical systems with complete diagnosis and treatment of various maladies. The leaves of the coca tree have been primarily chewed by Andean people to obtain well-known benefits. In 1860, Carl Koler isolated cocaine from the coca tree, the chemical responsible for its biological activity, and has become infamous as a drug of abuse. The other botanicals include atropine, hyoscine, digoxin, colchicine and emetine.

Medicinal and Aromatic Plant based industries and institutions in India

In India, it is estimated that there are about 25,000 licensed pharmacy of Indian system of medicine. Presently about 1000 single drugs and 3000 compound formulations are registered. Herbal Industry in India uses about 8000 medicinal plants. In India, herbal Research institute and manufacturer of herbal formulations. However none the pharma has standardized herbal medicine using active compounds as markers linked with confirmation of bioactivity of medicinal plants. There are about 8000 drug manufactures in India, there are however not more than 25 manufactures that can be classified as large scale manufactures. A large number of academic, industrial and government institutes are conducting research on the medicinal plants of India. There has been no systematic review of the massive work that is available from this nation. Many international data-bases and web-sites do not cover even the work published in the Indian Journals. Hence, there is a global lack of awareness of the mass and nature of work carried out on diverse aspects viz. ethnobotany, phytochemistry, pharmacognosy, pharmacology, clinical trials, safety studies and formulation-research. Following Table provides a short list of some of the eminent institutes which are active in research on medicinal plants and in Ayurveda.

Name	City	Postal code	e-mail
CCRAS(Central Council for Research in Ayurveda and Siddha)	New Delhi	110001	ccras_dir1@nic.in
RRL (Regional Research Laboratory) (CSIR)	Jammu-Tawi	180001	qazi_gn@yahoo.com
NBRI (National Botanical Research Institute) (CSIR)	Lucknow	226001	r.tuli@nbri.res.in
Gujarat Ayurveda University	Jamnagar	361008	info@ayurveduniversity.com
Bhavan's SPARC	Mumbai	400049	bhaspa@bom5.vsnl.net.in
National Institute of Ayurveda	Jaipur	302002	nia@raj.nic.in
ACARTS	Mumbai	400008	clinpharm@hathway.com
Arya Vaidya Shala	Kottakal	676503	mail@aryavaidyasala.com
Interdisciplinary School of Health Sciences	Pune	411007	shs@unipune.ernet.in
Banaras Hindu University	Vanarasi	221005	directorims@satyam.net.in
CIMAP (Central Institute for Medicinal and Aromatic Plants)	Lucknow	226015	director@cimap.res.in
ICMR (Indian Coucil for Medical Research)	New Delhi	110029	icmrhqds@sansad.nic.in
National Medicinal Plants Board	New Delhi	110001	ccras_dir1@nic.in
Indian Drug Manufacturers	Mumbai	400018	publications@idmaindia.com
Regional Medical Research Centre (ICMR)	Belgaum	590010	oicrmrcblm@yahoo.co.in
PERD Centre (Pharmaceutical Education and Research Development)	Ahmedabad	380054	perd@perdcentre.com
CCRUM (Central Council for Research in Unani Medicine)	New Delhi	110001	ccrum@del3.vsnl.net.in
NISCOM(National Institute of Science Communication)	New Delhi	110012	niscom@sirnetd.ernet.in
IMPCOPS (Indian Medical Practitoners Co-operative Pharmacy & Stores Ltd.)	Chennai	600041	admin@webhealthcenter.com
IHMMR (Indian Institute of History of Medicine and Medical Research)	New Delhi	110062	root@hamduni.ren.nic.in
Zandu Foundation	Mumbai	400025	zanduho@giasbm01.vsnl.net.in
Pharmexcil	Hyderabad	500038	info@pharmexcil.com
Chemexcil	Mumbai	400039	chemexcil@vsnl.com
CDRI (Central Drug Researech Institute) (CSIR)	Lucknow	226001	icmrrcdi@ ren.nic.in
IMPLANT Centre (Inter-university Medicinal Plant Laboratory for Analysis, Nurture and Therapeutics)	Rajkot	360005	rrkalariya@sauuni.ernet.in
NIMHANS (National Institute for Mental health and Neurosciences)	Bangalore	560029	sidda@nimhans.kar.nic.in
Panjab University	Chandigarh	600014	webman@puchd.ac.in
LM College of Pharmacy	Ahmedabad	380009	mukeshgohel@hotmail.com
NBPGR (National Bureau of Plant Genetic Resources)	New Delhi	110012	root@nbpgr.delhi.nic.in
NPRC (Nicholas Piramal Research Centre)	Mumbai	400013	recruitment@nicholaspiramal.co.in
NCL (National Chemical Laboratory)	Pune	411008	rs.malge@ncl.res.in
TBGRI (Tropical Botanical Garden & Research Institute)	Thiruvantpuram	695562	director_tbgri@rediffmail.com
BHU (Banaras Hindu University)	Varanasi	221005	vc_bhu@sify.com
Podar Hospital	Mumbai	400018	rapamc@rediffmail.com
Botanical Survey of India	Kolkata	700001	envis@cal2.vsnl.net.in
FRHLT (Foundation for Revitalisation of Local Health Traditions)	Bangalore	560024	Darshan.shankar@frlht.org.in
IASTAM (International Association for the Study of Traditional Asian Medicine)	Mumbai	400012	iastamindia@vsnl.net
ADMA (Ayurvedic Drug Manufacturing Association)	Mumbai	400012	amam2003@sify.com

Schedule T- Good manufacturing Practices of Indian Systems of Medicine

- **Components of GMP and its Objectives:** Good Manufacturing Practice (GMP) is a production and testing practice that helps to ensure a quality product. GMP guidelines are not prescriptive instructions on how to manufacture products. These are a series of general principles that must be observed during manufacturing. When a company is setting up its quality program and manufacturing process, there may be many ways it can fulfill GMP requirements. It is the company's responsibility to determine the most effective and efficient quality process. The Good Manufacturing Practices for ASU Drugs as described in Rule 157 of Drugs & Cosmetics Rules 1945 with conditions as specified in Schedule T / GMP are to ensure that:

  (I) Raw materials used in the manufacture of drugs are authentic, of prescribed quality and are free from contamination

  (II) The manufacturing process is as has been prescribed to maintain the standards

  (III) Adequate quality control measures are adopted

  (IV) The manufactured drug which is released for sale is of acceptable quality

  (V) To achieve the objectives listed above, each licensee shall evolve methodology and procedures for following the prescribed process of manufacture of drugs which should be documented as a manual and kept for reference and inspection. However, under IMCC Act, 1970 registered Vaidyas, Siddhas and Hakeems who prepare medicines on their own to dispense to their patients and not selling such drugs in the market are exempted from the purview of Good manufacturing Practice (GMP).

  Basic Principles of GMP

  Many countries have legislated that pharmaceutical and medical device companies must follow GMP procedures, and have created their own GMP guidelines that correspond with their legislation. Basic concepts of all of these guidelines remain more or less similar to the ultimate goals of safeguarding the health of the patient as well as producing good quality medicine.Although there are a number of them, all guidelines follow a few basic principles:

  - Manufacturing processes are clearly defined and controlled. All critical processes are validated to ensure consistency and compliance with specifications.
  - Manufacturing processes are controlled, and any changes to the process are evaluated.
  - Changes that have an impact on the quality of the drug are validated as necessary.
  - Instructions and procedures are written in clear and unambiguous language.
  - Operators are trained to carry out and document procedures.

- Records are made manually or by instruments during manufacture that demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that the quantity and quality of the drug was as expected
- Deviations are investigated and documented.
- Records of manufacture (including distribution) that enable the complete history of a batch to be traced are retained in a comprehensible and accessible form.

Duties regarding regulation of manufacture for sale of ASU drugs

Subject to the provisions of section 23 and of any rules made by the Central Government in this behalf, an Inspector may, within the local limits of the area for which he is appointed:

- Inspect,
  - (i) any premises wherein any ASU drugs is being manufactured and the means employed for standardizing and testing the ASU drugs;
  - (ii) any premises wherein any ASU drugs is being sold, or stocked or exhibited or offered for sale, or distributed .
- Take samples of any ASU drug,
  - (i) which is being manufactured or being sold or is stocked or exhibited or offered for sale, or is being distributed;
  - (ii) from any person who is in the course of conveying, delivering or preparing to deliver such ASU drugs to a purchaser or a consignee.
- At all reasonable times, with such assistance, if any, as he considers necessary,
  - (i) search any person, who, he has reason to believe, has secreted about his person, any ASU drugs in respect of which an offence under Chapter IV-A of D&C Act has been, or is being, committed; or
  - (ii) enter and search any place in which he has reason to believe that an offence under Chapter IV-A of D&C Act has been, or is being committed; or
  - (ii) Stop and search any vehicle, vessel, or other conveyance which, he has reason to believe, is being used for carrying any ASU drug in respect of which an offence under Chapter IV-A of D&C Act has been, or is being, committed, and order in writing the person in possession of the ASU drugs in respect of which the offence has been, or is being, committed, not to dispose of any stock of such ASU drugs for a specified period not exceeding twenty days, or, unless the alleged offence is such that the defect may be removed by the possessor of the ASU drugs, seize the stock of such ASU drugs and any substance or article by means of which the offence has been ,or is being, committed or which may be employed for the commission of such offence. (Clause c of Section 22 of D&C Act 1940)

Legal provisions for GMP certification

(Rules as in Drugs & Cosmetics Rules 1945 regarding) Manufacture for Sale of Ayurvedic (including Siddha) or Unani Drugs (Part XVI of D&C Rules 1945)

151. Manufacture on more than one set of premises: If Ayurvedic (including Siddha) or Unani drugs are manufactured on more than one set of premises, a separate application shall be made and a separate licence shall be obtained in respect of each such set of premises.

152. Licensing Authorities For this purpose of this Part the State Government shall appoint such Licensing Authorities and for such areas as may be specified in this behalf by notification in the Official Gazette.

153. Application for licence to manufacture Ayurvedic (including Siddha) or Unani drugs.

(1) An application for the grant or renewal of a licence to manufacture for sale any Ayurvedic (including Siddha) or Unani drugs shall be made in Form 24-D to the Licensing Authority along with a fee of rupees one thousand: Provided that in the case of renewal the applicant may apply for the renewal of the licence before its expiry or within one month of such expiry: Provided further that the applicant may apply for renewal after the expiry of one month but within three months of such expiry in which case the fee payable forrenewal of such licence shall be rupees one thousand and two hundred plus an additional fee of rupees six hundred.

(2) A fee of rupees three hundred shall be payable for a duplicate copy of a licence issued under this rule, if the original licence is defaced, damaged or lost.

153-A Loan Licence

(i) An application for the grant or renewal of a loan licence to manufacture for sale of any Ayurvedic (including Siddha) or Unani drugs shall be made in Form 24-E to the Licensing Authority along with a fee of rupees six hundred.

Explanation—For the purpose of this rule, a loan licence means a licence which a LicensingAuthority may issue to an applicant who does not have his own arrangements for manufacture but intends to avail himself of the manufacturing facilities owned by a licence in Form 25-D:

PROVIDED that in the case of renewal the applicant may apply for the renewal of the licence before its expiry or within one month of such expiry:

PROVIDED further that the applicant may apply for renewal after the expiry of one month, but within three months of such expiry in which case the fee payable for renewal of such licence shall be rupees six hundred plus an additional fee of rupees three hundred.

(ii) A fee of rupees one hundred and fifty shall be payable for a duplicate copy of a licence issued under this rule, if the original licence is defaced, damaged or lost.

154. Form of licence to manufacture Ayurvedic (including Siddha) or Unani drugs

(1) Subject to the conditions of rule 157 being fulfilled, a licence to manufacture for sale any Ayurvedic (including Siddha) or Unani drugs shall be issued in Form 25-D. The licence shall be issued within a period of three months from the date of receipt of the application.

(2) A licence under this rule shall be granted by the licensing authority after consulting such expert in Ayurvedic (including Siddha) or Unani Systems of medicine as the case may be, which the State Government may approve in this behalf.

155. Certificate of renewal : The certificate of renewal of a licence in Form 25-D shall be issued in Form 26-D. 155-A Certificate of renewal of a loan licence The certificate of renewal of a loan licence in Form 25-E shall be issued in Form 26-E. 155-B Certificate of award of G.M.P. of Ayurveda, Siddha and Unani Drugs

(i) The certificate of Good Manufacturing Practices to manufacturers of Ayurveda, Siddha or Unani drugs shall be issued for a period of five years to licensees who comply with the requirements of Good Manufacturing Practices (GMP) of Ayurveda, Siddha and Unani drugs as laid down in Schedule T.

(ii) The certificate referred to in sub rule (1) shall be issued for a period of five years from the date of issuance of the license.

156. Duration of licence: An original licence in Form 25-D or a renewed license in Form 26-D, unless sooner suspended or cancelled shall be valid for a period of five years from the date of its issue or renewed. PROVIDED that if the application for the renewal of a licence is made before its expiry

or within one month of its expiry, or if the application is made within three months of its

expiry after payment of the additional fee of rupees five hundred, the licence shall continue

to be in force until orders are passed on the application. The licence shall be deemed to have

expired, if the application for its renewal is not made within three months of its expiry.

156-A Duration of loan licence

An original loan licence in Form 25-E or a renewed loan licence in Form 26-E, unless sooner

suspended or cancelled, shall be valid for a period of five years from the date of its issue

or renewed:

PROVIDED that if the application for the renewal of a loan licence is made in accordance

with rule 153-A, the loan licence shall continue to be in force until orders are passed on the application. The licence shall be deemed to have expired, if the application for its renewal is not made within three months of its expiry.

157. Conditions for the grant or renewal of a licence in Form 25-D Before a licence in Form 25-D is granted or renewed in Form 26-D the following conditions shall be complied with by the applicant, namely—

(1) The manufacture of Ayurvedic (including Siddha) or Unani drugs shall be carried out in such premises and under such hygienic conditions as are specified in Schedule T.

(a) For issuing of the certificate of Good Manufacturing Practices, the Licensing Authority shall verify the requirements as per Schedule T and issue the Good Manufacturing Practices certificate in Form 26 E-I, simultaneously along with grant or renewal of License in Form 25-D.

(2) The manufacture of Ayurvedic (including Siddha) or Unani drugs shall be conducted under the direction and supervision of competent technical staff consisting at least one person, who is a whole time employee and who possesses the following qualifications, namely—

(a) A degree in Ayurveda or Ayurvedic Pharmacy, Siddha or Unani system of medicine, as the case may be, conferred by a University, a State Government or Statutory Faculties, Councils and Boards of Indian Systems of medicines recognized by the Central Government or a State Government for this purpose, or

(b) A diploma in Ayurveda, Siddha or Unani system of medicine granted by a State Government or an Institution recognised by the Central Government for this purpose, or

(c) A graduate in Pharmacy or Pharmaceutical Chemistry or Chemistry or Botany of a University recognized by the Central Government with experience of at least two years in the manufacture of drugs pertaining to the Ayurvedic or Siddha or Unani systems of medicines, or

(d) A Vaid or Hakim registered in a State Register of Practitioners of indigenous systems of medicines having experience of at least four years in the manufacture of Ayurvedic or Siddha or Unani drugs, or

(e) A qualification as Pharmacist in Ayurvedic (including Siddha) or Unani systems of medicine, possessing experience of not less than eight years in the manufacture of Ayurvedic or Siddha or Unani drugs as may be recognized by the Central Government.

(3) The competent technical staff to direct and supervise the manufacture of Ayurvedic drugs shall have qualifications in Ayurveda and the competent technical staff to direct and supervise

the manufacture if Siddha drugs and Unani drugs shall have qualification in Siddha or Unani, as the case may be.

Good Manufacturing Practices

Factory Premises: The manufacturing plant should have adequate space for:-

(i) Receiving and storing raw material;
(ii) Manufacturing process areas;
(iii) Quality control section;
(iv) Finished goods store;
(v) Office;
(vi) Rejected goods/drugs store.

General Requirements:

1.1 (A)Location and surroundings- The factory building for manufacture of Ayurveda, Siddha and Unani medicines shall be so situated and shall have such construction as to avoid contamination from open sewerage, drain, public lavatory or any factory which produces disagreeable or obnoxious odour or fumes or excessive soot, dust or smoke.

1.1(B) Buildings- The building used for factory shall be such as to permit production of drugs under hygienic conditions and should be free from cobwebs and insects/rodents. It should have adequate provision of light and ventilation. The floor and the walls should not be damp or moist. The premises used for manufacturing, processing, packaging and labeling will be in conformity with the provisions of the Factory Act. It shall be located so as to be:

(i) Compatible with other manufacturing operations that may be carried out in the same or adjacent premises.

(ii) Adequately provided with working space to allow orderly and logical placement of equipment and materials to avoid the risk of mix-up between different drugs or components thereof and control the possibility of cross- contamination by other drugs or substances and avoid the risk of omission of any manufacturing or control step.

iii. Designed, constructed andmaintainedtoprevententryofinsectsandrodents. Interior surface (walls, floors and ceilings) shall be smooth and free from cracks and permit easy cleaning and disinfection. The walls of the room in which the manufacturing operations are carried out shall be impervious to and be capable of being kept clean. The flooring shall be smooth and even and shall be such as not to permit retention or accumulation of dust or waste products.

iv. Provided with proper drainage system in the processing area. The sanitary fittings and electrical fixtures in the manufacturing area shall be proper and safe.

(v) Furnace/Bhatti section could be covered with tin roof and proper ventilation, but sufficient care should be taken to prevent flies and dust.

(vi)There should be fire safety measures and proper exits should be there.

(vii) Drying space- There should be separate space for drying of raw material, in process medicine or medicines which require drying before packing. This space will be protected from flies/insects/dusts, etc., by proper flooring, wire-mash window,glass pans or other material.

1.1(C) Water Supply- The water used in manufacture shall be pure and of potable quality.Adequate provision of water for washing the premises shall be made.

1.1(D) Disposal of Waste- From the manufacturing sections and laboratories the waste water and the residues which might be prejudicial to the workers or public health shall be disposed off after suitable treatment as per guidelines of pollution control authorities to render them harmless.

1.1(E) Containers' Cleaning- In factories where operations involving the use of containers such as glass bottles, vials and jars are conducted, there shall be adequate arrangement separated from the manufacturing operations for washing, cleaning and drying of such containers.

1.1(F) Stores- Storage should have proper ventilation and shall be free from dampness. It should provide independent adequate space for storage of different types of material, such as raw material, packaging material and finished products.

1.1(F)(A) Raw Materials- All raw materials procured for manufacturing will be stored in the raw materials store. The manufacture based on the experience and the characteristics of the particular raw material used in Ayurveda, Siddha and Unani system shall decide the use of appropriate containers which would protect the quality of the raw material as well as prevent it from damage due to dampness, microbiological contamination or rodent and insect infestation, etc. If certain raw materials require such controlled environmental conditions, the raw materials stores may be sub-divided with proper enclosures to provide such conditions by suitable cabinization. While designing such containers, cabins or areas in the raw materials store, care may be taken to handle the following different categories of raw materials:-

(1) Raw material of metallic origin.

(2) Raw material of mineral origin.

(3) Raw material from animal source.

(4) Fresh Herbs.

(5) Dry Herbs or plant parts.

(6) Excipients, etc.

(7) Volatile oils/perfumes & flavours.

(8) Plant concentrates/extracts and exudates/resins.

Each container used for raw material storage shall be properly identified with the label which indicates name of the raw material, source of supply and will also clearly state the status of raw material such as 'UNDER TEST' or 'APPROVED' or 'REJECTED'. The labels shall further indicate the identity of the particular supply in the form of Batch No. or Lot. No. and the date of receipt of consignment. All the raw materials shall be sampled and got tested either by the in-house Ayurvedic, Siddha and Unani experts (Quality control technical person) or by the laboratories approved by Government and shall be used only on approval after verifying. The rejected raw material should be removed from other raw materials store and should be kept in a separate room. Procedure of 'First in first out' should be adopted for raw materials wherever necessary. Records of the receipt, testing and approval or rejection and use of raw material shall be maintained.

1.1(F)(B) Packaging Materials- All packaging materials such as bottles, jars, capsules, etc. shall be stored properly. All containers and closures shall be adequately cleaned and dried before packing the products.

1.1(F)(C) Finished Goods Stores- The finished goods transferred from the production area after proper packaging shall be stored in the finished goods stores within an area marked"Quarantine". After the quality control laboratory and the experts have checked the correctness of finished goods with reference to its packing/labelling as well as the finished product quality as prescribed,, then it will be moved to 'Approved Finished Goods Stock"area.

1.1(G) Working Space- The manufacturing area shall provide adequate space (manufacture and quality control) for orderly placement of equipment and material used in any of the operations for which these are employed so as to facilitate easy and safe working and to minimize or to eliminate any risk of mix-up between different drugs, raw materials and to prevent the possibility of cross-contamination of one drug by another drug that is manufactured, stored or handled in the same premises.

1.1(H) Health, Clothing, Sanitation and Hygiene of Workers- All workers employed in the Factory shall be free from contagious diseases. The clothing of the workers shall consist of proper uniform suitable to the nature of work and the climate and shall be clean. The uniform shall also include cloth or synthetic covering for hands, feet and head wherever required. Adequate facilities for personal cleanliness such as clean towels, soap and scrubbing brushes shall be provided. Separate provision shall be made for lavatories to be used by men and women, and such lavatories shall be located at places separated from the processing rooms. Workers will also be provided facilities for changing their clothes and to keep their personal belongings.

1.1(I) Medical Services- The manufacturer shall also provide:-

(i) Adequate facilities for first aid;

(ii) Medical examination of workers at the time of employment and periodical checkup thereafter by a physician once a year, with particular attention being devoted to freedom from infections. Records thereof shall be maintained.

1.1(J) Machinery and Equipments- For carrying out manufacturing depending on the size of operation and the nature of product manufactured, suitable equipment either manually operated or operated semi-automatically (electrical or team based) or fully automatic machinery shall be made available. These may include machines for use in the process of manufacture such as crushing, grinding, powdering, boiling, mashing, burning, roasting, filtering, drying, filling, labelling and packing, etc. To ensure ease in movement of workers and orderliness in operations a suitably adequate space will be ensured between two machines or rows of machines. These machinery and equipments and machinery recommended is indicated in Part II-A. Proper standard operational procedures (SOPs) for cleaning maintaining and performance of every machine should be laid down.

1.1(K) Batch Manufacturing Records- The licensee shall maintain batch manufacturing record of each batch of Ayurvedic, Siddha and Unani drugs manufactured irrespective of the type of product manufactured (classical preparation or patent and proprietary medicines). Manufacturing records are required to provide and account of the list of raw materials and their quantities obtained from the store, tests conducted during the various stages of manufacture like taste, colour, physical characteristics and chemical tests as may be necessary or indicated in the approved books of Ayurveda, Siddha and Unani mentioned in the First Schedule of the Drugs and Cosmetics Act, 1940 (23 of 1940). These tests may include any in-house or pharmacopoeial test adopted by the manufacturer in the raw material or in the process material and in the finished product. These records shall be duly signed by Production and Quality Control Personnel respectively. Details of transfer of manufactured drug to the finished products store including dates and quantity of drugs transferred along with record of testing of the finished product, if any, and packaging, records shall be maintained. Only after the manufactured drugs have been verified and accepted quality shall be allowed to be cleared for sale. It should be essential to maintain the record of date, manpower, machine and equipments used and to keep in process record of various shodhana, bhavana, burning in fire and specific grindings in terms of internal use.

1.1(L) Distribution Records- Records of sale and distribution of each batch of Ayurveda, Siddha and Unani Drugs shall be maintained in order to facilitate prompt and complete recall of the batch, if necessary. The duration of record keeping should be the date of expiry of the batch, Certain categories of Ayurvedic, Siddha and Unani medicines like Bhasma, Rasa, Kupi- pakva, Parpati, Sindura, Karpu/Uppu/Puram, Kushta, Asava-arista, etc. do not have expiry date, in

contrast their efficacy increases with the passage of time. Hence, records need to be maintained up to 5 years of the exhausting of stock.

1.1(M) Record of Market Complaints- Manufacturers shall maintain a register to record all reports of market complaints received regarding the products sold in the market. The manufacturer shall enter all data received on such market complaints, investigations carried out by the manufacturers regarding the complaint as well as any corrective action initiated to prevent recurrence of such market complaints shall also be recorded. Once in a period of six months the manufacturer shall submit the record such complaints to the Licensing Authority. The Register shall also be available for inspection during any inspection of the premises. Reports of any adverse reaction resulting from the use of Ayurvedic, Siddha andUnani drugs shall also be maintained in a separate register by each manufacturer. The manufacturer shall investigate any of the adverse reaction to find if the same is due to any defect in the product, and whether such reactions are already reported in the literature or it is a new observation.

1.1(N) Quality Control- Every licensee is required to provide facility for quality control section in his own premises or through Government-approved testing laboratory. The test shall be as per the Ayurveda, Siddha and Unani pharmacopoeial standard. Where the tests are not available, the test should be performed according to the manufacturer's specification or other information available. The quality control section shall verify all the raw materials, monitor in process, quality checks and control the quality of finished product being released to finished goods store/warehouse. Preferably for such quality control there will be a separate expert. The quality control section shall have the following facilities:

(a) There should be 150 sq feet area for quality control section.

(b) For identification of raw drugs, reference books and reference samples should be maintained.

(c) Manufacturing record should be maintained for the various processes.

(d) To verify the finished products, controlled samples of finished products of each batch will be kept till the expiry date of product.

(e) To supervise and monitor adequacy of conditions under which raw materials, semifinished products and finished products are stored.

(f) Keep record in establishing shelf life and storage requirements for the drugs.

(g) Manufacturers who are manufacturing patent proprietary Ayurveda, Siddha and Unani medicines shall provide their own specification and control references in respect of such formulated drugs.

(h) The record of specific method and procedure of preparation, that is, “Bhavana”, “Mardana” and “Puta” and the record of every process carried out by the manufacturer shall be maintained.

(i) The standards foridentity,purity andstrengthas giveninrespectivepharmacopoeias of Ayurveda, Siddha and Unani systems of medicines published by Government of India Shall be complied with.

(j) All raw materials will be monitored for fungal, bacterial contamination with a view to minimize such contamination.

(k) Quality control section will have a minimum of-

(i) (a) Expert in Ayurveda or Siddha or Unani who possess a degree qualification recognized under Schedule II of Indian Medicine Central Council Act, 1970.

(b) Chemist, who shall possess at least a Bachelor Degree in Science or Pharmacy or Pharmacy (Ayurveda) awrded by a recognized University; and

(c) A Botanist (Pharmacognosist) who shall possess at least a Bachelor Degree in Science (Medical) or Pharmacy or Pharmacy (Ayurveda) awarded by a recognized University.

(ii) The manufacturing unit shall have a quality control section as explained under Section 35(ii). Alternatively, these quality control provisions will be met by getting testing, etc., from a recognized laboratory for Ayurveda, Siddha and Unani drugs; under Rule 160-A of the Drugs and Cosmetics Act. The manufacturing company will maintain all the record of various tests got done from outside recognized laboratory.

(iii) List of equipment recommended is indicated in Part II-C.

1.2 Requirement for Sterile Product:

(A) Manufacturing Areas– For the manufacture of sterile Ayurvedic, Unani and Siddha drugs, separate enclosed areas specifically designed for the purpose shall be provided. These areas shall be provided with air locks for entry and shall be essentially dust free and ventilated with an air supply. For all areas where aseptic manufacture has to be carried out, air supply shall be filtered through bacteria retaining filters (HEPA Filters) and shall be at a pressure higher than in the adjacent areas. The filters shall be checked for performance on installation and periodically thereafter the record of checks shall be maintained. All the surfaces in sterile manufacturing

areas shall be designed to facilitate cleaning and disinfection. For sterile manufacturing routine microbial counts of all Ayurvedic, Siddha and Unani drug manufacturing areas shall be carried out during operations. Results of such count shall be checked against established in-house standards and record maintained. Access to manufacturing areas shall be restricted to minimum number of authorized personnel. Special procedure to be followed for entering and leaving the manufacturing areas shall be written down and displayed. For the manufacturing of Ayurvedic, Siddha and Unani drug that can be sterilized in their final containers, the design of the areas shall preclude the possibility of the products intended for sterilization being mixed with or taken to be products already sterilized. In case of terminally sterilized products, the design of the areas shall preclude the possibility of mix-up between non-sterile products.

(B) Precautions against contamination and mix:

a) Carrying out manufacturing operations in a separate block of adequately isolated building or operating in an isolated enclosure within the building,

(b) Using appropriate pressure differential in the process area.

(c) Providing a suitable exhaust system.

(d) Designing laminar flow sterile air system for sterile products.

(e) The germicidal efficiency of UV lamps shall be checked and recorded indicating the burning hours or checked using intensity.

(f) Individual containers of liquids and ophthalmic solutions shall be examined against black-white background fitted with diffused light after filling to ensure freedom from contamination with foreign suspended matter.

(g) Expert technical staff approved by the Licensing Authority shall check and compare actual yield against theoretical yield before final distribution of the batch. All process controls as required under master formula including room temperature, relative humidity, volume filled, leakage and clarity shall be checked and recorded.