Part-I

Revised Draft GMP of AYURVEDA, SIDDHA AND UNANI Drugs.

Note - To achieve the objectives listed below, each licensee shall evolve appropriate methodology, systems and procedures which shall be documented and maintained for inspection and reference; and the manufacturing premises shall be used exclusively for production of Ayurveda, Siddha and Unani drugs and no other manufacturing activity shall be undertaken therein.

1. GENERAL REQUIREMENT:-

1.1 (A) - The Good Manufacturing Practices (GMP) are prescribed as follows in Part I and Part II to ensure:-

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 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 Practices (GMP).

1.1 (B) *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 sewrage, drain, public lavatory or any factory which produces disagreeable or obnoxious odour or fumes or excessive soot, dust or smoke.

1.1. *(C) Buildings:* The building used for factory shall be such as to permit production of Ayurveda, Siddha and Unani 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 and maintained to prevent entry of insects and rodents. Interior surface (walls, floors and ceilings) shall be smooth and free from cracks and permit easy cleaning and dis-infection. 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 of waste products.

IV. Provided with proper drainage system in the processing area. The sanitary fitting 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 require drying before packing. This space will be protected from flies/ insects/dusts etc., by proper flooring, wire mesh window, glass pans or other material.

1.1. *(D) Water System:* There shall be validated system for treatment of water drawn from own or any other source to render it potable in accordance with standards specified by the Bureau of nature of the operation. These shall also be suitable to the comforts of the Indian Standards or Local Municipality, as the case may be, so as to produce Purified Water conforming to Ayurveda, Siddha and Unani Pharmacopoeial specification. Purified Water so produced shall only be used for all the operations except washing and cleaning operations where potable water may be used Water shall be stored in tanks, which do not adversely affect quality of water and ensure freedom from microbiological growth. The tank shall be cleaned periodically and records maintained by the licensee in this behalf.

1.1.(E) Disposal of Waste:

i. The disposal of sewage and effluents (solid, liquid and gas) from the factory shall be in conformity with the requirements of Environment Pollution Control Board.
ii. All bio-medical waste shall be destroyed as per the provisions of the Bio-Medical Waste (Management and Handling) Rules, 1996.
iii. Additional precautions shall be taken for the storage and disposal of rejected drugs. Records shall be maintained for all disposal of waste.
iv. Provisions shall be made for the proper and safe storage of waste materials awaiting disposal. Hazardous, toxic substance and flammable materials shall be stored in suitably designed and segregated, enclosed areas in conformity with Central and State Legislations.

2. WAREHOUSING AREA:-

2.1. Adequate areas shall be designed to allow sufficient and orderly warehousing of various categories of materials and products like starting and packaging materials, intermediates bulk and finished products, products in quarantine, released, rejected, returned or recalled, machine and equipment spare parts and change items.
2.2. Warehousing areas shall be designed and adapted to ensure good storage conditions. They shall be clean, dry and maintained within acceptable temperature limits. Where special storage conditions are required (e.g., temperature humidity), these shall be provided, monitored and recorded. Storage areas shall have appropriate house-keeping

and rodents, pests and vermin control procedures and records maintained. Proper racks, bins and platforms shall be provided for the storage of materials.

2.3. Receiving and dispatch bays shall protect materials and products from adverse weather conditions.

2.4. Where quarantine status is ensured by warehousing in separate earmarked areas in the same warehouse or store, these areas shall be clearly demarcated. Any system replacing the physical quarantine, shall give equivalent assurance of segregation. Access to these areas shall be restricted to authorized persons.

2.5 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/labeling as well as the finished product quality as prescribed, then it will be moved to 'Approved Finished Goods Stock' area. Only approved finished goods shall be dispatched as per marketing requirements. Distribution records shall be maintained as required.

If any Ayurvedic, Siddha and Unani drug needs a special storage conditions, finished goods store shall provide necessary environmental requirements.

2.6. There shall be a separate sampling area in the warehousing area for active raw materials and excipients. If sampling is performed in any other area, it shall be conducted in such a way as to prevent contamination, cross-contamination and mix-up.

2.7. All packaging materials such as bottles, jars, capsules etc. shall be stored properly. All containers and closure shall be adequately cleaned and dried before packing the products. Segregation shall be provided for the storage of rejected, recalled or returned materials or products. Such areas, materials or products shall be suitably marked and secured. Access to these areas and materials shall be restricted.

2.8. Poisonous substances should be kept in safe storage condition. Adequate fire protection measures shall be provided in conformity with the rules of the concerned civic authority.

2.9. Printed packaging materials shall be stored in safe, separate and secure areas.

2.10. Sampling and dispensing of sterile materials shall be conducted under aseptic conditions, which can also be performed in a dedicated area within the manufacturing facility.

2.11. Regular checks shall be made to ensure adequate steps are taken against spillage, breakage and leakage of containers.

2.12 ***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 quality of the raw material as well as prevent it from damage due to dampness, microbiological contamination or rodent 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, cupboard or areas in the raw materials store, care may be taken to handle the following different categories of raw material:-

(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 containers 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 the 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 NABL or AYUSH approved laboratories and shall be used only on approval after verifying. The rejected raw material should be removed from other raw material store and should be kept in 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.

The licensee shall keep inventory of all raw materials to be used at any steps of manufacturing of drugs and maintain records as per schedule T-A.

3. PRODUCTION AREA

3.1. The production area shall be designed to allow the production preferably in uni-flow and with logical sequence of operations.

3.2. In order to avoid the risk of cross-contamination, separate dedicated and self-contained facilities shall be made available for the production of Ayurveda, Siddha and Unani drugs. 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.

3.3. Pipe-work, electrical fittings, ventilation openings and similar service lines shall be designed, fixed and constructed to avoid [accumulation of dust]. Service lines shall preferably be identified by colours and the nature of the supply and direction of the flow shall be marked/ indicated.

4. ANCILLARY AREA

4.1. Rest and refreshment rooms shall be separate from other areas. These areas shall not lead directly to the manufacturing and storage areas.

4.2. Facilities for changing, storing clothes and for washing and toilet purposes shall be easily accessible and adequate for the number of users. Toilets, separate for males and females, shall not be directly connected with production or storage areas. There shall be written instructions for cleaning and disinfection for such areas.

4.3. Maintenance workshops shall be separate and away from production areas. Whenever spares, changed parts and tools are stored in the production area, these shall be kept in dedicated rooms or lockers. Tools and spare parts for use in sterile areas shall be disinfected before these are carried inside the production areas.

5. QUALITY CONTROL AREA

5.1. Quality Control Laboratories shall be independent of the production areas. Separate areas shall be provided each for pharmacognostical, chemical, microbiological analysis. Separate instrument room with adequate area shall be provided for sensitive and sophisticated instruments employed for analysis.

5.2. Quality Control Laboratories shall be designed appropriately for the operations to be carried out in them. Adequate space shall be provided to avoid mix-ups and cross-contamination. Sufficient and suitable storage space shall be provided for test samples, retained samples, reference standards, reagents and records.

5.3. The design of the laboratory shall take into account the suitability of construction materials and ventilation. Separate air handling units and other requirements shall be provided for pharmacognostical, chemical, microbiological and testing areas. The laboratory shall be provided with regular supply of water of appropriate quality for cleaning and testing purposes .

5.4. Quality Control Laboratory shall be divided into separate sections i.e. for pharmacognostical, chemical and microbiological wherever required. These shall have adequate area for basic installation and for ancillary purposes. The microbiology section shall have arrangements such as airlocks and laminar air flow work station, wherever considered necessary.

5.5 Every licensee is required to provide facility for quality control section in his own premises. 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 manufacturers 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/ware house. Preferably for such quality control there will be a separate expert. The quality control section shall have the following facilities:

1) There should be adequate area for quality control section.
2) For identification of raw drugs, reference books such as Ayurveda, Siddha and Unani Pharmacopoeias Formularies and other scientific books and reference samples should be maintained.
3) Manufacturing record should be maintained for the various processes.
4) To verify the finished products, controlled samples of finished products of each batch will be kept for till the expiry date of product.

5) To supervise and monitor adequacy of conditions under which raw materials, semi-finished products and finished products are stored.
6) Keep record in establishing shelf life and storage requirements for the drugs.
7) Manufacturers who are manufacturing Patent Proprietary Ayurveda, Siddha, and Unani medicines shall provide their own specification and control reference in respect of such formulated drugs.
8) 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.
9) The standards for identity, purity and strength as given in respective pharmacopoeias of Ayurveda, Siddha and Unani systems of medicines published by Government of India shall be complied with.
10) All raw materials will be monitored for fungal, bacterial contamination with a view to minimise such contamination.
11) Quality control section will have a minimum of –
    (i) (a) Expert in Ayurveda or Sidha or Unani medicine who possesses a degree qualification recognized under Schedule II of Indian Medicine Central Council Act 1970;
    (b) Chemist, who shall possess at least Master Degree in Science or Pharmacy or Pharmacy (Ayurveda), awarded by a recognized University; and
    (c) Botanist (Pharmacognosist), who shall possess at least Bachelor Degree in Science (Medical) or Pharmacy or Pharmacy (Ayurveda) awarded by a recognized University.]
    (d) Microbiologist who shall process at least master degree in microbiology awarded by a recognized university.
    (ii) The manufacturing unit shall have a quality control section as explained under Section 35 (ii). The manufacturing company will maintain all the record of various tests got done from outside recognised laboratory.
    (iii) List of equipments recommended is indicated in Part II-C.

6. PERSONNEL:

6.1. The manufacture shall be conducted under the direct supervision of competent technical staff with prescribed qualifications and practical experience in the relevant dosage form of Ayurveda, Siddha and Unani drugs.
6.2. The head of the Quality Control Laboratory shall be independent of the manufacturing unit. The testing shall be conducted under the direct supervision of competent technical staff who shall be whole time employees of the licensee.
6.3. Personnel for Quality Assurance and Quality Control operations shall be suitably qualified and experienced.
6.4. Written duties of technical and Quality Control personnel shall be laid and followed strictly.
6.5. Number of personnel employed shall be adequate and in direct proportion to the workload.

6.6. The licensee shall ensure in accordance with a written instruction that all personnel in production area or into Quality Control Laboratories shall receive training appropriate to the duties and responsibility assigned to them. They shall be provided with regular in-service training.

7. HEALTH, CLOTHING AND SANITATION OF WORKERS:-

7.1. 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.

7.2. Prior to employment, all personnel, shall undergo medical examination including eye examination, and shall be free from Tuberculosis, skin and other communicable or contagious diseases. Thereafter, they should be medically examined periodically, at least once a year. Records shall be maintained thereof. The licnesee shall provide the services of a qualified physician for assessing the health status of personnel involved in different activities.

7.3. All persons, prior to and during employment, shall be trained in practices which ensure personal hygiene. A high level of personal hygiene shall be observed by all those engaged in the manufacturing processes. Instructions to this effect shall be displayed in change-rooms and other strategic locations.

7.4. No person showing, at any time, apparent illness or open lesions which may adversely affect the quality of products, shall be allowed to handle starting materials, packaging materials, in-process materials , and drug products until his condition is no longer judged to be a risk.

7.5. All employees shall be instructed to report about their illness or abnormal health condition to their immediate supervisor so that appropriate action can be taken.

7.6. Direct contact shall be avoided between the unprotected hands of personnel and raw materials, intermediate or finished, unpacked products.

7.7. All personnel shall wear clean body coverings appropriate to their duties. Before entry into the manufacturing area, there shall be change rooms separate for each sex with adequate facilities for personal cleanliness such as wash basin with running water, [clean towels or hand dryers], soaps, disinfectants etc. The change rooms shall be provided with cabinets for the storage of personal belongings of the personnel.

7.8. Smoking, eating, drinking, chewing or keeping plants, food, drink and personal medicines shall not be permitted in production, laboratory, storage and other areas where they might adversely influence the product quality.

8. MANUFACTURING OPERATIONS AND CONTROLS

8.1 All manufacturing operations shall be carried out under the supervision of technical staff approved by the Licensing Authority. Each critical step in the process relating to the

selection, weighing and me Ayurveda, Siddha and Unani ring of raw material addition during various stages shall be performed by trained personnel under the direct personal supervision of approved technical staff.

The contents of all vessels and containers used in manufacture and storage during the various manufacturing stages shall be conspicuously labeled with the name of the product, batch no., batch size and stage of manufacture. Each label should be initialed and dated by the authorized technical staff. Products not prepared under aseptic conditions are required to be free from pathogens.

8.2. Precautions against mix-up and cross-contamination—

8.2.1. The licensee shall prevent mix-up and cross-contamination of drug material and drug product (from environment dust) by proper air-handling system, pressure differential segregation, status labeling and cleaning. Proper records and Standard Operating Procedures thereof shall be maintained.

8.2.2. To prevent mix-ups during production stages, materials under-process shall be conspicuously labeled to demonstrate their status. All equipment used for production shall be labeled with their current status.

8.2.3. Packaging lines shall be independent and adequately segregated. It shall be ensured that all left-overs of the previous packaging operations, including labels, cartons and caps are cleared before the closing hour.

8.2.4. Before packaging operations are begun, steps shall be taken to ensure that the work area, packaging lines, printing machines, and other equipment are clean and free from any products, materials and spillages. The line clearance shall be performed according to an appropriate checklist and recorded.

8.2.5. The correct details of any printing (for example of batch numbers or expiry dates) done separately or in the course of the packaging shall be rechecked at regular intervals. All printing and overprinting shall be authorized in writing.

8.2.6. The manufacturing environment shall be maintained at the required levels of temperature, humidity and cleanliness.

8.2.7. Authorised persons shall ensure change-over into specific uniforms before undertaking any manufacturing operations including packaging.

8.2.8. There shall be segregated secured areas for recalled or rejected material and for such material which are to be re-processed or recovered.

9. SANITATION IN THE MANUFACTURING PREMISES.

9.1. The manufacturing premises shall be cleaned and maintained in an orderly manner, so that it is free from accumulated waste, dust, debris and other similar material. A validated cleaning procedure shall be maintained.

9.2. The manufacturing areas shall not be used for storage of materials, except for the material being processed. It shall not be used as a general thoroughfare.

9.3. A routine sanitation program shall be drawn up and observed, which shall be properly recorded and which shall indicate—

(a) specific areas to be cleaned and cleaning intervals;

(b) cleaning procedure to be followed, including equipment and materials to be used for cleaning; and

(c) personnel assigned to and responsible for the cleaning operation.

9.4. The adequacy of the working and in-process storage space shall permit the orderly and logical positioning of equipment and materials so as to minimise the risk of mix-up between different Ayurveda, Siddha and Unani products to avoid cross-contamination, and to minimise the risk of omission or wrong application of any of the manufacturing or control steps.

9.5. Production areas shall be well lit, particularly where visual on-line controls are carried out.

10. EQUIPMENTS

10.1. Equipment shall be located, designed, constructed, adapted and maintained to suit the operations to be carried out. The layout and design of the equipment shall aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt and, in general, any adverse effect on the quality of products. Each equipment shall be provided with a log book, wherever necessary.

10.2. Balances and other me Ayurveda, Siddha and Unani ring equipment of an appropriate range, accuracy and precision shall be available in the raw-material stores, production and in-process control operations and these shall be calibrated and checked on a scheduled basis in accordance with Standard Operating Procedures and records maintained.

10.3. The parts of the production equipment that come into contact with the product shall not be reactive, additive or adsorptive to an extent that would affect the quality of the product.

10.4. To avoid accidental contamination, wherever possible, non-toxic/edible grade lubricants shall be used and the equipment shall be maintained in a way that lubricants do not contaminate the Ayurveda, Siddha and Unani product being produced.

10.5. Defective equipment shall be removed from production and Quality Control areas or appropriately labeled.

10.6 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 steam 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, labeling 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 have to be properly installed and maintained with proper cleaning. List of 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.

11. DOCUMENTATION AND RECORDS:

Documentation is an essential part of the Quality assurance system and, as such, shall be related to all aspects of Good Manufacturing Practices (GMP). Its aim is to define the specifications for all materials, method of manufacture and control, to ensure that all personnel concerned with manufacture know the information necessary to decide whether or not to release a batch of a drug for sale and to provide an audit trail that shall permit investigation of the history of any suspected defective batch.

11.1. Documents designed, prepared, reviewed and controlled, wherever applicable, shall comply with these rules.

11.2. Documents shall be approved, signed and dated by appropriate and authorized persons.

11.3. Documents shall specify the title, nature and purpose. They shall be laid out in an orderly fashion and be easy to check. Reproduced documents shall be clear and legible. Documents shall be regularly reviewed and kept up to date. Any alteration made in the entry of a document shall be signed and dated.

11.4. The records shall be made or completed at the time of each operation in such a way that all significant activities concerning the manufacture of pharmaceutical products are traceable. Records and associated Standard Operating Procedures (SOP) shall be retained for at least one year after the expiry date of the finished products.

11.5. Data may be recorded by electronic data processing systems or other reliable means, but Master Formulae and detailed operating procedures relating to the system in use shall also be available in a hard copy to facilitate checking of the accuracy of the records. Wherever documentation is handled by electronic data processing methods, authorized persons shall enter or modify data in the computer. There shall be record of changes and deletions. Access, shall be restricted by 'passwords' or other means and the result of entry of critical data shall be independently checked. Batch records electronically stored shall be protected by a suitable back-up. During the period of retention, all relevant data shall be readily available.

12. LABELS AND OTHER PRINTED MATERIALS

Labels are absolutely necessary for identification of the drugs and their use. The printing shall be done in bright colours and in a legible manner. The label shall carry all the prescribed details about the product.]

12.1. All containers and equipments shall bear appropriate labels. Different colour coded labels shall be used to indicate the status of a product (for example: under test, approved, passed, rejected)

12.2. To avoid chance mix-up of printed packaging materials, product leaflets, relating to different products, shall be stored separately.

12.3. Prior to release, all labels for containers, cartons and boxes and all circulars, inserts and leaflets shall be examined by the Quality Control Department of the licensee.

12.4. Prior to packaging and labelling of a given batch of a drug, it shall be ensured by the licensee samples are drawn from the bulk and duly tested, approved and released by the quality control personnel.

12.5. Records of receipts of all labellig and packaging materials shall be maintained for each shipment received indicating receipts, control reference numbers and whether

accepted or rejected. Unused coded and damaged labels and packaging materials shall be destroyed and recorded.

12.6. The labels or accompanying document of reference standards and reference culture shall indicate concentration, lot number, potency, date on which container was first opened and storage conditions, where appropriate.

13. QUALITY ASSURANCES:

13.1 In addition to the use of modern analytical techniques (especially high performance thin-layer chromatography (HPTLC), gas chromatography (GC), high performance liquid chromatography (HPLC), capillary electrophoresis (CE), mass spectrometry (MS) and atomic absorption (AA) to characterize AYURVEDA, SIDDHA AND UNANI medicines, quality assurance also requires the control of starting materials, storage and processing. For this reason, an appropriate quality assurance system should be applied in the manufacture of Ayurveda, Siddha and Unani medicines.

13.2. The system of quality assurance appropriate to the manufacture of Ayurveda, Siddha and Unani products shall ensure that:

(a) the Ayurveda, Siddha and Unani products are designed and developed in a way that takes account of the requirements of Good Manufacturing Practices and other associated codes such as those of Good Laboratory Practice and Good Clinical Practices Guidelines;

(b) adequate arrangements are made for manufacture, supply, and use of the correct starting and packaging materials;

(c) adequate controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations, and validations are carried out;

(d) the finished Ayurveda, Siddha and Unani products is correctly processed and checked in accordance with established procedures laid in Ayurveda, Siddha and Unani books or respective formularies and pharmacopoeias.

(e) the Ayurveda, Siddha and Unani products are not released for sale or supplied before authorized persons have certified that each production batch has been produced and controlled in accordance with the requirements of the label claim and any other provisions relevant to production, control and release of Ayurveda, Siddha and Unani products;

14. SELF INSPECTION AND QUALITY AUDIT:

14.1 It may be useful to constitute a self inspection team supplemented with a quality audit procedure for assessment of all or part of a system with the specific purpose of improving it.

14.2. To evaluate the manufacturer's compliance with GMP in all aspects of production and quality control, concept of self-inspection shall be followed. The manufacturer shall constitute a team of independent, experienced, qualified persons from within or outside the company, who can audit objectively the implementation of methodology and procedures evolved. The procedures for self-inspection shall be documented indicating self-inspection results, evaluation, conclusions and recommended corrective actions with effective follow up program. The recommendations for corrective action shall be adopted.

14.3. The program shall be designed to detect shortcomings in the implementation of Good Manufacturing Practice and to recommend the necessary corrective actions. Self-inspections shall be performed routinely and on specific occasions, like when product recalls or repeated rejections occur or when an inspection by the licensing authorities is announced. The team responsible for self-inspection shall consist of personnel who can evaluate the implementation of Good Manufacturing Practice objectively; al recommendations for corrective action shall be implemented.

14.4. Written instructions for self-inspection shall be drawn up which shall include the following:

(a) Personnel.
(b) Premises including personnel facilities.
(c) Maintenance of building and equipment.
(d) Storage of starting materials and finished products.
(e) Equipment.
(f) Production and in-process controls.
(g) Quality control.
(h) Documentation.
(i) Sanitation and hygiene.
(j) Validation and revalidation programmes.
(k) Calibration of instruments or meAyurveda, Siddha and Unani rement systems.
(l) Recall procedures.
(m) Complaints management.
(n) Labels control.
(o) Results of previous self-inspections and any corrective steps taken.

15. QUALITY CONTROL SYSTEM:

Quality control shall be concerned with sampling, specifications, testing, documentation, release procedures which ensure that the necessary and relevant tests are actually carried and that the materials are not released for use, nor products released for sale or supply until their quality has been judged to be satisfactory. It is not confined to laboratory operations but shall be involved in all decisions concerning the quality of the product. It shall be ensured that all quality control arrangements are effectively and reliably carried out. The department as a whole shall have other duties such as to establish evaluate, validate and implement all Quality Control Procedures and methods.

15.1. Every manufacturing establishment shall establish its own quality control laboratory manned by qualified and experienced staff.

15.2. The area of the quality control laboratory may be divided into pharmacognostical, chemical, Microbiological testing and export of Ayurveda, Siddha and Unani systems.

15.3. Adequate area having the required storage conditions shall be provided for keeping Ayurveda, Siddha and Unani drug reference samples. The quality control department shall evaluate, maintain and store reference samples.

15.4. Standard operating procedures shall be available for sampling, inspecting, and testing of raw materials, intermediate, bulk finished products and packing materials and, wherever necessary, for monitoring environment conditions.

15.5. There shall be authorized and dated specifications for all materials, products, reagents and solvents including test of identity, content, purity and quality. These shall include specifications for water, solvents and reagents used in analysis.

15.6. No batch of the product shall be released for sale or supply until it has been certified by the authorised person(s) that it is in accordance with the requirements of the standards laid down.

15.7. Reference/retained samples from each batch of the products manufactured shall be maintained in a quantity which is atleast twice the quantity of the drug required to conduct all the tests. The retained product shall be kept in its final pack or a simulated pack for a period of three months after the date of expiry of Ayurveda, Siddha and Unani drugs.

15.8. Assessment of records pertaining to finished products shall include all relevant factors, including the production conditions, the results of in-process testing, the manufacturing (including packaging) documentation, compliance with the specification for the finished Ayurveda, Siddha and Unani product, and an examination of the finished pack. Assessment records should be signed by the in-charge of production and countersigned by the authorised quality control personnel before a product is released for sale or distribution.

15.9. Quality control personnel shall have access to production areas for sampling and investigation, as appropriate.

15.10. The in-charge of Quality Assurance shall investigate all product complaints and records thereof shall be maintained.

15.11. All instruments shall be calibrated and testing procedures validated before these are adopted for routine testing. Periodical calibration of instrument and validation of procedures shall be carried out.

15.12. Each specifications for raw materials, intermediates, final products, and packing materials shall be approved and maintained by the Quality Control Department. Periodic revisions of the specifications shall be carried out whenever changes are necessary.

15.13. Ayurveda, Siddha and Unani Pharmacopoeiae, reference standards, working standards, other reference materials and technical Ayurveda, Siddha and Unani books, as required, shall be available in the Quality Control Laboratory of the licensee.

15.14 ***Stability Studies***

15.14.1 The quality control department shall conduct stability studies of the Ayurveda, Siddha and Unani products to ensure and assign their shelf life at the prescribed conditions of storage. All records of such studies shall be maintained.

15.14.2 If the expiry date for a herbal raw material or Ayurveda, Siddha and Unani preparation is given, some stability data to support the proposed shelf-life under the specified storage conditions should be available. Stability data are always required to support the shelf-life for the finished Ayurveda, Siddha and Unani products.

15.14.3 Finished Ayurveda, Siddha and Unani products may contain several herbal raw materials or Ayurveda, Siddha and Unani preparations, and it is often not feasible to determine the stability of each active ingredient. Moreover, because the herbal raw material, in its entirety, is regarded as the active ingredient, a mere determination of the stability of the constituents with known therapeutic activity

will not usually be sufficient. Chromatography allows tracing of changes which may occur during storage of a complex mixture of biologically active substances contained in herbal raw materials. It should be shown, as far as possible, e.g. by comparisons of appropriate characteristics/fingerprint chromatograms, that the identified active ingredient (if any) and other substances present in the herbal raw material or finished Ayurveda, Siddha and Unani product are likewise stable and that their content as a proportion of the whole remains within the defined limits.

15.14.4 The fingerprint methods used for the stability studies should be as similar as possible to those used for quality control purposes.

15.14.5 For identified active ingredients, constituents with known therapeutic activity and markers, widely used general methods of assay, and physical and sensory or other appropriate tests may be applied.

15.14.6 To determine the shelf-life of finished Ayurveda, Siddha and Unani products, strong emphasis should also be placed on other tests in subsection 15.1 (Specifications), such as moisture content, microbial contamination and general dosage form control tests.

15.14.7 The stability of preservatives and stabilizers should be monitored. When these are not used, alternative tests should be done to ensure that the product is self-preserving over its shelf-life.

15.14.8 Samples used for stability studies should be stored in the containers intended for marketing.

15.14.9 Normally the first three commercial production batches should be included in the stability-monitoring programme to confirm shelf life or the expiry date. WHO guidelines on good manufacturing practices (GMP) for herbal medicines. However, where data from previous studies, including pilot batches, show that the product is expected to remain stable for at least two years. The testing frequency depends on the characteristics of the Ayurveda, Siddha and Unani products and should be determined on a case-by-case basis.

15.14.10 The protocol for ongoing stability studies should be documented. This would normally involve one batch per year being included in a stability-monitoring programme.

16. SPECIFICATION

16.1. For Raw materials and Packaging materials:- They shall include,-

(a) the designated name and internal code reference;

(b) reference, if any, to a respective formulary and pharmacopoeial monograph of Ayurveda, Siddha and Unani drugs

(c) qualitative and quantitative requirements with acceptance limits;

(d) name and address of manufacturer or supplier and original manufacturer of the material;

(e) specimen of printed material;

(f) directions for sampling and testing or reference to procedures;

(g) storage conditions; and

(h) maximum period of storage before re-testing.

16.2 *For Product Containers and Closures* -

16.2.1. All containers and closures intended for use shall comply with the Ayurveda, Siddha and Unani pharmacopoeial requirements. Suitable validated test methods, sample sizes, specifications, cleaning procedure, wherever indicated, shall be strictly followed to ensure that these are not reactive, additive, adsorptive, or leach to an extent that significantly affect the quality or purity of the drug. No second hand or used containers and closures shall be used.

16.2.2. Whenever bottles are being used, the written schedule of cleaning shall be laid down and followed. Where bottles are not dried after washing, they should be rinsed with de-ionised water or distilled water, as the case may be.

16.3. *For in-process and bulk products* - Specifications for in-process material, intermediate and bulk products shall be available. The specifications should be authenticated.

16.4. *For finished Products.* - Appropriate specifications for finished products shall include:-

(a) the designated name of the product and the code reference;
(b) the formula or a reference to the formula and the Ayurveda, Siddha and Unani Formulary and pharmacopoeial reference;
(c) directions for sampling and testing or a reference to procedures;
(d) a description of dosage form and package details;
(e) the qualitative and quantitative requirements, with the acceptance limits for release;
(f) the storage conditions and precautions, where applicable, and
(g) the shelf-life.

16.5. *For preparation of containers and closures.* – The requirements of machinery, equipments and premises required for preparation of containers and closures for different dosage forms and categories of Ayurveda, Siddha and Unani drugs. The suitability and adequacy of the machinery, equipment and premises shall be examined taking into consideration the requirements of each licensee in this respect.

17. MASTER FORMULA RECORD:

There shall be Master Formula records relating to all manufacturing procedures for each Ayurveda, Siddha and Unani product and batch size to be manufactured. These shall be prepared and endorsed by the competent technical staff i.e. head of production and quality control. The Master Formula shall include :-

(a) the name of the Ayurveda, Siddha and Unani product together with product reference code relating to its specifications;

(b) the patent or proprietary name of the product along with the generic name, a description of the dosage form, strength, composition of the Ayurveda, Siddha and Unani product and batch size;

(c) name, quantity, and reference number of all the starting materials to be used Mention shall be made of any substance that may 'disappear' in the course of processing;

(d) a statement of the expected final yield with the acceptable limits, and of relevant intermediate yields, where applicable;

(e) a statement of the processing location and the principal equipment to be used;

(f) the methods, or reference to the methods, to be used for preparing the critical equipment including cleaning, assembling, calibrating, sterilizing;

(g) detailed stepwise processing instructions and the time taken for each steps;

(h) the instructions for in-process controls with their limits;

(i) the requirements for storage conditions of the products, including the container, labelling and special storage conditions where applicable;

(j) any special precautions to be observed;

(k) packing details and specimen labels.

18. PACKAGING RECORDS:

There shall be authorised packaging instructions for each Ayurveda, Siddha and Unani product, pack size and type. Theses shall include or have reference to the following :-

(a) name of the product;

(b) description of the Ayurveda, Siddha and Unani dosage form and composition;

(c) the pack size expressed in terms of the number or dosage, weight or volume of the Ayurveda, Siddha and Unani product in the final container.

(d) complete list of all packaging material required for a standard batch size, including quantities, sizes and types, with the code or reference number relating to the specifications of each packaging material;

(e) reproduction of the relevant printed packaging materials and specimens indicating where batch number and expiry date of the product have been applied;

(f) special precautions to be observed, including a careful examination of the area and equipment in order to ascertain the line clearance before the operations begin;

(g) description of the packaging operation, including any significant subsidiary operations and equipment to be used;

(h) details of in-process controls with instructions for sampling and acceptance;

(i) upon completion of the packing and labeling operation, a reconciliation shall be made between number of labeling and packaging units issued, number of units labeled, packed and excess returned or destroyed. Any significant or unusual discrepancy in the numbers shall be carefully investigated before releasing the final batch.

19. BATCH PACKAGING RECORDS

19.1. A batch packaging record shall be kept for each batch or part batch processed. It shall be based on the relevant parts of the packaging instructions, and the method of preparation of such records shall be designed to avoid transcription errors.

19.2. Before any packaging operations begins, check shall be made and recorded that the equipment and the work stations are clear of the previous products, documents or materials not required for the planned packaging operations, and that the equipment is clean and suitable for use.

20. BATCH PROCESSING RECORDS

20.1. There shall be Batch Processing Record for each Ayurveda, Siddha and Unani product. It shall be based on the relevant parts of the currently approved Master Formula. The method of preparation of such records included in the Master Formula shall be designed to avoid transcription errors;

20.2. Before any processing begins, check shall be performed and recorded to ensure that the equipment and work station are clear of previous Ayurveda, Siddha and Unani products, documents or materials not required for the planned process are removed and that equipment is clean and suitable for use.

20.3. During processing, the following information shall be recorded at the time each action is taken and the record shall be dated and signed by the person responsible for the processing operations:

(a) the name of the Ayurveda, Siddha and Unani product (genric or proprietary)
(b) the number of the batch being manufactured,
(c) dates and time of commencement, of significant intermediate stages and of completion of production,
(d) initials of the operator of different significant steps of production and where appropriate, of the person who checked each of these operations,
(e) the batch number and/or analytical control number as well as the quantities of each starting material actually weighed,
(f) any relevant processing operation or event and major equipment used,
(g) a record of the in-process controls and the initials of the person(s) carrying them out, and the results obtained,
(h) the amount of product obtained after different and critical stages of manufacture (yield),
(i) Notes on special problems including details, with signed authorisation, for any deviation from the Master Formula, comments or explanations for significant deviations from the expected yield limits shall be given,
(j) Notes on special problems including details, with signed authorisation, for any deviation from the Master Formula,
(k) addition of any recovered or reprocessed material with reference to recovery or reprocessing stages.

21. STANDARD OPERATING PROCEDURES (SOPS)

21.1 Receipt of Material;

22.1.1. There shall be written Standard Operating Procedures and records for the receipts of each delivery of raw, primary and printed packaging material.

21.1.2. The records of the receipts shall include;

(a) the name of the material on the delivery note and the number of the containers;
(b) the date of receipt;
(c) the manufacturer ’s and/or supplier’s name;
(d) the manufacturer ’s batch or reference number;
(e) the total quantity, and number of containers, quantity in each container received;
(f) the control reference number assigned after receipt;
(g) any other relevant comment or information.

21.1.3 There shall be written standard operating procedures for the internal labelling, quarantine and storage of starting raw materials, packaging materials and other materials, as appropriate.

21.1.4 There shall be Standard Operating Procedures available for each instrument and equipment and these shall be placed in close proximity to the related instrument and equipment.

21.2 *Sampling.-*

21.2.1. There shall be written Standard Operating Procedures for sampling, which include the person(s) authorized to take the samples.

21.2.2 The sampling instructions shall include:

(a) the method of sampling and the sampling plan,
(b) the equipment to be used,
(c) any precautions to be observed to avoid contamination of the material or any deterioration in its quality,
(d) the quantity of samples to be taken,
(e) instructions for any required sub-division or pooling of the samples,
(f) the type of sample container to be used,
(g) any specific precautions to be observed, especially in regard to sampling of poisonous material used in Ayurveda, Siddha and Unani product.

21.3 *Batch Numbering.-*

21.3.1. There shall be Standard Operating Procedures describing the details of the batch (lot) numbering set up with the objective of ensuring that each batch of intermediate, bulk or finished Ayurveda, Siddha and Unani products is identified with a specific batch number.

21.3.2 Batch numbering Standard Operating Procedures applied to a processing stage and to the respective packaging stage shall be same or traceable to demonstrate.

21.3.3. Batch number allocation shall be immediately recorded in a logbook or by electronic data processing system. The record shall include date of allocation, product identity and size of batch.

21.4 *Testing.-*

21.4.1. There shall be written procedures for testing materials and products at different stages of manufacture, describing the methods and equipment to be used. The tests performed shall be recorded.

21.5 *Records of analysis.*

21.5.1. The records shall include the following data.

(a) name of the material or product and the dosage form,
(b) batch number and, where appropriate the manufacture and/or supplier;
(c) references to the relevant specifications and testing procedures,
(d) test results, including observations and calculations, and reference to any specifications (limits),
(e) dates of testing;
(f) initials of the persons who performed the testing;
(g) initials of the persons who verified the testing and the detailed calculations,
(h) a statement of release or rejection, and
(i) signature and date of the designated responsible person.

21.5.2. There shall be written standard operating procedures and the associated records of actions taken for:

(a) equipment assembly and validation;
(b) analytical apparatus and calibration;
(c) maintenance, cleaning and sanitation;
(d) personnel matters including qualification, training, clothing, hygiene;
(e) environmental monitoring;
(f) pest control;
(g) complaints;
(h) recalls made;
(i) returns received.

22. REFERENCE SAMPLES

22.1. Each lot of every active ingredients, in a quantity sufficient to carry out all the tests.

22.2. Samples of finished formulations shall be stored in the same or simulated containers in which the drug has been actually marketed.

23. REPROCESSING AND RECOVERIES

23.1. Where reprocessing is necessary, written procedures shall be established and approved by the Quality Assurance Department that shall specify the conditions and limitations of repeating chemical reactions. Such reprocessing shall be validated.

23.2. If the product batch has to be reprocessed, the procedures shall be authorized and recorded. An investigation shall be carried out into the causes necessitating re-processing and appropriate corrective me Ayurveda, Siddha and Unani res shall be taken for prevention of recurrence. Re-processed batch shall be subjected to stability evaluation.

23.3. Recovery of product residue may be carried out, if permitted, in the master production and control records by incorporating it in subsequent batches of the product.

24. 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 category 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 upto 5 years of the exhausting of stock.

25. VALIDATION AND PROCESS VALIDATION

25.1. Validation studies shall be an essential part of Good Manufacturing Practices and shall be conducted as per the pre-defined protocols. These shall include validation of processing, testing and cleaning procedures.

25.2. A written report summarizing recorded results and conclusions shall be prepared, documented and maintained.

25.3. Processes and procedures shall be established on the basis of validation study and undergo periodic revalidation to ensure that they remain capable of achieving the intended results. Critical processes shall be validated, prospectively or retrospectively.

25.4. When any new master formula or method of preparation is adopted, steps shall be taken to demonstrate its suitability for routine processing. The defined process, using the materials and equipment specified shall be demonstrated to yield a product consistently of the required quality.

25.5. Significant changes to the manufacturing process, including any change in equipment or materials that may affect product quality and/or the reproducibility of the process, shall be validated.

26. PRODUCT RECALLS

26.1. A prompt and effective product recall system of defective products shall be devised for timely information of all concerned suppliers, up to the retail level within the shortest period. The licensee may make use of both print and electronic media in this regard.

26.2. There shall be an established written procedure in the form of Standard Operating Procedure for effective recall of products distributed by the licensee. Recall operations

shall be capable of being initiated promptly so as to effectively reach at the level of each distribution channel.

26.3. The distribution records shall be readily made available to the persons designated for recalls.

26.4. The designated persons shall record a final report issued, including a reconciliation between the delivered and the recovered quantities of the products.

26.5. The effectiveness of the arrangements for recalls shall be evaluated from time to time.

26.6. The recalled products shall be stored separately in a secured segregated area pending final decision on them.

27. COMPLAINTS AND ADVERSE REACTION

27.1. All complaints thereof concerning Ayurveda, Siddha and Unani product quality shall be carefully reviewed and recorded according to written procedures. Each complaint shall be investigated/evaluated by the designated personnel of the company and records of investigation and remedial action taken thereof shall be maintained.

27.2. Reports of serious adverse drug reactions resulting from the use of a drug along with comments and documents shall be forthwith reported to the concerned State Licensing Authority (AYUSH).

27.3. There shall be written procedures describing the action to be taken, recall to be made of the defective Ayurveda, Siddha and Unani product.

28. SITE MASTER FILES: The licensee shall prepare a succinct document in the form of 'Site Master File' containing specific and factual Good Manufacturing Practices about the production and/or control of Ayurveda, Siddha and Unani manufacturing preparations carried out at the licensed premises. It shall contain the following :-

28.1. *General information.*-

(a) brief information of the firm;

(b) Ayurveda, Siddha and Unani Drugs manufacturing activities as permitted by the State licensing authority (AYUSH);

(c) other manufacturing activities, if any, carried out on the premises;

(d) type of Ayurveda, Siddha and Unani products and all categories of Ayurveda, Siddha and Unani products licensed for manufacture with flowcharts mentioning procedures and process flow;

(e) number of employees engaged in the production, quality control, storage and distribution;

(f) Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis;

(g) short description of the Quality Management system of the firm;

(h) Ayurveda, Siddha and Unani products details registered with foreign countries.

28.2. *Personnel.*-

(a) organisational chart showing the arrangement for quality assurance including production and quality control;

(b) qualification, experience and responsibilities of key personnel;

(c) outline for arrangements for basic and in-service training and how the records are maintained;

(d) health requirements for personnel engaged in production;

(e) personnel hygiene requirements, including clothing.

28.3. *Premises.-*

(a) simple plan or description of manufacturing areas drawn to scale;

(b) nature of construction and fixtures / fittings;

(c) brief description of ventilation systems. More details should be given for critical areas with potential risk of airborne contamination (schematic drawing of systems). Classification of the rooms used for the manufacture of Ayurveda, Siddha and Unani products should be mentioned;

(d) special areas for the handling of the poisonous , materials;

(e) brief description of water systems (schematic drawing of systems), including sanitation;

(f) description of planned preventive maintenance programs for premises and of the recording system.

28.4. *Equipment.-*

(a) brief description of major equipment used in production and quality control laboratories (a list of equipment required);

(b) description of planned preventive maintenance programs for equipment and of the recording systems;

(c) qualification, including the recording systems and arrangements for computerized systems validation.

28.5. *Sanitation-*

(a) availability of written specifications and procedures for cleaning manufacturing areas and equipment.

28.6. *Documentation-*

(a) arrangements for the preparation, revision and distribution of

(b) necessary documentation for the manufacture;

(c) any other documentation related to product quality that is not mentioned elsewhere (e.g. microbiological controls about air and water)

28.7. *Production-*

(a) brief description of production operations using, wherever possible, flow sheets and charts specifying important parameters;

(b) arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage;

(c) arrangements for the handling of rejected materials and products;

(d) brief description of general policy for process validation.

28.8. *Quality control-*

(a) description of the quality control system and of the activities of the quality control department. Procedures for the release of the finished Ayurveda, Siddha and Unani products.

28.9. *Loan licence manufacture and licensee-*

(a) description of the way in which compliance of Good Manufacturing Practices by the loan licensee shall be assessed.

28.10. Distribution, complaints and product recall-

(a) arrangements and recording systems for distribution;

(b) arrangements for the handling of complaints and product recalls.

28.11. *Self-Inspection-*

(a) short description of the self-inspection system indicating whether an outside, independent and experienced external expert was involved in evaluating the manufacturer 's compliance with Good Manufacturing Practices in all aspects of production.

28.12. *Export of drugs-*

(a) Ayurveda, Siddha and Unani products exported to different countries;

(b) complaints and product recall, if any.

Part-II

A. LIST OF RECOMMENDED MACHINERY, EQUIPMENT AND MINIMUM MANUFACTURING PREMISES REQUIRED FOR THE MANUFACTURE OF VARIOUS CATEGORIES OF AYURVEDIC, SIDDHA SYSTEM OF MEDICINES

One machine indicated for one category of medicine could be used for the manufacturing of other category of medicine also. Similarly some of the manufacturing areas like powdering, furnace, packing of liquids and Avaleha, Paks, could also be shared for these items.

S No.	Category of Medicine	Minimum Manufacturing space required	Machinery/equipment recommended
		1200 sq. ft. covered area with separate cabins or partitions for each activity. If Unani medicines are manufactured in same premises an additional area of 400 sq feet will be required.	
1.	Anjana/Pisti	100 sq. ft.	Kharal/mechanised/motorised Kharal, End Runner/Ball-Mill, Sieves/Shifter.
2.	Churna/Nasya Manjan/Lepa Kwath Churn	200 sq. ft.	Grinder/Disintegrator/ Pulverisar/Powder mixer / Sieves /Shifter
3.	Pills / Vati/ Gutika Matrica and tablets	100 sq. ft.	Ball Mills, Mass Mixer/Powder mixer, Granulator, drier, tablet compressing machine, pill/ vati cutting machine, stainless steel trays / container for

			storage and sugar coating, polishing pan in case of sugar coated tablets, mechanized chatoo, (for mixing of guggulu) where required.
4.	Kupi pakva / Ksara / Parpati / Lavana Bhasma Satva / Sindura Kapu / Uppa / Param / Qushta / Jawhar	150 sq. ft.	Bhatti, Karahi / stainless steel vessels/patila flask, Multani Matti /Plaster of Paris, Copper Rod, Earthen container, Gaj Put Bhatti, Muffle furnace (electrically operated) End/Edge Runner, Exhaust Fan, Wooden, S.S. Spatula
5.	Kajal	100 sq. ft.	Earthern lamps for collection of Kajal, Tripple Roller Mill, End Runner, Sieves, S.S. Patila, Filling packing and manufacturing room should be provided with Exhaust fan & ultra violet lamps
6.	Capsules 100 sq. ft.	Capsules 100 sq. ft.	Air Conditioner, De-humidifier, hygrometer Thermometer, Capsule filling machine and balance
7.	Ointment/Marham Pasai	100 sq. ft.	Tube filling machine, Crimping machnie/Ointment Mixer, End Runner/Mill (Where required), S.S. Storage container, S. S. Patila
8.	Pak/Avaleh/ Khand Modak/Lakayam	100 sq. ft.	Bhatti section fitted with Exhaust fan and should be fly proof, Iron Kadah i/ S.S. Patila an d S.S. Storage container
9.	Panak Syrup/Pravahi Kwath Manapaku	150 sq. ft.	Tinctum press, exhaust fan fitted and flyproof, Bhatti section , B ottle wash in g Mach in e, filter Press/Gravity filter liquid filling Machine, P.P. Capping Machine
10.	Asava/Aristha	200 sq. ft.	Same as mentioned above. Fermentation tanks containers and distillation plant where necessary, Filter Press.
11.	Sura	100 sq. ft.	Same as mentioned above plus distillation plant and transfer pump
12.	Ark/ Tinir	100 sq. ft.	Maceration tank, Distillation plant, Liquid filling tan k with tap/Gravity Filter/Filter press, visual Inspection box.
13.	Tail/Ghrit /Ney	100 sq. ft.	Bhatti, Kadah i/S.S. Patila, S.S. Storage containers, Filtration equipment, filling tank with tap/Liquid filling machine
14.	Asch yotan / Netra Malham Panir/ Karn Bindu /Nasabindu	100 sq. ft.	Hot air oven electrically heated with thermostatic control, kettle Gas or electrically heated with suitable mixing arrangement collation mill or ointment mill, tube filling equipment, mixing and

			storage tanks of stainless steel or of other suitable material sintered glass funnel, seitz filter or filter candle, liquid filling equipment, autoclave.
15.	Each manufacturing unit will have a separate area for Bhatti, furnace, boilers, puta, etc. This will have proper ventilation, removal of smoke, prevention of flies, insects, dust etc. The furnace section could have a tin roof.	200 sq. ft.	

B. LIST OF MACHINERY, EQUIPMENT AND MINIMUM MANUFACTURING PREMISES REQUIRED FOR THE MANUFACTURE OF VARIOUS CATEGORIES OF UNANI SYSTEM OF MEDICINES.

One machine indicated for one category of medicine could be used for the manufacturing of other category of medicine also. Similarly some of the manufacturing areas like powdering, furnace, packing of liquids could also be shared for these items.

S No.	**Category of Medicine**	**Minimum Manufacturing space required**	**Machinery/equipment recommended**
		1200 sq. ft. covered area with separate cabins or partitions for each activity. If Ayurveda/Siddha, Medicines are also manufactured in same premises an additional area of 400 sq feet will be required.	
1.	Itrifal Tiryaq/ Majoon/Laooq Jawarish Khamiras	100 sq. ft.	Grinder/Pulveriser, sieves, powder mixer (if required), S.S. Patilas, Bhatti and other accessories, Plant mixer for Khamiras.
2.	Araq	100 sq. ft.	Distillation plant (garembic) S.S. stor age tank, boiling vessel, gravity filter, bottle fillin g machine, bottle washing machine, bottle drier
3.	Habb(Pills) and Tablets	100 sq. ft.	Ball Mills, Mass Mixer/Powder mixer, Granulator, drier, tablet compressing machine, pill/ vati cutting machine, stainless steel

			trays / container for storage and sugar coating, polishing pan in case of sugar coated tablets, mechanized chatoo, (for mixing of guggulu) where required.
4.	Sufoof(Powder)	200 sq. ft.	Grinder/Pulveriser, sieves, Trays, Scoops, powder mixer (where required),
5.	Raugha n (Oils) (Crushing and Boiling)	100 sq. ft.	Oil Expeller, S.S. Patilas Oil filter bottle filling machine, bottle drier, Bhatti
6.	Shiyaf, Surma, Kajal	100 sq. ft.	End runner, mixing S.S. Vessel.
7.	Marham, Zimad (ointment)	100 sq. ft.	Kharal, Bhatti, End runner, Grinder , pulviser, Tripple Roller Mill (if needed)
8.	Qurs (Tab)	100 sq. ft.	Gr inder /Pulver iser, Sieves, Powder mixer (where needed), Granulator, Drier, Tablet compressing machine, Die punches trays, O.T. Apparatus, balance with weights, scoops, sugar coating pan, polishing pan, heater
9.	Kushta	100 sq. ft.	Bhatti, Kharal, Sil Batta, earthern pots.
10.	Murabba	100 sq. ft.	Aluminium vessels 50-100 kgs capacity Gendna, Bhatti.
11.	Capsule	100 sq. ft.	Pulveriser, Powder mixer (where needed), capsule filling machine, Air conditioner, Dehumidifier, balance with weights, storage-container s, glass.
12.	Sharbat & Jushanda	100 sq. ft.	Tinctum press, exhaust fan fitted, bhatti section, bottle washing machine, filter press gravity filter, liquid filling tank with tap/liquid filling machine, hot air oven electrically heated with thermostatic control, kettle.
13.	Qutoor-e-Chashm and Marham (Eye drops Eye ointment)	100 sq. ft.	Hot air oven electrically heated with Thermostatic control, kettle.
14.	Each manufacturing unit will have a separate area for Bhatti, furnaces, boilers, putta etc. This will have proper ventilation, removal of smoke, prevention of flies, insects, dust etc.	200 sq. ft.	

C. LIST OF EQUIPMENT RECOMMENDED FOR IN HOUSE QUALITY CONTROL SECTION.

(Alternatively unit can get the testing done from the Government approved laboratory).

(A)	CHEMISTRY SECTION	PHARMACOGNOSY SECTION	Microbiology Section:
1.	Analytical Balance of 220 gram capacity with sensitivity of 0.0001gram;	Abbe Refractometer;	Autoclave;
2.	Binocular Research Microscope capable of magnification up to 100X with oil immersion facilities and a four turret objective unit with corresponding eyepieces;	Alcohol determination apparatus with all accessories;	Biochemical Oxygen Demand (BOD) Incubator;
3.	Dissection and Surgical Instruments;	Analytical Balance of 220 gram capacity with sensitivity of 0.0001gram;	Colony Counter;
4.	Electric Mantles;	Boiling Point determination apparatus;	Essential glassware and other materials including reagents required for microbiological analysis.
5.	Essential glassware and other materials including reagents required for pharmacognostical testing;	Bulk density apparatus;	High power Microscope;
6.	Hot Air Oven;	Centrifuge machine;	Hot Air Oven;
7.	Hot Plate or equivalent heating apparatus;	Clevenger apparatus for volatile oil determination;	Laminar Air Flow (L.A.F.) bench;
8.	Micro-slide cabinet;	Conductivity meter;	Plain Incubator;
9.	Micrometers-stage, ocular, linear and net ruled Types;	Essential glassware and other materials including reagents and chemicals required for chemical analysis;	Refrigerator; and
10.	Mixer Grinder;	Flame photometer;	Serological Water bath.
11.	Prism and Mirror type Camera Lucida;	High Performance Liquid Chromatography (HPLC)	Autoclave;

		apparatus, High Performance Thin Layer Chromatography (HPTLC) apparatus, Gas Chromatography (GC) apparatus, Atomic Absorption Spectroscopy (AAS) apparatus or arrangement with other laboratories;	
12.	Refrigerator;	Hot air oven;	Biochemical Oxygen Demand (BOD) Incubator;
13.	Sieves as per Ayurvedic, Siddha and Unani Pharmacopoeias of India and Bureau of Indian Standards (BIS) specifications;	Hot plates and heating mantles;	Colony Counter;
14.	Sledge Microtome;	pH meter;	Essential glassware and other materials including reagents required for microbiological analysis.
15.	Stereo zoom microscope with incident and transmitted light facilities and with minimum 60X magnification;	Polarimeter;	High power Microscope;
16.	Top-Pan Balances of 1kilogram capacity with sensitivity of 1.0gram; and	Refrigerator;	Hot Air Oven;
17.	Water baths;	Sieves from 10 to 120 size with sieve shaker;	Laminar Air Flow (L.A.F.) bench;
18.		Water Purification System/ deionized system, where required;	
19.		Melting point determination apparatus;	
20.		Moisture determination apparatus;	
21.		Muffle Furnace;	
22.		Tablet Disintegration apparatus;	

23.		Tablet Dissolution tester;	
24.		Tablet Friability tester;	
25.		Tablet Hardness Tester;	
26.		Thin Layer Chromatography (TLC) apparatus with all accessories;	
27.		Ultra-Violet (UV) Cabinet;	
28.		UV- Visible Spectrophotometer;	
29.		Viscometer; and	
30.		Water bath with temperature control.	

D. Specific Requirements for Manufacturing of Rasaushadhies or Rasamaraunthukul and Kushtajat (herb-mineral-metallic compound) of Ayurveda, Siddha and Unani Medicines.

The guidelines are to provide general and minimum technical requirements for quality assurance and control in manufacturing rasaushadhies or rasamaraunthukuland kushtajat (Herb-mineral-metallic formulations). These guidelines deal with Bhasmas, satwa(of Metals and Minerals origin) Drutiparpam, karpu and kushta etc. used in Ayurveda, Siddha and Unani Medicines.

The GMP guidelines for Rasaushadhies or Rasamaraunthukuland Kushtajat are needed to establish the authenticity of raw drug minerals and metals, in process validation quality control parameters to ensure that these formulations are processed and prepared in accordance with classical texts and for which safety measures are complied. Only those manufacturing units which have Good Manufacturing Practices for Ayurveda, Siddha and Unani Drugs and certificate for Rasaushadhies or Rasamaraunthukuland Kushtajat formulations shall be allowed to manufacture the same. Good Manufacturing Practices certificate for Rasaushadhies shall be issued by the State Licensing Authority only after thorough inspection by an expert team including Rasashastra experts nominated by the Department of AYUSH.

2. Manufacturing Process Areas: For the Manufacturing of bhasma and kupipakawa and Rasaaushadhi preparations made from metals and minerals the following specific areas shall be provided, which should be completely segregated from the production areas used for preparations of plants and animals by product based formulations to avoid cross contamination. The following exclusive areas are required for Rasaushadhies or Rasamaraunthukuland Kushtajat.

2.2 (a) Bhatti or Heating Devise Section for Bhasma and Rasaaushadhi:- 100 sq. feet for heating, burning, putta and any heat related work with proper ventilation, exhaust and chimney. This could be tin shed also.

(b) Grinding, Drying and Processing Section for Bhasma and Rasaaushadhi:- 10sq. feet (Manual or mechanical, oven etc.). drying may be done in a space which is covered by glass or other transparent material to allow entry of sunrays on the material to keep for the purpose. If drying is being in oven the temperature of the same may be selected specific temperature.

(c) Rasaushadhis Related Store:-100 sq. ft.

The size and Dimensions of each Bhatti section would be so designed ti suit the batch size or quantity of materials to be processed, keeping in mind the processed, keeping in mind the processing is done as per the conditions of Drugs and Cosmetics Act mentioned under Schedule I official books.

In additions to the fuel prescribed in the schedule books namely coal, fire woods, cow dung cakes etc., use of other heating devices e.g. electrical heating, oil or gas fired furnace and other may be employed so as to provide the required temperature as per the nature of material and object of heating. Depending on the formulation being manufactured, manufacturers may adopt aerobic or anaerobic process. Properly baked and clean earthen pots of other crucibles and glass containers or appropriate design shall be used.

The manufacturing areas should be designed with special attention to process the products that generate toxic fumes like SO2, arsenic and mercury vapour, etc. When heating and boiling is necessary, suitable ventilation and air exhaust flow mechanism should be provided to prevent accumulation of unintended fumes and vapors. Such areas may be provided with properly designed chimneys or ducts fitted with exhaust systems and suitable scrubbing system to remove fumes and smokes, so that safety of personnel and environment is taken care of.

Since processing of Rasaaushadhi may introduce heavy metal contamination and cross contamination etc., therefore, cleaning of equipment is particularly important after every process by using appropriate cleaning agent which should not react with material of equipment and must be free unwanted properties e.g. corrosiveness.

2.3 Records shall be maintained specially for temperatures attained during the entire process of Bhasmikaran, while employing different kinds of classical puta, furnace using oil, gas or electricity. Appropriate temperature me Ayurveda, Siddha and Unani ring instrument should be employed such as pyrometer and, pyrograph for manual reading or recording by heat sensors, connected to computer, as the case may be.

In order to handle large quantities, appropriate technology like use of hand operated extruders for making chakrikas or pellets may be adopted. However, such equipment made of aluminum or its alloys should not be used.

Access to manufacturing areas shall be restricted to minimum number of authorised personal only.

3. Quality Control

A. In Process Quality Control

The registers as indicated below should exclusively be maintained for ready reference:-

(a) Shodhan Register with following details:

1. Sl. No.
2. Batch no. and Size
3. Date, time and duration
4. Name of the Raw-material with Quality reference and quantity
5. Quantity of ShodhanaDravya
6. Book reference followed
7. Methodology

(b) Bhavana and Putta Register with following details:

1. Sl. No.
2. Batch no. and Size
3. Date, time and duration
4. Name of the material with Quantity of starting materials
5. Quantity of nirvapya Dravya
6. Quantity of Bhavana Dravya
7. Date and Time of Starting and completion of Bhavana or Mardana and duration
8. Type and Number of Puttas
9. Time and Date of completion Puttas
10. Colour and texture of the products or standards
11. In process tests followed (BhasmaPariksha and any other tests)
12. In case heating at a particular temperature is required, record of attainment of that temperature.

(c) Grinding Records Register: (Finished Products/Intermediate Procedure)

1. Sl. No.
2. Batch no. and Size
3. Date, time and duration
4. Name of the material with Quantity
5. Name of the equipment (SS/granite)
6. Duration of grinding
7. Repeat the grinding if required (number of repetition)

(d) Packing details:

1. Name of Rasaushadhi
2. Type of Dosage Form (e.g. Powder, pill tablet etc.)
3. Weight of Rasaushadhis in each unit.

B. Product Quality Control

The specifications for finished Rasaushadhi are primarily intended to define the quality rather than to establish full characterization, and should focus on those characteristics found to be useful in ensuring the quality. Consistent quality for Rasaushadhi can only be assured if the starting material-metals and minerals are used of pharmacopoeial standards. In some cases more detailed information may be needed on aspects of their process. The manufacture will ensure in-house standards for the uniform quality of products.

Quality testing will be carried out as per official Pharmacopoeia or Schedule books for texts namely, colour, taste, varitaratwa, Rekhapurnatwa, Laghutva, Nirudhumatwa, Dntagreekachakacha, Niruttha, Apunarbhava and Nischandratwa.

The Particle size of products should be tested adopting microscopic fitted with micrometre of particle size analyser or any appropriate other techniques. Required physio-chemical characterization of the product should be undertaken by appropriate analytical equipment. The Standard Manufacturing Process of the product should be evolved/follow up. The disintegration time of pills-vati and tablets should also be recorded.

4. Product recalls

Literature inserted inside the products package should indicate the name, address of the manufacturing unit or email or telephone number for reporting of any adverse drug reaction by physicians or patients. On receipt of such Adverse Drug Reaction report, it will be the responsibility of the manufacturer to ensure the recall the product from the market.

Standard operating procedures (SOP) should be included for storage of recalled Rasaushadhies in a secure segregated area, complying with the requirements specified for storage, till their final disposal.

5. Medical Examination of the employees

Employees engaged in manufacturing should be medically examined periodically at least once a year for any adverse effect of the drug during manufacturing process fir which necessary investigations may be carried out for ensuring that there is no effect of material on the vital organs of the employees. Annual examination reports of the employees shall be made available to statuary inspectors during Good Manufacturing Practices inspections

6. Self- Inspection

The release of Rasaushadhis should be under the control of a person who has been trained in the specific features of the processing and quality assurance of Rasaushadhis Personnel dealing with the production and quality assurance of Rasaushadhis manufacturing section should have an adequate training in the specific subject of Rasaushadhis manufacturing. He will be at least a degree holder in Ayurveda/Siddha/ Unani medicine or B. Pharma degree holder in Ayurveda/Siddha/ Unani medicine.

7. Dosage form of Rasaushadhis

The Rasaushadhis may be made into an acceptable dosage forms such as, churna, vati, guti, tablet, capsule etc. after adding suitable permissible fillers or binding agents as permissible under the Ayurvedic Pharmacopoeia of India or Indian Pharmacopoeia as updated from time to time. In such cases the label must indicate the Ayurveda/Siddha/ Unani medicine in one Tablet or Pill or Capsule in addition to the filters. The crystalline product may be grinded before packing in the individual dispensing size. All the Rasaushadhies or Rasamaraunthukuland Kushtajat shall be packed in a dosage form which is ready for use for the consumer. Grinding and weighting of individual dose of potentially poisonous products will not be permissible in patient consumer pack. This arrangement may reduce the Adverse Drug Reaction of Rasaushadhies which takes place due to dose variation. However for hospital bulk pack, it will not be applicable and label will not be applicable and label will clearly indicate the "Hospital Pack".

8. Area Specification/requirement for an applicant companies only to have GMP of Rasaushadhies or Rasamaraunthukul and Kushtajat (Herbo-mineral-metallic compounds) of Ayurveda, Siddha and Unani Medicines:

S. no.	**Category of Medicine/ Manufacturing area**	**Minimum Manufacturing space required (1500 sq. ft.)**	**Machinery equipment recommended**
1	Pisti/ Grinding area for Bhasma. Phisti, Kushtajat.	100 sq. ft.	Kharal/mechanized/motorized Kharal, End runner/Ball-Mill Sieves/Shifter
2	Powdering area for raw drugs of plant origin giving in Rasaushadhies (Herbo-metallic formulations)	200 sq. ft.	Grinder/ Disintegrator/Pulverisar/Powder mixer/ sieves/ Shifter
3	Pills/Vati/Gutika Matrica and tablets/Habb making area.	100 sq. ft.	Ball Mill, Mass Mixer/Powder mixer, Granulator drier, tablet compressing machine, pill/vati cutting machine, stainless steel trays/container for storage and storage and sugar coating, polishing pan in case of sugar coated tablets, mechanized chattoo (for mixing of guggulu) where required.
4	Kupipakva/Ksara/Parpati/Lavana BhasmaSatva/SinduraKarpu/Upp	150sq. ft.	Bhatti, Karahi/stainless steel vessels/patila flask, MultaniMatti/

	uParam/Qushta/Jawhar		palster of Paris, Copper Rod, Earthen container, Gaj Put Bhatti, muffle furnace (electrically operated) End/ Edge Runner, Exhaust Fan, Wooden, S.S. Sapatula.
5	Receiving and storing raw material	200 sq. ft.	
6	Quality Control Section	150 sq. ft.	
7	Quarantine/observation	50 sq. ft.	
8	Finished goods store	150 sq. ft.	
9	Rejected Good Store	50 sq. ft.	
10	Bhatti-Putta Area	200 sq. ft.	
11	Area for water and washing etc.	50 sq. ft.	
12	Office	100 sq. ft.	
	Total	**1500 sq. ft.**	

Note:- The above requirements of machinery, equipment's, space are made subject to the modification at the discretion of the Licensing Authority; if he is of the opinion that having regard to the nature and extent of the manufacturing operations it is necessary to relax or alter them in the circumstances in a particular case (he may do so after recording reasons in writing)