GOOD MANUFACTURING PRACTICES GUIDELINES FOR UNANI, AYURVEDIC AND HERBAL MEDICINES

Directorate General of Drug Administration
Ministry of Health and Family Welfare

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Preface

Unani and Ayurvedic medicine, prominent part of traditional system of medicine plays a pivotal role in healthcare of huge world population and mostly practiced in the middle-east and south-Asian countries. Due some intrinsic advantages Unani and Ayurvedic medicines are gaining popularity in both developed and developing countries.

Apart from Ayurvedic and Unani systems of medicine, herbal medicine is a modern approach of ancient medicinal practice. Now a day's herbal medicine is addressing special interest of western world. It has got noticeable popularity among the developed worlds.

The World Health Organization (WHO) has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety and efficacy.

Good Practices are essential measurement for ensuring the quality control of such traditional medicines. "GMP" expression is used to describe all measures, which are taken during the manufacturing process and quality control leading to a reproducible quality. The manufacturing process is one of the key steps where, quality control is required to ensure quality of medicinal products, including Uani and Ayurvedic medicines. Good manufacturing practices(GMP) is one of the most important for this measure.

With the worldwide increase in the use of Unani and Ayurvedic medicines and the rapid expansion of the global market, the safety and the quality of such medicines has become a major concern for health authorities, pharmaceutical industries and consumers. The safety and efficacy of any medicine largely depend on their quality.

Requirements and methods for the quality control of finished Unani and Ayurvedic medicines are far more complex than for chemical drugs, particularly for the polyherbal and herbo-mineral combined or mixed Unani and Ayurvedic medicines. Furthermore, the quality of Unani and Ayurvedic medicines is influenced both by the quality of procedure used during their production and the quality of the raw materials . Products which meet high quality standards are needed to allow the patient to make safe use of the such medicines. Nowaday, this is more and more important because, as

a consequence of market globalization, many of the raw materials and medicines used in the Unani and Ayurvedic systems come from different countries.

In the recent time, Directorate General of Drug Administration, Ministry of Health and Family Welfare, Government of People's Republic of Bangladesh formulated Standardization and Quality Control Parameters Required for testing of Unani, Ayurvedic, Herbal and Homeopathic medicines emphasized on various quality parameters for testing of single and combined formulation as per requirements of the WHO and other International Drugs Regulatory Authorities and Health Agencies.

To fulfill the goal of development of traditional and Homeopathic medicine to highest standard and stringent control over, Directorate General of Drug Administration of Bangladesh is going to frame out GMP Guidelines for Unani, Ayurvedic, Herbal and Homeopathic Medicine.

There is no doubt that this GMP Guidelines will play a vital role in ensuring the quality, safety and efficacy of Unani, Ayurvedic and Herbal medicines. However, meeting GMP requirements requires investment from manufactures and this may be especially difficult for small manufactures in developing countries. Investing the GMP may increase production costs, leading to an increase in the price of the final product. This will impact on the affordability of such medicines. Therefore, relevant national health authorities need to take this impact into consideration and take the appropriate measures to encourage and ensure that manufacturers are willing and able to improve their GMP. According to the experiences of some countries, giving a transition period to manufactures for them to improve the GMP is one good example. Therefore, these guidelines are only a reference and the national health authorities will, based on the guideline, further develop their own GMP requirements according to their circumstances, nature of drugs and the limitation of testing of polyherbal combitional, herbo-mineral Unani and Ayurvedic medicine in general and partcularly Ayurvedic medicine containing nano particulate metalic compounds and admixture of herbs, metals and animal organs.

Major General Md. Mahbubur Rahman

Director General

Abbreviations and Acronyms

WHO	: World Health Organization :
GMP	: Good manufacturing practices
DRA	: Drugs Regulatory Authorities
IDRA	: Drugs Regulatory Authorities
DGDA	: Directorate General of Drug Administration,
DA	: Drug Administration
MOHFW	: Ministry of Health and Family Welfare,
GOB	: Government of People's Republic of Bangladesh
QC	: Quality Control
QA	: Quality Assurance
QO	: Quality Operation
OOS	: Out-of-Specification
PD	: Product Development
PDD	: Product Development Department
R&D	: Research and Development
ICH	: International Conference on Harmonisation (guide line)
PM	: Packaging Materials
RM	: Raw Materals
BP	: British Pharmacopoeia
USP	: United State Pharmacopeia
BAMS	: Bachlor of Ayurvedic Medicine and Surgery
BUMS	: Bachlor of Unani Medicine and Surgery
DAMS	: Diploma in Ayurvedic Medicine and Surgery
DUMS	: Bachlor in Unani Medicine and Surgery
	Standard Operational Procedures (SOPs : Standard Operational Procedures
BPR	: Batch Processing Record, Batch Packing Record
BMR	: Batch Manufacturing Record
S.S	: Stainless Steel
Sq. ft	: Square foot
TLC	: Thin Layer Chromatography
UV	: Ultra Vioet
IR	: Infra Red
HPLC	: High Performance Liquid Chromatography
HPTLC	: High Performance Thin Layer Chromatography
AAS	: Atomic Absorption Spectrophotometer
GC	: Gas Chromatography
FTIR	: Fourier Transform-Infrared Spectroscopy
TEM	: Travelling Electronic Microscope
SEM	: Simulation Electronic Microscope
SME	: Small and Medium Enterprise
LAF	: Laminar Air Flow
pH	: Negative logarithm of Hydrogen Ion Concentration
LOD	: Loss on drying

IPQC	: In Process Quality Control
IPQA	: In Process Quality Assurance
BNAF	: Bangladesh National Ayurvedic Formulary
BNUF	: Bangladesh National Unani Formulary
DM	: De-Mineralized

Unani, Ayurvedic, Homeopathic and Herbal GMP Guideline Committee

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1. INTRODUCTION

With the constant increase in the use of Unani, Ayurveda & Herbal medicines worldwide and the rapid expansion of the global market, the safety and quality of Unani, Ayurveda & Herbal materials and finished herbal products have become a major concern for health authorities, pharmaceutical industries and the public. The safety and efficacy of traditional medicines largely depend on their quality. Requirements and methods for quality control of finished products, traditional medicinal products particularly for combining/mixing herbal products, are far more complex than for chemical drugs. The quality of finished products is also influenced by the quality of the raw materials used.

WHO has committed to the development of a series of technical guidelines related to quality assurance and control of herbal medicines, as well as to updating existing guidelines.

The manufacturing process is one of the key steps where quality control is required to ensure quality of medicinal products, including herbal medicines. Good Manufacturing Practices (GMP) is one of the most important tools for this measure.

Unlike conventional pharmaceutical products, which are usually produced from synthetic materials by means of reproducible manufacturing techniques and procedures, herbal medicines are prepared from materials of herbal origin, which are often obtained from varied geographical and/or commercial sources. As a result it may not always be possible to ascertain the conditions to which they may have been subjected. In addition, they may vary in composition and properties. Furthermore, the procedures and techniques used in the manufacture and quality control of herbal medicines are often substantially different from those employed for conventional pharmaceutical products.

Because of the inherent complexity of naturally grown medicinal plants and the often variable nature of cultivated ones, the examples of contamination with toxic medicinal plants and/or plant parts and the number and small quantity of defined active ingredients, the production and primary processing has a direct influence on the quality of Unani, Ayurveda & Herbal medicines. For this reason, application of GMPs in the manufacture of herbal medicines is an essential tool to assure their quality.

2. GMP: An Overview

Good Manufacturing Practice (**GMP**) Guidelines provide guidance for manufacturing, testing and quality assurance practice in order to ensure that a quality drug product is safe for human consumption. 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. But mostly it is the company's responsibility to determine the most effective and efficient quality process. The Good Manufacturing Practice is prescribed here to ensure-

(i) The raw materials used in the manufacture of drugs are authentic, of prescribed quality and are free from contamination;

(ii) The manufacturing processes it has been prescribed to maintain the standards;

(iii) To adopt adequate quality control measures;

(iv) The manufactured medicines which are released for sale are of acceptable quality;

(v) To achieve the above objectives, each licensed manufacturing unit shall evolve its methodology and procedures for manufacturing of medicines following prescribed processes which should be well documented as a manual, will keep for future reference and inspection when required.

2.1 Importance of GMP

Unlike conventional pharmaceutical products, which are usually produced from synthetic materials by means of reproducible manufacturing techniques and procedures, Unani, Ayurveda & Herbal medicines are mainly prepared from materials of plant, mineral and animal origin, which are often obtained from varied geographical and/or commercial sources. As a result it may not always be possible to ascertain the conditions to which they may have been subjected. In addition, they may vary in composition and properties. Furthermore, the procedures and techniques used in the manufacture and quality control of such medicines are often substantially different from those employed for conventional pharmaceutical products. Because of the inherent complexity of naturally grown medicinal plants and the often variable nature of cultivated ones, the examples of contamination with toxic medicinal plants and/ or plant parts and the number and small quantity of defined active ingredients, the production and primary processing has a direct influence on the quality of Homoeopathic medicines. For this reason, application of GMPs in the manufacture of Homoeopathic medicines is an essential tool to assure their quality.

3. Basic Principles of GMP

Govt. of Bangladesh has included in drug policy that pharmaceutical 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.

- Production operations must follow clearly defined procedures in accordance with approved formularies and or pharmacopeial manufacturing and marketing authorizations, with the objective of obtaining products of the requisite quality.
- All critical processes are validated to ensure consistency and compliance with specifications *but there are short coming in case of some products with high potencies.*
- 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 where 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.
- A system is available for recalling any batch of drug from sale or supply.
- Complaints about marketed drugs are examined, the causes of quality defects are investigated, and appropriate measures are taken with respect to the defective drugs and to prevent recurrence.

3.1 Good practices in production

General:

3.1.1. All handling of materials and products, such as receipt and cleaning, quarantine, sampling, storage, labeling, dispensing, processing, packaging and distribution should be done in accordance with written procedures or instructions and, where necessary, recorded.

3.1.2. Any deviation from instructions or procedures should be avoided as far as possible. If deviations occur, they should be done in accordance with an approved procedure. The authorization of the deviation should be recorded in writing by a designated person, with the involvement of the quality assurance department, when appropriate.

3.1.3. Checks on yields and reconciliation of quantities should be carried out as necessary to ensure that there are no discrepancies outside acceptable limits.

3.1.4 Operations on different products should not be carried out simultaneously or consecutively in the same room or area unless there is no risk of mix-up or cross-contamination.

3.1.5 At all times during processing, all materials, bulk containers, major items of equipment, and where appropriate, the rooms and packaging lines being used should be labeled or otherwise identified with an indication of the product or material being processed, its strength (where applicable) and the batch number. Where applicable, this indication should also mention the stage of production. In some cases it may be useful to record also the name of the previous product that has been processed.

3.1.6 Access to production premises should be restricted to authorized personnel.

3.1.7 Normally, non-medicinal products should not be produced in areas or with equipment destined for the production of pharmaceutical products.

3.1.8 In-process controls are usually performed within the production area. The performance of such in-process controls should not have any negative effect on the quality of the product or another product (e.g. cross-contamination or mixup).

Prevention of cross-contamination and bacterial contamination during production:

3.1.9 When dry materials and products are used in production, special precautions should be taken to prevent the generation and dissemination of dust. Provision should be made for proper air control (e.g. supply and extraction of air of suitable quality).

3.1.10 Contamination of a starting material or of a product by another material or product must be avoided. This risk of accidental cross-contamination arises from the uncontrolled release of dust, gases, particles, vapours, sprays or organisms from materials and products in process, from residues on equipment, from intruding insects, and from operators' clothing, skin, etc. The significance of this risk varies with the type of contaminant and of the product being contaminated.

Processing operations:

3.1.11 Before any processing operation is started, steps should be taken to ensure that the work area and equipment are clean and free from any starting materials, products, product residues, labels or documents not required for the current operation.

3.1.12 Any necessary in-process controls and environmental controls should be carried out and recorded.

3.1.13 Means should be instituted of indicating failures of equipment or of services (e.g. water, gas) to equipment. Defective equipment should be withdrawn from use until the defect has been rectified. After use, production equipment should be cleaned without delay according to detailed written procedures and stored under clean and dry conditions in a separate area or in a manner that will prevent contamination.

3.1.14 Containers for filling should be cleaned before filling. Attention should be given to avoiding and removing any contaminants such as glass fragments and metal particles.

3.1.15 Any significant deviation from the expected yield should be recorded and investigated.

3.1.16 Checks should be carried out to ensure that pipelines and other pieces of equipment used for the transportation of products from one area to another are connected in a correct manner.

3.1.17 Pipes used for conveying distilled or deionized/purified water and, where appropriate, other water pipes should be cleaned and stored according to written procedures.

3.1.18 Measuring, weighing, recording, and control equipment and instruments should be serviced and calibrated at pre-specified intervals and records maintained. To ensure satisfactory functioning, instruments should be checked daily or prior to use for performing analytical tests. The date of calibration and servicing and the date when recalibration is due should be clearly indicated, preferably on a label attached to the instrument.

3.1.19 Repair and maintenance operations should not present any hazard to the quality of the products.

Packaging operations:

3.1.20 When the programme for packaging operations is being set up, particular attention should be given to minimizing the risk of cross-contamination, mix-ups or substitutions. Different products should not be packaged in close proximity unless there is physical segregation or an alternative system that will provide equal assurance.

3.1.21 Before packaging operations are begun, steps should be taken to ensure that the work area, packaging lines, printing machines and other equipment are clean and free from any products, materials or documents used previously and which are not required for the current operation. The line clearance should be performed according to an appropriate procedure and checklist, and recorded.

3.1.22. The name and batch number of the product being handled should be displayed at each packaging station or line.

3.1.23. Normally, filling and sealing should be followed as quickly as possible by labeling. If labeling is delayed, appropriate procedures should be applied to ensure that no mix-ups or mislabeling can occur.

3.1.24 The correct performance of any printing (e.g. of code numbers or manufacturing expiry dates) done separately or in the course of the packaging should be checked and recorded. Attention should be paid to printing by hand, which should be rechecked at regular intervals.

3.1.25 Special care should be taken when cut labels are used and when overprinting is carried out off-line, and in hand-packaging operations. Roll-feed labels are normally preferable to cut labels in helping to avoid mix-ups. When labels are attached manually, in-process control checks should be performed more frequently.

3.1.26 Printed or embossed (where applicable) information on packaging materials should be distinct and resistant to fading or erasing.

3.1.27 Regular on-line control of the product during packaging should include at least checks on:

a. The general appearance of the packages;
b. Whether the packages are complete;
c. Whether the correct products and packaging materials are used;
d. Whether any overprinting is correct;
e. Correct functioning of line monitors.
f. Whether approved label, carton, insert, batch no., Mfg & Exp date are printed of relevant products are being used.

Samples taken away from the packaging line should not be returned.

3.1.28 Products that have been involved in an unusual event during packaging should be reintroduced into the process only after special inspection, investigation and approval by authorized personnel. A detailed record should be kept of this operation.

3.1.29. Upon completion of a packaging operation, any unused batch-coded packaging materials should be destroyed and the destruction recorded. A documented procedure requiring checks to be performed before returning unused materials should be followed if un-coded printed materials are returned to stock.

3.2 *Good practices in quality assurance and control*

3.2.1 Quality control is the part of GMP concerned with sampling, specifications and testing, and with the organization, documentation and release procedures which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory with standard specifications. Quality control is not confined to laboratory operations but must be involved in all decisions concerning the quality of the product.

3.2.2 The independence of quality control from production is considered fundamental.

3.2.3 Each manufacturer (the holder of a manufacturing authorization) should have a quality control function. The quality control function should be independent of other departments and under the authority of a person with appropriate qualifications and experience, who has one or several control laboratories at his or her disposal. Adequate resources must be available to ensure that all the quality control arrangements are effectively and reliably carried out. The basic requirements for quality control are as follows:

a. Adequate facilities, trained personnel and approved procedures must be available for sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products, and where appropriate for monitoring environmental conditions for GMP purposes;
b. Samples of starting materials, packaging materials, intermediate products, bulk products and finished products must be taken by methods and personnel approved of by the quality control department;
c. Qualification and validation must be performed;
d. Records must be made (manually and/or by recording instruments) demonstrating that all the required sampling, inspecting and testing procedures have actually been carried out and that any deviations have been fully recorded and investigated;
e. The finished products must contain ingredients complying with the qualitative and quantitative composition of the product described in the

marketing authorization; the ingredients must be of the required purity, in their proper container and correctly labeled;

f. Records must be made of the results of inspecting and testing the materials and intermediate, bulk and finished products against specifications; product assessment must include a review and evaluation of the relevant production documentation and an assessment of deviations from specified procedures;

g. No batch of product is to be released for sale or supply prior to certification by the authorized person(s) that it is in accordance with the requirements of the marketing authorization.

h. Sufficient samples of starting materials and products must be retained to permit future examination of the product if necessary; the retained product must be kept in its final pack unless the pack is exceptionally large.

3.2.4 Quality control as a whole will also have other duties, such as to establish, validate and implement all quality control procedures, to evaluate, maintain, and store the reference standards for substances, to ensure the correct labeling of containers of materials and products, to ensure that the stability of the active pharmaceutical ingredients and products is monitored, to participate in the investigation of complaints related to the quality of the product, and to participate in environmental monitoring. All these operations should be carried out in accordance with written procedures and, where necessary, recorded.

3.2.5 Assessment of finished products should embrace 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 product, and an examination of the finished pack.

3.2.6 Quality control personnel must have access to production areas for sampling and investigation as appropriate.

Control of starting materials and intermediate, bulk and finished products

3.2.7 All tests should follow the instructions given in the relevant written test procedure for each material or product. The result should be checked by the supervisor before the material or product is released or rejected.

3.2.8 Samples should be representative of the batches of material from which they are taken in accordance with the approved written procedure.

3.2.9 Sampling should be carried out so as to avoid contamination or other adverse effects on quality. The containers that have been sampled should be marked accordingly and carefully resealed after sampling.

3.2.10 Care should be taken during sampling to guard against contamination or mix-up of, or by, the material being sampled. All sampling equipment that comes into contact with the material should be clean. Some particularly hazardous or potent materials may require special precautions.

3.2.11 Sampling equipment should be cleaned and, if necessary, sterilized before and after each use and stored separately from other laboratory equipment.

3.2.12 Each sample container should bear a label indicating:

a. The name of the sampled material;
b. The batch or lot number;
c. The number of the container from which the sample has been taken;
d. The number of the sample;
e. The signature of the person who has taken the sample;
f. The date of sampling.

3.2.13 Out-of-specification (OOS) results obtained during testing of materials or products should be investigated in accordance with an approved procedure. Records should be maintained.

Test requirements:

Starting and packaging materials

3.2.14 Before releasing a starting or packaging material for use, the quality control manager should ensure that the materials have been tested for conformity with specifications for identity, strength, purity and other quality parameters.

3.2.15 An identity test should be conducted on a sample from each container of starting material

3.2.16 Each batch (lot) of printed packaging materials must be examined following receipt.

3.2.17 In lieu of testing by the manufacturer, a certificate of analysis may be accepted from the supplier.

Certificates must contain at least the following information:

a. Identification (name and address) of the issuing supplier;

b. Signature of the competent official, and statement of his or her qualifications;
c. The name of the material tested;
d. The batch number of the material tested;
e. The specifications and methods used;
f. The test results obtained;
g. The date of testing.

In-process control :

3.2.18. In-process control records should be maintained and form a part of the batch records.

Finished products

3.2.19. For each batch of drug product, there should be an appropriate laboratory determination of satisfactory conformity to its finished product specification prior to release.

3.2.20. Products failing to meet the established specifications or any other relevant quality criteria should be rejected.

Batch record review:

3.2.21 Production and quality control records should be reviewed as part of the approval process of batch release. Any divergence or failure of a batch to meet its specifications should be thoroughly investigated. The investigation should, if necessary, extend to other batches of the same product and other products that may have been associated with the specific failure or discrepancy. A written record of the investigation should be made and should include the conclusion and follow-up action.

3.2.22 Retention samples from each batch of finished product should be kept for at least one year after the expiry date. Finished products should usually be kept in their final packaging and stored under the recommended conditions. If exceptionally large packages are produced, smaller samples might be stored in appropriate containers. Samples of active starting materials should be retained for at least one year beyond the expiry date of the corresponding finished product. Retention samples of materials and products should be of a size sufficient to permit at least two full re-examinations.

3.3 Research and Development

Research and development (R&D) is the work where pharmaceutical company innovates, introduces, and improves products and dosage forms. It is a series of investigative activities to improve existing products to lead to the development of new products. It is challenging venture for local and global market and development of novel Unani, Ayurvedic and Herbal phyto-medicines. The Unani, Ayurvedic and Herbal industries shall built up Research and Development section separate or as a part of Quality Control with required expert manpower and equipment, space and environment

The R & D personnel shall discharge the following functions diligently

3.3.1 Pre-formulation studies to check pharmacological actions and uses of ingredients.

3.3.2 Trials to assess efficiency and reproducibility of any formulation and develop self-explanatory methods and manufacturing processes

3.3.3 Stability studies both at accelerated conditions and at real time life following ICH guide line to check physical, chemical, and microbiological aspects of any formulation.

3.3.4 Determine shelf life of products and to ensure that all batches of the released products are maintaining within specification limits throughout their entire shelf life

3.3.5 Standardize processes for consistency and uniformity in product quality.

3.3.6 Technical Transference to production and quality operation division/department

3.3.7 Analytical method validation supported by the Quality Control Department.

3.3.8 Improvement of new and existing products for customer satisfaction, environmental change, technology change and other competitors.

3.3.9 Formulation and method development, re-formulation and method up gradation to achieve superior quality medicines at affordable prices by implementing efficient cost-effective measures and management system.

Stability studies :

3.3.10. Research and Development section / Product Development Department (PDD) should evaluate the quality and stability of finished products and, when necessary, starting materials and intermediate products.

3.3.11. Research and Development section should establish expiry dates and shelf-life specifications on the basis of stability tests related to storage conditions.

3.3.12. A written program for ongoing stability determination should be developed and implemented to include elements such as:

a. a complete description of the drug involved in the study;
b. the complete set of testing parameters and methods, describing all tests for potency, purity, and physical characteristics and documented evidence that these tests indicate stability;
c. provision for the inclusion of a sufficient number of batches;
d. the testing schedule for each drug;
e. provision for special storage conditions;
f. provision for adequate sample retention;
g. A summary of all the data generated, including the evaluation and the conclusions of the study.

3.3.13. Stability should be determined prior to marketing and following any significant changes in processes, equipment, packaging materials, etc.

GOOD MANUFACTURING PRACTICES GUIDELINES FOR UNANI, AYURVEDIC AND HERBAL MEDICINES

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 Unani, Ayurvedic and Herbal medicines and no other manufacturing activities shall be undertaken therein.

The Good Manufacturing Practices (GMP) prescribed in Part I and Part II shall ensure the followings:

i. Raw materials used in the manufacture of medicines are authentic, of prescribed quality and are free from contamination;
ii. The manufacturing process as prescribed shall maintain the standard;
iii. Adequate quality control measures shall be adopted;
iv. The manufactured drug which is released for sale shall be acceptable quality;
v. Each licensee shall evolve methodology and procedures as per prescribed process of manufacturing of medicines which shall be documented as manual (either in written or electronically) and shall be kept for reference and inspection.

However, Unani and Ayurvedic physicians registered under The Bangladesh Unani and Ayurvedic Practitioners Ordinance 1983 as Hakim, Kabiraj and/or registered practitioners from any lawful authority, who prepares medicines on his/her own to dispense to his/her patients and not for selling such medicines commercially, shall be exempted from the purview of Good Manufacturing Practices (GMP) and this GMP Guidelines shall not be binding upon them.

PART 1

1. FACTORY PREMISES

The manufacturing plant shall have adequate space for -

(I) Raw Materials Stores
(II) Packing and Packaging Materials Stores
(III) Spare parts, Engineering and other Materials Stores
(IV) Manufacturing Process Areas
(V) Intermediate and Semi-processed Goods Stores
(VI) In-Process Quality Control Area
(VII) Quality Operation Areas
(VIII) Finished Goods Stores
(IX) Rejected Goods Store
(X) Office and Ancillary Areas

1. GENERAL REQUIREMENTS

1.1.1 Location and Surrounding*:* The factory building for manufacturing of Unani, Ayurvedic and Herbal medicines

The factory building for manufacturing of Unani, Ayurvedicand Herbal medicines shall be situated and constructed 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.

1.1.2 Buildings: The building(s) used for factory shall be such as to permit production of Unani, Ayurvedic and Herbal medicines under hygienic conditions and shall be free from cobwebs, insects and rodents. It shall have adequate provision of light and ventilation. The floor and the walls shall not be damped or moist. The premises used for manufacturing, processing, packaging and labeling shall be in conformity with the rules and regulations prevailed in the country. It shall be located so as to be:
I. Compatible with other manufacturing operations that shall be carried out in the same or adjacent premises.

II. Adequate working space for orderly and logical placement of equipment and materials shall be allowed 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 shall permit easy cleaning and disinfection. The walls of the room in which the manufacturing operations to be carried out shall be impervious to and shall be capable of being kept clean. The floor 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 as well as connection in the manufacturing area shall be proper and safe.

V. Furnace/Bhatti section shall be covered with tin roof or cement sheet or burned earthen slab known as tally and with proper ventilation, but sufficient measure shall be taken to prevent flies and dust.

VI. There shall be fire safety measures and proper exit facilities.

VII. There shall have separate space for drying of raw materials, in process or bulk medicines or medicines required for drying before processing or packing/packaging. This space shall be protected from flies, insects, dusts etc. by proper flooring, wire netted windows, glass panels or with other suitable devices.

1.1.3 Water System: There shall be DM water system or as appropriate system (validated system) for treatment of water drawn from own or any other source to render it potable in accordance with specific standard and DM water conforming to BP/USP specification. Purified Water so produced shall only be used for all the operations except washing and cleaning operations where potable water shall 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 shall be maintained by the licensee manufacturer in this behalf.

1.1.4 Disposal of Waste: The Waste water and the residues from the manufacturing areas, Laboratories and other sites which shall be prejudicial to the workers or public health and shall be disposed off after suitable treatment.

i. The disposal of sewage and effluents (solid, liquid and gas) from the factory shall be in conformity with the requirements of Department of Environment.

ii. Additional precautions shall be taken for the storage and disposal of rejected medicines. Records shall be maintained for all disposal of waste.

iii. Provisions shall be made for the proper and safe storage of waste materials waiting for disposal. Hazardous, toxic substances and inflammable materials shall be stored in suitably designed and segregated enclosed areas.

2. WAREHOUSING AREA

i. 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; released, rejected, returned, recalled or in quarantine products, spare parts and change items of machine and equipment.

ii. 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 and humidity), these shall be provided, monitored and recorded. Storage areas shall have appropriate house-keeping and rodents, pests and vermin control procedures and records shall be maintained. Proper racks, bins, pallets and platforms shall be provided for the storage of materials.

iii. Receiving and dispatch bays shall be such as to protect materials and products from adverse weather conditions.

iv. 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 only authorize persons.

2.1 Raw Materials Store: All raw materials procured for manufacturing shall be kept in raw materials store. The manufacture based on the experience and the characteristics of the particular raw material used in Unani, Ayurvedic and Herbal medicines shall decide the use of appropriate containers which shall protect quality of the raw materials as well as prevent those 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 store shall be sub-divided with proper enclosures to provide such conditions by suitable cabinet. While

designing such containers, cupboard or areas in the raw materials store, care shall be taken to handle the following different categories of raw material:

(I) Raw material of metallic origin
(II) Raw material of mineral origin
(III) Raw material from animal source
(IV) Fresh Herbs and biologicals
(V) Dry Herbs and plant materials.
(VI) Intermediate and semi processed materials
(VII) Excipients etc.
(VII) Empty hard gelatin or vegetable capsule shell etc.

Each container used for raw material storage shall be properly identified with the label which shall indicate name of the raw material, source of supply, date of receipt, expiry date, reference number and shall also clearly state the status of raw material such as 'QUARANTINE', 'UNDER TEST' , 'APPROVED' or 'REJECTED'.

All raw materials shall be sampled and got tested either by the in house Unani, Ayurvedic or Herbal experts working as Quality Control technical personnel or by the government approved laboratories and shall be used only on approval after verifying. The rejected raw materials shall be removed from other raw material store and shall be kept in separate room. Procedure of 'First in First out' shall be adopted for raw materials wherever necessary. Records of the receipt, testing and approval or rejection and use of raw material shall be maintained.

2.1.1 Special Protected Areas: Poisonous and precious 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

2.2. Sampling Areas: 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.

2.3. Packaging Materials: All packaging materials such as bottles, jars, cartons, master cartons, shipping cartons, boxes, strip and blister foils, caps, measuring spoons etc. shall be stored properly. All containers and closure shall be adequately cleaned before storing. 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.

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

ii. Regular checkup shall be made to ensure adequate steps against spillage, breakage and leakage of containers.

2.4 Finished Products: The finished goods transferred from the production area after proper packaging shall be kept 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 and labeling as well as the finished product quality as prescribed, then it shall be shifted to 'Approved Finished Goods Store'. Distribution records shall be maintained as required.

If Unani, Ayurvedic and Herbal medicines needs any special storage conditions, finished goods store shall ensure required conditions.

3. PRODUCTION

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

ii. In order to avoid the risk of cross-contamination, separate dedicated and self-contained facilities shall be made available for the production of Unani, Ayurvedic and Herbal medicines. The manufacturing area shall provide adequate space for orderly placement of equipment and materials to be used in any operation for which these are consumed so as to facilitate easy and safe working environment and to minimize or to eliminate any risk of mix-up between different drugs, raw materials and also to prevent the possibility of cross contamination among drugs those are manufactured, stored or handled in the same premises.

iii. 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 or indicated.

iv. The manufacture of Unani, Ayurvedicand Herbal medicines shall be conducted under the direct supervision of minimum one expert (Hakim/Kaviraj) in Unani or Ayurvedic system of medicine who possesses a degree (BAMS/BUMS) qualification from any University or Institute or a registered diploma holder (DAMS/DUMS) with at least one year experience.

v. Number of personnel employed shall be adequate and direct proportion to the workload.

vi. The licensee manufacturer shall ensure that all personnel in Production area or in Quality Control Laboratories shall receive training appropriate to the duties and responsibilities assigned to them. They shall be provided with regular in-service training.

4. HEALTH, CLOTHING AND SANITATION OF WORKERS

i. 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. It shall be clean too. The uniform includes 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 areas. Workers shall also be provided with the facilities for changing clothes and to keep their personal belongings.

ii. Prior to employment, all personnel shall undergo medical examination including eye examination and shall be free from skin and other communicable or contagious diseases.

Thereafter, they shall be medically examined periodically, at least once a year. Records shall be maintained thereof. The licensee manufacturer shall provide the services of a qualified physician for assessing the health status of personnel involved in different activities.

iii. All personnel, 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.

iv. No person showing, at any time, apparent illness or open lesions which may adversely affect the quality of products, shall not 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.

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

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

vii. 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.

viii. 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.

ix. There shall be adequate facilities of First Aid.

5. MACHINERY AND EQUIPMENT

i. For carrying out manufacturing depending on the size of operation and the nature of product manufactured, suitable machines and equipment shall be made available. These shall 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.

ii To ensure ease in movement of workers and orderliness in operation a suitably adequate space shall be ensured between two machines or rows of machines. These machinery and equipment have to be properly installed and maintained with proper cleaning.

iii. List of equipment 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.

6. BATCH MANUFACTURING RECORDS

i. There shall be Batch Processing Record (BPR)/ Batch Manufacturing Record (BMR) for each Unani, Ayurvedic and Herbal product. It shall be based on the relevant parts of the currently approved Master Formula (MF). The method of preparation of such records included in the Master Formula shall be based on BNAF/ BNUF and designed to avoid transcription errors.

ii. Before any processing begins, checking shall be performed and recorded to ensure that the equipment and work station, documents or materials not required for the planned process are removed and cleared of previous Unani, Ayurvedic and Herbal medicines and that equipment are clean and suitable for use.

iii. 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 product both in generic and proprietary,
(b) The number of the batch being manufactured,
(c) Date and time of commencement, of significant intermediate stages and of completion of production,
(d) initials of the operators 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 quality control 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 that is yield calculation,

(i) Notes on special problems including details, with signed authorization for any deviation from the master formula, comments or explanations for significant deviations from the expected yield limits shall be given,

(j) Addition of any recovered or reprocessed material with reference to recovery or reprocessing stages.

7. BATCH PACKAGING RECORDS

i. Batch Packaging Record (BPR) 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.

ii. Before any packaging operations begins, checking 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 operation, and that the equipment is clean and suitable for use.

8. DISTRIBUTION RECORDS

Records of sale and distribution of each batch of Unani, Ayurvedic and Herbal medicines shall be maintained in order to facilitate prompt and complete recall of the batch, if necessary. The duration of record keeping shall be one year plus date of expiry of the batch.

9. COMPLAINTS AND ADVERSE DRUG REACTION

i. All complaints thereof concerning quality of Unani, Ayurvedic,and Herbal medicine shall be carefully reviewed and recorded according to written procedures. Each complaint shall be investigated and evaluated by the designated personnel of the company and records of investigation and remedial action taken thereof shall be maintained.

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

iii. There shall be written procedures describing the action to be taken, recall to be made of the defective Unani, Ayurveda and Herbal medicine.

10. QUALITY CONTROL

i. There shall be adequate facilities for quality control (QC) section/department in the same premises. The test shall be as per pharmacopoeia standard. Where the test facilities are not available, the tests shall be performed with the help of approved accredited laboratories.

ii The quality control section shall verify all the raw materials, monitor in process, quality checks and control the quality of finished product(s) being released to finished goods store/ware house. Preferably for such quality control there shall be a separate expert. The quality control section shall have the following facilities:

i) There shall be adequate area for quality control section/ department.
ii) Reference books such as Unani, Ayurvedic and Herbal Pharmacopoeias, Formularies, Monographs and other Scientific Books, Herbarium Sheets and Reference Samples shall be maintained for proper identification.
iii) Manufacturing record shall be maintained for the various steps of processes.
iv) Controlled samples of finished products of each batch shall be kept for till one year ahead of the expiry date of the product for future reference.
v) Adequate conditions under which raw materials, semi-finished products and finished products are stored shall be ensured for supervision and monitoring**.**
vi) Record to be kept in establishing shelf life and storage requirements for the medicines
vii) Record of specific method and procedure of preparation, that is, ‘Bhavana’, ‘Mardana, ‘Puta’, Gal-e-Hikmat, DeqVapka, and the record of every process carried out by the manufacturer shall be maintained.

viii) Standard for identity, purity and strength as given in respective pharmacopoeias of Unani, Ayurvedic and Herbal systems of medicine published by the government or any lawful authority shall be complied with.
ix) All raw materials shall be routinely monitored to check fungal and bacterial contamination with a view to minimize such contamination.
x) 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(**s**) who shall be whole time employees of the licensee.

Xi) Personnel for Quality Assurance (QA) and Quality Control (QC) operations shall be suitably qualified and experienced and shall have a minimum-
(a) One expert in Unani or Ayurveda medicine who possesses a degree (BAMS/BUMS) from any University or Institute or a registered diploma holder (DAMS/DUMS) with at least one year experience.
(b) One expert who possess at least four (4) years honors or Master Degree in Chemistry or Pharmacy or Biochemistry or Applied Chemistry awarded by any recognized University; and
(c) One Botanist who possess at least four (4) years honors or master degree in Botany having specialization in Pharmacognosy or Taxonomy awarded by any recognized University.
(d) One Microbiologist who possess at least four (4) years honors or Master Degree in Microbiology awarded by any recognized University.
xii) The manufacturing unit shall have a quality control section as explained under Section 35 (ii). The manufacturing company shall maintain all the records of various tests got done from outside recognized laboratory.
xiii) List of machines and equipment recommended is indicated in Part III-Colum 4.

PART II

LIST OF MACHINERIES, EQUIPMENT AND MINIMUM PRODUCTION PREMISES REQUIRED FOR MANUFACTURING OF VARIOUS DOSAGE FORMS OF UNANI, AYURVEDIC AND HERBAL MEDICINES

As outlined minimum factory premises of 5,000 square feet area shall be required for each system of manufacturing unit mentioned below. The well painted covered areas shall be separated by partition for each activity entitled for the manufacture of particular category of dosage form. The area designated or shown for a particular dosage form shall be subtracted from the minimum area noted. On the other hand, additional area as permissible shall be required if any dosage form of either system of medicines if manufactured in the same premises.

SL	Dosage form	Minimum space required	Minimum machineries/ equipment recommended
01	Powders: Sufoof /Churna, Sanoon/ Manjan, Zuroor/ Lepa, Nasya,KwathChurna,	200 Sq. ft Divided into two area, one for processing and other for packing	Powder Mixer, SS Vat or Bin, Dryer, Powder filling and sealing machine or proper arrangement. Sachet filling and sealing machine for

	Nimak/Labon		sachet packing
02	Calcined Powders: Kushta/Bhasma	100 Sq. ft Considering filling, sealing and packaging in same Powder manufacturing area	Manual or mechanical Kharal, Earthen pots, Furnace or Bhatti, Triturating machine
03	Fine Processed Powder: Jawhar/, Pisti ,Satwa, Kupipakka,Parpati,	100 Sq. ft Considering filling, sealing and packaging in same Powder manufacturing area	GeleHikmat/Putpak, Manual or mechanical Kharal, **End Runner Mill**, S.S Vat or Bin
03	Semi-solid Preparations: Etrifal, Jawarish, Majun, Laooq, Lubob, Halwa, Khamira, Murabba/ Ableh, Modak, Pak, Prash	150 Sq. ft Considering basic process and heating in same heating room as of Liquid processing	S.S Vat or Bin, Semi-solid filling and sealing machine or proper arrangement
04	Tablets: Haboob, Qurse/ Botti, Batika, Gutika/ Pills	150 Sq. ft	S.S Vat or Bin, Tablet Compressing Machine
05	Capsules	150 Sq. ft	S.S Vat or Bin, Dehumidifier, Capsule filling and sealing machine.
06	Distillates: Arq/ Ark	100 Sq. ft	Maceration tank, Distillation Machine/Qarambik, S.S tank/ Vessel, Filter machine or filtering arrangement
07	Syrups: Sharbat, Sikanjabeen, Saiyal/ Kwath, Asava, Arishta	400 Sq. ft	Filter, Holding tank, Compounding vessel, Emulsifier, Stirrer
08	Ointments and Suppositories: Qeerooti, Zimad, Marham, Furzaza/Malam, Malhar, Barti	200 Sq. ft Extra 350 sq. ft space shall be necessary for Suppositories	Double jacketed or heating cum Compounding vessel, Emulsifier, Container/ Tube filling and crimping machine
09	Medicated Oils: Tila, Rowghan/ Taila, Ghreeta	100 Sq. ft	Storage and compounding vessel, Filter machine or Filtering arrangement, Bottle filling and sealing machine/ arrangement
10	ENT Drops: Qutur,Gargara, Mazmaza, Sawoot /Bindu	200 Sq. ft	Thermostatically controlled hot air oven/ heating kettle, Sterilizer/ autoclave, aseptic filling area, filling machine or arrangement
11	Collyriums: Surma, Shiaf/ Kajal/Anjan	200 Sq. ft	Triturating machine, Sieve, Filling and sealing arrangement under UV Lamp. Earthen Lamp for collection and Triple or End Roller Mill, for refining of Kajal/Anjan
12	Basic Processing Area	250 Sq. ft	Herb cutter/Size reducer, Washing machine/Arrangement, Crusher, Grinder, Pulveriser, Sifter/ Sieve, Powder Mixer/ Blender, Granulator, Dryer
13	Liquid Processing Area	200 Sq. ft Extra 350 sq. ft	Gas Burner or other heating arrangement for herb extraction.

		dedicated space shall be necessary for Fermentation tank/ container and distillation machine for AyurvedicAsava and Arista	The area shall have proper ventilation, removal of smoke, prevention from flies, insects and dust.
14	Solid Processing Area	300 Sq. ft	Crusher, Grinder, Pulveriser, Sifter/ Sieve, Powder Mixer/ Blender, Granulator, Dryer
15	Liquid Packing and Packaging Area	300 Sq. ft Extra space shall be necessary for online Bottle washing, filling, sealing and packing facility	Bottle washing Machine/arrangement, Bottle dryer/ arrangement, Liquid filling and Capping Machine, Visual inspection arrangement, Bottle Labelling Machine/arrangement, Conveyer/ Packaging Table
16	Solid Packing Area	200 Sq. ft Extra 250 Sq. ft shall be needed for coating and Strip/ Blister packing	Container filling, sealing and Packing arrangement in addition to space specified above, Packaging/ Conveyer Table Coating Machine and Strip/ Blister Machine in case of coated tablet and Strip/Blister packing
17	General Utility	------	There shall sufficient number of Air shower, Insect Killer/Trapper, Air cooler/conditioner, Humidifier, Air Circulation and ventilation arrangement
Total Area except extra space		**3,300 Sq. ft**	

PART III

EQUIPMENT AND MINIMUM AREA REQUIRED FOR DISCHARGING QUALITY ASSURANCE AND QUALITY CONTROL OF VARIOUS DOSAGE FORMS OF UNANI, AYURVEDIC AND HERBAL MEDICINES

Sl. No.	**Section**	**Minimum space required**	**Equipment recommended**
01	**Metrology Lab**	**200 Sq ft**	
			Electronic Balance
			Digital Balance
			Platform Scale
			Standard Weight Sets
			Digital Calipers
			Hardness Tester
			Friability Tester
02	**Chemical Lab**	**400 Sq ft**	

			Muffle Furnace
			Vacuum Oven
			Fume Hood
			Vibratory Sieve Shaker
			Lab. Water Distillation Plant
			Filtration Unit(Vacuum Pump)
			Liebig Condenser / Distilled Condenser
			Melting Point Apparatus
			Boiling Point Apparatus
			Volatile oil determination Apparatus
			Desiccator
			Infra-Red Moisture Analyzer/ Meter
			Water Bath
			Flask Shaker
			Centrifuge
			Auto-Titrate
			pH Meter
			Conductivity Meter
			Viscometer
			Density bottle /Pycnometer
			Digital Thermometer
			Micro Pipette
			Vortex Meter
			Soxhlet Apparatus
			Rota evaporator
			Kjeldel Apparatus
			Hot plate with Magnetic Stirrer
			Dissolution Tester, 6 Chamber
			Disintegration Tester
			Ultrasonic Bath
			Refrigerator
			Leak Tester
			Karl Fischer with Potentiometer
			Color Index or Colorimeter
			Dehumidifier.
			Glassware and Reagents for testing
03	**Pharmacognosy/ Botany Lab**	**200 Sq ft**	
			Herbs Disintegrator
			Sieve Analyzer
			SS / Aluminum Shade Trays
			Stage Micrometer
			Camera (Prism and Mirror Type
			Binocular Microscope
			Dissecting Microscope
			TLC Chamber or Kits
			Specimen Sample
			Herbarium Sheet Press
			Glass Ware, Chemicals etc
			Screw Gauze
			Slide Calipers

04	**Instrumental Lab**	**200 Sq ft**	
			Thin Layer Chromatography (TLC) plate viewing UV cabinet
			HPLC with computerized system
			UV Spectrophotometer
			Atomic Absorption Spectrophotometer (AAS)
			Flame Photometer
			GAS Chromatography (GC) with Sampler
			FTIR Spectrophotometer
			High Performance Thin Layer Chromatography (HPTLC)
			Travelling Electronic Microscope (TEM)
			Simulation Electronic Microscope(SEM)
			X-Ray Diffraction Microscope
	Note: 1. Above instruments shall be required for testing of Bhasma, Kushtajat, Herbo-mineral products, constituent raw materials, heavy metal contents, pesticidal constituents in starting materials as well as in intermediates and finished products. 2. Instrumental Laboratories required for Chemical and other Tests shall be shared with other laboratories where the facilities existed.		
05	**R & D /PD Product Development Lab**	**400 Sq. ft**	
			Physio-chemical Balance
			Digital Table Top/ Kitchen balance
			Mini Herbs Cutter
			Electrical Herbs Crusher
			Mini Herbs Grinder
			Mixture/ Blender
			Granulator
			S. S Sieve, Different mesh size
			Hot air Dryer
			Development Dryer
			Mini Tablet Compression Machine
			Mini Tablet Coating Machine
			Capsule filling & sealing Machine
			S. S Vessel for developmental work
			Mini Electric Stirrer/ Emulsifier
			Hot Plate with Magnetic Stirrer
			Tablet Hardness Tester
			Slide calipers
			Tablet Friability Tester
			Disintegration Tester
			Digital pH Meter
			Moisture Balance
			Pycnometer/Hydrometer
			S S Scoop & utensils
			Beaker, Flask etc Glassware

			Test Chemicals and reagents
			Stability Chamber
	Note: Instrument support for test sample development and quality parameter check shall be shared with Production and Quality Assurance department/section until facilities built up		
06	**Microbiology Lab**	**200 Sq ft**	
			Dry Heat Sterilizer
			Air Sampler
			Air Born Particle Counter
			Incubator
			Laminar Air Flow (LAF)Cabinet
			Colony Counter
			Zone Reader
			Autoclave
			Electronic Microscope
			Glassware and Media for testing
	Total Area	**1,600 Sq Ft**	
	Note: 3. Sufficient number of Air curtain/ Air shower, Insect catcher/ Insect repellent light, Air condition/ Air cooler, ventilation system etc. should be arranged		

PART IV

PARTICULARS TO BE SHOWN IN MANUFACTURING RECORDS

I. Substances other than parenteral preparation in general.`

1. Serial number
2. Name of the product
3. Reference of Master Formula Records.
4. Lot/Batch Size.
5. Lot/Batch Number
6. Date of commencement of manufacture and date of completion of manufacture and assigned date of expiry.

7. Name of all ingredients, specifications quantities required for the lot/Batch size and quantities actually used. All weighing and measurements shall be carried out by a responsible person and initialed by him and shall be counter-checked and signed by the competent technical staff under whose personal supervision the ingredients are used for manufacture.
8. Control Numbers of raw materials used in the formulation.
9. Date, time and duration of mixing.
10. Details of environmental controls like room temperature, relative humidity.
11. Date of granulation, wherever applicable.
12. Theoretical weight and actual weight of granules/powder blend.
13. Records of in-processes controls (Periodically whenever necessary)
    - i Uniformity of mixing.
    - ii Moisture content of granules/powder in case of Tablet/Capsules.
    - iii pH of solution in case of liquid.
    - iv Weight variation of tablet.
    - v Disintegration time of tablet.
    - vi Hardness of tablet
    - vii Friability test of tablet
    - viii Leak test in case of strip packing.
    - ix Filled volume of liquids.
    - x Quantity of tablets/capsules in the final container.
    - xi Content of ointment in the filled containers.
14. Date of compression in case of Tablets/date of filling in case of capsules.
15. Date of sealing/coating polishing in case of tablets/capsules wherever applicable.
16. Reference to analytical Report number stating the result of test and analysis.
17. Separate records of the disposal of the rejected batches and of batches withdrawn from the market.
18. The theoretical yield and actual productions yield and packing particulars indicating the size and quantity of finished packing.
19. Specimen of label/strip, carton with batch coding information like Batch Number, date of manufacture, date of expiry, retail prices as applicable, stamped thereon and inserts used in the finished packing's.
20. Signature with date of competent technical staff responsible for the manufacture.

21. Counter-signature of the head of the testing units or other approved person-in-charge of testing for having verified the batch records and for having released and batch for sale and distribution, the quantity released and date of release.
22. Date of release of finished packaging and quantity released for sale and distribution.
23. Quantity transferred to warehouse.

II. RECORDS OF RAW MATERIALS

Records in respect of each raw material shall be maintained indicating the date of receipt, invoice number, name and address of the manufacturer/supplier, batch number, quantity received, pack size, date of manufacture, date of expiry, if any, date of analysis and release/rejection by quantity control, analytical report number, with special remarks, if any, quantity issued, date of issue and the particulars of the name and batch numbers of products for the manufacture of which issued and the proper disposal of the stocks.

NOTE 1: The Licensing Authority may permit the licensee to maintain records in such manner as is considered satisfactory, provided the basic requirements laid down above are complied with.

NOTE 2: The licensing Authority may direct the licensee to maintain records for such additional particulars, as it may consider necessary in the circumstances of a particular case

III. PARTICULARS TO BE RECORDED IN THE ANALYTICAL RECORDS.

A. TABLETS AND CAPSULES.

1. Analytical report number.
2. Name of the sample
3. Date of receipt of sample
4. Batch/Lot number
5. Protocols of tests applied.
    a) Description
    b) Identification
    c) Uniformity of weight
    d) Uniformity of diameter (if applicable).

e) Disintegration test (time in minutes)

f) Hardness

g) Friability

Note: - Records regarding various test applied (including readings and calculations) should be maintained and necessary reference to these records should be entered in Col. 5 above whenever necessary.

6. Signature of the Analyst.
7. Opinion and signature of the approved Analyst.

Note: - Records regarding various test applied (including readings and calculations) should be maintained and necessary reference to these records should be entered in Col. 7 above, wherever necessary.

8. Signature of the Analyst.
9. Opinion and signature of the approved Analyst.

B. BHASMA/ SINDURA/KUSHTA (CALX)

1. Analytical report number.

2. Name of the sample

3. Date of receipt of sample
4. Batch/Lot number
5. Protocols of tests applied

a) Description: Colour, Odour

b). Identification- Chemically

c).Particle size: Mesh Size 200 – 300

d) Loss on drying at 105 degree C

e) Total ash

f) Acid- insoluble ash

g) Water soluble ash

h) Assay of elements

6. Ayurvedic Specifications

a) Lustreless (Nishchandrica)

b) Fine enough to enter the crevices of finger (rekhapurnatva)

c) Floats on water (varitara)

d) Smokeless (Nirdhoom)

e) Tasteless (Niswadu)

f) Irreversible (Apunarbhav)

7. Chemical Tests

Identification: Qualitative Test

Loss on drying at 105

Total ash

Acid-insoluble ash

Water soluble ash

Hydroxide Value

8Instrumental Tests

Assay/ Qualitative Test

Microscopic Test

X-Diffraction

SEM/TEM Confirmative Test

Spectrophotometric and Microscopic finger print to be attached

FOR OTHER DRUGS

1. Analytical report number.
2. Name of the sample.
3. Batch/Lot number.
4. Date of receipt of sample.
5. Protocol of tests applied.
   - i Description.
   - ii Identification.

iii Any other tests.
iv Results of Assay.

Note :- Particulars regarding various tests applied (including readings and calculations) shall be maintained and necessary reference to these records shall be entered in Column 5 above, wherever necessary.

6. Signature of Analyst.
7. Opinion and signature of the approved Analyst.

C. **RAW MATERIALS**

l. Serial number,

2. Name of the materials.
3. Name of the manufacturer/supplier.
4. Quantity received.
5. Invoice/ Challan number and date.
6. Protocols of test s applied.

Note: - Particulars regarding various tests applied (including readings and calculations) shall be maintained and necessary reference to these records shall be entered in Column 6 above, wherever necessary.

D. **CONTAINER, PACKING MATERIALS ETC.**

1. Serial number.
2. Name of the item.
3. Name of the manufacturer/supplier.
4. Quantity received.
5. Invoice/ Challan number and date . 6, Results of tests applied

Note:-Particulars regarding various tests applied shall be maintained and necessary reference to these records shall be entered in column 6 above.

7. Remarks.
8. signature of the examiner.

Note: - 1. The foregoing provisions represent the minimum requirements to be complied with by the licensee. The Licensing Authority, may however, direct the nature of records to be maintained by the licensee for such products as are not covered by the categories described above.

2. The Licensing Authority may permit the licensee to maintain records in such manner as are considered satisfactory, provided the basic requirements laid down above are complied with.
3. The Licensing Authority may at its discretion direct the licensee to maintain records for such additional particulars as it may consider necessary in the circumstances of a particular case.

ANALYTICAL SPECIFICATIONS OF BHASMA/ SINDURA (CALX)

1. Description : Colour, Odour

2. Identification- Chemically

3. Particle size : mesh size 200 – 300

4. Loss on drying (LOD) at 105 degree centigrade

5 Total ash

6 Acid- insoluble ash

7 Water soluble ash

8 Assay of elements

9 Ayurvedic specifications

a) Lustreless (Nishchandrica)

b) Fine enough to enter the crevices of finger (rekhapurnatva)

c) Floats on water (varitara)

d) Smokeless (Nirdhoom)

e) Tasteless (Niswadu)

f) Irreversible (Apunarbhav)

PART V

Specific Requirements for Manufacturing of Bhasma (calyx) and Rasaushadhies (herb-mineral-metallic compound) of Ayurvedic or Kushtajat (calcined products) of Unani Medicines.

1. Introduction: The guidelines are to provide general and minimum technical requirements for quality assurance and control in manufacturing rasaushadhies or and kushtajat (Herb-mineral-metallic formulations). These guidelines deal with Bhasmas, satwa (of Metals and Minerals origin) Drutiparpam, karpu and kushta etc. used in Ayurveda and Unani Medicines. The GMP guidelines for Rasaushadhies or and 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:- 10 sq. 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 to 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: 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 (IPQC)

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 Shodhana Dravya

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 (Bhasma Pariksha 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 materialmetals 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 pillsvati 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:**

Sl. no.	**Category of Medicine/ Manufacturing area**	**Minimum Manufacturing space required (1500 sq. ft.)**	**Machinery equipment recommended**
01	Pisti/ Grinding area for Bhasma. Phisti, Kushtaja	100 sq. ft.	Kharal/mechanized/motorized Kharal, End runner/Ball-Mill Sieves/Shifter
02	Powdering area for raw drugs of plant origin giving in Rasaushadhies (Herbo-metallic formulations)	200sq. ft	Grinder/ Disintegrator/Pulverisar/Powder mixer/ sieves/ Shifter
03	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

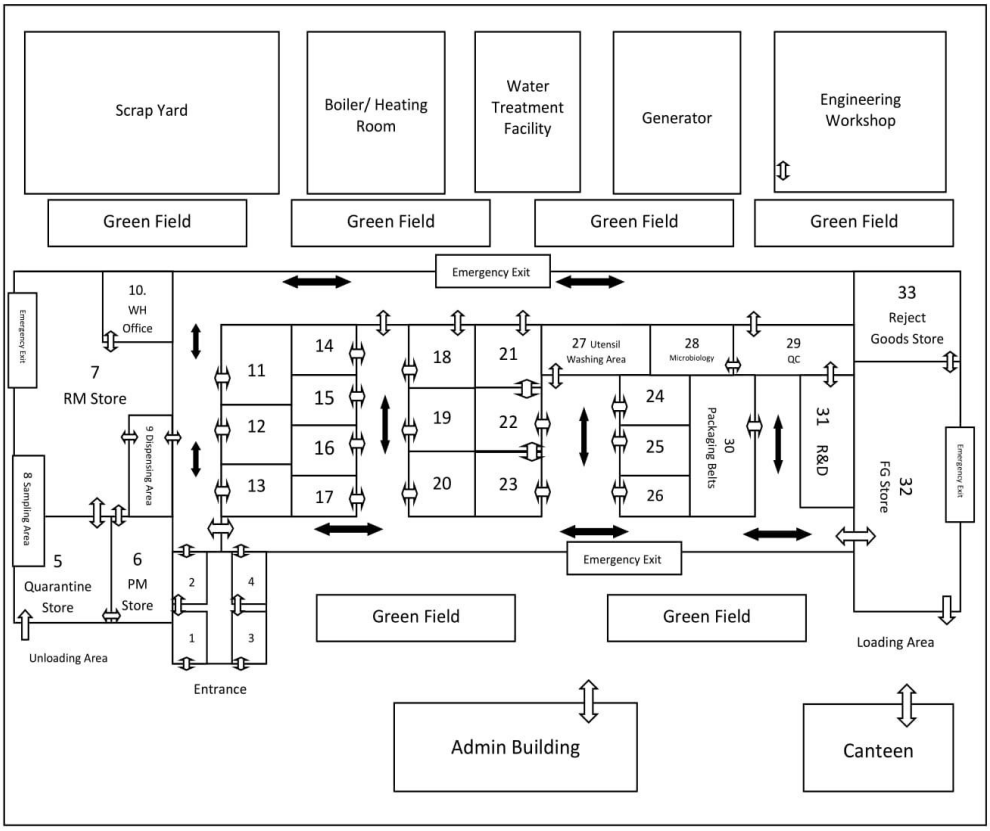
			storage and sugar coating, polishing pan in case of sugar coated tablets, mechanized chattoo (for mixing of guggulu) where required
04	Kupipakva/Ksara/Parpati/Lavana BhasmaSatva/SinduraKarpu/UppuParam/Qushta/Jawhar	150sq. ft.	Bhatti, Karahi/stainless steel vessels/patila flask, MultaniMatti/ palster of Paris, Copper Rod, Earthen container, Gaj Put Bhatti, muffle furnace (electrically operated) End/ Edge Runner, Exhaust Fan, Wooden, S.S. Sapatula
05	Receiving and storing raw material	150 sq. ft.	
06	Quality Control Section	150 sq. ft	
07	Quarantine/observation	50 sq. ft	
08	Finished goods store	150 sq.ft	
09	Rejected Good Store	50 sq. ft.	
10	Bhatti-Putta Area	50 sq. ft.	
11	Area for water and washing etc	200 sq. ft	
12	Office	100 sq. ft.	
	Total Area	**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)

APPENDIX I : A Typical General Factory Layout for Unani, Ayurvedic and Herbal Manufacturing Plant

Directorate General of Drug Administration (DGDA)
General Factory for Unani, Ayurvedic and Herbal Manufacturing Plant

Not to be scaled



Numbers indicate Room as denoted below-

1. Male Washroom, Entrance and Exit
2. Male Dress Change Room
3. Female Washroom, Entrance and Exit
4. Female Dress Change Room
5. Quarantine Store
6. PM Store
7. RM Store
8. Sampling Area
9. Dispensing Area
10. WH Office
11. Crushing Room
12. Solid dosage Room
13. Bulk Product Store
14. Tablet Compression Machine
15. Capsule Filling and Polishing Machine
16. Sachet Processing & Filling
17. Blister/ Strip/ Bottle filling
18. Change Parts Room
19. WIP- Intermediate store
20. IPQA- In process Quality Control
21. Extraction Room/ Processing
22. Process Room (Liquid)
23. Liquid Filling and Sealing Room
24. Semi-solid Process
25. Semi-solid Filling and Sealing
26. Production Office Room
27. Utensil Washing Area
28. Microbiology
29. QC
30. Packing Belts
31. R&D
32. FG Store
33. Reject Goods Store

Both way entry and exit Both way movements Unidirectional Movement

APPENDIX-II: CHECKLIST OF GMP INSPECTION FOR DRUG INSPECTORS

Sl. No.	Areas/Activities to be Autited	Remarks	
1	GENERAL		
	Name and address of Unit MFG. Lic No.		
	Telephone Fax:		
	Email:		
	Names and designation of the inspection team:		
2	PERSONAL		
	Name of In charge		
	a) production		
	b) quality control		
	Number of Production Supervisors/Asstt. Mfg./Chemist Number of Analysts		
	Have all personal received GMP Training? Is Training Documented?		
	What is the periodicity of the training?		
3	FACTORY PREMISES		
	Does manufacturing unit have adequate space for Receiving and storing raw material.		
	Manufacturing process areas. Quality control section. Finished goods store.		
	Office		
	Rejected goods/drugs store.		
	Does manufacturing unit have adequate space for Receiving and storing raw material.		
	Manufacturing process areas. Quality control section.		

	Finished goods store.		
	Office		
	Rejected goods/drugs store.		
	FACTORY PREMISES		
	Does manufacturing unit have adequate space for Receiving and storing raw material.		
	Manufacturing process areas. Quality control section. Finished goods store.		
4	LOCATION AND SURROUNDINGS		
	Is the establishment located away from environmentally polluted areas?		
	Is the establishment located away from areas adjacent to open sewerage, drain/public lavatory or any factory which produces excessive, disagreeable odour?		
	Are sewage, trash and other effluent disposal provided?		
5	BUILDINGS		
	Do the internal design and layout of establishment permit good hygiene practices including protection from cross contamination?		
	Are surfaces of walls, partitions and floors made of impervious materials and capable of being kept clean?		
	Do walls and partitions have smooth surface?		
	Are floors constructed to allow adequate cleaning and drainage?		
	Are doors, windows, ceiling and overhead fixtures constructed and finished to minimize buildup of dirt, condensation and shedding of particles and easy to clean?		
	Are working surfaces that come into direct contact with drugs of sound condition, durable and easy to clean, maintain and disinfect?		
	Any open drain blocked sewer or public lavatory nearby?		
	Are any products other than drugs manufactured in the same building?		

	Is there adequate space for equipment, material and movement of personal and materials?		
	Is there adequate space for equipment, material and movement of personal and materials?		
	Is there any programme/system to check of birds, rodents and insects?		
	Are lightening and ventilation adequate?		
	Are facilities for changing street clothes, footwear, washing and toilets adequately and satisfactorily maintained?		
	Is the space for drying of raw materials satisfactory?		
6	WATER SUPPLY		
	Is there adequate supply of potable water?		
	Does the potable water meet the specifications published API specifications?		
	Is only potable water Used in ASU medicines?		
7	DISPOSAL OF WASTE		
	Are drainage and water disposal systems designed, constructed and maintained in such a way as to avoid contamination of ASU products?		
	Are the waste water and residues disposed of after suitable treatment as per guidelines of pollution control authorities?		
	Are the arrangements for the following adequate? Disposal of solid/semi solid waste Disposal of sewage Disposal of Liquid laboratory waste? Disposal of Management of gaseous pollutants?		
	Is efficient treatment plant in existence / if yes, give comment on it?		
	Are fume hoods of adequate design in existence and used wherever necessary?		

8	CLEANING OF CONTAINERS		
	Is there proper arrangement for washing, cleaning and drying of containers?		
	Is this area separated from manufacturing area?		
9	STORES		
	Is there independent adequate space for storage of different types of materials such as raw material, packaging material and finished products?		
	Are ASU medicine storage facilities designed and constructed to Permit adequate maintenance and cleaning? Avoid pest ace and harbourage? Enable drugs to be effectively protected from contamination?		
	Provided the necessary environment to prevent spoilage?		
10	RAW MATERIALS STORES		
	Are raw materials or ingredients checked for parasites, undesirable microorganisms, pesticide or decomposed or extraneous substances		
	Are raw materials or ingredients inspected and tested before processing?		
	Are raw materials or ingredients subjected to effective stock rotation?		
	Is the area adequate?		
	Are the ventilation and lighting of stores adequate?		
	Is the Raw Material store segregated for different types of Raw Material? - Raw materials of metallic origin - Raw materials of mineral origin - Raw materials of animal source - Fresh herbs - Dry herbs or plant parts - Excipients etc. - Volatile oils/perfumes and flavours - Plant extracts and exudates/resins Others		

	Is special area with special condition provided for special Raw Materials?		
	Are there labels for material of different status i.e. quarantine, tested and releases for use and rejected?		
	Are these labels of different colours?		
	Are labels on containers of RM to be used in manufacture checked with regard to identity, quantity and QA approval? If not give details/		
	Is there the following information on the labels?Name of material Batch number Analysis number Date of release/rejection? Date of testing? Date of expiry? Is the sampling performed by quality control personal? Are there sampling procedures? Are the containers provided for storage of raw material suitable to preserve the		
	Is the sampling performed by quality control personal?		
	Are there sampling procedures?		
	Are the containers provided for storage of raw material suitable to preserve the quality		
	Is exterioe storage available for : Solvent storage area? Inflammable material storage area? Whether safety measures provided have been assessed by regulatory agency if any? Is SOP's available for handling of these materials? Are SOP's for cleaning of containers and closures available before packing of products?		
	Is the weighing area segregated?		
	Are lighting and ventilation adequate? Is		
	the area clean?		
	Do the personal wear appropriate clothing?		
	Is there danger of cross contamination during weighing?		
	Are the scales and balance calibrated regularly and records maintained?		
	Are the containers of the raw materials to be weighed, cleaned before opening?		
	After weighing, are these containers sealed		
	Are the raw materials for each batch, after weighing properly identified and checked ? Are adequately clean and dried equipment used for dispensing materials from the containers ?		
	Is FIFO principle adopted		
11	PACKING MATERIALS		
	Is the area adequate with reference to packing material		
	Are the containers and closures adequately cleared and checked		
12	FINISHED GOODS STORES		
	Is the area adequate with reference to materials stored?		
	Are lighting and ventilation adequate?		
	Are there inventory records to show:		

	Quantities Batch		
	number Date of receipt		
	Have the distribution records been maintained?		
	Do distribution records provide sufficient information for drug recall purpose?		
	Is there segregation area for retrieved good? Are		
	records available for the retrieved goods? Is		
	there any marked quarantine area?		
	Is there space for special storage conditions (environmental condition), if required?		
13	WORKING SPACE		
	Is space adequate as per manufacturing operations?		
	Is machinery along with working manual orderly placed with adequate space?		
	Are there adequate precautions to check cross contamination ?		
14	HEALTH ,CLOTHING, SANITATION AND HYGIENE OF WORKERS		
	Are workers free from contagious disease?		
	Are workers properly uniformed?		
	Are there separate lavatories for men and women?		
	Is there provision for changing their cloth and to keep personal belongings?		
	Are adequate facilities like wash-basin with running water hand drier & clean towels, etc., available for personal hygiene before entering into production area ?		
	Are personnel instructed to observe personal hygiene ?		
	Are hygiene instructions displayed in change rooms and strategic locations ?		
	Is the sanitation system monitored for effectiveness?		
	Is the sanitation system periodically verified by inspections? Is microbiological sampling of environment and ASU drugs contact surfaces carried out		
	Is the sanitation system regularly reviewed and adapte		
	Is the sanitation system regularly reviewed and adapted to reflact changed circumstances		
15	MEDICAL SERVICES		
	Is medical file of each worker maintained separately ?		
	Is recruitment of an employee preceded by medical examinations ?		
	What is the periodicity of subsequent medical examinations ?		
	Is an employee whose state of health is doubtful immediately removed from work site until he is fully recovered ?		
16	MACHINERY AND EQUIPMENT		
	Is manually operated or semioperated or automatic machines are used for Crushing, grinding, powdering boiling, mashing, burning, roasting, filtering, drying, filling, labelling and packing ?		

	Are equipment and containers coming into contact with ASU drugs designed such that they can be adequately cleaned, disinfected and maintained ?		
	Are equipment made of nontoxic materials?		
	Are equipment used to cook, heat, treat, cool, store designed to achieve the required temperature as rapidly as necessary ?		
	Are equipments used to cook, heat, treat, cool, store designed to monitor and control the required temperature?		
	Are containers for waste suitably identified?		
	Are containers for waste closable to prevent malicious or accidental contamination of ASU Medicines?		
	Is the equipment adequate for intended use?		
	Is it constructed in such a way that lubricants, coolant, etc. cannot contaminate the drug product?		
	Does the equipment permit cleaning and maintenance?		
	Does the equipment show its status i.e. clean, dirty, batch contents?		
	Do all apparatus/equipment bear appropriate labels to identify the product for which the equipment is used, its batch no., date of manufacturing etc .		
	Are SOPS available for cleaning maintenance and sanitation of major equipment?		
	Are log books maintained for cleaning maintenance and sanitation of major equipment?		
	Are SOP's readily available to operators?		
	If automatic electronic or mechanical equipment is used ,are there : Written programs for calibration/inspection Checks to ensure that may changes are made only by authorized persons/ Are suitable closures or lids available to protect the changes in properties of material exposed to outside atmosphere ?		
17	BATCH MANUFACTURING RECORDS		
	Are appropriate records of processing, production and distribution kept? Are SOP's available for the following Receipt of raw material and other components? Quarantine and storage? Quality control system and approval/rejection Release of production In process testing and control Finished product ? Storage of finished product? Distribution Returned goods Recalls and complaints Cleaning and maintenance? Quality control of water For reworking of non-conforming batches in existence? If yes, check)		
	Are there additional documents like log books, notebooks or other similar records available to show execution of various functions ?		
	Are there records of receipts of materials and do these have following information? (goods receipt Note-GRN) Receiving GRN documents number ? Date of receipt ? Supplier ? Manufacturer? Manufacture's batch number? Type and size of containers ? Number of containers and conditions ?		

	Are specifications available for all materials?		
	Are they dated authorized?		
	Are test methods validated?		
	Are periodic reviews of specification carried out to ensure compliance with new /revised National/international pharmacopoeia? Are these records of stock and issue of raw materials and do these have following information: Opening balance ? Date of receipt? Quantity received? Name and batch number assigned by the manufacturer? Invoice number, date name and address of supplier? Analysis receipt no. and date? Date of expiry, if any? Name and batch number of product for manufacture for which issued? Balance? Signature of issuing person?		
	Are there master formulation records for each drug product being produced		
	Is there a separate master production documents for each dosage form/batch size		
	Are these master production records signed and dated by competent person		
	Is a batch production record prepared for every batch produced		
	Is it reproduction of the appropriate master production documents or it has all critical information about the batch?		
	Are batch records retained for at least one year after expiry date		
	Has it been checked for accuracy, signed and dated by a responsible person Are the records maintained by QC for all the tests carried out? Do these records include: The name of the product Number of the batch being manufactured? Issue slip with lab ref. No Job cards ? Graphs, chart, spectra, etc ? List of major equipment used? In-process testing reports? Calculations of yield? Notes on deviations with signed authorization? Signature of individuals of who performed the tests? Material returns to store slip? Lab report of final product? Review of results for any raw material issued under "positive Recall" ? Signature of the designated person responsible for the review of records for accuracy and compliance with established standards?		
	Are other associated records available?		
	Is documentation available readily for examination?		
	Are batch production records capable of giving complete history of the batch right from the raw material stage to the distribution of finished products ?		
18	DISTRIBUTION RECORD		
	Are records of sale and distribution of each batch of ASU drugs maintained ? Are records maintained at least up to 5 years of the exhausting of stock ?		
19	RECORD OF MARKET COMPLAINTS		

	Are the firm maintain a record of complaint received from market ?		
	Does the firm have investigated the complaint and has taken any corrective action?		
	Does the firm has intimated such complaint six monthly to the Licensing Authority?		
	Does the firm maintain register of any ADR report received?		
	Are written procedure available for receipt and control of return products ?		
	Are returned or salvaged drug products destroyed unless QC determines their reprocessing ?		
	Are records of the returned products maintained including their disposition ?		
	Is a safety manual available?		
20	QUALITY CONTROL		
	Is the QC area more than 150 sq ft ?		
	Has Quality Control section minimum of : a) One person with Degree qualification in Ayurveda/ Herbal/Unani ; b) One chemist with bachelor in Science or Pharmacy or Pharmacy (Ayurveda) and; c) One Botanist (Pharmacognosist) with bachelor in Science (medical) or Pharmacy or Pharmacy (Ayurveda)?		
	Are master control procedures signed and stated by authorised persons?		
	Do these control procedure include specifications, test procedure or other control procedure for?		
	Raw materials		
	In process materials		
	Packaging and labeling materials?		
	Finished products?		
	Are the procedure in written form and readily available to QC personnel for acceptance of reprocessed material ?		
	Are the procedure in written form and readily available for acceptance of reprocessed material?		
	Do these control procedure include specifications test procured or other control procedure for :		
	Raw material		
	In process material		
	Packaging and labeling materials		
	Finished products?		
	Are samples collected by QC personal		
	Is there special room for microbiological and sterility testing?		
	Is the environment of room controlled		
	Are only materials, containers and appliance necessary for the job in hand stored in the vicinity of the manufacturing areas and are these properly labelled with name of the product, batch no. date etc.?		
	Are all raw materials, containers, closures, label and printed packaging material approved and released by QC for use in manufacture of drugs products		
	Are in-process controls carried out by QC personnel?		
	Are semi-finished products tested for appropriate tests when necessary?		
	Is bulk finished product tested for established		

	specifications before packing?		
	Is every finished product tested for established specifications before release for sale?		
	Does the QC maintain records of all the tests carried out?		
	Does the QC review all production and control records to ensure compliance with established written procedure before a batch of the product is released for sale?		
	Reference standards: Are reference standards (R.S) available? Are these RS or working standards (WS)? Are WS standardised against RS or CRS? Are RS stored properly (at appropriate temperature under dehumidified conditions) ? Are records of R.S and their standard maintained ?		
	Are samples in sufficient quantity for testing twice retained of starting materials and finished products for future examination, in case of need ?		
	Are quality control procedures validated ?		
	Is written programs available for stability including the following:		
	Sample storage condition		
	Room temperature		
	Sample size and test intervals?		
	Reliable and specific test methods?		
	Testing in the same containers closure system in which it is marketed?		
	Date and expiration date if any?		
	Established of in-house specification?		
	Does the firm provided the equipment as recommended in Part II C?		