

DRUGS (LICENSING, REGISTERING AND ADVERTISING) RULES, 1976

S.R.O. 145 (I)/76 dated 12th February 1976:- In exercise of the powers conferred by Section 41 of the Drugs Ordinance, 1976 (IV of 1976), the Federal Government is pleased to make the following rules, namely :-

CHAPTER I	Preliminary.
CHAPTER II	Manufacture Of Drugs For Sale.
CHAPTER III	Registration Of Drugs.
CHAPTER IV	Advertising Of Drugs, Etc.
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CHAPTER I - PRELIMINARY

1. Short title and commencement: .(1) These rules may be called the Drugs (Licensing, Registering and Advertising) Rules, 1976.

(2) They shall come into force at once.

2. Definitions.-- In these rules, unless there is anything repugnant in the subject or context:--

(a) "active pharmaceutical ingredient" means a substance or compound that is intended to be used in the manufacture of a pharmaceutical product as a pharmacologically active compound (ingredient);

(b) "airlock" means an enclosed space with two or more doors, which is interposed between two or more rooms of differing classes of cleanliness for the purpose of controlling the airflow between those rooms when they need to be entered and an airlock is designed for and used by either people or goods;

(c) "authorized person" means a person responsible for the release of batches of product for sale;

(d) "basic manufacture" means manufacture of a drug from basic raw material to a product which is ready for use as a starting material for the formulation of a finished drug or for repacking and such manufacture may involve chemical, bio-chemical, photochemical, microbial or such other processes or a combination of any of such processes;

(e) "batch (or lot)" means a defined quantity of starting material, packaging material, or finish product processed in a single process or series of processes so that it could be expected to be homogeneous in the case of continuous manufacture the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity, and to complete certain stages of manufacture it may sometimes be necessary to divide a batch into a number of sub-batches, which are later brought together to form a final homogeneous batch;

(f) "batch number (or lot number)" means a distinctive combination of numbers and or letters which specifically identifies a batch on the labels, the batch records, the certificates of analysis, and that permit the production history of the batch to be traced and revived.

(g) "batch numbering system" means a standard operating procedure describing the details of the batch numbering;

(h) "batch records" means all documents associated with the manufacture of a batch of bulk product or finished product showing a history of each batch of product and of all circumstances pertinent to the quality of the final product;

(i) "biological agents" means micro-organisms, including genetically engineered micro-organisms, cell cultures and endoparasites, whether pathogenic or not;

(j) "bulk product" means any product that has completed all processing stages up to, but not including, final packaging;

(k) "calibration" means the set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or measuring system for especially weighing, recording and controlling, or the values represented by a material measure and the corresponding known values of a reference standard and the limits for acceptance of the results of measuring;

(l) "clean area" means an area with defined environmental control of particulate and microbial contamination, constructed and used in such a way as to reduce and or eliminate introduction, generation and retention of contaminants within the area;

(m) "compounding" means scientific combination of two or more ingredients with a view to make a finished drug;

(n) "consignment or delivery" means the quantity of starting material or of a drug product, made by one manufacturer and supplied one time in response to a particular request or order, a consignment may comprise one or more packages or containers and may include material belonging to more than one batch;

(o) "critical process" means a process that may cause variation in the quality of the pharmaceutical product;

(p) "cross-contamination" means contamination of a starting material intermediate product, or finished product with another starting material or drug during production;

(q) "finished product" means a product that has undergone all stages of production, including packaging in its final container and labeling;

(r) "Form" means a form set forth in Schedule A;

(s) "formulation" means all operations involved in converting a drug into a final pharmaceutical dosage form ready for use as a finished drug including compounding, processing, formulating, filling, packing, finishing, labelling and other like processes;

(t) "good manufacturing practices for pharmaceutical products" means part of quality assurance which:--

(i) ensure that products are consistently produced and controlled to the quality standards appropriate to their intended use as required by the marketing authorization or product specification; and
(ii) diminish the risks, inherent in any pharmaceutical production, including contamination, cross contamination and mix ups (confusion) that cannot be detected completely through the testing of final products;

(u) "half-finished product" means any material or mixture of materials that has to undergo further manufacture;

(v) "in-process control" means checks performed during production in order to monitor and if necessary to adjust the process to ensure that the product conforms to its specifications and control of the environment or equipment may also be regarded as a part of in-process control;

(w) "intermediate product" means partly processed material that must undergo further manufacturing steps before it becomes a bulk product;

(x) "large-volume parenterals" means sterile solutions intended for parenteral application with a volume of more than 100ml in one container of the finished dosage form;

(y) "manufacture" means all operations of production, quality control, release, storage and the related controls;

(z) "manufacturer" means a company that carries out at least one step of manufacture;

(aa) "marketing authorization" means a document, issued by the Drug Registration Board set up under the Drugs Act, 1976, as a certificate of drug registration;

(ab) "master formula" means a document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a description of the procedure and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls;

(ac) "master record" means a document or set of documents that serve as a basis for the batch documentation (blank batch record);

(ad) "new drug" means a drug that has not been commonly sold or distributed to the public in Pakistan and is introduced for the first time;

(ae) "Ordinance" means the Drugs Ordinance, 1976 (IV of 1976);

(af) "packaging" means all operations, including filling and labelling which a bulk drug has to undergo in order to become a finished product;

Note: Sterile filling would not normally be regarded as part of packaging, the bulk product being the filled, but not the finally packaged, primary container.

(ag) "packaging material" means any material, including printed material, employed in the packaging of a pharmaceutical product, excluding any outer packaging used for transportation or shipment and packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product;

(ah) "pharmaceutical product" means any drug intended for human use or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form;

(ai) "processing instructions or procedures" means a defined in clause (ab) of this section;

(aj) "production" means all operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing and packaging, to its completion as the finished product;

(ak) "purity" means the degree to which other chemical or biological entities are present in any substance;

(al) "quality assurance" means the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use and so incorporates good manufacturing practices, Quality Control and other factors including product design and development and good laboratory practices;

(am) "quality control" means the part of good manufacturing practices concerned with sampling, specifications, and testing as well as 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 finished products released for sale or supply until their quality has been judged to be satisfactory and it is involved in all decisions concerning the quality of the product;

(an) "quarantine" means status of starting or packaging materials intermediate, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their release, rejection, or reprocessing;

(ao) "reconciliation" means a comparison, making due allowance for normal variation between the amount of product or materials theoretically produced or used and the amount actually produced or used;

(ap) "recovery or blending" means the introduction of all or part of previous batches, or of redistilled solvents and similar products, of the required quality into another batch at a defined stage of manufacture;

(aq) "repacking" means all operations involved in the transfer of a drug from a larger container or packing into smaller containers or packings including filling, packing and labeling with a view to make it ready for retail sale or wholesale, but does not include any compounding, or processing with a view to formulate it in any dosage form;

(ar) "retail sale" means a sale other than wholesale;

(as) "reprocessing" means the reworking of all or part of a batch of product of an unacceptable quality from a refined stage of production so that its quality may be rendered acceptable by one or more additional operations;

(at) "returned product" means finished product sent back to the manufacturer or distributor;

(au) "Schedule" means Schedule to these rules;

(av) "semi-basic manufacture" means manufacture from an intermediate substance of a drug to be used as a starting material for the formulation of a finished drug or to be used for repacking;

(aw) "specification" means the requirements with which the products or materials used or obtained during manufacture must conform as specified in the Drugs (Specification) Rules, 1978;

(ax) "standard operating procedure" means an authorized written procedure indicating instructions for performing operations not necessarily specific to a given product or material but of a more general nature such as equipment operation, maintenance and cleaning validation, cleaning of premises and environmental control sampling and inspection, and certain standard operating procedures may be used to supplement product specific master and batch production documentation;

(ay) "starting material" means any substance used in the production of a pharmaceutical product but excluding packaging materials;

(az) "system" means a regulated pattern of interacting activities and techniques which are united to form an organized whole;

(ba) "validation" means the documented act of proving that any procedure, process, equipment, material, activity or system works correctly and actually leads to the expected result; and

(bb) "wholesale" means sale to a person who purchases for the purpose of selling again and includes sale to a hospital or dispensary, or to medical, educational or research institute.

CHAPTER II MANUFACTURE OF DRUGS FOR SALE

3. Types of licences to manufacture drugs: Licences to manufacture drugs shall be of the following types, namely :--

- (i) licence to manufacture by way of basic manufacture.
- (ii) licence to manufacture by way of semi-basic manufacture;
- (iii) licence to manufacture by way of formulation;
- (iv) licence to manufacture by way of repacking; and
- (v) licence to manufacture for experimental purposes.

4. Manufacture on more than one set of premises: If drugs are manufactured on more than one set of premises, a separate application shall be made and a separate licence shall be issued in respect of each such set of premises.

5. Application for licence to manufacture drugs and fee therefor: (1) An application for the grant or renewal of a licence referred to in clauses (i) to (iv) of rule 3 shall be made in Form 1 or I-A to the Central Licensing Board addressed to its Secretary.

(2) An application under sub-rule (1) shall be accompanied by the proper fee as specified in Schedule F.

Proviso: Added vide S.R.O. 536(1)/93 dated 23rd June 1993. Omitted vide S.R.O. 277 (1)/96 dated 21st April 1996.

(3) If the application for renewal of the licence is made after the expiry of the period of the validity of the licence, it shall be treated as a fresh application for the grant of a licence.

(4) A fee of rupees one hundred shall be paid for a duplicate copy of the licence if the original is defaced, damaged or lost. Such copy of the licence shall bear the words "DUPLICATE COPY".

(5) Any fee deposited under sub-rule (2) Shall in no case be refunded.

6. Duration of a licence to manufacture drugs: A licence issued under this Chapter shall, unless earlier suspended or cancelled, be in force for a period of five years from the date of issue and may thereafter be renewed for periods of five years at a time:

Provided that an application for renewal shall not be entertained unless it has been made within sixty days after the expiry of the licence and when an application has been made as aforesaid the licence shall subject to the orders passed on the application for renewal continue in force for the next period of two years.

Provided further that duration of a licence issued under rule 21 shall be two years unless earlier suspended or cancelled.

7. Certificate of licence to manufacture drugs: A licence to manufacture by way of basic manufacture, semi-basic manufacture, formulation or repacking, as the case may be, shall be issued in Form 2.

. 8. Central Licensing Board: (1) The Central Licensing Board shall consist of the following members, namely :--

- (a) the Director-General Health, Government of Pakistan, who shall be its ex-officio Chairman;
- (b) the Director, Health Services of, each Provincial Government;
- (c) two pharmacologists, to be nominated by the Federal Government.

- (d) one pharmacist, to be nominated by the Federal Government;
- (e) one medical specialist from the Army Medical Corps. to be nominated by the Federal Government.
- (f) one pharmaceutical chemist or expert in quality control, to be nominated by the Federal Government;
- (g) the Drugs Controller, Ministry of Health, Government of Pakistan who shall be its ex-officio Secretary;
- (h) one representative, not below the status of an officer of BBPS- 19 [.....], of each of the Ministries of Commerce Industries & Justice to be nominated by the Federal Government; and
- (i) one representative of the Central Board of Revenue, not below the status of an officer of B-20, to be nominated by the Federal Government;
- (j) Cost Accountant of the Ministry of Health;
- (k) One physician, to be nominated by the Federal Government;
- (l) One Surgeon, to be nominated by the Federal Government. or an officer of the Provincial Health Department not below the status of Additional Secretary, to be nominated by the Secretary, Health Department of that Province. and
- (m) one expert in veterinary medicine to be nominated by the Federal Government.

(2) No person who is a member of the Appellate Board shall be nominated to the Central Licensing Board.

(3) The members of the Central licensing Board, other than its ex officio members, shall hold office for three years and shall be eligible for renomination.

(4) The Central Licensing Board may co-opt any other person who is expert in the pharmaceutical or medical profession for advice on any particular matter under consideration.

(5) The meetings of the Central Licensing Board may be held at such time as the Board may deem fit and, on the request of any of its members, the Chairman may at any time call a meeting if there is any important matter for its consideration.

(6) In the absence of the Chairman, the Board may elect one of its members to preside over a meeting.

(6-A) The quorum to constitute a meeting of the Board shall be one third of its total membership.

(7) The Central Licensing Board may authorise the Chairman to any of its members to perform any specific function of the Board for a specified period.

(8) The Central Licensing Board shall follow such policy directing as the Federal Government may issue from time to time.

(9) No act or proceeding of the Central Licensing Board shall be invalid merely on the ground of the existence of any vacancy in, or any defect in the constitution of the Board.

(10) The chairman and the Secretary of the Central Licensing Board shall, after the Board has approved the issuance of a licence sign the licence.

(11) Subject to rule 14, the Central Licensing Board may appoint a licensing authority or authorities for such purpose as it may deem fit.

9. Powers of the Central Licensing Board: (1) The members of the Central Licensing Board shall exercise all the powers of an Inspector without restriction as to area, and shall have the powers of a Provincial Inspector in relation to Section 30.

(2) In the exercise of their powers the members of the Central Licensing Board shall follow the

procedure prescribed for the Federal Inspector -

Provided that member nominated by a Provincial Government may follow the procedure as laid down for a Provincial Inspector.

10. Procedure of Central Licensing Board: (1) The Central Licensing Board may, before issuing a licence, cause the premises in which the manufacture is proposed to be conducted to be inspected by itself or by its sub-committee or by a panel of Inspector or experts appointed by it for the purpose, which may examine all portions of the premises and the plant and appliances, inspect the process of manufacture intended to be employed and the means to be employed for standarizing, if necessary, and analysing substances to be manufactured and enquire into the professional qualifications of the technical staff employed.

(2) Where inspection under sub-rule (1) is carried out by a sub-committee or panel of experts of Inspectors appointed under the said sub-rule it shall forward to the Central Licensing Board a detailed report of the result of the inspection.

(3) If the Central Licensing Board, after' such further enquiry, if any, as it may consider necessary, is satisfied that the requirements of the rules have been complied with, it may issue a licence in Form 2.

(4) If the Central Licensing Board is not so satisfied, it shall reject the application and shall inform the applicant of the reasons for such rejection and of the conditions which must be satisfied before a licence may be issued.

(5) No application shall be entertained within three months of the rejection of an application under sub-rule (4).

(6) If after the expiry of three months but within six months of the rejection of an application under sub-rule (4), the applicant informs the Central Licensing Board that the requirements of the rules have been fulfilled, the Board may if after causing a further inspection to be made, is satisfied that the conditions for the grant of a licence have been complied with, issue a licence and no further fee shall be required to be deposited for such an application.

(7) In case an application for licence to manufacture is made after the expiry of six months from the date of rejection of an application under sub-rule (1), such application shall be treated as a fresh application and full fee shall have to be deposited.

11. Special provisions regarding grant of a licence: (1) Where a manufacturer intends to manufacture a drug a part of the process of which is of specialised nature and would be uneconomical for him to conduct it, the Central Licensing Board may permit such process to be undertaken at another licensed premises specialised for this purpose, subject to such conditions, if any, as may be specified in this behalf.

(2) If a person is conducting a part of the process of the manufacture on behalf of another manufacturer in accordance with the permission granted under sub-rule (1), and he is not responsible for the quality of the final product, the Central Licensing Board may not require him to establish an independent quality control laboratory for such products.

(3) If a person possesses, or applies for, more than one type of licences to manufacture drugs in the same premises, he may establish one Quality Control Department for the purpose of both the licences.

12. Cancellation or suspension of licences: (1) If licensee does not comply with any of the conditions of a licence or violates any of the provisions of the Ordinance or the rules, or fails to deposit the requisite amount of the Central Research Fund due from him, the Central Licensing Board

may, by an order in writing stating the reasons thereof, cancel a licence or suspend it for such period as it thinks fit, either wholly or in respect of some of the drugs to which it relates.

(2) The Central Licensing Board shall, before cancelling or suspending a licence under sub-rule (1), provide an opportunity of being heard to the licensee.

(3) When a licence is cancelled or suspended, an entry to that effect shall be recorded on the licence.

(4) A licensee whose licence has been cancelled or suspended may appeal to the Appellate Board within sixty days of the date of receipt of the decision of the Central Licensing Board by the licensee and until the Appellate Board has given its order, the licence shall remain cancelled or suspended, as the case may be.

13. Renewal of a licence: On application being made for renewal, the Central Licensing Board may cause an inspection to be made, and if satisfied that the conditions of the licence and the rules are and will continue to be observed, shall issue a certificate of renewal or otherwise reject the application and inform the licensee accordingly.

14. Licensing authority: For the purpose of Section 18 of the Ordinance the Secretary to the Government of Province in the Health Department shall be the licensing authority for that Province.

15. Conditions for grant or renewal of a licence to manufacture drugs by way of basic or semi-basic manufacture: (1) Before a licence to manufacture by way of basic or semi-basic manufacture is granted or renewed, the Central Licensing Board shall satisfy itself that the following conditions are complied with by the applicant, namely :--

(a) The applicant shall provide premises which shall be suitable for intended use, in size and construction and shall be located in an area free from offensive and obnoxious odours and other possible sources of contamination.

(b) The applicant shall provide adequate space, plant and equipment for the manufacturing operations;

(c) The manufacture shall be conducted under the active directions and personal supervision of competent technical staff consisting of at least one person holding a degree in pharmacy, medicine, science with chemistry or chemical engineering from a university in Pakistan or any other institution, recognised by the Federal Government for the purposes of the Ordinance, and shall possess qualifications and experience which, in the opinion of the Central Licensing Board, is appropriate and adequate for the manufacture and handling of the drug to be, or being, manufactured.

(d) The applicant shall establish an independent Quality Control Department and maintain separate staff, premises and adequate laboratory equipment for carrying out tests of the strength, potency, quality and purity of the substances being or to be used in the manufacture.

(e) The Quality Control Department shall be independent of the manufacturing units and its incharge shall be a whole-time employee of the manufacturer and shall possess a degree in pharmacy, or a degree in science with chemistry, or a degree in medicine, microbiology, pharmacology, or bacteriology from a university in Pakistan or any other institution recognised by the Federal Government for the purposes of Ordinance, as the Central Licensing Board may deem fit for any particular unit; and shall be independent of the incharge of the manufacture (Production Units).

(f) the applicant shall ensure that--

(i) the manufacturing premises shall be maintained properly and shall, as far as possible, be orderly, clean and free from accumulated waste and vermin;

- (ii) unhygienic practices eating and smoking shall not take place in any production or quality control area;
- (ii) sufficiently clean, appropriately ventilated toilet facilities, including facilities for washing and room for changing clothes, shall be available for the use of manufacturing personnel where required;
- (iv) hygienic garments shall be worn by all staff in processing and packaging areas;
- (v) high standard of personnel hygiene shall be observed by all persons concerned with production processes, and
- (vi) no person known to be suffering from communicable disease or to be a carrier of such a disease and no person with open lesions or skin infection shall be engaged in production areas.

(g) The applicant shall provide--

- (i) adequate facilities for first aid;
- (ii) medical inspection of workers at the time of employment and periodical check up thereafter at least once a year;
- (iii) facilities for vaccination and inoculation against the enteric or any other epidemic group of diseases; and
- (iv) adequate precautions for safe-guarding the health of the workers, including measures to avoid industrial accidents or diseases.

Provided that where a person possess or applies for a licence to manufacture by way of basic and he also intends to conduct semi-basic manufacture of drugs, he may conduct such manufacture under the same license, subject to the approval of, and under such conditions as, the Central Licensing Board may specify, and

16. Conditions for the grant or renewal of licence to manufacture drugs by way of formulation:

Before a licence to manufacture drugs by way of formulation is granted or renewed, the Central Licensing Board shall satisfy itself that the following conditions are being complied with by the applicant namely :--

- (a) The factory premises shall comply with the conditions specified in Schedule B.
- (b) The applicant shall provide adequate space, plant and equipment for the manufacturing operations, the minimum space, plant and equipment for various operations are specified in Schedule B-1.

(bb) An applicant for registration of insecticides, pesticides and household disinfectants shall, in addition to the conditions specified in Schedule B and Schedule B-I, comply with the conditions specified in Schedule B-I, A.

(c) The manufacture shall be conducted under the 'active directions and personal supervisions of competent technical staff consisting of at least one person who is a whole-time employee and who has-

(i) a degree in Pharmacy from a university in Pakistan or any other institution recognised by the Federal Government for the purpose of the Ordinance and has at least twelve months of practical experience in the manufacture of drugs; or

(ii) a degree in science with chemistry or pharmaceutical chemistry as the principal subject who, for the time being is working as incharge of a licensed pharmaceutical manufacturing unit, has not less than ten years practical experience in the manufacture of drugs intended to be manufactured knowledge of pharmacy which, in the opinion of the Central Licensing Board is adequate for the purposes; or

(iii) any foreign qualification the quality and content of the training of which are comparable with those described in sub-clause (i) or sub-clause (ii) and is approved for the purposes, of this sub-rule by the Central Licensing Board: Provided that the Central Licensing Board may, in the case of manufacture

of drugs included in Schedule C, permit the manufacture of such drugs under the active direction and personal supervision or a person holding a degree in medicine or veterinary sciences of a university in Pakistan or any other institution recognised by the Federal Government, with at least three years experience in the manufacture, testing and analysis of biological products which are intended to be produced:

Provided further that the Central Licensing Board, may, in the case of manufacture of disinfectant fluids, insecticides liquid paraffin, medicinal gases, non-chemical contraceptives, plaster of paris, surgical dressing or chemicals for the manufacture of which the knowledge of pharmacy or pharmaceutical chemistry is not essential, permit manufacture of the drug under the active direction and personal supervision of competent staff who, [....] has in the opinion of the Central Licensing Board, adequate knowledge and experience in the manufacture of the drug (s) to be produced.

(d) The applicant shall establish an independent Quality Control Department and maintain separate staff, premises and adequate laboratory equipment for carrying out tests of strength, quality and purity of the substances being or to be used in the manufacture.

Provided further that a person already approved by the Central Licensing Board as the production incharge of a pharmaceutical firm shall continue to be the technical supervisor of that firm for the purposes of this rule.

(e) The Quality Control Department shall be independent of the manufacturing unit and its incharge shall be whole time employee of the manufacturer and shall possess a degree in pharmacy, or a degree in science with chemistry or a degree in medicine or pharmacology (for pharmacological testing) or a degree in microbiology (for microbiological testing) and has sufficient experience in testing of drugs:

Provided that in the case of drugs specified in Schedule C, the Central Licensing Board may allow the applicant to make arrangements with some other institution approved by the Central Licensing Board for such tests to be regularly carried out on his behalf by that institution.

17. Licence to manufacture drugs by way of repacking: (1) A licence to manufacture drugs by way of repacking is required for the repacking of such drugs, and under such conditions, as are specified in Schedule D.

(2) Where a person possesses or applies for a licence to manufacture by way of formulation and he also intends to conduct repacking of drugs, he may conduct such repacking under the same licence subject to the approval of, and under such conditions as, the Central Licensing Board may specify.

18. Condition for the grant or renewal of a licence to manufacture drugs by way of repacking: Before a licence to manufacture drugs by way of repacking is granted or renewed, the Central Licensing Board shall satisfy itself that the following conditions are complied with by the applicant, namely :--

- (a) adequate space and equipment shall be provided;
- (b) repacking operation shall be carried out under hygienic conditions and under supervision of technical staff provided for in clause (c) of rule 16;
- (c) adequate arrangements shall be provided for carrying out the tests for strength potency, quality and purity of the drugs to be repacked.

19. Conditions of licence to manufacture, by way of basic manufacture, semi-basic manufacture formulation and repacking of drugs: (1) A licence to manufacture by way of basic, semi-basic manufacture, formulation or repacking of drugs shall be subject to the conditions stated herein, if any, and to the further condition that the licensee shall continue to maintain conditions on the basis of which he was granted a licence.

- (2) The licence shall be kept on the licenced premises and shall be produced at the request of any member of the Central Licensing Board or of Provincial Quality Control Board or an Inspector.
- (3) Any change in the expert staff or significant alteration in the licensed premises or equipment shall be immediately notified to the Central Licensing Board.
- (4) The licensee shall maintain in the inspection book provided by the Central Licensing Board at the time of the issuance of the licence on which a member of the said Board or of a Provincial Quality Control Board or an Inspector shall record proceedings of each of his visits, his impressions and the defect or irregularities noticed, if any, by him and such inspection book shall be signed by him as well as the licensee or his authorised agent.
- (5) If any defects or irregularities are recorded in the inspection book under sub-rule (4) the manufacturer shall take steps to remove such defects or irregularities.
- (6) A licensee who for any purpose is engaged in the culture or manipulation of pathogenic spore bearing micro-organisms shall provide, to the satisfaction of the Central Licensing Board, separate laboratories, utensils and apparatus required for the culture or manipulation of such .micro-organisms, and they shall not be used for the manufacture of any other substance.
- (7) The licensee shall comply with the provisions of the Ordinance and the rules and with such further requirements, if any, as may be specified in any rule subsequently made-in this behalf or any other condition that may be imposed at the time of grant of a licence in the special circumstances of each case.
- (8) The licensee shall allow any member of the Central Licensing Board or of a Provincial Quality Control Board or an Inspector to enter, withg or without prior notice, any premises and to inspect the plant and the process of manufacture & the means employed in standardising and testing the drugs and to take samples for test and analysis.
- (9) The licensee shall allow any member of the Central Licensing "Board or of a Provincial Quality Control Board of an Inspector to inspect all registers and records maintained under these rules and to take samples of the manufactured drugs and shall supply to such member or Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Ordinance and the rules have been observed.
- (10) The Licensee shall, on demand, furnish to the Central Licensing Board or the Provincial Quality Control Board or to such authority as the Central Licensing Board may direct, from every batch of a drug, or from such batch or batches of drugs as it may from time to time specify, a sample for examination and, if required, furnish full Protocols of the tests which have been applied.
- (11) If the Central Licensing Board or a Provincial Quality Control Board so directs, the licensee shall not sell or offer for sale any batch of a drug in respect of which a sample is, or protocols are, furnished under clause (10) until a certificate authorising the sale of the batch of such drug has been issued to him by or on behalf of the Central Licensing Board or the Provincial Quality Control Board, as the case may be.
- (12) The licensee shall on being informed by the Central Licensing Board or a Provincial Quality Control Board that any part of any batch of a drug has been found not to conform with the requirements of the Ordinance or the rules and on being directed so to do, withdraw the remainder of the batch of such drug from sale and, so far as may in the particular circumstances of the case be practicable, recall all issues already made from that batch and dispose it of in such manner as may be directed by the said Board.

(13) No drug manufactured under licence shall be sold unless the precautions necessary for preserving its properties have been observed throughout the period after manufacture.

(13-A) The licensee or his authorised agent shall issue a warranty in Form 2-A For any drug sold by him for the purpose of re-sale or distribution.

(14) The Licensee shall, by the 30th June and the 31st December each year, Whichever is immediately after the annual financial closing of the company. contribute one per cent of his gross profit before deduction of income-tax towards the Central Research Fund to be maintained by the Federal Government and utilised by it in accordance with the Drugs (Research) Rules, 1978:

Provided that the Central Licensing Board may allow a portion of such contribution to be spent by the firm itself for research and development of new drugs or for establishing research laboratories when it is fully satisfied that such expenditure will be utilised for the said purpose effectively and properly.

Explanation: In this sub-rule, "profit" means gross profit before payment of income tax or other tax.

(14-A) The contributions made towards the Central 'Research Fund under sub-rule (14) shall be kept in such bank as the Federal Government may specify and shall be utilised in accordance with the Drugs (Research) Rules, 1978.

(15) The licensee shall, on or before the 31st July each year, submit a duly Signed profit and loss statement as per "PROFORMA" given in FORM-1 of SCHEDULE-A alongwith an evidence of deposit of 1 per cent of profit towards the Central Research Fund;

20. Additional conditions of licence to manufacture drugs by way of formulation: A licence to manufacture drugs by way of formulation shall, in addition to the conditions laid down in rule 19, be subject to the following further conditions, namely :--

(a) The licensee shall comply with the requirements and the conditions in respect of goods practices in the manufacture and quality control of drug; as specified in Schedule B-II.

(b) The licensee shall record in Schedule B-III the particulars of manufacture of each batch of drugs manufactured by him and shall retain such records, in the case of a substance for which expiry date is fixed for a period of two years from the expiry of such date and, in the case of other substances, for a period of five years from the date of manufacture.

(c) The licensee shall either in his own laboratory or, where so authorised under the proviso to clause (e) of rule 16, in any other laboratory approved by the Central Licensing Board, test each batch of the raw materials used by him for the manufacture of drugs and also each batch of the final drug, shall maintain records showing the particulars in respect of such tests as specified in Schedule B-III and shall retain such records, in the case of a substance for which expiry date is fixed for a period of two years from the expiry of such date and, in the case of other substances, for a period of five years from the date of manufacture.

20A. Contract Manufacture.-- Manufacture or analysis on contract is permissible on behalf of a licensee or of a pharmaceutical company whose products are registered in Pakistan for sale subject to the conditions laid down in Schedule G," as a special case and for genuine reasons as approved by the Registration Board.

SCHEDULE 'G'

1. Contract production and analysis

1.1 Contract of manufacture shall be undertaken only by a manufacturer who hold a valid drug manufacturing license, and the contract acceptor shall/have adequate facilities, knowledge, experience and competent personnel to satisfactorily carry out the work ordered by the contract giver.

1.2 General.-- Contract production and analysis shall be correctly defined, agreed and controlled in

order to avoid misunderstandings that could result in a drug or work or analysis of unsatisfactory quality. A written contract between the contract giver and the contract acceptor shall clearly establish the duties of each party had state the way in which the authorized person shall exercise his full responsibility in releasing each batch of product for sale or issuing the certificate of analysis and a copy of such a contract shall be supplied to the Central Licensing Board also.

1.3 All arrangements for contract manufacture and analysis, including any proposed changes in technical or other arrangements, shall be in accordance with the registration of the drug concerned.

1.4 There shall be a written contract covering the manufacture and or analysis arranged, under contract and any technical arrangements made in connection with it.

1.5 The contract shall permit the contract giver to audit the facilities of the contract acceptor.

1.6 In the case of contract analysis, the final approval for release must be given by the authorised person(s).

2. Contract Giver

2.1 The contract giver shall be responsible for assessing the competence of the contract acceptor in successfully carrying out the work or tests required and for ensuring by means of the contract that the principles of good manufacturing practices are followed.

2.2 The contract giver shall provide the contract acceptor with all the information necessary to carry out the contracted operations correctly in accordance with the registration and any other legal requirements and the contract giver shall ensure that the contract acceptor is fully aware of any problem associated with the product, work, or tests that might pose a hazard to premises, equipment , personnel, other materials or other products.

2.3 The contract giver shall ensure that all processed products and materials delivered by the contract acceptor to comply with their specifications or that the product has been released by the authorised person(s).

3. Contract acceptor

3.1 The contract acceptor shall not pass to a third party any of the work entrusted to him or her under the contract without the written consent of the contract giver and prior evaluation and approval by the arrangements of the Central Licensing Board, and arrangements made between the contract acceptor and any third party shall ensure that the manufacturing and analytical information is made available in the same way as between the original contract giver and contract acceptor.

3.2 The contract acceptor shall refrain from any activity that may adversely affect the quality of the product manufactured and or analyzed for the contract giver.

4. The contract

4.1 A contract shall be drawn up between the contract giver and contract acceptor that specifies their respective responsibilities relating to the manufacture and control of the product, and technical aspects of the contract shall be drawn up by competent persons suitably knowledgeable in pharmaceutical technology, analysis, and good manufacturing practices. All arrangements for production and analysis must be in accordance with the registration and agreed by both parties.

4.2 The contract shall specify the way in which the authorized person releasing the batch for sale ensures that each batch has been manufactured in, and checked for, compliance with the requirements of the marketing authorization.

4.3 The contract shall be describe clearly who is responsible for purchasing, testing and releasing materials and for undertaking production and quality controls, including in-process controls, and who

has responsibility for sampling and analysis, and in the case of contract analysis, the contract shall state whether or not the contract acceptor shall take samples at the premises of the manufacturer.

4.4 Manufacturing, analytical and distribution records and reference samples shall be kept by, or be available to, the contract giver, and any records relevant to assessing the quality of a product in the event of complaints or a suspected defect shall be accessible and specified in the defect or recall procedures of the contract giver.

4.5 The contract shall describe the handling of starting materials, intermediate and bulk products and finished products if they are rejected and it shall also describe the processing of information if the contract analysis shows that the tested product must be rejected.

21. Licence to manufacture drugs for experimental purposes: (1) If a person intending to manufacture a drug for experimental purposes does not hold a licence to manufacture drugs, he shall before commencing such manufacture, apply in Form 3 for the grant or renewal of a licence to the Central Licensing Board addressed to its Secretary.

(2) An application under sub-rule (1) shall be countersigned by the head of the institution in which, or the director or manager of the firm or company by which, the drug will be manufactured.

(3) The licence for the manufacture of drugs for experimental purposes shall be in Form 4.

22. Conditions of licence to manufacture drugs for experimental proposes: A licence issuing under rule 21 shall be subject to the following conditions, namely :--

(a) That licensee shall use the drugs manufactured under the licence exclusively for experimental purposes and shall carry on the manufacture and experimental work at the place specified in the licence.

(b) The licensee shall allow a member of the Central Licensing Board or of a Provincial Quality Control Board or an Inspector to enter, with or without notice, the premises where the drugs are manufactured and to satisfy himself that the manufacture is being conducted for experimental purposes.

(c) The licensee shall comply with such further requirements, if any, as may be specified under any rule subsequently made.

23. Labeling of drugs manufactured for experimental purposes: (1) Any drug manufactured for experimental purposes shall be kept in containers bearing labels indicating the purpose for which it has been manufactured.

(2) If any drug manufactured for experimental purposes is supplied by the manufacturer to any other person, the container shall bear a label on which shall be stated the name and address of the manufacturer, the accepted scientific name of the drug, if known, or, if not known, a reference which will enable the drug to be identified and the purpose for which it has been manufactured.

CHAPTER 3 REGISTRATION OF DRUGS

24. Registration Board: (1) The Registration Board shall consist of such members, including the Chairman and the Secretary, and its members shall hold office for such term, as is prescribed for the Central Licensing Board set up under rule 8.

(2) The Registration Board may refer any case for detailed examination to the committee of experts on the Drugs Evaluation constituted under Section 10 of the Act.

(3) The Registration Board may appoint a sub-committee consisting of at least one Clinical Professor, one pharmacologist and one pharmacist to make a detailed examination of each case and to submit a report for the consideration of the Board.

(4) The Registration Board may appoint a panel of experts or inspectors to inspect on behalf of the Board the premises of a manufacturer of drugs and to submit its report to the Board.

(5) The Chairman and the Secretary of the Registration Board shall, after the Board has approved the registration of a drug, sign the certificate of registration.

(6) For the manner and conduct of the meetings of the Registration Board, the provisions of sub-rules (3), (4), (5), (6), (7), (8), and (9) of rule 8 shall mutatis mutandis apply.

25. Powers of Registration Board: The members of the Registration Board shall exercise all the powers of Inspector without restriction as the area, and shall have the powers of a Provincial Inspector in relation to Section 30.

26. Application for registration of drugs and fees thereof: (1) An application for registration of a drug shall be made in Form 5 or 5-A in duplicate to the Registration Board addressed to its Secretary, and separate application shall be made for each drug.

(2) The applicant shall furnish such further information and material as may be required by the Registration Board for the proper evaluation of the drug.

(3) An application under sub-rule (1) shall be accompanied by fee or--

(a) rupees one thousand for the registration of new drug;

(b) rupees five hundred for the registration of any other drug; and

(c) rupees two hundred and fifty for the renewal of the registration of a new or any other drug:

Provided that the application for the renewal of registration is made before the expiry of the validity of the certificate of registration.

(3-A) Application for renewal of registration of a drug shall be made in Form 5-B.

(3-B) Any application under sub-rule (1) or sub-rule (3) shall be accompanied by the proper fee specified in Schedule F.

(4) If the application for renewal of registration is made after the expiry of the period of the validity of the certificate or registration, it shall be treated as a fresh application for the registration of drug.

(5) A fee of rupees fifty shall be paid for a duplicate copy of the certificate of registration if the original is defaced, damaged or lost, and such copy of the certificate shall bear the words "Duplicate Copy".

(6) Any fee deposited under sub-rule (3) shall in no case be refunded.

27. Duration of certificate of registration: A certificate of registration under this chapter, shall, unless earlier suspended or cancelled, be in force for a period of five years from the date of Registration of the drug and may thereafter be renewed for periods not exceeding 5 years at a time.

Provided that an application for the renewal of registration shall not be entertained unless it has been

made within sixty days after the expiry of the registration and when an application has been made as aforesaid the registration shall be subject to the orders passed on the application for the renewal to continue in force for the next period of five years :

Provided further that, if in the opinion of the Registration Board it is necessary so to do in the Public interest, it may provisionally register a [...] drug for a period of two years.

28. Certificate of registration: A certificate of registration of drug shall be issued in Form 6.

29. Procedure for registration: (1) The Registration Board may, if it considers necessary, cause the application for registration and the information and material supplied to it under rule 26 to be evaluated by a Committee on Drugs Evaluation consisting of experts related to the aspect of the drug to be evaluated and obtain its report.

(2) The Registration Board may, before issuing a registration], cause the premises in which the manufacture is proposed to be conducted to be inspected by itself or by its sub-committee or by a panel of Inspectors or experts appointed by it for the purpose, which may examine all portions of the premises and the plant and appliances, inspect the process of manufacture intended to be employed and the means to be employed for standardising, if necessary, and testing the substances to be manufactured and enquire into the professional qualifications of the technical staff employed.

(3) Where inspection under sub-rule (2) is carried out by a Sub-Committee or panel of experts or Inspectors appointed under the said sub-rule, it shall forward to the Registration Board a detailed report of the result of the inspection.

(4) If the Registration Board, after such further enquiry, if any, as it may consider necessary, is satisfied of its safety, efficacy, quality and economical value or where the public interest so requires, it may register the drug and issue a certificate of registration in Form 6, subject to such specific conditions as it may specify.'

(5) The Registration Board may, while registering a drug under sub-rule (4), approve the details as supplied by the applicant or approve them with amendments as it may deem fit in respect of the following particulars, namely :--

- (a) the name under which the drug may be sold;
- (b) the labelling;
- (c) the statement of all the representations to be made for the promotion of the drug in respect of--
 - (i) the claims to be made for the drug;
 - (ii) the route of administration;
 - (iii) the dosage;
 - (iv) the contra-indications, the side effects and precautions if any; and

(d) Omitted by S.R.O. 551(1)/93, dated 3. 7. 1993.

(5-A) Where the Registration Board registers a new drug, it may recommend to the Federal Government for fixation of maximum price of such drug.

(6) The Registration Board shall, before registering a new drug for which the research work has been conducted in other countries and its efficacy, safety and quality has been established therein, require the investigation on such pharmaceutical, pharmacological and other aspects, to be conducted and clinical trials to be made as are necessary to establish its quality and, where applicable, the biological, availability, and its safety and efficacy to be established under the local conditions:

Provided that under special circumstances to be recorded in writing, the Registration Board may

register a drug and require such investigations and clinical trials to be conducted after its registration.

(7) A new drug, where new method of manufacture is contemplated or a change is proposed in source, standard or specification of the active ingredient or the finished product, may not require full investigations and clinical trials except in so far as they are necessary for the purpose of establishing bio-equivalence, absorption, acceptability or other such features.

(8) Where it is necessary in the public interest so to do, the Registration Board may register a drug on its own motion without having received any application for registration.

(9) If the Registration Board is not satisfied as to the safety, efficacy, quality or economic value of a drug, or where the public interest so requires it may, [.]..., reject the application for registration and inform the applicant of the reasons for such rejection in writing.

(10) Rejection of an application for the registration of a drug shall not debar an applicant from submitting a fresh application under rule 26.

30. Conditions or registration of drug: (1) The relevant provisions of the Ordinance and the rules in respect of the registered drug, shall be complied with.

(2) The import, manufacture and sale of drugs shall be in accordance with the information contained in the applications in respect of those drugs or in any supplementary information or, where such information was amended by the Registration Board, in accordance with such amended information on the basis of which such drugs were registered:

Provided that deviations from any such information may be made only after obtaining prior approval of the Registration Board.

(3) The indications, contra-indication, side effects, the dosage and cautions, if any, as have been approved for the purpose of registration of a drug shall be clearly specified in the labelling and promotion.

(4) Every drug shall be produced in sufficient quantity so as to ensure its regular and adequate supply in the market.

(5) The manufacture of any drug shall not, without the prior approval of the Registration Board, be discontinued for period which may result in its shortage:

Provided that in the circumstances beyond the control of a manufacturer,, of a drug which may lead to reduction in the production of that drug, the circumstances may be intimated to the Registration Board.

(6) A record of quarterly production and disposal of a drug shall be maintained and supplied to the Chairman of the Registration Board in Form 7 in the months of January, April, July and October each year.

(7) In case of an imported drug, the indenter or any other approved representative in Pakistan of the foreign firm shall ensure regular and adequate supply of tee drug in Pakistan.

(7-A) The indenter, importer or manufacturer's authorised agent shall issue a warranty in Form 2-A for any drug indented or sold by him for the purpose of re-sale or distribution; and

(8) In respect of new drug, records, including adequately organised and indexed files, shall be maintained containing full information regarding--

- (a) animal or clinical investigations and tests conducted by the manufacturer or reported to him by any person concerning that drug;
- (b) reports from the scientific literature or the bibliography therefrom that are available to him concerning that drug;
- (c) experiences, investigations, studies and tests involving the chemical or physical properties or any other properties of that drug;
- (d) any substitution of another substance for that drug or any mixing of another substance with that drug;
- (e) any error in the labelling of that drug;
- (f) any bacteriological or any significant chemical or physical or other change or deterioration in any batch of that drug;
- (g) any failure of one or more distributed batches of that drug to meet the required specifications;
- (h) any unexpected side effects, injury, toxicity or sensitivity reaction associated with the clinical uses, studies, investigations and tests respecting that drug; and
- (i) any unusual failure of that drug to product it expected pharmacological activity.

(9) The following information shall be supplied to the Registration Board--

- (a) on request, report in duplicate of all records respecting the information contemplated by paragraphs (d), (e), and (f) of sub-rule (8); and
- (b) immediately upon receipt by him, reports in duplicate of all records respecting the information contemplated by paragraphs (d), (e) and (f) of sub-rule (8); and
- (c) as soon as possible and in any event within fifteen working days of their receipt by him, reports in duplicate of all records respecting the information contemplated by paragraphs (g), (h) and (i) of sub-rule (8).

(10) If a drug or any of its ingredients, which is imported or manufactured by a company in Pakistan is also approved for registration and free sale by its subsidiary, sister concern, associate or parent company in the country where it was originally developed or in any of the countries namely, USA, European Union Countries, Canada, Japan, Australia, and--

(a) if that drug at any time, for safety reasons is withdrawn or banned or certain restrictions are imposed in any of the said countries, then it shall be the responsibility of the manufacturer in Pakistan or as the case may be, the indenter, to immediately withdraw the drug from the market in Pakistan or, as the case may be to impose similar restriction and to inform the registration Board within fourteen days of such an information having come to his knowledge and having taken the necessary action. The Registration Board after getting the said intimation shall take similar action for the same drug available from other sources within the shortest possible time;

(b) if a clinical information for a drug is approved by the Drug Regulatory Authority in any of the said countries, the same clinical information shall be considered as approved for drug registration in Pakistan unless modified by the Registration Board on the basis of scientific data available to it, and such clinical information may include indication, contra-indications, side effects, precautions, dosage, etc;

(c) if any adverse drug reaction not otherwise included in the application for registration, is registered in any of the said countries, it shall be the responsibility of the concerned manufacturer or in case of imported drugs the indenter or manufacturer's agent in Pakistan, to be aware of such adverse action and to report to the Registration Board within thirty days of becoming so aware.

(11) The manufacturer or as the case may be, the indenter shall follow the ethical criteria for medical drug promotion as given in Schedule G.

(12) The manufacturer or, as the case may be, the indentor shall supply the information in relation to safety, efficacy, production, quality, or availability of the drugs as and when required by the Registration Board with a view to ensure safety, efficacy or quality of the drug, and

CHAPTER IV ADVERTISING OF DRUGS, Etc.

31. Conditions for Advertising: (1) The Federal Government may, after seeking advice of the Committee on Advertising, allow the advertisement of a drug, or any substance or a remedy as specified in Schedule D-1 or a treatment or offer of a treatment for any disease. approve the contents of such advertisement and specify conditions subject to which such advertisement shall be made:

Provided that the Federal Government may, if in its opinion the public interest so required, withdraw the approval granted to any advertisement or modify or alter any condition subject to which the advertisement was approved.

(1-A) An application for advertisement of any drug, substance, remedy, treatment or offer of treatment for any disease shall be made in Form-8, addressed to the Secretary of the Commissioner on Advertising and there shall be made a separate application for each advertisement.

(1-B) An application under sub-rule (1-A) shall be accompanied by the proper fee specified in Schedule F : and

(1-C) The approval of the advertisement, granted under sub-rule (1), shall be valid for a period of two years only.

(2) A drug or any substance referred to in clause (ii) of Sec. 24 may be advertised to the medical, pharmaceutical and allied professions, without referring to the Federal Government, through medical representatives or through professional journals and publication which are meant for circulation exclusively amongst the members of the medical, pharmaceutical and allied professions .

Provided that:

- (i) one copy of each issue of such journal or publication is sent to the Drug Administration of the Health Division; and
- (ii) the Federal Government may, after giving an opportunity of being heard, prohibit the publication of any advertisement in any such journal as it is found to violate any of the conditions specified under sub-rule (1).

(3) Advertisements under sub-rule (2) shall be subjected to the following conditions, namely :--

- (i) All claims shall be made in accordance with those approved for registration of that drug.
- (ii) Where the usual information on indications and dosage is provided, that advertisement material shall contain information on contra-indications, side effects and other necessary precautions as may be applicable.

(4) A drug or any substance referred to in clause (ii) of Section 24, may be advertised through Press without reference to the Federal Government if it is merely intended to inform the public of the availability or the price of such drug or any substance referred to in clause (ii) of Section 24 subject to the condition that the Federal Government may prohibit such advertisement if, in its opinion, the public interest so requires.

(5) A drug or any substance referred to in clause (ii) of Section 24, may be advertised to the medical, pharmaceutical and allied professions through a documentary film.

(6) No advertisement under this rule shall contain any direct or indirect comparison in any way with any other drug or substance or remedy for any disease for the purpose of attracting customers or with a view to discredit other such product.

(7) Advertisement material shall be presented with courtesy and good taste and words and phrases implying urgency, uniqueness or such expressions which are absolute in character, such as "the most

potent", "the most rapid", "the most efficacious", or which make exaggerated claims or to general claims, such as "effective in all cases" or "effective against all complaints" or superlatives shall be avoided.

(8) Advertisement of a drug or any substance referred to in clause (ii) of Section 24 shall include such information or any risks and other precautions as may be necessary for the protection of public health, and in the case of drug also its maximum retail price fixed under Section 12.

(9) No drug or any other substance shall be advertised in a manner which encourages self-medication or use to the extent that it endangers health.

(10) No drug or any remedy, treatment or after treatment of any disease specified in Schedule 'E' shall be advertised except as provided in sub-rule (2).

(11) Reminder publications for the medical, pharmaceutical and allied professions shall include the name of the drug and its exact composition, the price, the name and address of the manufacturer and a statement to the effect that "Full information is available on request".

32. Sampling of drugs: Samples of drugs may be provided to the physicians or dentists or Pharmacists or Veterinarians or a medical institution in a reasonable quantity and in reduced packings marked with the words "Physicians Sample Not for Sale".

33. Expenditure on advertisement: No person shall spend more than five per cent of his turnover on advertisement, sampling and other promotional activities in respect of drugs,

Explanation: The expenditure on pay and allowances of the field force connected with the promotional activities shall not be included in expenditure for the purpose of this rule.

34. Substances required to be prescribed under Section 24: Any substance or a mixture of substances offered for sale which is injurious, or likely to become hazardous, to the health of a person shall be deemed to be a substance for the purpose of Section 24 of the Ordinance.

35. Retailer's discount: The retailers discount shall be 15% of the maximum retail price.

SCHEDULE A

[See rule 2 (e)]

Form 1

[See rule 5 (/)]

**APPLICATION FORM GRANT OF A LICENCE TO MANUFACTURE BY WAY OF
FORMULATION/BASIC MANUFACTURE/SEMI-BASIC MANUFACTURE/REPACKING**

I/Weofhereby apply for the grant of a licence to manufacture by way of.....on premises situated at

2. The drug(s) or class(es) of drugs intended to be manufactured :-

- (1) Class(es) of drugs.
- (2) Dosage form(s) of drugs.
- (3) Name of the drug(s).

3. I enclose :-

(i) Particulars regarding the legal status of the applicant (i.e. in case of proprietorship the names) of proprietors and their address (es), in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).

(ii) Details of the premises including layout plan of the factory.

(iii) Details of the section-wise equipment and machinery for manufacture and quality control.

(iv) Names and qualifications of the Production Incharge and Quality Control Incharge for supervising manufacturing processes and Quality Control Department, and other technical staff working in these departments.

4. The premises and plan will be ready for inspection or are ready for inspection.

Dated.....

Signed.....

Place.....

Name, designation and address

PROFORMA
DETAILS OF THE FIRM

Name of the CompanyType of ownership (Partnership, Proprietorship, Public limited, Private limited, etc.)

Name(s) of Proprietor(s)/Director(s)/Partner(s).

Date of Establishment.

Initial investment (and details of equity shares).

Present investment (and details of equity shares).

Profit and loss statement as per audited accounts for the last five years :

<u>Year</u>	Investment Turnover	Profit before tax	Percentage 1% before tax for Central Research Fund	percentage of Profit	
			Calculated Paid	investment	Turnover

Note: Copies of balance sheets to be enclosed with the application for renewal only"; and

(6) in. Schedule B, in paragraph (2), in clause (k), for the semi colon and word"; and" a colon shall be substituted and thereafter the following proviso shall be inserted, namely:

Provided that the conditions of location may be relaxed by the Board in suitable cases for grant or renewal or a licence subject to such conditions as it may deem fit, if the surroundings and the premises, in the opinion of the Board, are satisfactory for the intended manufacture.

FORM 1-A
[See rule (5(l))]
APPLICATION FORM FOR RENEWAL OF A LICENCE TO MANUFACTURE DRUGS BY WAY OF FORMULATION/BASIC MANUFACTURE/SEMI-BASIC MANUFACTURE/REPACKING

I/We of hereby apply for the renewal of a licence to manufacture by way of on premises situated at

2. The drug(s) or class(es) of drugs intended to be continued to be manufactured:-

- (i) Class(es) of drugs.
- (ii) Dosage form(s) of drugs.
- (iii) Name of the drug(s) registered/approved.

3. There have been/have not been any change in respect of

- (i) Name of the proprietor/directors/partner(s)
- (ii) Details of the premises including layout plan of the factory.
- (iii) Details of the section-wise equipment and machinery for manufacture and quality control.
- (iv) Names and qualifications of the Production Incharge and Quality Control Incharge for supervision of manufacturing processes and Quality Control Departments, and other technical staff working in these departments

4. Statement of the Central Research Fund.

Attested copies of the last two income tax assessment orders of the Income Tax Department attached.

Following statement, as per audited accounts/based on Income Tax Return for the last five years:-

Year	Investment	Turn-over	CRF due	C R F paid as per Col. 4
1	2	3	4	5

Date

Signed.....

Place

Name, designation and address of the signatory

Note:-Strike off which is not applicable

FORM 2
[See rule 7] GOVERNMENT OF PAKISTAN
Licence to Manufacture

is/are hereby licensed to manufacture by way of Basic Manufacture/Semi Basic manufacture/Formulation/Repacking at the following premises:-

2. This licence permits the manufacture of

3. This licence shall, in addition to the conditions specified in the rules made under the Drugs Ordinance/Act, 1976, be subject to the following conditions namely:-

(i) The licence will be in force for a period of five years from the date of issue unless earlier suspended or cancelled.

(ii) The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the products manufactured under this licence, subject to the conditions applicable to licences for sale.

(iii) Name of the approved expert staff.

.....
.....

.....
.....

Date of issue

Secretary, Central Licensing
Board.

(Seal)

Chairman, Central Licensing
Board.

FORM 2A
(See rules 19 and 30)
Warranty under Section 23(I)(i) of the Drugs Act, 1976

I.....being a person resident in Pakistan, carrying on business at (full address)
under the name of.....(and being an importer/indenter/authorised agent of), do
hereby give this warranty that the drugs here-under described as sold/indented by me/specified and
contained in the bill of sale, invoice, bill of lading or other document describing the goods referred to
herein do not contravene in any way the provisions of section 23 of the Drugs Act, 1976.

Dated

(Signed)

1. Name(s) of the drug(s):

Batch number(s)

(i)
(ii)

2. Description of bill of sale, invoice, bill of lading or other document (if any).

Signed

FORM 3
[See rule 21(l)]
APPLICATION FOR LICENCE TO MANUFACTURE DRUG(S) FOR EXPERIMENTAL PURPOSES.

I/We of hereby apply for a licence to manufacture drug(s) specified below for experimental purposes at and I/We undertake to comply with the conditions applicable to the licence under rule 22 of the Drugs (Licensing, Registering and Advertising) Rules, 1976.

1. Name and quantity of drug(s) to be manufactured for the said purposes:.

Signature.....
Name
Address
Countersigned by

FORM 4
[See rule 21(3)]
LICENCE TO MANUFACTURE DRUG(S)
FOR EXPERIMENTAL PURPOSES

Mr./Messrs of is/are hereby licensed to manufacture the drug(s) specified below for experimental purposes at :. or at such other place(s) at the. Central Licensing Board may from time to time permit.

2. The licence is subject to the conditions prescribed in rule 22 of the Drugs (Licensing, Registering and Advertising) Rules, 1976, and such other conditions as may be subsequently prescribed or Specified by the Central Licensing Board in this behalf.

3. This licence shall unless previously suspended or cancelled be in force for a period of two years from the date specified below:-

Name of drugs with quantity to be manufactured.

Date:.....
Place:.....

Licensing Authority.

FORM 5
[See rule 26(l)]

APPLICATION FORM FOR REGISTRATION OF A DRUG FOR LOCAL MANUFACTURE

I/we.....ofhereby apply for registration of the drug namelydetails of which are enclosed.

Date

Place

ENCLOSURE OF THE APPLICATION FOR REGISTRATION OF A DRUG

1. Name and address of the manufacturer ·
- 2, Name of drug ·
 - (a) Generic/international non-proprietary name:
 - (b) Proprietary name, if any:
- 3 Name under which drug is proposed to be sold
4. Dosage form of the drug:
5. Composition of the drug, stating quantity of each active and non-active ingredient(s) per unit or as a percent age of total formulation :
6. Proposed dosage :
 - (a) for adults.
 - (b) children by age group.
 - (c) infant
 - (d) special groups.
7. Main Pharmacological group to which the drug belongs:
8. Pharmacological and clinical data :
 - (a) recommended clinical use and the claims to be made for the drug.
 - (b) contra-indications.
 - (c) toxicity or the side-effects.
 - (d) any directions for the use to be included in the labelling, warning and precautions in use : symptoms of over dosage should be given alongwith the treatment including antidotes, where required.
9. Proposed route of administration.
10. Description of the method of manufacture and quality control with details of the equipment.
11. Specifications, with details of analytical procedure for each ingredient and the finished drugs (not required in case of a drug for which pharmacopocial standards recognised under the Drugs Act, 1976, are claimed).

12. Bio-availability, Bio-equivalence and Pharmacokinetics Analysis (For Dosage Form Introducing first time in Pakistan).

13. Stability Summary :

(a) A complete description of and date derived from studies on the stability of new drug, including information pertaining to the suitability of the analytical methods used

(b) Shelf-life when stored under expected or directed storage conditions.

(c) Recommended storage conditions and expiration date to be assigned to the specific formulation and package..

(d) Extreme Temperature Fluctuations Study for all liquid and semi-solid preparations. (Such observations should be utilized for appropriate labelled storage conditions or warning statements).

(e) Type of container/package, with the nature of material, package testing (chemical, mechanical, environmental).

14. Labelling : Specimen or draft with colour scheme, alongwith the undertaking to refrain from counterfeiting shall also be submitted.

15. Pack size (s) and proposed maximum retail price with the following details:-

(i) Cost per retail pack of each active and non-active. Ingredients :

(ii) Cost of each packing material.

(iii) Cost of direct labour,

16. Justification : (Only in case of a new entity).

17. Patent number, if any, with date and its date of expiry.

18. In case of a new drug (entity) not yet registered in Pakistan :

(i) enclose certificate of registration and Free Sale from any of the following countries: Japan, USA and European Company Member countries.

(ii) Any other relevant information that may be required by the Board for consideration of this application.

FORM -5(A)
[See rule 26 (1)]
APPLICATION FORM FOR REGISTRATION OF AN IMPORTED DRUG

I/Weofhereby apply for registration of the drug,
namely.....details of which are enclosed.

Date
Place

Signed.....

ENCLOSURES OF THE APPLICATION FOR REGISTRATION OF A DRUG

1. Name, address and status of the applicant:
2. Name and address of the manufacturer:
3. Name of the drug:
 - (a) Generic international non-proprietary name:
 - (b) Proprietary name, if any:
4. Name of drug, under which it is proposed to be sold:
5. Dosage form of the drug:
6. Composition of the drug stating quantity of each active and non-active ingredients per unit dose or percentage of total formulation:
7. Proposed dosage:
 - (a) for adults.
 - (b) children by age group.
 - (c) infants.
 - (d) special groups,
8. Main Pharmacological group to which the drug belongs:
9. Proposed route of administration:
10. Pharmacological and clinical data :
 - (a) recommended clinical use and the claim to be made for the drug.
 - (b) contra-indications.
 - (c) toxicity or the side-effects.
 - (d) any directions for. use to be included in the labelling warnings and precautions in use: symptoms of overdosage should be given alongwith the treatment including antidotes where required.
11. Specifications with details of analytical procedure (not required in case of a drug for which the pharmacopocial standards recognised under the Drugs Act, 1976 are claimed):
12. Bio-availability studies:
13. Stability studies :
14. Proposed shelf life with storage conditions, if any :

15 Type of container :

16. Labelling : (Specimen to be enclosed alongwith a .sample and undertaking to refrain from counterfeiting shall also be submitted) :

17. Proposed C and F and maximum retail price (in case of imported drug) :

18. Justification :

19. Certificate regarding sale and G.M.P. in the country of origin (in English and in Form 5 (c) :

20. Certificate of registration by F.D.A. of USA. Committee on Safety of Medicines of U.K. or corresponding agencies of France, West Germany, Japan, Sweden. and Denmark.

21. Patent number, if any, with date and its date of expiry :

22. Undertaking to manufacture drug locally within two years. If it is not possible, the reasons therefor.

FORM-5B
[See rule 26(3A)]
APPLICATION FORM FOR RENEWAL OF REGISTRATION OF ALL KINDS OF DRUGS

I/We of hereby apply for renewal of registration of the drug, namelydetails of which are as follows ·

1. Name and address of the manufacturer:
2. Name and address of the agent or indentor in case of imported drug -
3. Whether the drug is registered for local manufacture or import ·
4. Name of the registered drug, with its registration number and date or initial ,registration and last renewal '
5. Changes, if any, in information furnished at the time of initial registration or last renewal
6. If withdrawn from the market anywhere ·
 - (i) Country.
 - (ii) Reasons thereof.

Place.....

Signature

Date.....

Name, and address of the signatory

FORM-5C
TO WHOM IT MAY CONCERN CERTIFICATE OF DRUGS REGISTERED UNDER
THE DRUGS ACT, 1976

Name and dosage form of product

Name and amount of each active ingredient

.....

Manufacturer and or when applicable the person responsible for Placing the Product on the market

..... Address(es).....

It is certified :

* This product has been authorised to be place of the market for use in this country.

*Number of Registration and date of issue if plicable.

*This product has not been authorised to be placed on the market for use in this country for the following reason-

.....

.....

.....

.....

It is also certified that (a) the manufacturing plant in which the product is produced is subject in inspections at suitable intervals, and (b) the manufacturer conforms to requirements for good practices in the manufacture and quality control, in respect of products to be sold or distributed within the country of origin or to be exported.

(Signature of designated authority

(Place and date)

FORM 6
[See rules 28 and 29(4)]
GOVERNMENT OF PAKISTAN
CERTIFICATE OF REGISTRATION

Certified that following drug(s) are hereby registered under the Drugs Ordinance/Act, 1976:-

Name of Drug(s).

Name of Manufacturer.

Name of Indenter/Manufacturer's agent/Importer (in case of imported drugs only).

2. This registration shall be valid for a period of five years unless earlier suspended or cancelled.

3. This registration is subject to the conditions specified in the Drugs Ordinance/Act, 1976, and .the rules thereunder and to the conditions specified in the enclosure.

Date of Registration Secretary
Registration Board

(Seal)

Chairman. Registration Board

FORM 7
[See rule 30(6)]
STATEMENT SHOWING QUARTERLY PRODUCTION TO BE SUBMITTED IN DUPLICATE

Name of drug. _____

Pharmacological group _____

Name of the Firm. _____

Address. _____

For the quarter ending. _____

Pack size.	No. of Pack	Total quantity in terms of individual units e.g., total No. of tablets, injections tubes litres etc.	
1	2	3	
VALUE (in Rs.)		Details of Disposal	
On trade price	On retail price	Indicate whether supplied through normal distribution, channels or exported or supplied to any specific institution.	Value of raw materials used (Active & inactive) (in Rs.)
4	5	6	7

Total.

SCHEDULE B

CONDITIONS FOR GRANT OF A LICENSE TO MANUFACTURE BY WAY OF FORMULATION

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<p><u>4. Storage Areas</u> 4.1 Capacity 4.2 Design 4.3 Bays 4.4 Quarantine 4.5 Sampling 4.6 Rejected Materials 4.7 Special Materials 4.8 Packaging Materials 4.9 Weighing Area</p>
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SCHEDULE B-I
[See rule 16 (6) (b)]

REQUIREMENTS OF PLANT AND EQUIPMENT

(A) The following equipment is required for the manufacture of drugs for external appliances or suspense:

- (1) Mixing tanks where applicable:
- (2) Kettles, steam, gas or electrically heated.
- (3) A suitable power driven mixer.
- (4) Storage tanks or pots.
- (5) A colloid mill or a suitable emulsifier or homogeniser, where applicable.
- (6) A triple-roller mill or an ointment mill, where applicable.
- (7) Liquid filling equipment.
- (8) Jar or tube filling equipment, where applicable.

Area of minimum of 200 square feet is required for the basic installation.

(B) The following equipment is required for manufacture of Syrups, Exlixirs and Solutions :--

- (1) Mixing and storage tanks.
- (2) Mixer.
- (3) Filter press or other suitable filtering equipment such as metafilter or sparklet filter or Also-pad filter.
- (4) Water still or Deioniser.
- (5) Various liquid measures and weighing scale.

An area of maximum 300 square feet is required for the basic installations.

(C) Equipment for the manufacture of Pills and Compressed Tablets including Hypodermic Tablets. For efficient operation, the tablet production department shall be divided into the following three distinct and separate sections situated in different rooms,

- (i) Granulating Section;
- (ii) Tableting Section;
- (iii) Coating Section.

The following equipment is required in each of the three sections :-

- 1. Granulating Section:**
- (1) Disintegrator, where applicable.
 - (2) Power Mixer or granulation mixer with stainless steel cabinet
 - (3) Granular
 - (4) Oven thermostatically controlled.

2. Tableting Section:

- (1) Tablet machine, single punch or rotary.
- (2) Pill machine, where applicable.
- (3) Punch and dyes storages cabinet.

The Tableting Section shall be free from dust and floating particles. For this purpose, it is desirable that each tablet machine is connected either to an exhaust system or isolated into cubicles.

3. Coating Section:

- (1) Jacketed kettle, or equivalent steam, gas or electrically heated for preparing solution.
- (2) Coating pan.
- (3) Polishing pan, where applicable,
- (4) Heater and exhaust system, where applicable.

The coating section shall be made dust-free and suitable exhaust provided to remove excess powder and the fumes resulting from solvent evaporation.

A total area of not less than 900 square feet for the three Sections is required for basic installations.

The manufacture of Hypodermic Tablets shall be conducted under aseptic conditions in a separate air-conditioned room, the walls of which shall be smooth and washable. The granulation, tableting and packing shall be done in this room.

(D) The following equipment is required for the manufacture of Powders :--

- (1) Disintegrator, where applicable.
- (2) Mixer.
- (3) Sifter or sieve.
- (4) Stainless steel vessels and scoops of suitable material,
- (5) Filling equipment,

In the case of operations involving floating particles of fine powder or dust a suitable exhaust system shall be provided, Workers shall be provided with suitable marks during operation.

If a manufacturer has a tablet section where the powder of the granules can be manufactured, provided that such granules or powder are non-toxic, no separate equipment will be required for manufacture of such powder as granules.

(E) The following equipment is required for filling of Hard Gelatin Capsules:-

- (1) Mixing and blending equipment.

- (2) Capsule filling units.

An area of minimum of 200 square feet is required for the basic installations. The room shall be air-conditioned and also dehumidified wherever necessary.

(F) The following equipment is required for the manufacture of Surgical Dressings other than Absorbent Cotton Wool

- (1) Rolling machine.
- (2) Trimming machine.
- (3) Cutting equipment.
- (4) Folding and pressing machine for gauze.
- (5) Mixing tanks for processing medicated dressings.
- (6) Hot air drying ovens.
- (7) Steam steriliser or dry heat steriliser.

An area of minimum of 300 square feet is required for the basic installations. In case medicated dressings are to be manufactured, room with an area of minimum of 300 square feet shall be provided.

(G) The following equipment is required for the manufacture under aseptic conditions of Eye-Ointments, Eye-Drops, Eye-Lotions and other use :-

- (1) Hot air oven electrically heated with thermostatic control.
- (2) Kettle, gas or electrically heated with suitable mixing arrangement.
- (3) Colloid mill or homogeniser.
- (4) Tube filling equipment.
- (5) Mixing and storage tanks of stainless steel or of other suitable material.
- (6) Sintered glass funnel, seitz filter or filter candle.
- (7) Liquid filling equipment.
- (8) Autoclave.

An area of minimum of 250 square feet is required for the basic installation. The manufacture and filling shall be carried out in art air-conditioned room under aseptic conditions. The room shall be further dehumidified if preparations containing antibiotics are manufactured.

(H) The following equipment is required for the manufacture of Pessaries and Suppositories :-

- (1) Mixing and pouring equipment.
- (2) Moulding equipment.

An area of minimum of 200, square feet required far the basic installation,

In case of pessaries manufactured by granulation compression, if the licence does not have a tablet section, a separate area of minimum of 300 squared feet and the following equipment is necessary :--

- (1) Mixer.
- (2) Granulator.
- (3) Drier.
- (4) Compressing machine.
- (5) Pessary and tablet counter.

(I) The following equipment is required for the manufacture of inhalers end Vitralae:

- (1) Mixing equipment.
- (2) Graduated delivery equipment for measurement of the medicament.
- (3) Sealing equipment,

An area of minimum of 200 square feet is required for the basic installations.

(J) The following equipment is required for the repacking installation of drugs and Pharmaceutical Chemicals

- (1) Sifter.
- (2) Stainless steel scoops end vessels.
- (3) Weighing and measuring equipment.
- (4) Filling equipment.

An area of minimum of 300 square feet is required for basic packing operations. In the case of operations involving floating particles of fine powder or dust, a suitable exhaust system should be provided.

(K) Requirements for the manufacture of Parenteral Preparations: The whole process of the manufacture of parenteral preparations may be divided into the following separate operations:

(a) Preparations of the container: This includes, cutting. washing, drying sterilisation of ampoules or vials prior to

(b) Preparation of solution: This includes preparation and filtration of solution.

(c) Filling and sealing: This includes filling and sealing of ampoules or filling and capping of vials.

(d) Sterilisation.

(e) Testing,

The following basic hygienic requirement shall be complied with

- (1) Strict sanitation shall be maintained throughout the entire plant in order to prevent contamination and to keep out pyrogens, Masks and overalls shall be worn wherever necessary.
- (2) The preparation room where the solution is prepared shall be of such a nature that may be kept scrupulously clean. This room shall be air-conditioned.
- (3) The filling and sealing rooms shall likewise be air-conditioned under positive pressure with air locks provided to prevent the entry of air from outside. The walls and floor shall be such as may permit their being sprayed and washed with an antiseptic solution. The benches shall preferably have stainless steel or laminated plastic tops capable of being washed.
- (4) In the room provided for aseptic filling and sealing, necessary measures for maintaining sterility and to preventing contamination shall be adopted.
- (5) A separate room shall be provided for sterilisation, testing (for leaks and floating particles) and drying.
- (6) Finished products shall be stored in a suitable separate place.

The following equipment required :-

Manufacturing Area :

- (1) Storage equipment for ampoules and vials
- (2) Ampoule washing and drying equipment.
- (3) Dust proof storage Cabinets.
- (4) Water still.
- (5) Mixing and preparation tanks or other containers. The tanks or containers shall be made of either glass or such material which will not react with the liquid
- (6) Filtering equipments such as filter press or sintered glass funnel.
- (7) Autoclave,
- (8) Hot Air Steriliser,

Filling and Sealing Room:

- (9) Benches for filling and sealing.
- (10) Filling and sealing unit

Aseptic Filling and sealing room:

- (11) Bacteriological filters such as Seitz filter, candles or sintered glass filters,
- (12) Filling and sealing unit,

General Room:

- (13) Inspection table with draft and light background
- (14) Leak testing equipment.
- (15) Labelling and packing benches,
- (16) Storage equipment including cold storage and refrigerators, if necessary

Note /: The above requirements of this schedule are subject to modifications, at the discretion of the Central Licensing Board if it is of the opinion that having regard to the nature and extent of the manufacturing operations it is necessary to relax or alter in the circumstances of a particular case:

Provided that such variation shall be recorded in writing with reasons therefor and also communicated in writing to the manufacturer for his record,

Note//: This Schedule gives equipment and space required for certain categories of drugs only. There

are, in addition, other categories such as drugs miscellaneous pharmaceuticals such as Ferries Ammonii Citras. Potassium Citras, Glycerin, Paraffin, Oxygen gas, Disinfectant fluids, mechanical contraceptives, surgical cotton and tinctures which are not listed in this Schedule. The Central Licensing Board shall, in respect of such categories of drugs, have the discretion to examine the adequacy or otherwise of factory premises, space, plant, machinery and other requirements having regard to the nature and extent of the manufacture to carry out necessary modifications in them and, on the modification. having been made, approve of the manufacture of such categories of drugs. Any drug so permitted to be manufactured by the Central Licensing. Board shall be deemed to be an additional category of drug for the purpose of this Schedule.

SCHEDULE B I-A.
[See rule 16 (bb)-7]
CONDITIONS OF FACTORY PREMISES

1. Location and surrounding: The premises should be away from drinking water sources and an area liable to flooding.

2. (a) Building: Building should be provided with both good general ventilation and protection against direct sunlight, with easy access for fire-fighting equipment including fire-extinguishers, fire-blankets, .hose, reels and fire-alarm, etc. Sufficient water must be available for fire-fighting.

(b) Walls: Walls as far as possible should be protected by non-flammable or slow burning material.

(c) Doors; Doors must be fire resistant preferably with self-closing system,

(d) Floors: Floors should be impermeable to liquids, smooth and free from cracks. There should be no drains at all in plants and in warehouse. If drains are absolutely necessary they must not contract directly with waterways or public sewers,

(e) Signs: Signs indicating smoking restrictions, location of emergency kits, fire-fighting equipment, telephone and escape routes must be prominently displayed. Local exhaust system must be effective,.

3. Personnel: To void intoxication by skin contact, inhalation of fumes, vapours and dust, accidental ingestion, the protected clothing and equipments, e.g., protective helmet or cloth cap, eye protection (safety spectacles, goggles or face shield) dust or light fume masks, one piece worksuit with closely fitting trouser bottoms, rubber or plastic gloves Or gauntlets, rubber or plastic apron, and workboots with protective toecaps, must be provided.

Staff must not be allowed to go home wearing the same clothing they wore at work; emergency showers and eye washing facilities must be provided in the premises. Safety instructions should be strategically displayed in local language. All emergency and safety equipment must be frequently and regularly checked and maintained to ensure its conditions satisfactory.

4. Medical Services: There must be pre-employment medical; , examination for all staff members whether working permanently or on contract basis. When organophosphates or carbamates are handled, pre-exposure baseline blood cholinesterase level must be determined for all operational staff. Staff regularly engaged in formulation and packing procedures and maintenances must have their cholinesterase levels checked regularly and detailed records must be kept. The checks should be carried .out by a properly equipped hospital or laboratory under qualified expert.

"Levels of cholinesterase activity should be interpreted by a doctor, but the following guide might be helpful :--

(i) A decrease of more than 20% in blood cholinesterase activity,. from the pre-exposure value indicates that the cause should be investigated.

(ii) A decrease of more than 40% in blood cholinesterase activity from the pre-exposure value indicates that the worker concerned should be removed from further exposure to organophosphates or carbamates.

Workers should not be exposed again to cholinesterase inhibiting compounds until further tests show a blood cholinesterase activity within 20% of the pre-exposure value.

SCHEDULE B-II

**GOOD MANUFACTURING PRACTICES (GMPs) FOR LICENCE TO
MANUFACTURE BY WAY OF FORMULATION**

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Eliminate fibers

Checking integrity of filters

Frequency of use of filter

Filter safety

15. Finishing of sterile products

General

Use of vacuum

Inspection of containers

SECTION -- 7

16. Quality control

Sterility testing

Sterility test as the last measures

Monitoring endotoxin

SCHEDULE B-III
[See rule 20 (b)]
PARTICULARS TO BE SHOWN IN MANUFACTURING RECORDS

A. Substances Parenteral preparation in general:

1. Serial Number.
2. Name of the drug.
3. Batch Size,
4. Batch number.
5. Date of commencement of manufacture and date when manufacture was completed,
6. Name of all ingredients, quantities required for the batch size, quantities actually used. (All weighings and measurements shall be checked initiated by the competent person in the section).
7. Control reference numbers in respect of raw materials used in formulation.
8. Date of mixing in case of dry products, e.g., powder, powder mixture for capsule products, etc.
9. Date of granulation wherever applicable.
10. Weight of granules.
11. Date of compression in case of tablets/date of filling in case of capsules.
12. Dates of coating wherever applicable.
13. Records of test to be carried out in case of tablets as under
 - (a) Average weight every thirty minutes.
 - (b) Disintegration time as often as practicable.
14. Records of readings taken to check weight variation in case of capsules,
15. Reference to Analytical Report number stating whether of standard quality or otherwise.
16. Records on the disposal of rejected batches and batches with-drawn from the market.
17. Actual production and packing particulars indicating the size and quantity of finished packings,
18. Date of release of finished packings for distribution or sale,
19. in case of Hypodermic tablets and ophthalmic preparations which are required to be manufactured under aseptic conditions, records shall be maintained indicating the precautions taken during the process of manufacture to ensure that aseptic conditions are maintained,
20. Signature of the expert staff responsible for the manufacture,

B. Parenteral preparation:

1. Serial Number,
2. Name of the drug,
3. Batch Size,
4. Batch number (if bulk lot is divided into various batches and processed separately, a batch number distinctly different from that of the bulk lot should be assigned to each of the processed batch),

5. Date of commencement of manufacture and date of completion.
6. Name of all ingredients, quantities required for the lot size, quantities actually used. (All weighings and measurements shall be checked and initialled by the competent person in the section).
7. Control reference numbers in respect of raw materials used.
8. PH of the solution wherever applicable.
9. Date and methods of filtration.
10. Sterility test reference on bulk batch wherever applicable. (If bulk lot is divided into various batches and processed separately, a batch number distinctly different from that of the bulk lot should be assigned to each of the processed batch.
11. Date of filling.
12. Records of tests employed :--
 - (a) To ensure that sealed ampules are leak-proof,
 - (b) To check the presence of foreign particles.
 - (c) For pyrogens wherever applicable.
13. Records of sterilisation in case of parenteral preparation which are heat sterilised including particulars of time temperature and pressure employed.
14. Number and size of containers filed and number rejected.
15. Reference to Analytical Report numbers stating whether of standard quality or otherwise.
16. Records of the disposal of rejected batch and batches with-drawn from the market.
17. Actual production and packing particulars.
18. Date of release finished packings for distribution or sale.
19. Particulars regarding the precautions taken during manufacture to ensure that aseptic conditions are maintained.
20. Control reference numbers in respect of the lot of glass containers used for filling.
21. Signature of the expert staff responsible for manufacture.

II. RECORDS OF RAW MATERIALS

Records in respect of each raw material shall be maintained indicating the quantity received, control reference numbers, the quantities issued from time to time, the names and batch Nos. of the products for the manufacture of which the quantities have been issued and the particulars relating to the proper disposal of the stocks.

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 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) Any other tests.
 - (g) Results of assay.

Note: Records racer, cling various tests applied (including reading and calculation) should be maintained and necessary reference to these records should .be entered in serial No. 5 whenever necessary.

6. Signature of the Analyst.

7. Opinion and signature of the approved Analyst.

B. Parenteral Preparations

1. Analytical report number.
2. Name of the sample.
3. Batch number.
4. Date of receipt of sample.
5. Number of containers filled.
6. Number of container packed
7. Protocols of tests applied
 - (a) Clarity,
 - (b) PH wherever applicable,
 - (c) Identification.
 - (d) Volume in container,
 - (e) Sterility--(/) Bulk sample wherever applicable (ii) container sample.
 - (f) Pyrogen test, wherever applicable.
 - (g) Toxicity test, wherever applicable.
 - (h) Any other teats.
 - (i) Results of assay.

Note: Records regarding various tests applied (including readings and calculations) should be maintained and necessary reference to these records should be entered in Serial No.7. wherever necessary

8. Signature of the Analyst.

9, Opinion and signature of the approved Analyst Pyrogen Tests:-

1. Test Report number.
2. Name of the sample.
3. Batch number.
4. Number of rabbits used.

5. Weight of each rabbit.
6. Normal temperature of each rabbit.
7. Mean initial temperature of each rabbit,
8. Dose and volume of solution injected into each rabbit and time of injection.
9. Temperature of each rabbit noted at suitable intervals,
10. Maximum temperature.
11. Response.
12. Summed response,
13. Signature of the Analyst,
14. Opinion and signature of the approved Analyst

Toxicity Test:

1. Test Report number.
2. Name of the Sample
- 3, Batch number
4. Number of mice used and weight of each mouse, Strength and volume of the drug injected,
- 6, Date of injection,
7. Results and remarks,
8. Signature of Analyst,
9. Opinion and signature of the approved Analyst.

C. For other drugs:

1. Analytical report number
2. Name of the sample
3. Batch number.

4. Date of receipt of sample
5. Protocols of tests applied:
 - (a) Description.
 - (b) Identification.
 - (c) Any other tests
 - (d). Results of assay.

Note: Particulars regarding various tests applied (including reading and calculations) shall be maintained and necessary reference to these records shall be entered in serial No. 5 wherever necessary.

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

D. Raw materials:

1. Serial number
2. Name of the material

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

Note: Particular regarding various tests applied (including reading and calculations) shall be maintained and necessary reference these records shall be entered in serial No. 6 wherever necessary.

E. Container, packing material, 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 serial No. 6 wherever necessary.

7. Remarks.
8. Signature of the examiner.

Note 1: The foregoing provisions represent the minimum requirements to be complied with by the licensee. The Central Licensing Board may, however, direct the nature of records to be maintained by the licensee for such drugs as are not covered by the categories described in this Schedule.

Note 2: The Central Licensing Board may permit the licensee to maintain records in such manner as are considered satisfactory, provided the basic requirements laid down in the Schedule are complied with.

Note 3: The Central Licensing Board may as its discretion direct the licensee to maintain records for such additional particulars as it may consider necessary in the circumstances of a particular case.

SCHEDULE C

[See rule 16(c) (iii) and (e)]

1. Sera.
2. Solution of serum proteins intended for injuction.
3. Vaccines.
4. Toxins.
5. Antigen.
6. Antitoxins.
7. Insulin.
8. Pituitary (Posterior Lobe) Extract.
9. Sterilized surgical lignature and sterilized surgical suture.
10. Bacteriophages.

SCHEDULE D
[See rule 17(1)]
DRUGS FOR REPACKING

1. Aluminium Hydroxide Gel Dried.
2. Ammonium Bicarbonate.
3. Ammonium Chloride.
4. Ammonium Carbonate.
5. Benzoic Acid.
6. Bismuth Carbonate.
7. Bismuth Subnitrate.
8. Boric Acid.
9. Borax.
10. Caffeine and its Salts.
11. Calamine.
12. Calcium Carbonate.
13. Calcium Lactate.
14. Calcium Gluconate.
15. Calcium Hydroxide.
16. Castor Oil.
17. Cetrimide Powder.
18. Chloral Hydrate.
19. Ephedrine Hydrochloride.
20. Ephedrine Sulphate.
21. Ferrous Sulphate.
22. Ferric Ammonium Citrate.
23. Gentian Violet.
24. Glycerin.
25. Iodine.
26. Ichthammol.
27. Kaolin.
28. Liquid Paraffin Heavy.
29. Magnesium Carbonate.
30. Magnesium Hydroxide.
31. Magnesium Sulphate.
32. Methylene Blue.
33. Magnesium Trisilicate.
34. Methyl Salicylate.

35. Phenothlazine (B. VET. C.).
36. Pix Carb.
37. Potassium Acetate.
38. Potassium Bromide.
39. Potassium Bicarb.
40. Potassium Chloride.
41. Potassium Citrate.
42. Potassium Iodine.
43. Potassium Permanganate.
44. Procaine Hydro-Chloride.
45. Pulv Gentian.
46. Resorcin.
47. Salicylic Acid.
48. Sentonin.
49. Sena.
50. Sodium Benzoate.
51. Sodium Bicarbonate.
52. Sodium Chloride.
53. Sodium Bromide.
54. Sodium Carbonate.
55. Sodium Citrate.
56. Sodium Iodide.
57. Sodium Metabisuphite.
58. Sodium Potassium Tartrate.
59. Sodium Salicylate.
60. Sodium Sulphate.
61. Sodium Thiosulphate.
62. Soft yellow Paraffin.
63. Sulphonilamide Powder (B. VET. C).
64. Sulphur Precipitated.
65. Sulphur Sublime.
66. Tannic Acid.
67. Zinc Oxide.
68. Zinc Sulphate.

SCHEDULE D-I
[See rule (31)1]

Household remedies including--

Analgesics:

Aspirin and Paracetamol in tablets and liquid forms.

(2) Analgesic Balms/Plasters.

(3) Antiseptics and disinfectants for household use, excluding those containing hormone and antineoplastic.

(4) Antidandruff preparations.

(5) Dental preparations.

(6) Antacid and carminatives:

Compound Effervescent Salts, [--] , Milk of Magnesia.

(7)

(8) Contraceptives.

(9) Miscellaneous.

Fish Liver Oil and its equivalents.

SCHEDULE E
[See rule 31 (10)]
**DISEASES, ADVERTISEMENT FOR TREATMENT OF
WHICH IS PROHIBITED**

1. [Omitted vide S.R.O. 871(I)/78, dated 8th July, 1978.]
2. [Omitted vide S.R.O. 871(I)/78, dated 8th July, 1978.]
3. Venereal diseases.
4. Sexual impotence.
5. Amenorrhoea metrorrhagia, metorthagia, metrosalpingitis, ovaritis, fibromas, cysts.
6. Bright's disease, cataract, glaucoma, epilepsy, [..] locomotive ataxia, multiple sclerosis, lupus, paralysis, blindness.
7. Complaints requiring surgical operation (e.g., appendicitis, stomach ulcers, prostatic disorders, hernias, sinusitis, mastoiditis).
8. Serious illness liable to endanger the life of the patient (e.g., pneumonia, pleurisy, abscess of the lungs).
9. Gripe Waters.
10. Cough Preparations.

SCHEDULE F

[See rule 5 (2)]

1. DRUG MANUFACTURING LICENCE FEE

(a) For the grant of licence:

Type of licence	Fee
By way of basic	Rs. 10,000
By way of semi-basic	Rs. 10,000
By way of formulation	Rs. 25,000
By way of repacking	Rs. 15,000

(b) For the renewal of licence

(i) If the application for renewal is made before the expiry of period of validity of licence.

Type of licence	Fee
By way of basic	Rs. 5000
By way of semi-basic	Rs. 5,000
By way of formulation	Rs. 12,500
By way of repacking	Rs. 7,500

(ii) If the application for renewal is made after the expiry of the period of validity of licence but within sixty days after expiry of the period validity:

Type of licence	Fee
By way of basic	Rs. 10,000

By way of semi-basic	Rs. 10,000
By way of formulation	Rs. 25,000
By way of repacking	Rs. 15,000

II. DRUG REGISTRATION FEE
[See rule 26 (3)]

(A) For the grant of Registration	Rs. 5,000
(B) For the renewal of Registration	
(i) if the application for renewal is made before the expiry of the validity of a certificate	Rs. 2,500
(ii) if the application for renewal is made within thirty days after the expiry of the period of validity of a certificate	Rs. 5,000

III. FEE FOR ADVERTISEMENT
[See rule 31 (1A) and (1B)]

Application fee for Advertisement.	Rs. 1,000 per advertisement
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SCHEDULE G

[See rule 30 (11)]

ETHICAL CRITERIA FOR MEDICINAL DRUG PROMOTION

1. Promotion of drugs.- (1) For the purposes of this Schedule, "promotion" means all informational and persuasive activities by manufacturer and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs.

(2) All claims concerning a drug for the purposes of promotion shall be reliable, accurate, truthful; informative, balanced, up to date, capable of substantiation and in good taste. Such claims shall not contain misleading, unverifiable statements, omissions likely to induce medically unjustifiable use of a drug or to give rise to under risks. The word "safe" shall not be used with respect to promotion unless properly qualified. Comparison of products shall be factual, fair and capable of substantiation. Promotional material shall not be designed so as to disguise its real nature.

(3) Scientific data in the public domain shall be made available, on request, to prescribers and any other person entitled to receive it as appropriate to their requirements. Promotion in the form of financial or material benefits shall not be offered to or sought by health care practitioners to influence them in the prescription of drugs.

2. Advertisements in any form made to physicians and health-related professionals.- (1) The wording and illustrations in advertisements to physicians and related health professionals shall be fully consistent with the approved scientific data sheet for the drug concerned or other source of information with similar content. The text shall be fully legible.

(2). While introducing the drug to the physician for the first time in shall contain full product information, on the basis of the approved scientific data sheet or similar document and shall contain, among others, the following information:-

- (a) The generic name(s) of the active ingredient(s);
- (b) the content of active ingredient(s) per dosage form or regimen;
- (c) the generic name(s) of other ingredient(s) known to cause problem(s)
- (d) the approved therapeutic uses;
- (e) dosage form or regimen;
- (f) side-effects and major adverse drug reactions;
- (g) precautions, contra-indications and warnings;
- (h) major interactions;
- (i) the name and address of manufacturer or distributor; [-]
- (j) reference to appropriate scientific literature ; and
- (k) Price of the drug, ; and

(3) Reminder advertisements shall include, amongst others, at least the international non-proprietary name or generic name, the name of each active ingredient and the price of drug and the name and address for the manufacturer or distributor for the purpose of receiving further information.

3. Advertisements in any form to the general public.- (1) Advertisements to the general public, where permissible, shall help people to make rational decisions on the use of drugs determined to be legally available without a prescription. While advertisements shall take account of people's legitimate desire for information regarding their health they shall not take undue advantage of people's concern about their own health. Advertisement shall not generally be permitted for prescription drugs or to promote drugs for certain serious conditions that can be treated only by qualified health practitioners. The scheduled narcotic and psychotropic drugs shall not be advertised to the general public in connection with fight against drug addiction and dependency. Although health education aimed at children is highly desirable, drug advertisements shall not be directed at children. Promotional material shall be factual and claims for cure, prevention or relieve of an ailment shall be made only if this can be substantiated. Advertisements shall also indicate, where applicable, appropriate limitations to the use of the drug.

(2) When lay language is used the information shall be consistent with the approved scientific data or other legally determined scientific basis for approval. Language which brings about fear or distress shall not be used.

(3) Taking into account the media employed, advertisements to the general public may amongst others, contain, the following information:-

- (a) The generic name(s) of the active ingredient(s);
- (b) major indication(s) for use; (S.R.O. 1362(I)/96-28.11.96).
- (c) major precautions, contra-indications and warnings, if any; and
- (d) name of manufacturer or distributor.

4. Information on price to the consumer shall be accurately and honestly portrayed.

4. Medical Representatives.- (1) Medical representatives shall have an appropriate educational background. They shall be adequately trained so as to possess sufficient medical and technical knowledge and integrity to present information on products and carry out other promotional activities in an accurate and responsible manner. Employers shall be responsible for the basic and continuing training of their representatives. The training shall include instructions regarding appropriate ethical conduct taking into consideration the W.H.O. criteria.

(2) Medical representatives shall make available to prescribers and dispensers complete and unbiased information for each product discussed, such as an approved scientific data or other source of information with similar contents.

(3) Employers shall be responsible for the statements and activities of their medical, representatives. Medical representative shall not offer inducements to prescribers and dispensers. Prescribers and dispensers shall not solicit such inducements. In order to avoid over-promotion, the main part of the volume of sales they generate.

5. Free samples of prescription drugs for promotional purposes.- Free samples of drugs may be provided in modest quantities to prescribers, preferably on request.

6. Free samples of non-prescription drugs to the general public for promotional purposes.- There shall be no free sampling of non-prescription drug to the general public for promotional purposes.

7. Symposia and other scientific meetings.- The intimation regarding scientific symposia, seminars, conferences and such meetings where sponsored by a pharmaceutical manufacturer or distributor

shall be clearly communicated in advance. The invitation letter should accurately reflect the presentations and discussions to be held. Entertainment or other hospitality, offered to members of the medical and allied professions shall be secondary to the main purpose of the meeting and shall be kept to a modest level.

8. Post-marketing scientific studies, surveillance and dissemination of information.- (1) The Registration Board shall be made aware of any post-marketing clinical trials for drugs that are conducted and the results thereafter as soon as possible.

(2) Post-marketing scientific studies and surveillance shall not be misused as a disguised form of promotion.

(3) Substantiated information on hazards associated with the drug shall be reported to the Registration Board as a priority.

9. Packaging and labelling.- Appropriate information being important to ensure the rational use of drugs, all packaging and labelling material shall provide information consistent with that approved by the Registration Board and if no such approval is available it shall be, consistent with that approved by the drug regulatory authority of the country from which the drug is imported or other reliable sources of information with similar content. Any wording and illustration on the package and label shall conform to the principles of ethical criteria enunciated in this Schedule.

10. Information for patients contained in package inserts, leaflets and booklets.- (1) Adequate information on the use of drugs shall be made available to the patients where it is necessary for rational use of a drug. In package inserts or leaflets the manufacturers or distributors shall ensure that the information reflected is correct. If package inserts or leaflets are used for promotional purposes, they shall comply with the ethical criteria enunciated in this Schedule. The wording of the package inserts or leaflets, if prepared specially for patients, shall be in lay language subject to the condition that the medical and scientific content is properly reflected.

(2) In addition to approved package inserts and leaflets wherever available the preparation and distribution of booklets and other information material for patients and consumer shall also comply with the ethical criteria enunciated in this schedule.

[No. F. 8-1/90--AU (Vol-11.)]

DR. F.R.Y. FAZLI,

Deputy Director General (Pharmacy)/Drugs Controller.

(S.R.O. 1362(I)/96 28.11.1997)