REGISTERED No. M - 302
L.-7646

The Gazette of Pakistan

EXTRAORDINARY
PUBLISHED BY AUTHORITY

ISLAMABAD, WEDNESDAY, MARCH 5, 2014

PART II

Statutory Notifications (S.R.O.)

GOVERNMENT OF PAKISTAN

MINISTRY OF NATIONAL HEALTH REGULATION SERVICES AND COORDINATION

(Drug Regulatory Authority of Pakistan)

NOTIFICATION

Islamabad, the 4th March, 2014

S.R.O. 152 (I)/2014.—In exercise of the powers conferred by section 23 of the Drug Regulatory Authority of Pakistan Act, 2012 (XXI of 2012), read with clause (a) of section 7 thereof and section 43 of the Drug Act, 1976 (XXXI of 1976), the Drug Regulatory Authority of Pakistan, with the approval of the Federal Government is pleased to direct that the following further amendments shall be made in the Drugs (Licensing, Registering and Advertising) Rules, 1976. The same having been previously published *vide* Notification No. SRO 1086 (I)/2013 dated 2nd January, 2014 as required by sub-section (3) of the section 43, namely:—

In the aforesaid Rules,—

(1) for rule 20A, the following shall be substituted, namely:—

"20A. **Contract manufacture.**—(1) Manufacture or analysis on contract is permissible on behalf of a licensee or of a licensed

Price : Rs. 5.00

[4226(2014)/Ex. Gaz.]

pharmaceutical company whose products are registered for sale in Pakistan or as may be registered by the Registration Board and for the purposes including the following categories, namely:—

(a) for encouraging local production of imported drugs;

(b) for meeting export requirements of a local manufacturer or a foreign pharmaceutical company, provided that a drug manufactured under this arrangement shall not be sold in Pakistan; and

(c) as a special case and for genuine reasons, including break down, renovation, up-gradation, as may be determined by the Registration Board, provided that the contract manufacturing under this clause shall be for a period not exceeding thirty months;

(2) The provisions of sub-rule (1) shall be subject to the following conditions, namely:—

(a) The Provisions of rule 29 *mutatis mutandis* apply;

(b) Contract manufacturing shall be allowed only on the basis of similar category of drugs including human to human, veterinary to veterinary, cotton to cotton, medical devices to medical devices or as the case may be, etc;

(c) Contract manufacturing of controlled drugs (narcotic drug or psychotropic substances or precursor chemicals) shall not be allowed;

(d) Contract manufacturing shall also be subject to the conditions laid down in Schedule-H."; and

(2) for Schedule-G, the following shall be substituted, namely:-

"SCHEDULE H

1. **Contract production and analysis.—**

1.1. Contract of manufacture or analysis shall be undertaken only by a manufacturer that holds a valid drug manufacturing licence 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 mis-understandings that could result in a product or work or analysis of un-satisfactory quality.

1.3. All arrangements for contract manufacture and analysis, including any proposed changes in technical or other arrangements, shall be in accordance with the regulation in force and condition of registration of the drug concerned if it is for sale in Pakistan. In case of a foreign pharmaceutical company getting its products manufactured in Pakistan the manufacturing specification shall be the responsibility of the contract giver however a copy of such specifications shall be provided to the Registration Board for the purpose of information.

1.4. There must be a written contract (drawn by the people having suitable knowledge in pharmaceutical technology, analysis and cGMP requirements) between the contract giver and the contract acceptor that shall clearly establish the duties of each party. The quality management system of contract giver must clearly state responsibilities and the way in which the authorized person of each party 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 Registration Board.

1.5. The contract shall have explicit provision for auditing the facilities of the contract acceptor and contract giver at any time to ensure that manufacturing or analysis of contracted products are being done as per specifications and the contract.

1.6. In the case of contract analysis, final approval for release must be given by the authorized persons.

2. **Contract giver.-**

2.1 The contract giver before submission of application for contract manufacturing permission shall be responsible for assessing the legality, suitability and competence of the contract acceptor in successfully carrying out the work or tests required and for ensuring that the principles of good manufacturing practices are followed. This assessment report shall be a part of contract manufacturing or analysis application submitted to the Registration Board.

2.2 Upon receiving of contract manufacturing or analysis application, the Registration Board may cause to inspect the manufacturing or analysis facility of contract acceptor by a panel of experts as determined by the Board to verify the report submitted by contract giver, evaluation of cGMP compliance for manufacturing, quality control, validation, stability and storage facilities of both contract giver and contract acceptor etc.

2.3 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. Contract giver shall ultimately be responsible to ensure that processes are in place and complied with during contract manufacturing period and will inform Registration Board in case of any breach of any facility of the contract.

2.4 The contract giver shall ensure that all processed products and materials delivered by the contract acceptor comply with their specifications and that the product has been released by the authorized persons.

2.5 Contract manufacturing shall be allowed for five registered products per section as approved by the Central Licensing Board only up to maximum thirty products, on part of contract giver, excluding drugs registered for export purpose.

3. **Contract acceptor.-**

3.1 The contract acceptor must have adequate premises, equipment, knowledge, facilities, experience and competent personnel to carry out satisfactorily the work ordered by the contract giver.

3.2 The contract acceptor shall not pass to a third party any of the work entrusted to him under the contract without the written consent of the contract giver 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.

3.3 The contract acceptor shall refrain from making any change outside the terms of the contract or any activity that may adversely affect the quality of the product manufactured, packed and analyzed for the contract giver.

3.4 Any change required in manufacturing process, raw or packaging material by the contract acceptor shall be made through a change control mechanism approved by both contract giver and acceptor and properly validated through required processes like stability testing, validation etc. before the product is produced after change and is released for sale.

3.5 Contract acceptor is responsible for keeping the record of production and analysis. Both the contract giver and the contract acceptor shall retain sufficient number of samples of each batch to allow double testing of product, till the expiry of the product for reference. The record shall be made accessible to the contract giver or Registration Board or any other investigating agency etc. at all times for the purpose of compliance to law.

3.6 Contract manufacturer shall submit details of production of each batch of drug manufactured under contract on Form-7 to the Registration Board quarterly, as required by Drugs (Licensing, Registering and Advertising) Rules, 1976.

3.7 In case of change of source of raw material and machinery by the contract manufacturer, proper validation and stability study shall be conducted and recorded for cGMP compliance.

4. **The contract.-**

4.1 A contract shall be drawn up between the contract giver and contract acceptor that specify 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 having suitable knowledge in pharmaceutical technology, analysis and good manufacturing practices. All arrangements for production and analysis must be in accordance with the registration or marketing authorization in country of origin in case of foreign pharmaceutical company 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 clearly describe the person responsible for knowledge management, technology transfer, quality, supply chain, purchasing, testing and releasing of materials (active and inactive) and for undertaking production and quality controls, including in-process controls, and the person responsible 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. Contract shall also clearly describe the mechanism for any change in all of the above responsibilities.

4.4 The contract shall clearly specify the mechanism for keeping of record pertaining to manufacturing, analytical, sale and reference samples by contract acceptor. It shall also specify the availability of the aforementioned record and samples to the contract giver (the samples if required shall be other than the retention samples). All records pertaining to the contract manufactured product will be accessible for assessing the quality of a product in the event of a complaint or a suspected defect. Recall procedure must be clearly mentioned, if required.

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.

4.6 The contract shall include an SOP for pharmacovigilance and the responsibilities of both parties in case of any Adverse Drug Reaction (ADR) and reporting of the same to the Drug Regulatory Authority of Pakistan.

4.7 The SOP for recall of defective products shall also be part of the contract that clearly defines the responsibilities of both parties and a comprehensive recall procedure.

5. **Miscellaneous.-**

5.1 The specifications for drugs shall be in accordance with the Drugs (Specification) Rules, 1978.

5.2 Fee for contract manufacturing permission will be fifty thousand rupees per product. However, in order to promote export, fee will be twenty thousand rupees per product for grant of registration for export purpose.

5.3 Contravention to any provision of the Drug Regulatory Authority of Pakistan Act, 2012, Drugs Act, 1976 and rules made there under including Schedule-H, or any condition of registration by the contract giver or contract acceptor shall be liable to the cancellation of contract manufacturing registration by the Registration Board.

5.4 If any drug manufactured on contract basis is found or reported in contravention of any of the provisions of Drugs Act, 1976 and rules made thereunder, then both the contract giver and acceptor shall be liable to any action under the said Act and rules.

5.5 Apart from the labeling requirements as per Drug (Labeling and Packaging) Rules 1986, name, address, and DML number of contract giver (if manufacturer), in case of contract manufactured drugs registered for import, pharmaceutical company name and address of contract giver will also appear on all labels and packaging materials.

5.6 Contract manufactured products registered for export purpose will not be permitted for sale in Pakistan. In case of violation contract manufacturing permission will be withdrawn in addition to other legal proceedings. Moreover exporter will also furnish confirmation about receiving of stock in importing country after export.

5.7 Change of contract manufacturer shall be allowed during contract period only on genuine reasons including *Force Majeure*, the fee for this will be fifty thousand rupees per product. New contract manufacturer shall ensure the stability and validation of the product and all other quality assurance specifications. If the previous contract manufacturer is still manufacturing the drug after change of its status, then it would be treated as spurious drug and would be dealt with under relevant provision of the Drugs Act, 1976 or the Drug Regulatory Authority of Pakistan Act, 2012.".

[F. No.1-13/2013-DDG (Reg-I).]

GHULAM RASOOL DUTANI,
Director (Pharmaceutical Evaluation & Registration),
Drug Regulatory Authority of Pakistan.

PRINTED BY THE MANAGER, PRINTING CORPORATION OF PAKISTAN PRESS, ISLAMABAD.
PUBLISHED BY THE DEPUTY CONTROLLER, STATIONERY AND FORMS, UNIVERSITY ROAD, KARACHI.