No.F.313-DRB/2021 (PE&R)
Government of Pakistan
Ministry of National Health Services, Regulation and Coordination
(Drug Regulatory Authority of Pakistan)
TF Complex Sector G-9/4
****

"SAY NO TO CORRUPTION"

Islamabad, the 29th December, 2021

Subject: - **Good Manufacturing Practices for Pharmaceutical Products.**

I am directed to say that Registration Board in its 313th meeting held on 16th–18th November, 2021 has decided to issue advisory for compliance to GMP in addition to already applicable requirements and guidelines; as follows:-

i. It is preferable to have product development area with requisite facilities for relevant dosage form in each licensed unit endorsed from Central Licensing Board.
ii. Pharmaceutical manufacturers shall ensure that they have valid operational qualification (OQ) and performance qualification (PQ) for already installed manufacturing equipment and shall perform installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) for equipment to be installed within their premises.
iii. Pharmaceutical manufacturers shall ensure to have written procedures and protocols for all activities to be carried out in the licensed premises under the supervision of qualified personnel.
iv. Quality control laboratory should be equipped with necessary equipment required to carry out testing of drug substances and drug products intended to be manufactured within the facility. All tests mentioned in official pharmacopoeia shall be performed as per the pharmacopoeial recommendations without any deviation using the same equipment preferably calibrated from an ISO certified firm and procedure as specified within the latest edition of relevant official pharmacopeia.
v. The drug product manufacturers shall have primary reference standard or secondary reference standards traceable to the primary standards, and the potency of any working standard shall be verified using the primary or secondary standard.
vi. For all compendial as well as non-compendial drug substances, the drug product manufacturer shall perform analytical method verification studies including specificity, accuracy and repeatability (method precision) etc.
vii. For drug products with non-compendial methods, the drug product manufacturers shall develop the method keeping in view the recommendations and tests specified in general monographs of the official pharmacopoeia and validate the analytical method as per ICH guidelines/pharmacopoeial requirements.
viii. For the drug products for which officially recognized compendial methods are available, the drug product manufacturer shall perform verification studies which shall include a demonstration of specificity, repeatability (method precision), accuracy etc.
ix. Adequate facilities for microbiological testing to comply the requirements of official pharmacopeia for all type of drug substances, drug products being manufactured within the facility and for the area monitoring, where required.
x. Adequate systems for vendor qualification for purchase of materials including Active Pharmaceutical Ingredient (API)/Drug Substance (DS), excipients and other materials through authorised sources. Active Pharmaceutical Ingredient (API)/Drug Substance shall be procured from pharmaceutical manufacturers having valid Drug Manufacturing License (DML)/Good Manufacturing Practices (GMP) certificate issued by concerned regulatory authority of country of origin.
xi. Adequate water treatment facility to ensure that water used in manufacturing, testing operations etc. of all drug products is of required quality.

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xii. Suitable Heating, Ventilation, and Air Conditioning (HVAC) system along with proper controls to ensure environment monitoring and to avoid cross contamination.

xiii. Manufacturers shall perform product development studies including pharmaceutical equivalence, comparative dissolution profile (where applicable, preferably using dissolution apparatus with 12 basket assembly) against the innovator / reference drug product as approved by reference regulatory authorities. In case where the innovator/reference drug product is not available in Pakistan, the manufacturer shall get approval from QA&LT Division for import of innovator / reference drug product as per Drugs (Import & Export) Rules, 1976. The Board further advised QA&LT Division, DRAP to permit import of innovator or reference drug product on priority for performing aforementioned studies.

xiv. Preferable to have 21 CFR compliant High-performance liquid chromatography (HPLC) system with enabled audit trail report system. Such systems need to be reviewed and audited during regulatory inspection by QA&LT/Licensing/PE&R Divisions and the details of such system along with its model including information whether gradient or isocratic, 21 CFR compliance status, audit trail report etc. should be made part of the inspection report.

xv. Adequate number of stability chambers with digital data logger for temperature and humidity monitoring along-with backup power supply for conducting accelerated as well as real time stability studies of their products (real time stability for already registered drug products and both real time & accelerated stability studies for trial products). The stability chambers should be reviewed and reported during regulatory inspections by QA&LT/Licensing/PE&R Divisions.

2. Registration Board further advised that auditors/panels of DRAP during various regulatory inspections of QA&LT/Licensing/PE&R Divisions review these points and record them accordingly in their reports.

3. Accordingly, above decision of Registration Board is hereby circulated for compliance of all relevant stakeholders.

29/12/21

(Sayyad Hussain Khan)
Additional Director (PE&R)/
Secretary, Registration Board

Distribution:

i. Chairman, Pakistan Pharmaceutical Manufacturer's Association, Islamabad.
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