National Pharmaceutical Control Bureau (NPCB)
Ministry of Health
MALAYSIA

Berita Ubat-ubatan
NEWSLETTER OF THE DRUG CONTROL AUTHORITY MALAYSIA

CLASSIFICATION OF GMP NON-CONFORMITIES

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In tune with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) requirements, a system to classify GMP non-conformities into 3 different categories, namely critical, major and minor have been introduced and implemented recently.

Non-conformities identified during a recent routine GMP inspection carried out by the National Pharmaceutical Control Bureau (NPCB) on a pharmaceutical manufacturing premises producing both sterile and non-sterile products were categorized accordingly as critical, major and minor. Consequently, the Drug Control Authority (DCA) has taken punitive action by temporarily suspending the Manufacturing License of the factory based on these non-conformities. A summary of the categorized non-conformities is presented as follows:

Critical Non-conformities

- Key production personnel do not understand the concept of white and black areas. Personnel move freely, as they like.
- Penicillin raw material kept without proper segregation in general store.
- Quality of water used for production not properly monitored and not according to procedures.
- Product complaints not dealt with appropriately. No corrective nor preventive actions taken.
- Poor label control.
- Overall tablet processing not properly monitored and controlled. Critical parameters neglected.
- Training for sterile production personnel did not include critical aspects and techniques.
- No planned preventive maintenance programme for equipment used for sterile production.
- Laminar air-flow cabinet could not fit the ampoule filling machine and filling process exposed to external environment.
- No written procedures for treatment and sanitation of water, operation for dry heat sterilizer, sampling of packaging materials, intermediates, bulk and finished products.
- No bioburden testing carried out on raw materials.
- Sterilization process controls not suitable and incomplete.
- No records of sterility test.
- Validation data not satisfactory.
- Calibration of laboratory equipment not done.
- Suitability of dissolution testing equipment never carried out.
- Records for standardization of reference substances incomplete.
- Not all tests on raw materials conducted.
- IPQC tests not carried out consistently.
- Results of IPQC tests used for finished products.

Major Non-conformities

- Emergency door in the non-sterile area not well-maintained and not effective.
- Washing area in the blending room very dirty and poorly maintained.
- Motorcycle kept in raw material store.
- No records to evaluate the effectiveness of UV treatment to determine quality of water.
- Deactivation of penicillin residual waste not properly carried out.
- No corrective actions taken on reports of internal quality audits.

- No duty lists documented for key personnel.
- Effectiveness of GMP training program not conducted.
- No log books for crucial equipment.
- Time interval from filling to sterilization of bulk product not specified.
- Maintenance work carried out on sterile production equipment not recorded.
- No written procedures for maintenance of major equipment used in sterile production.
- No action taken against a low temperature reading during sterilization of ampoules using a dry heat sterilizer.
- Laboratory safety facilities incomplete.
- Organization chart for company and quality control different.
- Records of standardization and handling of reference substances incomplete.
- Tests done on reference substances not complete.
- Actual results on tests carried out not stated.
- No procedure for sampling of samples for IPQC.
- Tests and calculations carried out not according to procedure.
- Format used for stability studies incomplete.
- Actual stability tests reports not satisfactorily recorded.
- Frequency and tests carried out not according to stability guidelines and not satisfactory.
- Limits and specifications used for stability tests not specified.
- Stability information submitted for product registration different from actual practice.

Minor non-conformities

- Lay-out plan for production area not updated.
- Soap container and sink for washing hands in the Change Room found to be dirty.
- Rooms used for several activities labelled differently.
- No status labels for clean machines and equipment.
- Functions of Quality Assurance not clear.
- Organization chart not updated.
- Documents have many typographical errors, scribbling and incomplete.
- Laboratory personnel lack training.
- No calibration schedule for laboratory equipment.