Pakistan Journal of Pharmaceutical Sciences
Vol. 8(1), January 1995, pp.63.67

SHORT COMMUNICATION

GUIDELINES TO GOOD MANUFACTURING PRACTICES (G.M.P.) IN PHARMACEUTICAL MANUFACTURING

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The object of the GMP and associated rules is the assurance of the quality of the products for the safety, well being and protection of the patient. In achieving this aim it is impossible to over-emphasis the importance of people, at all levels, in the assurance of the quality of medicinal products. The great majority of reported defective medicinal products has resulted *from* human error or carelessness and not from failure in technology. All the people involved with the production, quality control or distribution of medicinal products, whether key personnel, production or quality control staff, inspectors or other involved in the many activities which lead to a patient taking a medicine, should bear this constantly in mind when performing their duties.

Quality Assurance is a wide ranging concept which, in case of drugs, extends from research and development through manufacturing and quality control, storage and distribution, dispensing and patient's use and which covers all matters which individually or collectively influence the quality of a product. All aspects of quality assurance are important and none more so than manufacturing and quality control which, if carried out incorrectly, can result in deviation from the product design specification. Pharmaceutical manufacturers and the Licensing Authority have a duty to assure the general public that patients are properly protected and that the drug products meet appropriate requirement of safety, quality and efficacy. To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance, incorporating Good Manufacturing Practice and thus quality control. It should be fully documented and its effectiveness monitored. All parts of Quality Assurance system should be adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities. The attainment of this quality objective is the responsibility of the senior management and requires the participation and commitment by staff in many department and at all levels with in the company, the company's suppliers and the distributors. The legal framework is provided by the Government under the Drugs Act, 1976 and rules framed their under and by subsequent statutory instructions. All the drugs for human and veterinary use manufactured or imported into

the country, including the drugs intended for export should be manufactured in accordance with the Drugs Act, 1976 and the principles of GMP.

The principle of GMP should primarily concern personnel, premises, equipment, documentation, production, quality control, complaints, product recall and self inspection. The basic concept of quality assurance, good manufacturing practice and quality control are inter-related. Ultimately the quality and safety of a product depends on the application of appropriate procedures based on GMP leading to a product with in the recognised specification. Standard procedures and recognised specifications cannot be divorced.

The GMP stresses the underlying principle relating to manufacturing and quality control practices, properly designed premises, validated processes, trained personnel, effective storage and distribution and overlying all of these an orderly system of working and documentary procedures. The GMP is concerned with both production and quality control and all personnel should be aware of the principles of GMP that affects them and receive initial or continuing training including hygiene instruction, relevant to their needs. Following points should be given due consideration:

1. All the manufacturing methods, processes and procedures should be well-defined and reviewed regularly in the light of scientific and technical progress and should undergo periodic critical re-validation to ensure that they remain capable of achieving the intended results. Production operations, including the handling of material such as receipt and quarantine, sampling, storage, labeling, dispensing, processing, packaging and distribution must be clearly defined and documented in order to obtain products of the requisite quality.

2. The manufacturer should have sufficient number of competent and appropriately qualified personnel to achieve the pharmaceutical quality assurance objective(s), and they should receive initial and continuing training including the theory and application of the concept of quality assurance and GMP and its practical effectiveness should be periodically assessed.

3. Layout, design and operation must aim to minimize the risk of error and permit effective cleaning and maintenance in order to avoid contamination, cross contamination, build up of dust or dirt and in general any adverse effect on the quality of the product. Lighting, temperature, humidity and ventilation should be appropriate and such that they do not adversely affect the storage or accurate functioning of the equipments.

4. Good documentation constitutes an essential part of the quality assurance system. Proper documentation, free from errors, based upon specifications, manufacturing formulae and processing and packaging instructions, procedure and records covering the various manufacturing operations, sampling programmes, analytical test methods and appropriate specification for ingredients, printed and unprinted packaging components and finished dosage forms, be kept and updated accordingly. The legibility of the documents is of paramount importance.

5. Production operations should be carried out according to the pre- established procedures and instructions and in such a way as to ensure that the drug products conforms with the standards of strength, quality, purity and all such operations be inaccordance with the Good Manufacturing Practice. Checks on yields and reconciliation of quantities should be carried out as necessary to en-sure that there arc no discrepancies outside acceptable limits.

6. Manufacturing processes should be regularly and critically revalidated to ensure that they remain capable of achieving the intended results. Any new or important modification in the manufacturing process should be validated Validation studies should reinforce Good Manufacturing Practice and be conducted in accordance with defined procedures. Results and conclusions should be recorded.

7. All possible and appropriate technical and/or organizational measure should be taken to avoid any possibility of contamination and cross contaminations including mix-ups. Operations on different products should not be carried out simultaneously or consecutively in the same room unless there is no risk of mix-up or cross-contamination. Access to production premises should be restricted to authorised personnel and should not be used as right of way. Measure to prevent cross-contamination and their effectiveness should be checked periodically ac-cording to set procedures.

8. An effective pharmaceutical quality assurance system be implemented involving the active participation of the management. Adequately equipped and properly (appropriately) staffed independent quality control department having the required qualification and technical knowledge of the subject including the authority in relation to quality control and being independent from all other department in exercise of that authority should be established for carrying out the necessary examination and testing of starting material, packaging material, intermediates and the finished product.

9. The quality control department, before release for sale or distribution of finished products, should takes into accounts in addition to the analytical results:
   (a) the condition of production
   (b) the result of in-process controls
   (c) the examination of manufacturing documents, and
   (d) the conformity of products to specification.

10. A system for recording and reviewing complaints in relation to registered products manufactured or assembled (in case of contract manufacturing) together with an effective system of recalling promptly and effectively products known or suspected to he defective from the market, sale, distribution network, supply or exportation be implemented. The complaint should be properly investigated and defect which could result in a recall of the drug be also reported to the licensing authority. The effectiveness of the arrangements for recalls should be evaluated from time to time.

11. Rejected materials and products should be clearly marked as such and stored separately in restricted areas. They should either be returned to the suppliers or where appropriate, reprocessed or destroyed. The action taken should be recorded. Reprocessing should be exceptional and permitted only if the quality of the final products is not affected. Where any doubt arises over the quality of the product, it should not be considered suitable for re-issue or re-use, although basic chemical re-processing to recover active ingredient may be possible. Any action taken should be appropriately recorded.

12. Self inspection should be conducted periodically in an independent and detailed *way* by designated competent person(s) in order to monitor the implementation and compliance with GMP principle and to propose necessary corrective measures. All self inspections should be recorded. Reports should contain all the observation made during the inspection and, where applicable, proposals for corrective measures. Actions taken subsequently should also be recorded.

References

Chemical Stability of Pharamaceuticals, Kenneth A. Connors, Gordon L. Amidon and Valentino J. Stella, 2nd Edn., 1986, JohnWiley & Sons, Inc. New York.

Good Manufacturing Practices for Pharmaceuticals 1982, Vol.16, Sidney H. Willig, Murray M. Tuckerman, William S. Hitchings, 2nd Edn., Marcel Dekker, Inc., New York.

Pharmaceutical Practices, Edited by Diana M. Collett, Michael E. Aultion 1910, Churchill Livingstone, UK.

Pharmaceutical Process Validation 1984, Edited by Bernard T. Lotus, Robert A. Nash, Mercel Dekker, Inc. Vol.23, New York.

Process Validation for Solid Dosage Forms, Pharmaceutical Technology, 1989.

Role of Product and Process Design in Assuring Quality, Good Manufacturing Practices Conference 1982, Cherry Hill, New Jersey.

Rule and Guidance for Pharmaceutical Manufacturers 1993, London.

Sterility Testing and Sterility Testing of Pharmaceutical Preparations and Biological Substances 1980, World Health Organisation, Geneva, Switzerland.

The Drugs Act 1976, Drugs (Licensing Registering and Advertising) Rules 1976, Pakistan.