EDITORIAL

QUALITY ASSURANCE OF PHARMACEUTICAL PRODUCTS

Quality Assurance (QA) in the pharmacy context refers to the total sum of all those processes that are necessary to ensure the drug product is of good quality, effective and safe up to the point it is administered to the patient within its stated shelf-life. It involves several aspects which broadly fall into four categories.

The first aspect of QA involves registration of the drug product prior to marketing in the recipient country. A dossier containing all relevant information on the product is submitted and evaluated by a committee of experts representing different specialities. Information sought includes evidence of quality, safety and efficacy. QA measures must meet internationally accepted standards as defined in such compendia as European Pharmacopoeia, British Pharmacopoeia, US Pharmacopoeia etc. Stability data to support recommended shelf life must be submitted. The stability data to be presented must focus on physical characteristics of the finished product (colour, friability, viscosity, non-sedimentation etc.) disintegration and dissolution profiles; amount of active ingredients and absence of degradation products. Both accelerated data (40 ˚C, RH 75%) for 6 months and actual shelf life data (25 ˚C, RH 60%) are acceptable, but the latter is considered more useful. For certain products (eye and parenteral preparations) the sterility within the stated shelf-life must be confirmed. Other information includes evidence of registration in country of origin and other countries where quality assurance measures are enforced. The World Health Organization (WHO) certificate regarding the origin of the drug is considered valuable as it confirms that GMP is enforced by the manufacturer. The requirements are very comprehensive and demanding and therefore help to weed out those manufacturers/importers who do not comply with registration requirements.

The second aspect of QA is evidence of Good Manufacturing Practice (GMP), which must focus on the standard of raw material, the manufacturing facility, the in-house production and control measures, packaging, storage, quality control of finished product, qualifications and competence of personnel. In earlier years emphasis had been on analysis of finished product, but later in the 1970s emphasis shifted to GMP.

The third aspect of QA is the quality control of finished product. Although the manufacturer of a drug product is expected to carry out analysis of the product as part of GMP, it is necessary for such results to be validated by an independent and reputable laboratory. Tests include confirmation of label specifications, dissolution rates, and limit tests for contaminants and degradation products. For a generic product, the innovator product serves as point of reference. For antibiotics, chemical assay serves a limited purpose and the antimicrobial assay is preferable. For generic drugs, bioequivalence studies are considered mandatory. The development of immunoassay analytical techniques in the 1970s made it possible to assay blood concentration of drugs in the nanogram range and hence monitor blood concentration profiles more accurately. Other simple laboratory models such as the ‘inverted rabbit ileum’ have been found useful in ascertaining the bioavailabity of drug.

The fourth aspect of QA is pharmacosurveillance (post marketing surveillance) of drug products. Despite all the precautionally measures taken to ensure a safe and effective product, there are some unpredictable variables which could impact negatively as the product moves along the supply line from the manufacturer, wholesaler, retailer/hospital and eventually the patient. Real time stability data often determined at 25 – 30 °C, do not take into account extreme variation in temperature and humidity particularly in the tropics as the drug moves along the supply chain. It is not uncommon to find precipitation in solutions or caking in suspensions due to physical or chemical changes in the product. It is also possible for the drug to interact with containers (cations, antioxidants preservatives, etc) leading to

accelerated deterioration. The cost of pharmacosurveillance is high and few countries are able to monitor the quality of drugs in the market effectively.

Quality assurance measures have progressively improved over the past 30 years but more needs to be done. Pharmaceutical manufacturers are not charitable organizations and the cost of QA is passed on to the patient. This argument is often invoked by transnational pharmaceutical manufacturers to justify the high price of their products as compared to those of small companies. There are minor differences especially in labelling requirements and generally dissemination of information. Recently the European Community (EC) countries decided that the drugs literature insert should be directed to the patient, rather than the prescriber. The main reason is that a literature insert is not necessary to a prescriber because he does not handle products. Adoption of international conventions, preferably under World Health Organization would minimize discrepancies in QA requirements. At all stages of QA it is important to remember Murphy's Law which states, "Whatever can go wrong, will go wrong." This need not be the case if proper attention is given.

Editor-in-Chief