



Ensuring the quality of medicines through Post Marketing surveillance

Medicinal products including drugs, vaccines and biologicals are necessary to maintain and promote better health. Maintaining good quality of drugs from manufacturing to the point of administration to patients requires collaboration and commitment of several stakeholders and continuous good practices in the manufacturing distribution, storage, dispensing and administration of drugs. Therefore regulatory agencies, pharmaceutical manufacturers, traders, wholesalers, distributors, pharmacists, health care professionals and patients all have a unique role in ensuring quality and safety of medicines.

The Bureau of Food and Drugs (BFAD) is the national regulatory agency that oversees the registration of all medicinal products and licensing of the manufacturers, distributors, retailers handling them, to ensure the efficacy, safety and quality of all marketed medicines.

BFAD also conducts Post-Marketing Surveillance (PMS) of all marketed drug products to ensure that their quality is maintained (quality monitoring) and to monitor their ongoing safety (adverse drug reaction monitoring or pharmacovigilance) to be able to assess benefits and harm associated with the use of marketed medicines. Pharmacovigilance is necessary, because clinical trials that are used to establish efficacy and safety of drugs before registration of a product cannot accurately detect all potential harmful effects of a drug. PMS involves the active, systematic and scientifically valid collection, analysis and interpretation of data and other information about marketed drugs to continually assess benefits and harm associated with their use and to take regulatory action when harm outweigh the benefits.

Drug products in the market are regularly sampled by BFAD and validated for their quality to ensure that they conform to the approved labels and standards. Manufacturer's inspection conducted by BFAD is also an important activity for PMS to ensure maintenance of standards for productions of good quality medicines. Current Good Manufacturing Practice (GMP) requirements for manufacturing of medicines have been in place since 1999 as determined by Administrative Order No. 43 of BFAD. GMP requirements command that manufacturers and packagers of drugs take proactive steps to ensure that their products are safe, pure, and effective. GMP regulations require a quality approach to manufacturing, enabling companies to minimize or eliminate instances of contamination, mix-ups, and errors that may lead to manufacturing of sub-standard or poor quality drugs. This in turn, protects the patients from purchasing a product which is not effective or even dangerous. GMP inspections can be initiated by BFAD at any time. Other violations of the

company/ product in terms of compliance to regulations are also considered during Post Market Surveillance.

Drug products are also continually monitored for their possible health risks and adverse effects via BFAD's adverse drug reaction reporting program. Alerts from consumers, patients, health professionals and other national drug regulatory agencies or international bodies like the World Health Organization are considered in regulatory actions that are necessary to ensure the safety of Filipinos.

The Goal of the PMS system of BFAD

The main objective of the PMS is to reduce public health risks associated with the safety, efficacy and quality of marketed drug products. This objective is achieved through the shared responsibility of the regulatory agency, the Bureau of Food and Drugs (BFAD), and the marketing authorization holder. With this objective in mind, the BFAD is guided by the following specific points:

1. Use results-driven, risk-based approaches to develop and implement strategies to increase industry compliance with regulations and conformance with good practices.
2. Utilize science-based surveillance programs and strategic problem-solving to identify, evaluate, and prioritize risk related to drug safety, efficacy and quality.
3. Use both surveillance and strategic problem-solving expertise to develop and support innovative compliance and risk reduction activities

Focused Product Monitoring

With its limited resources and the protection to health risks, the Bureau aims to focus on and give priority to the different activities of the Post-Marketing Surveillance such as market monitoring, audit and inspection, strategic sampling and inspection, improved drug quality reporting system, and product recalls.

Market Monitoring

Before granting a market authorization to a new drug, the aspect of safety, efficacy and quality are studied and reviewed by BFAD to ensure the maximum safety of the drug. In some cases, however,

this cannot be achieved through scientific evaluation of the clinical trials submitted in the application. It may be necessary to conduct continuous surveillance of the newly marketed drug so as to vigilantly monitor its safety. New drugs have a high probability of unforeseen health risks because their safety profiles are limited to results of clinical trials. Other drugs may also be monitored for unexpected health risks. The BFAD always and immediately notify or advise the public on the risks posed by the drugs under investigation.

Audit and Inspection

The BFAD and the industry shall have the shared responsibility for consumer safety and satisfaction. The manufacturer is responsible for guaranteeing the safety, efficacy and quality of drug products and ensuring that the products are manufactured in accordance with current Good Manufacturing Practices (cGMP).

The following factors will warrant inspection of manufacturing establishment:

1. Market information and feedback from consumers
2. BFAD's surveillance and compliance activities, and
3. Type and risk level of products

The BFAD shall also review the following documents that may provide additional information so as to manage the risks:

1. Assure the authenticity and accuracy of data submitted in the applications
2. Compliance with full pharmacopeial requirements/ Technical specifications
3. Microbial contamination
4. Limits of impurities/ toxic heavy metals
5. Adherence to requirements for tamper-resistant packaging
6. Stability studies – real time and accelerated
7. Labeling and packaging

Changes in manufacturing procedures, ingredients or equipment must be fully disclosed whenever there will be investigations concerning the drug product.

The Bureau is planning to implement GMP audit on graveyard shifts which will strengthen the assurance of the products manufactured in the company regardless of shifts.

Strategic Product Sampling and Testing

Regular routine sampling and testing shall be reinforced to make it a proactive PMS activity. Risk based assessment shall be applied on sampling surveillance. Sampling of products that has a higher risk shall be prioritized. Sampling from all channels of the marketing chain shall also be considered. Adulteration, misbranding, drug-related complaint, adverse event, labeling and packaging issues will also be considered as triggers for BFAD PMS-initiated sampling.

The BFAD Central Office shall test the products for compliance with official pharmaceutical standards or with specifications set by the product manufacturer.

Drug Quality Reporting System

Drugs quality reporting is essential in BFAD as it encourages consumers and health care professionals to voluntarily report observed or suspected defects or quality problems with marketed drug products. This will assist BFAD to rapidly identify significant health hazards and areas or trends requiring corrective and/or preventive action. Reports received from consumers and health professionals shall be collated, analyzed, prioritized and forwarded to the PMS Task force and other divisions (if needed) for investigation and appropriate action.

Product Recall

Post-marketing surveillance plays an important part in the action of product recall. BFAD Bureau Circular No. 08 s. 2001 sets the guidelines to be observed on the recall of all types of regulated products from the market. Recalls are actions taken to remove a product from the market. These may be ordered by BFAD or are voluntary actions on the part of the manufacturers and distributors to carry out their responsibility to protect the public health and well-being from products that present risk of injury or gross deception or are otherwise deceptive. The nature and extent of risk shall also in accordance with implementing product recall classification.

BFAD's responsibility in product recall

BFAD shall notify the public on all recall actions through Public Health Alerts. It shall also review recall status reports during the recall and set reporting intervals about the firm's accomplishments during the recall. Based on also on the recall status report, it shall communicate risk information to health care professionals and the public.

Products which have been subject of a recall must immediately be removed from the market and must not be allowed for distribution and sale. Upon completion of the recall procedure, the concerned company shall notify BFAD of the final disposition of the product. Such activities may include labeling changes on the product, reprocessing of the returned products or destruction of the returned products which shall be witnessed by a BFAD representative.

Minimizing risk maximizing safety

BFAD's role doesn't end when products are approved for sale. Equally important to protecting the health of Filipinos is BFAD's work to monitor the safety, efficacy

and quality of health products after they have reached the marketplace. This post-market surveillance is essential to maintaining the balance between the health benefits and risks posed by all health products. Within BFAD, post-market surveillance activities are the responsibility of the PMS Taskforce. The ADR unit first collects and reviews health-product safety data, conducts risk assessments and evaluates therapeutic effectiveness of marketed health products. The available data shall be forwarded to the PMS Taskforce. The PMS Taskforce works collaboratively with other BFAD divisions to perform post-market surveillance. Should a health product's safety, efficacy or quality come into question, PMS Taskforce will take appropriate action ranging from informing the public and health care community of new product safety information, to removing the product from the market. Appropriate advisories and notices shall be created by the PMS Taskforce as appropriate.

Challenges for BFAD

In spite of the initiatives being undertaken by BFAD, there is a continuing challenge for the agency to ensure public health by monitoring the safety, efficacy and quality of registered products which are on the market.

1. As a consequence of the opportunities provided by the private sector and the opening of foreign markets to Filipino professionals the BFAD's human resources which is its most vital asset has been dwindling. Records reveal that at present, there are only 24 BFAD FDRO Drug Inspectors and 118 Regional FDROs. All these are tasked to effectively inspect and monitor 35, 000 establishments.
2. The laboratory support service of BFAD needs to be strengthened. BFAD is routinely tasked to test samples of products given market authorizations. As of now, there are 20,000 drug products registered in BFAD. Sampling of these registered products are carried out routinely and tested to ensure their consistency in conforming to set standards.
3. The BFAD as the national drug regulatory agency has to ensure adherence by manufacturers to all licensing provisions and specifically to GMP. More specifically Administrative Order No. 43 s. 1999 states "*license to manufacture drugs shall be issued upon compliance to*

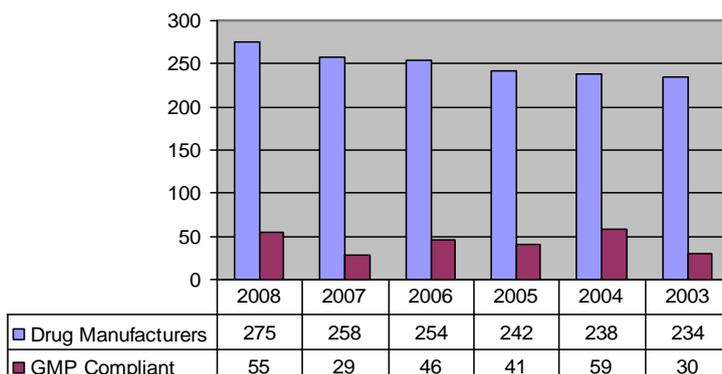
current good manufacturing practice guidelines". Statistical records reveal the following:

4. Continuous public assurance on the quality of all medicines due to the foreseen deluge of submission of applications for registration of drug products
5. Effective mechanism for collecting and investigating product quality defects.

Strategies to assure quality medicines

BFAD should be abreast with emerging knowledge, standards, and technologies. BFAD functions should be strengthened in monitoring health products that are still for clinical studies and health products that have already been granted market authorization to ensure their long-term safety and usage. The post market surveillance capability of BFAD should match the growth of the products it regulates. Listed below are several strategies identified by BFAD to assure quality of medicines in the country:

1. Utilize a risk-based sample surveillance approach to select products for analysis that have the greatest risk of quality problems and/or health impact. Surveillance of newly marketed products shall be enhanced and intensified.
2. Promote compliance with cGMP by providing capacity building to the industry to conform to ASEAN/ international standards
3. Review and revise existing regulations on multisource pharmaceutical products to conform with WHO guidelines on registration requirements to establish interchangeability
4. Centralized reporting system for marketed drug quality problems
5. Improvement and operationalization of the Cebu and Davao Satellite Laboratories
6. Strengthen communications and working relationships with the field offices, investigators and other stakeholders
7. Increase transparency through public disclosure of information on drug quality from the BFAD website (www.bfad.gov.ph)



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