a 50922

WHO/PHARM/96.588
ORIGINAL: ENGLISH
DISTR.: LIMITED

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

GOOD MANUFACTURING PRACTICES:

Authorized Person - the role, functions and training

This text does not constitute additional requirements in the area of GMP. It is offered with the view to assist manufacturers wishing to strengthen their Quality Assurance systems. Reference to ISO standards of 9000 series are relevant primarily to manufacturers, that are not in a position to immediately implement in full GMP requirements. The reason for this may be the lack of resources or a limited involvement in contractual manufacturing/testing of drugs. For such manufacturers/testing laboratories the implementation of Quality Systems along the lines of ISO standard will be one step in the right direction. Manufacturers fully complying with GMP requirements may wish to adopt on a voluntary basis certain elements found in ISO standards of 9000 series, e.g. quality manuals. Nothing in this text may be interpreted as a suggestion that drug manufacturers need external certification under ISO standards.

We would appreciate your views and comments to be mailed to Quality Assurance, Division of Drug Management & Policies, World Health Organization, 1211 Geneva 27, Switzerland, Fax: (0041 22) 791 07 46, or e-mail: schmidm@who.ch, by 31 January 1997 at the latest.

The WHO GMP guide defines the Authorized Person as a person (among key personnel of a manufacturing establishment) responsible for the release of batches of finished products for sale. In some other GMP guides and legal texts a term Qualified Person is used to describe analogous functions. In particular, according to the European Community Directives and other documents, the Qualified Person is responsible for securing that each batch of proprietary medicinal product has been manufactured and checked in compliance with the laws in force in that Member State and in accordance with the requirements of the marketing authorization.

The role and position of the Authorized Person in the company

The Authorized Person as the overall quality controller is responsible for the quality function, which includes the following major areas:

- implementation (and when needed - establishment) of the quality system;
- participation in the development of the company's Quality Manual;
- supervision of the regular functioning of the internal audits or self-inspections;
- oversight of the Quality Control department;
- participation in external audit (vendor audit);
- participation in validation programmes.

Whilst the Authorized Person may not have line management responsibility for many activities within this function (although he/she should be involved in these activities as much as possible), he or she has to be aware of any changes that may affect compliance with technical or regulatory requirements related to the quality of finished products. When there is any aspect of the company's operations which is not in accordance with GMP guidelines or relevant legislation in force, the Authorized Person has a duty to bring this to the attention of Senior Management. This duty should be reflected in the Authorized Person job description.

The availability of an Authorized Person should be a prerequisite for the issuance of a manufacturing licence (authorization). The name(s) of the Authorized Person(s) (as well as names of persons responsible for Production and Quality Control) should appear on the licence. The licence holder should have an obligation to immediately inform the Drug regulatory authority (DRA) or other responsible authority depending on national (regional) regulations, if the Authorized Person is replaced unexpectedly. Such provisions will assure to a considerable degree the independence of the Authorized Person from the management of the company in the fulfilment of his/her duties even when under undue pressure to depart from professional and technical standards.

As it is indicated in the WHO GMP guide, in certain countries, depending on the national legislation or regulations, two Authorized Persons are designated: one for Production and another for Quality Control department. Moreover, a company may have either a complex structure, or operate at several locations, or both. Sometimes a separate Authorized Person may be designated who is responsible for the manufacture of clinical trials materials. Consequently it may be necessary to nominate several Authorized Persons, one of them having responsibilities of the overall quality controller and other responsible for site or branch operations. The person authorizing batch release should be independent from production activities, as far as possible, unless batch release is a joint responsibility between Authorized Persons from the production and quality control functions.

The DRA should approve the Authorized Person on the basis of his/her professional curriculum vitae. Authorized Persons have duties not only to their employer but also to the competent authorities such as DRA. They should establish good working relations with inspectors and as far as possible provide information on request during site inspections.

It must be recognized that the Authorized Person depends upon many of his/her working colleagues for the achievement of quality objectives. It is therefore of paramount importance that he or she establish and maintain a very good working relationship with other persons in position of responsibility, especially with persons responsible for production and quality control.

Implementation of the Quality System

The Authorized Person has a personal and professional responsibility for ensuring that each batch of finished products has been manufactured in accordance with the marketing authorization, GMP rules and all related legal and administrative provisions. This does not necessarily mean that he/she must himself/herself have directly supervised all manufacturing and quality control operations. The Authorized Person must be satisfied either directly or, more usually, by proper operation of quality systems that manufacturing and testing has complied with all relevant requirements. Therefore it is recommended for the successful functioning of the Authorized Person that the manufacturer establishes and maintains a comprehensive quality system, covering all aspects of GMP.

A useful reference material, in addition to rules and regulations on GMP, may be International Standards ISO 9000 family (9000-9004). These standards describe quality systems requirements that can be used for external quality assurance purposes. The important element of these documents is a quality manual, describing the quality policy and objectives (commitment to quality) of the company, the organizational structure, responsibilities and authorities together with the description of or references to documented quality system procedures.

An important aspect of a comprehensive quality system, not covered by GMP guides, concerns R&D activities and transfer of results of the developmental work to routine manufacture. In the pharmaceutical industry this includes original product design, formulation, processes development and validation and preparation of medicinal products for use in clinical trials. It is of vital importance that the quality of routine production batches corresponds to a specification derived from the composition of development batches. The quality and safety of a pharmaceutical product depends on the application of appropriate procedures based on GMP leading to a product within the recognized specification. Standard procedures and recognized specifications cannot be divorced.

Routine duties of an Authorized Person

Before approving a batch for release the Authorized Person doing so should always ensure that the following requirements have been met:

- The Marketing Authorization and the Manufacturing Authorization requirements for the product have been met for the batch concerned.
- The principles and guidelines of Good Manufacturing Practices as laid down in the WHO GMP guide have been followed.
- The principal manufacturing and testing processes have been validated.
- All the necessary checks and tests have been performed and account taken of the production conditions and manufacturing records.
- Any planned changes or deviations in manufacturing or quality control have been notified in accordance with a well defined reporting system before any product is released. Such changes may need notification to and approval by the Drug Regulatory Authority.
- Any additional sampling, inspection, tests and checks have been carried out or initiated, as appropriate, to cover planed changes and deviations.

- All necessary production and quality control documentation has been completed and endorsed by supervisors, trained in appropriate disciplines.
- Appropriate audits, self-inspections and spot-checks are being carried out by experienced and trained staff.
- Approval has been given by the Head of the Quality Control Department.
- All relevant factors have been considered including any not specifically associated with the output batch directly under review (e.g. sub-division of output batches from a common input, factors associated with continuous production runs etc.).

In certain circumstances the Authorized Person may be responsible for the release of intermediates manufactured on contract.

Education and training

The pool of expertise which is drawn upon for persons to fill this position may differ from country to country. Basic qualifications of a scientific education and practical experience for the key personnel, including Authorized Persons, are outlined in the GMP Guide (section 10, "Personnel").

Additional requirements may include subjects such as principles of Quality Assurance and Good Manufacturing Practices, principles of Good Laboratory Practice as applicable to R&D as well as to Quality Control function, detailed knowledge of Authorized/Qualified Person duties and responsibilities, International Standards ISO 9000-9004 and relationships with suppliers, principles and problems of formulation of pharmaceutical preparations, pharmaceutical microbiology, principles and practice of sampling and testing of starting materials, packaging components and finished dosage forms. A more detailed list of issues is given in the Annex.

Selected references

WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-second Report, Annex 1. WHO Technical Report Series 823, 1992.

Second Council Directive on the approximation of provisions laid down by law, regulation of administrative action relating to proprietary medicinal products (75/319/EEC), 1975.

Guide to Good Manufacturing Practice for Medicinal Products. The Rules governing Medicinal Products in the European Community, Volume IV, 1992.

Code of Practice for Qualified Persons. Rules and Guidance for Pharmaceutical Manufacturers. Medicines Control Agency, London, 1993.

International Standard ISO 8402, Quality management and quality assurance - Vocabulary, 1994.

International Standard ISO 9001, Model for quality assurance in design, development, production, installation and servicing, 1994.

International Standard ISO 9004, Quality management and quality system elements, 1994.

International Standard ISO 10013, Guidelines for developing quality manuals, 1995.

* * *