

**GUIDELINES ON THE IMPLEMENTATION OF THE WHO CERTIFICATION SCHEME
ON THE QUALITY OF PHARMACEUTICAL PRODUCTS.**Nidhi S. Ghetiya*, Darshil B. Shah² and Dr. Dilip G. Mahesvari³

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Article Received on 27/05/2016

Article Revised on 18/06/2016

Article Accepted on 09/07/2016

ABSTRACT

To facilitate use of the World Health Organisation (WHO) Certification Scheme, a set of guidelines was developed in 1996, which includes model certificates for use by Member States. Today, the scheme provides transparent information, particularly about the regulatory status of a product in export the country. If used properly, the product certificate and batch certificate can provide a basis for product registration. This article covers the strengths and weaknesses of the scheme.^[1]

KEYWORDS: World health organization; Certificat Scheme; Good Manufacturing practice (GMP); Health Systems and Innovation (HIS); Essential Medicines and Health Products (EMP).

INTRODUCTION

The WHO Essential Medicines and Health Products (EMP) Department works with countries to promote affordable access to quality, safe and effective medicines, vaccines, diagnostics and other medical devices.

Medicines at WHO Headquarters

At WHO headquarters, Essential Medicines and Health Products activities are situated within the Cluster of Health Systems and Innovation (HIS).

Core functions Of WHO

Panel 1-1 summarizes the core functions of WHO in humanitarian response – what is expected of WHO. For each function, WHO is expected to provide leadership and technical guidance so that: (i) all health actors are aware of relevant international standards and best practices in emergency health (including IHR requirements), and (ii) the strategies adopted to address current needs and risks are appropriate.

Typically, this involves

Providing information to MoH and all other health actors on international standards and regulations (including the IHR); providing technical advice and guidance on best practices to MoH and all other health actors in relation to current and potential health problems and service provision; and working with MoH and all other health actors to (i) agree on the most appropriate strategies to address current problems and risks, and (ii) develop an overall health sector response plan.^[2]

WHO's program for primary health care comprises eight essential elements:

1. Education concerning prevalent health problems and the methods of preventing and controlling them;
2. Promotion of food supply and proper nutrition;
3. Maintenance of an adequate supply of safe water and basic sanitation;
4. Provision of maternal and child health care, including family planning;
5. Immunization against the major infectious diseases;
6. Prevention and control of locally endemic diseases;
7. Appropriate treatment of common diseases and injuries; and
8. Provision of essential drugs.

These eight elements were defined in the Declaration of Alma-Ata, which emerged from the International Conference on Primary Health Care, held in Alma-Ata, USSR, in 1978.^[3]

Provisions and objectives

1.1 A comprehensive system of quality assurance must be founded on a reliable system of licensing and independent analysis of the finished product, as well as upon assurance obtained through independent inspection that all manufacturing operations are carried out in conformity with accepted norms, referred to as "good manufacturing practices" (GMP).

1.2 These standards are fully consonant with those operative within the countries participating in the Convention for the Mutual Recognition of Inspection in Respect of the Manufacture of Pharmaceutical Products, and other major industrialized countries. They also

provide the basis for the WHO Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce (referred to henceforth as "the Scheme") recommended initially in resolution WHA22.50.^[1] The Scheme is an administrative instrument that requires each participating Member State, upon application by a commercially interested party, to attest to the competent authority of another participating Member State that:

- A specific product is authorized to be placed on the market within its jurisdiction or, if it is not thus authorized, the reason why that authorization has not been accorded.
- The plant in which it is produced is subject to inspections at suitable intervals to establish that the manufacturer conforms to GMP as recommended by WHO.
- All submitted product information, including labelling, is currently authorized in the certifying country.

Eligibility for participation

2.1 Any Member State intending to participate in the Scheme may do so by notifying the Director-General of the World Health Organization, in writing, of:

- Its willingness to participate in the Scheme;
- Any significant reservations it intends to observe relating to this participation; and
- The name and address of its national drug regulatory authority or other competent authority.

2.2 A Member State may opt to participate solely to control the import of pharmaceutical products and active substances. This intention should be stated explicitly in its notification to the World Health Organization.

2.3 A Member State intending to use the Scheme to support the export of pharmaceutical products should first satisfy itself that it possesses:

- an effective national licensing system, not only for pharmaceutical products, but also for the responsible manufacturers and distributors;
- GMP requirements, consonant with those recommended by WHO, to which all manufacturers of finished pharmaceutical products are required to conform;
- effective controls to monitor the quality of pharmaceutical products registered or manufactured within its country, including access to an independent quality control laboratory;

2.4 Each Member State assumes the responsibility to determine, through a process of self-evaluation, whether it satisfies these prerequisites. The Scheme contains no provision, under any circumstance, for external inspection or assessment, either of a competent national authority or of a manufacturing facility. However, should a Member State so wish, it could approach WHO, or a well-recognized Drug Regulatory Authority, to occasionally delegate consultants to act as advisors in the

course of national inspections, and inspector training activities.^[4]

Requesting a certificate

3.1 Three documents can be requested within the scope of the scheme:

- A certificate of a pharmaceutical product (product certificate).
- A statement of licensing status of pharmaceutical product(s).
- A batch certificate of a pharmaceutical product

1. Certificate of a pharmaceutical product

3.2 The Certificate of a Pharmaceutical Product issued by the exporting country, is intended for use by the competent authority within an importing country in two situations:

1. When the product in question is under consideration for a product licence that will authorize its importation and sale;
2. When administrative action is required to renew, extend, vary or review such a licence. The applicant should submit the following information for each product to the authority issuing the certificate:
 - Name and dosage form of product.
 - Name and amount of active ingredient(s) per unit dose (International Nonproprietary Name(s) where such exist(s)),
 - Name and address of product licence holder and/or manufacturing facility,
 - Formula (complete composition including all excipients; also particularly when no product licence exists or when the formulation differs from that of the licensed product),
 - Product information for health professionals and for the public (patient information leaflets) as approved in the exporting country.

2. Statement of licensing status

3.3 Statement of Licensing Status. This attests only that a licence has been issued for a specified product, or products, for use in the exporting country. It is intended for use by importing agents when considering bids made in response to an international tender, in which case it should be requested by the agent as a condition of bidding. It is intended only to facilitate the screening and preparation of information. The importation of any product that is provisionally selected through this procedure should be determined on the basis of a Certificate of a Pharmaceutical Product.

3. Batch Certificate

3.4 The provision of a Batch certificate is usually a mandatory element in tender and procurement documents. A Batch certificate is normally issued by the manufacturer and only exceptionally, as in the case of vaccines, sera and some other biological products, by the competent authority of the exporting country. The Batch Certificate is intended to accompany and provide an attestation concerning the quality and expiry date of a

specific batch or consignment of a product that has already been licensed in the importing country. The Batch Certificate should include the specifications of the final product at the time of batch release and the results of a full analysis undertaken on the batch in question.^[5]

Issuing a certificate

4.1 When the applicant is the manufacturer of the finished dosage form, the certifying authority should satisfy itself, before attesting compliance with GMP, that the applicant:

- applies identical GMP standards to the production of all batches of pharmaceutical products manufactured within the facility.

4.2 GMP as recommended by WHO assigns to the manufacturer of the finished dosage form responsibility for assuring the quality of active ingredients. National regulations may require that suppliers of active ingredients be identified in the product licence, but the competent authority may have no power to inspect them.

4.3 The certifying authority should officially stamp and date all copies of product information submitted to it in support of an application for a certificate and intended to be appended to the certificate. Every effort should be made to ensure that certificates and all documentation are consonant with the version of the product licence operative on the date of issue.

4.4 Any additional attachment to a certificate submitted by the applicant, such as price lists of products for which bids are offered, should be clearly identified as not comprising part of the attestation made by the certifying authority. If requested, an identical copy, clearly marked as duplicate, should be forwarded by the certifying authority on demand directly to the importing country authority.^[6]

Notifying and investigating a quality defect

5.1 Each certifying authority undertakes to institute enquiries into any quality defect reported in a product exported in accordance with the provisions of the Scheme, on the understanding that:

- The complaint is transmitted, together with the relevant facts, through the competent authority in the importing country;
- The complaint is considered to be of a serious nature by the latter authority; and
- The defect, if it appeared after delivery of the product into the importing country, is not attributable to local conditions.

5.2 In the case of obvious doubt, a participating national authority may request WHO to assist in identifying an independent quality control laboratory to carry out tests for the purposes of quality control.

5.3 Each certifying authority undertakes to inform WHO and, as far as is possible, all competent national

authorities, of any serious hazard newly associated with a product exported under the provisions of the Scheme or of any criminal abuse of the Scheme directed, in particular, to the export of falsely labelled, spurious, counterfeited or substandard pharmaceutical products. On receipt of such notification, WHO will transmit the message immediately to the competent national authority in each Member State.

5.4 WHO stands prepared to offer advice should difficulty arise in implementing any aspect of the Scheme or in resolving a complaint, but it cannot be a party to any resulting litigation or arbitration.^[7]

Implementation

In 1982 WHO undertook a reorientation of health education, designed to expand its community approach and include communication theories and practice. In 1987 the term "health education" was changed to "health promotion" to denote a broader, ecological approach to the work of facilitating "informed choices" by people on health matters.

WHO maintains a network of collaborating centers, which engage in work in various specific fields. It also maintains a working relationship with a large number of nongovernmental organizations involved in health and development. These organizations are accredited and approved by the World Health Assembly.^[8]

YEAR 2020 GOALS OF WHO

The World Health Assembly has adopted the following set of new goals to be reached by, or before, 2020:

- By 2005, health equity indices will be used within and between countries as a basis for promoting and monitoring equity in health.
- By 2010, transmission of Chagas' disease will be interrupted, and leprosy will be eliminated.
- By 2020, maternal mortality rates will be halved; the worldwide burden of disease will be substantially decreased by reversing the current trends of incidence and disability caused by tuberculosis, malaria, HIV/AIDS, tobacco-related diseases, and violence; measles will be eradicated; and lymphatic filariasis eliminated.
- By 2020, all countries will have made major progress in making available safe drinking water, adequate sanitation, food and shelter in sufficient quantity and
- quality; all countries will have introduced and be actively managing monitoring strategies that strengthen health-enhancing lifestyles and weaken health-damaging ones, through a combination of regulatory, economic, educational, organization-based, and community-based programs.
- By 2005, member states will have operational mechanisms for developing, implementing, and monitoring policies that are consistent with the HFA policy.

- By 2010, appropriate global and national health information, surveillance, and alert systems will be operational; research policies and institutional mechanisms will be operational at global, regional, and country levels; and all people will have access throughout their lives to comprehensive, essential, quality health care, supported by essential public health functions.

WHO has also launched a series of initiatives, including programs to roll back malaria, stop the spread of tuberculosis, fight the AIDS pandemic, and curtail tobacco use. A breakthrough in the drastic reduction of the cost of AIDS treatment drugs is likely to impact the AIDS fight. Negotiation for a tobacco-control convention may lead to greater success for WHO's Tobacco-Free Initiative. With additional resources from private foundations, WHO, in partnership with the World Bank and UNICEF, has launched an ambitious Global Alliance for Vaccines and Immunization (GAVI). Malnutrition, which accounts for nearly half of the 10.5 million deaths each year among preschool children, will continue to be a priority item in the years to come.

WHO has also undergone a number of reorganizations, the latest resulting in nine clusters, each covering a number of programs.

In addition to the two clusters on management and governing bodies, the program clusters are: communicable diseases, noncommunicable diseases, sustainable development and health environments, family and community health, evidence and information for policy, health technology and pharmaceuticals, and social change and mental health.^[9]

Summary

WHO plays an important role in regulating international drug approval and marketing. Quality, safety and efficacy (QSE) are the fundamental requirements for marketing a drug in any country.^[10]

Certificate of Medicinal Product (CPP) is a confidential document provided by the exporting country's regulatory authorities to the approved product's license holder or its agent in the importing country. It is to be presented in the filing application to the target country's health authority when the product in question is under consideration for new registration for authorized importation and sale, or when action is required to renew, modify or review a prelicensed product. WHO provides a recommended model certificate in three languages: English, French and Spanish.^[11]

When requesting a CPP, the applicant should indicate the type of information required. Supplementary information may be attached to the CPP at the applicant's request and at the certifying authority's discretion. The certifying authority is responsible for assuring the authenticity of the certified data.^[12]

WHO recommends the CPP as part of a broad scheme detailed in its guidelines. This scheme is an administrative instrument that requires each participating member state to attest to another's health authority that: a specific product is authorized to be placed on the market within its jurisdiction, or if not authorized, the reason why that authorization has not been accorded; the plant in which the product is manufactured is subject to inspections at suitable intervals to ensure that the manufacturer conforms to GMP standards recommended by WHO; and all submitted product information, including labeling, is currently authorized in the certifying country.^[13]

CONCLUSION

The WHO Certification Scheme in its present form and with the model certification documents provides transparent information, particularly about the regulatory status of a given product in the exporting country. The advantage of using the same formate and content of certificates worldwide is that this facilitates and rationalizes the issuance of certificates and also their interpretation at thereciving end. If used properly, the information provided under the scheme, through the product certificate and batch certificate can provide an important basis for product registration in the importing country.

On the other hand, it must be acknowledge that three scheme in its present form still has an inherent weakness in that it is based on the self-assessment of regulatory competence and there is no external assessment mechanism. In order to strength then this point the guidelines on the scheme mention under that a should a member state so wish, it could approach WHO, or a well recognized drug regulatory authority, to occasionally delegate consultants to act as advisors in the course of national inspections. WHO, however, being an international and not a supranational organization, does not carry out its own inspections nor would it have the authority to do so. There is thus no such thing as WHO GMP certificate.^[1]

ACKNOWLEDGMENTS

The authors are thankful to Dr. K. Pundarikakshudu Director of L.J. Institute of pharmacy, for providing all guidance and supports.

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