

General Policy Topics

A last word on the WHO Certification Scheme

At a time when some national markets are undermined by illicit and substandard pharmaceutical products, everyone holding relevant responsibility has a duty to ensure that confidence is maintained in products in international commerce through vigorous promotion and implementation of the WHO Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce. For the Scheme to be successful, it must be portrayed in a positive light and everyone involved must have a general understanding of its objectives. A detailed account of its workings was provided in the previous issue of *WHO Drug Information* and its basic principles are reasserted here in the form of a dialogue intended to dispel misconceptions. Suggestions for improving the Scheme would be welcomed from anyone involved in regulatory affairs, whether in government or the pharmaceutical industry.

Q: I am greatly concerned about reports of substandard and fake drugs circulating in international commerce. We cannot afford a sophisticated drug regulatory authority in my country and we feel helplessly vulnerable. I have heard of the WHO Certification Scheme, which is obviously intended to help us, yet I sometimes hear that it is little used and that it lacks teeth. Is there nothing that we can do to protect ourselves?

You must look carefully at the provisions of the Scheme and make up your own mind. It is certainly intended to meet your needs, since it informs you whether or not a medicinal product under consideration for importation into your country meets the standards of safety, efficacy and quality required in the exporting country.

Q: Who provides these assurances?

The national regulatory authority in the exporting country. Every country holds sovereign responsibility for the performance of its own industry. There is no international supervisory body.

Q: But surely the certificates must be based on tangible and enforceable standards that are internationally respected?

Indeed they are, and in this respect they differ from the "Certificates of Free Sale" that many countries used to issue in the past. A government participating in the WHO Scheme undertakes, when preparing a certificate, to establish whether the manufacturer of the product is operating to standards defined by WHO and to investigate any quality defects sub-

sequently found in products exported under the Scheme. Not least, it also agrees to issue certificates in a standard format.

Q: Does the certificate provide any additional assurances?

Yes. If a product is not registered for sale on the domestic market in the exporting country, it explains the reasons for this. It also provides the date on which the manufacturing facility was last inspected. A copy of the product information, as approved in the country of export, may also be obtained on request.

Q: Can any government participate in the Scheme?

The Scheme is open to all Member States of WHO. By the beginning of this year, 128 countries had announced their intention to participate but the large majority of these use it only as a means to control imports. No test of competence is applied to countries wishing to participate. It is for each government to determine and to declare whether it has in place the governmental systems of registration and control — and particularly the trained pharmaceutical inspectors — required to perform the task effectively.

Q: Is the Scheme not sometimes criticized adversely because it lacks a supranational administrative body?

Yes, but this is not politically feasible. Nor would external inspection be either practicable or reliable. Concerns regarding commercial confidentiality have to be respected, and rights of inspection and powers

of enforcement raise issues of national sovereignty. Moreover, the number of pharmaceutical manufacturing plants in the world runs into tens of thousands and the number of small generic companies is fast expanding. Some require more attention than others and, on occasion, adequate assurance regarding their working practices may be obtained only after several visits. In the last analysis, every participating government appreciates that it is required to investigate and report upon circumstances resulting in substandard or fraudulent products that have been exported under the Scheme.

Q: Can a certificate be obtained for any medicinal product?

The participating countries have undertaken to supply a certificate — at the specific request of the competent authority in the importing country — for any finished pharmaceutical or biological product or vaccine that is intended for human use, and also for veterinary products and growth-promoting agents intended for food-producing animals. They will also supply certificates for any active ingredient that must be registered before it may be used in products intended for the domestic market.

Q: Does an analysis of the finished product not provide comparable assurance of quality?

No. Pharmacopoeal analysis may fail to detect unanticipated impurities or contaminants. It will not provide information on the prospective stability of the product and it may not provide adequate assurance of bioavailability. In fact, the only way for the certifying authority to obtain direct assurance that successive batches of the product are dependable in these respects is through regular inspection of documentation and operations within the manufacturing facility.

Q: What assurances does the Scheme offer if the certificate holder is engaged only in the last stages of the manufacturing process or, perhaps, merely in relabelling a pre-existing product?

It is true that many importing countries rely heavily on wholesalers and brokers who sometimes sell repackaged products, and on generic manufacturers who formulate small batches of different products, often to specific order, that are made from ingredients obtained from many different sources. Such products will not be registered for use in the export-

ing country. Occasional inspection of the company's premises can then provide only limited assurance of their quality. The certifying authority has a responsibility to define these limitations in the certificate. There should be a clear statement to indicate what contribution the certificate holder has made to the manufacture of the product and its packaging, and what assurances, if any, can be provided regarding the source of the formulated product and its active ingredients.

Q: Does this mean that products should necessarily be bought directly from the initial manufacturer rather than through an intermediary?

Not necessarily. Reputable wholesale agents exercise an important role in the distribution of medicinal products internationally. You must have assurance, however, that they conform to certain basic standards. They should be operated by pharmacists experienced in drug procurement, they should be subject to independent inspection, they should use the WHO Certification Scheme in their own procurement activities and they should provide copies of relevant certificates to the clients they serve. If buyers and users of drugs do not know where the finished dosage form was made, quality defects cannot be adequately investigated, and the manufacturer escapes responsibility and liability for the product.

Q: But cannot certificates be forged as readily as pharmaceutical products?

Of course, and they certainly have been. But a simple remedy exists. The issuing authority should supply the original of the certificate to the applicant, who needs to append it to the product importation papers and another identical copy should be sent to the competent authority in the importing country.

Q: When should the importing authority request a certificate?

Ideally, whenever a consignment of a certifiable product is ordered. At very least, whenever an order is placed for the first time for a new product or with an unknown manufacturer or intermediary. Particular consideration needs to be given to products that are not registered and consequently not specifically controlled in the exporting country. In such cases the certification of each consignment — by providing assurances that good manufacturing practices remain in operation — may offer the only tangible basis for its acceptance. For registered products it is

prudent to request a new certificate, including a copy of the approved prescribing information, every two years or so. These are decisions that require the professional judgement of a pharmacist experienced in drug procurement who maintains an awareness of regulatory actions in other countries through WHO's information systems and other sources.

Q: What needs to be done in the importing country to ensure that the Scheme operates effectively?

National drug control is directed everywhere to fulfilling two basic objectives. Firstly, a requirement for registration of marketed products, both imported and locally produced, provides a basis for the control of the market through statutory provisions and regulations. Secondly, by implementation and

enforcement of regulations, prescribed standards of safety, quality and efficacy can be applied as a prerequisite to registration, and unregistered products that remain illicitly on the market can be removed from circulation. WHO has prepared Guiding Principles for Small National Drug Regulatory Authorities that are concerned primarily with the importation of finished pharmaceutical products. These place emphasis on the need for an effective medicines inspectorate and depict the WHO Certification Scheme as the fulcrum of the administrative process. The Scheme is, in fact, nothing less than the international corollary to the national regulatory process. It is intended to ensure, without burdensome legislative provisions, that all the controls that a drug-exporting country applies to its domestic market are also reliably reflected in the products that it ships abroad.