

General Policy Topics

Drug regulation and developing countries

A decade or so ago, concerns were commonly expressed about large-scale dumping in developing countries of pharmaceutical products that were either approaching or past their expiry dates or likely to be withdrawn from the market in the country of origin. These are practices that have been largely consigned to history by efficient interchange of information between national drug regulatory authorities. In the meantime, genuine changes in attitude have undoubtedly occurred within many pharmaceutical companies. All is not well, however, in pharmaceutical export markets. The focus of attention has moved ominously to a new threat posed by the proliferation of counterfeit and other spurious products that escape every modality of control. There is also a new-found appreciation that product-related information needs to be controlled as assiduously as manufacturing practices and product specifications.

To help developing countries control their markets in imported products, a total ban on the export of products not registered in the country of origin has frequently been proposed. This was the policy followed by the United States of America until 1986. In recognition of the international character of the drug development process this policy was subsequently relaxed. Subject to specific safeguards, exportation of legitimate but non-registered products was permitted to countries with comparable systems of regulatory control (1) and, for products indicated for the treatment and prevention of tropical diseases. This exemption was extended to all countries in which these diseases are endemic.

This carefully judged relaxation of the exportation of pharmaceutical products from the USA to developing countries greatly facilitated, for instance, the clinical development of ivermectin in the management of onchocerciasis and of eflornithine as a treatment for African trypanosomiasis. Notwithstanding these benefits, if comparable provisions were to become the norm in major drug exporting countries, a complex schedule of exemptions would need to be drawn up to avert non-tariff barriers to

legitimate but non-registered products required within developing countries. Not least, special consideration would be needed to accommodate generic versions of products manufactured on contract specifically for export, and products that have been repackaged or reformulated to satisfy requirements determined in the country of destination.

The practicalities, the costs, and the possible adverse effect on legitimate trade in pharmaceutical products, of implementing such legal provisions would need to be carefully weighed. Developing countries would need to be fully involved in the consultative process. In any event, such legislation would do nothing to staunch the flow within export markets of products that are legitimately registered but which are irrelevant, or trifling, given the priorities that need to be respected within the developing world. Nor would it obstruct the movement of products that may still be explicitly registered — but without clear reason — “for export only”.

A mechanism of export control that offers greater latitude to the importing country is the system of “prior informed consent” that has been proposed (2) to control trade in products included in the *United Nations consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not-approved by governments* (3). This proposal would inhibit the export of a listed product unless the competent authority within the importing country, after having been notified of the associated risks, explicitly authorizes its acceptance. However, there would be drawbacks in applying this system widely to pharmaceutical products. Agents in importing countries might tend to favour dealing with countries where controls are less rigorous simply to avoid bureaucratic constraints. Moreover, the *UN Consolidated List* includes products that are “severely restricted” as well as banned. Many products in this category — including potent antimicrobial and anticancer drugs — are used in life-saving situations. Several are included in the WHO Model List of Essential Drugs (4).

As an alternative strategy, the majority of Member States of WHO subscribe to the WHO Certification

Scheme on the Quality of Pharmaceutical Products moving in International Commerce (5). Increasingly — and notably among the Member States of the European Community (6) — it has been accorded statutory recognition. In essence, the Scheme simply provides a channel of communication between the competent regulatory authorities in the importing and exporting countries. The certification process is activated only at the request of the competent authority in the importing country.

There might be advantage in introducing a parallel notification system activated within the exporting country as a prerequisite to authorizing the export of a non-registered product. Newly-introduced provisions in France (7), for example, prohibit the export of products that have been suspended or withdrawn on grounds of public health. Export of other non-registered products is now permitted only after the importing country has given its assent to accept them, after having received documentation from the manufacturer, via the French regulatory authority, explaining why the product is not authorized for sale on the domestic market.

Supplementary legislative measures may well prove advantageous in some circumstances, but the WHO Certification Scheme will long remain the basic channel for international exchange of product-specific information between national drug regulatory authorities. A query may be raised about any product at any time, and it may be directed as readily to the information that accompanies the product as to its quality or its regulatory status. Concerns about the quality and consistency of the information supplied when products are exported are likely to be sensitized very shortly with the long-awaited publication of the results of the labelling study undertaken by the US Congressional Office of Technology Assessment. That there have been inexcusable shortcomings that must be exorcized is not contested and there will certainly be calls for new policies and for national and international action. It would be disappointing, however, if the appeal for new initiatives were to underrate the scope and potential of the Certification Scheme.

An innate advantage of the Certification Scheme is that, as a channel of information on the drug licensing process, it assists in the development of effective drug regulatory capability within developing countries. This capability is vital, whatever the characteristics of the domestic market, but nowhere more so than where domestic manufacture is fast expanding. Effective controls need to be applied to both imported and locally-produced products. In the

last analysis, each country must assume responsibility for the management of its own drug market. Where resources are limited, national policy must be geared to maintaining essential supplies and to assuring their quality. This can be achieved only through effective control of all aspects of domestic manufacture, and this supervision must be directed not only to the physical quality of the product but also to the legitimacy of the labelling and promotional claims.

Over the past two decades the structure of the industry has changed in many developing countries, where large numbers of relatively small companies that manufacture generic versions of pharmaceutical products have entered into the market. This diversification of the industry, and the concomitant increase in the numbers of marketed products is straining the capacity of regulatory authorities in many countries. Within the past few years, frailty of control has been reflected not only in reports of continued availability in many developing countries of products long withdrawn from other markets on grounds of obsolescence or toxicity (8), but in a disturbing prevalence of counterfeit and spurious products (9) and grave lapses in quality assurance that in some instances have resulted in tragedy on a scale not revisited since the time of thalidomide (10).

Many countries are in urgent need of advice and support in developing a sound manufacturing and regulatory infrastructure. There are no cure-all solutions and no secure alternatives to current licensing systems that embrace all products and all manufacturers. Markets must be precisely defined before they can be effectively controlled. Implementation of WHO's guiding principles for small regulatory authorities (11), coupled with the use of the Certification Scheme, provides a tried and tangible basis for this control. With the development by WHO of a simple drug registration software package operable on a freestanding desktop computer it is reasonable to hope that a breakthrough has at last been made towards bringing an efficient licensing mechanism within the reach of a far wider constellation of countries.

References

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