

General Policy Topics

Adverse drug-related events: need for increased efficiency in international transfer of information

Multilateral harmonization of the controls applied to the registration and marketing of pharmaceutical products has been given impetus in recent years, both as a result of a broad political commitment throughout the world to free-trading policies, and the development of single markets between close trading partners, notably among the Member States of the European Union. International alignment of technical requirements for assessing and monitoring pharmaceutical products advances public health interests as well as economic objectives: it creates a basis for developing a rigorous, internationally accepted technical mechanism for admitting new products into national markets and for monitoring their subsequent performance, and it provides a means of rationalizing, expediting and reducing the costs of developing products that are offered to a wide spectrum of national markets.

A scheme for harmonizing and integrating national drug monitoring programmes, directed primarily at creating an international data base of reports of suspected adverse drug reactions, was first developed under the aegis of WHO some 25 years ago. The need for efficient international interchange of information concerning potential and proven risks of newly-marketed products, in particular, is manifest. Worldwide over the past 10 years, over 100 products have been withdrawn from use within two years of their introduction because of unanticipated concerns regarding their safety.

Some 10 years ago, moves were taken by several highly evolved national authorities to complement the WHO system — which relies upon informal collaboration between national regulatory authorities — with a requirement imposing a statutory responsibility upon product-licence holders to generate this information. As a condition of product registration these authorities oblige licence holders to report, within a short defined time-frame, any serious or unanticipated adverse event associated with use of the product, wherever in the world the event may have occurred.

The latter arrangement holds some advantage as an early warning system, in that it places a formal obligation upon those responsible for marketing pharmaceutical products to participate actively, and within an international framework, in the monitoring process. It does not supersede the WHO system, however, since the international data base continues to provide a unique research facility for national regulatory authorities faced with the need to consider restrictive action against a product licence on grounds of safety.

Such decisions, which are taken to protect the public health, need to be formulated as expeditiously as possible. This implies rapid transmission and processing of adverse drug related events reported within each of the countries in which the product in question is available. Full advantage can be taken of the rapid development of telecommunications and automated data storage and processing only if there is international agreement on the terminology used to describe these events and on the classification that determines how they are stored within the international data base. As yet, consensus has not been achieved either on terminology or classification. This adversely prejudices the speed at which data transmitted across national boundaries can be processed and assessed; the reliability with which data derived from different countries can be compared; and the effectiveness with which national regulatory authorities can collaborate in investigating matters of mutual concern.

It is understandable that individual regulatory authorities should be protective of their established national systems, and it is inevitable that those responsible for maintaining national data bases should be reluctant to reorganize a data base with which they have become familiar. However, these considerations no longer provide tenable justification for inactivity. For more than 20 years two internationally recognized but independent adverse reaction terminologies (COSTART and WHOART) have existed in parallel. The difficulties that this divergence poses for international communication have been compounded in recent years, firstly because both systems continue to evolve independently, and secondly, because they are increasingly subjected to unilaterally-determined

revisions by various users and, thirdly, because a new hybrid terminology (ADROIT) is now under consideration as an international standard between the Member States of the European Union.

Given this situation, the US Food and Drug Administration (FDA) and the World Health Organization have proposed that national regulatory authorities and users of these terminologies within the research-based pharmaceutical industry should collaborate, under the aegis of the Council for International Organizations of Medical Sciences (CIOMS), with the aim of achieving a broad international consensus on the terminology and classification to be adopted for describing and classifying adverse drug-related events in collaborative programmes.

In the first instance, it is proposed that a task force be created consisting of representatives of the US FDA (as the custodian of COSTART); WHO (as the custodian of WHOART); and representatives of the research-based pharmaceutical industry (as users of these two classifications), with a view to:

- reviewing the present status of the two currently-used classifications;
- preparing a technical document describing the strengths, deficiencies and extent of the differences between the two systems;
- presenting a limited set of options for addressing the deficiencies and/or reconciling the differences; and

- proposing how a project directed to such reconciliation, and conducted under the auspices of CIOMS, might be organized, implemented, budgeted and funded.

It is proposed, secondly, that the report of the task force be presented by CIOMS to a meeting of interested parties, with the following objectives:

- to review and to discuss the report of the task force as a basis for international harmonization of terminology and classification of adverse drug-related events;
- to offer proposals with regard to the scope of the proposed project and consultative arrangements to be adopted during its execution;
- to discuss criteria for the selection of a steering committee, and the terms of reference of this overseeing body; and
- to discuss modalities of funding.

Invitations to the meeting of interested parties will be cast widely to include representatives of all national drug regulatory authorities, and all potential users of the system within the pharmaceutical and related industries, including manufacturers of supplemented foods and medical devices. The intention is to set up and to maintain on an open-ended basis an internationally representative body, operating through effective consultation with all interested parties, that will create and update a single globally-accepted operational system.