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Commentary

Pharmaceutical Marketing in the European Community: The 1992 Changes

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Harmonization is the term used to describe the removal of barriers to the movement of goods and services within the European Community (EC) to create a market without frontiers. This process has been under way for several years but is due to take a big leap forward in 1992, when the schedule calls for the internal market to be virtually complete. Among the changes will be adoption of three procedures for authorization of medicinal products (the equivalent of approval for marketing in the United States). Elements of the three approaches exist now and form the basis for the post 1992 system.

Market development is being closely followed by policy makers and interested members of the pharmaceutical industry because harmonization of authorization requirements across the Community essentially creates a larger market for prescription pharmaceuticals. Final regulations have not been released but a discussion document from the Commission of the European Communities specifies an approach that Member States have agreed to in principle. It seems clear that the post 1992 procedures will contain three pathways to authorization:

(1) a *decentralized* procedure based on mutual recognition among the Member States,
(2) a *centralized* procedure valid for all 12 Member States, and
(3) a *national* procedure used primarily for a single Member State.

The Decentralized Approach. This approach is based on the principle of mutual recognition. That is, a marketing authorization granted in one Member State should be accepted by other Member States. The process is derived from the current multistate procedure but allows for progressive penetration of other national markets. The decentralized approach is particularly important for smaller pharmaceutical firms since it permits a phased approach to market access. It appears now that the decentralized approach will continue to be the most commonly used after 1992.

Once authorization is received in the first Member State, the firm applies to other Member States for recognition of the original authorization by providing an application together with a copy of the initial authorization, the summary of product characteristics, product labeling, and package insert as approved by the first Member State. The Member State which first authorized the product forwards a copy of its assessment report to the other Member State(s). The request must be acted upon by each recipient Member State within 120 days of receipt.

Since this is a mutual recognition system, only the first Member State will prepare an assessment report. Subsequent Member States would review the report and a limited part of the original application provided by the authorizing Member State. If a Member State does not want to recognize the original authorization, it may request the full original application for review. If this occurs the evaluation must be completed and sent to the authorizing Member State within 120 days. Where differences cannot be resolved between Member States, the matter is referred to an agency within the European Community Commission (the CPMP, described later), which attempts to resolve disagreements. Currently their role is only to rule on the grounds for objections and their opinion does not replace national decisions. The CPMP opinion is issued within 60 days of receiving the necessary information. The concerned Member States have 60 days in which to decide what action to take on the CPMP opinion. It is anticipated that after 1992 the CPMP opinion will carry more weight and would become the basis for deliberation on a Commission binding decision if necessary.

In theory, the decentralized procedure reduces paperwork redundancy and decreases the time for receiving marketing approval. In practice it appears that many obstacles to the process still exist which will result in a large percentage of authorizations being challenged and ultimately sent to the CPMP for review. An efficient decentralized process may take several years to emerge.

The Centralized Procedure. This mechanism has been in operation for biotechnology-derived products and certain other high-technology medicinals since 1987. After 1992 the procedures will be improved and made available on a voluntary basis for new chemical entities.

Applications for authorization will be submitted directly to a Commission agency known as the reinforced CPMP/CVMP (Committee for Propriety Medicinal Products/Committee for Veterinary Medicinal Products). The CPMP/CVMP is expected to make a single evaluation which will be accepted throughout the Community and thus avoid the waste of resources associated with multiple applications. The CPMP/CVMP will select rapporteurs and experts from lists of nominated national experts to prepare the assessment report (these are the same individuals that now make evaluations for their Member States).

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The current system limits the role of the CPMP to assessment of product quality, safety, and efficacy. Their opinion, which is not binding, is provided to the Member State where the application was originally filed. Member States concerned with the application are required to reach a decision within 30 days of receiving the CPMP opinion.

After 1992 the rapporteur's evaluation would be presented to the CPMP/CVMP for its scientific opinion and rendering of a binding decision. Normally the evaluation must be completed in 210 days, however, it is possible that requests for additional information could extend this period. If there are objections to an approval or refusal (by the applicant or Member States), an administrative mechanism will provide for acceptance and review of written comments as well as a hearing. Where disagreements persist there are legal procedures to be followed.

The expectation is that a centralized procedure will create more efficient review of applications and bring the benefits to Community citizens more quickly and at less expense. As described above the expected changes provide a greater role for the CPMP and remove some flexibility from the competent authorities of Member States in the consideration of specific applications. Success of the revised system will depend upon the willingness to accept the collective judgment of the CPMP.

National Procedures After 1992. These procedures will remain unchanged. The Commission will have the right to examine Member State authorizations in cases where interests of the Community are involved. It appears that national procedures will be of interest to very small pharmaceutical firms or for products with only local interest.

The Postmarketing Role of the Commission. Regardless of the procedure used to obtain marketing authorization, the Commission will take responsibility for "pharmacovigilance" across the Community. This concept covers a wide range of methods designed to collect and interpret adverse drug reactions (ADRs). The system will apply to all products authorized for marketing in the Community regardless of the producer's location. The Directives clearly apply to firms outside the Community as well as those located in Member States.

The Commission role is accomplished through the CPMP, which works with the comparable authorities in each Member State. This CPMP role is likely to increase as pharmaceuticals become more specialized and potent. The EEC pharmacovigilance system is seen as complementing and harmonizing the efforts of Member States and also the activities of WHO. Pharmaceutical firms will be affected since EEC Directives specify actions for Member States and place reporting and record-keeping responsibilities on firms marketing in the Community.

It is important to recognize that authorization is a necessary but not a sufficient condition for *successful* marketing of a product. A second requirement in many Member States is a price determination made by the individual Member States' competent authority. Since the dominant share of market in each Member State is reimbursed by the government health plan or by insurance plans, an official price is a practical limitation to market access.

Another barrier to access is found in those countries that use positive or negative formularies. In these countries the product must be admitted to the formulary or, alternatively, not placed on the negative drug list to be eligible for reimbursement.

Finally, the problem of price transparency between Member States must be resolved before an internal market can be said to exist. Currently there are some substantial price variations for (virtually) the same product in different Member States. These conditions promote the practice of "parallel trading," which has a detrimental effect on manufacturer profitability and encourages inefficient marketing practices. Directives have been proposed to improve price transparency.

This overview of the emerging marketing authorization process for pharmaceuticals in the EC attempts to describe the basic procedures in the context of other marketing realities. The description is necessarily brief but should convey the message that harmonization will not remove all national boundaries to marketing but will attempt to reduce the time and cost of authorization for pharmaceuticals in the Community. The result is intended to be better access to a large market with the benefit of greater efficiency for producers and consumers of medicinal products.

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