BROADER USES OF POST-MARKETING SURVEILLANCE

Judith K. Jones, M.D., Ph.D.
Director, Division of Drug Experience
Office of Biometrics and Epidemiology
Bureau of Drugs, Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

I. DEFINITION OF POST-MARKETING SURVEILLANCE FROM A BROADER PERSPECTIVE

Since post-marketing surveillance has been functionally defined in many ways and can encompass a large number of activities, it is important to keep the output of any effort or system combining various efforts in mind. Various efforts of coordinating information on drug use go through a prolonged process and have various outcomes, but the overall goal is to optimize drug utilization and minimize preventable adverse effects.

Another perspective on this view of drug effects relates to the longitudinal view of post-marketing surveillance. There is a progression of knowledge over time in the development of a drug both before and after its marketing. A certain proportion of information on efficacy and safety is known at the time of marketing, partially determined by the uniqueness of a molecular entity. From the time of marketing on, more and more information about the drug's actions are gradually accrued, and the goal of post-marketing surveillance is to ideally obtain as much of that information as early as possible. There are several major limitations to early detection by any post-marketing surveillance method. One relates to the inability to discover, at an early stage, latent effects which occur long after the drug has been taken, as in the case of drug-associated cancer. Another limitation relates to special populations at higher risk.
discovery is dependent on sufficient exposure of these special high risk populations to allow discovery. For example, for a drug that is used predominantly in a younger age population, if a particular effect occurs in 1% of a special population, such as post-menopausal women, its detection may be delayed. Finally, the detectability of an effect, particularly if it is clinically obscure (e.g., a change in immunological function) and/or it occurs in a setting confounded by other diseases or drugs, provides some broad limitations.

In the United States there are some legal mandates for post-marketing surveillance which are embodied in the regulations promulgated by the Food and Drug Administration under 21 CFR 310.300-304. These regulations require annual reports on all approved drug products, which include information not only on adverse reactions, but also on labeling, advertising, manufacturing, and amounts of drug produced. This information can potentially give an overview of the entire status of the drug on the market. Specific regulations (21 CFR 310.301) are directed towards reports of adverse reactions, and other regulations (21 CFR 310.304) support the request for specific post-marketing surveillance studies in cases where there are special questions which require an answer but do not require further delay in approval of the drug.

II. GOALS OF POST-MARKETING SURVEILLANCE

At least three goals of post-marketing surveillance can be defined, which include the following:

1. Detect unexpected problems as early as possible and modify labeling or drug use accordingly.

2. To communicate appropriately and effectively to the physician in the medical community information to optimize the use of a drug.

3. To predict problems which may occur at the time of marketing and ideally define these problems prior to marketing. This implies that these problems will eventually be identified earlier in the drug development process.

III. SOURCES OF POST-MARKETING SURVEILLANCE DATA IN THE UNITED STATES

There are a large number of sources of post-marketing surveillance data available to the U.S. Food and Drug Administration as summarized in Table I. A number of these sources come by