In September 2010, the US Food and Drug Administration (FDA) conducted a webinar for the media to review the basic information concerning FDA’s approval of generic drugs in an attempt to promote the public’s understanding of generics and dispel common misconceptions about this growing branch of pharmaceutical products that are surrounded by a veil of confusion and controversy. Although much of the information provided by the FDA in that webinar could be considered common knowledge, such reiteration of the basic facts should not be seen as redundant, considering that the “drug wars” among generic and brand-name pharmaceutical makers (that stem largely from cost concerns) often are positioned as issues related to patient safety and product efficacy rather than finances.

Robert L. West, Deputy Director of the FDA’s Office of Generic Drugs (OGD) conducted the webinar. Mr West’s foremost concern was the message of safety and efficacy of generics, while simultaneously acknowledging that generic utilization continues to grow and by now constitutes the bulk of all prescriptions written in the United States. This in itself did not seem to pose a problem for him. If generics “represent 70% of the total prescriptions dispensed in the United States,” which is a considerable increase from “about 50% just a year ago,” according to Mr West, it would seem unnecessary to tout generic drugs yet again as being as safe and effective as brand-name drugs. Such a growth in the utilization rate should be sufficient evidence for these qualities (patient safety and product efficacy).

To receive FDA approval for a generic drug, Mr West indicated, the manufacturer must demonstrate that its product:
• Contains the same active ingredient as the brand-name drug
• Has the same strength of the active ingredient as in the brand drug
• Is of the same dosing formulation (eg, tablet, capsule)
• Has the same route of administration as the brand drug (eg, oral, injection).

Furthermore, although generic drugs rely on evidence collected in the original clinical studies conducted by the brand drug manufacturer, generic manufacturers must also demonstrate that the specific generic formulation carries bioequivalence and pharmaceutical equivalence to the brand-name drug. This is often the cause for concern and contention about the actual benefit of and justification for generic product utilization.

This very concern was recently evaluated by FDA/OGD investigators (including many pharmacists) in a study published late last year. The investigators compared the evidence used by the FDA between 1996 and 2007 to establish the bioequivalence of generics and brand-name drugs. The goal of the study was to evaluate how well the bioequivalence measures used to approve generics compared with those used for the brand-name drugs. A total of 2070 studies were included in this analysis.

The results showed a mean standard deviation of geometric mean ratios of 1.00 ± 0.60 for drug peak plasma concentration (Cmax) and 1.00 ± 0.40 for area under the curve (AUC) plasma drug concentration. The average differences between generic and brand-name drugs in these measures (Cmax and AUC) were 4.35% and 3.56%, respectively. And in 98% of these studies, the generic AUC differed from that of the brand product by <10%. The investigators concluded that these studies support the FDA’s use of its criteria for the approval process of generic formulations for brand-name products. This analysis, although scientifically sound, is anything but simple.
Mr West admitted that the issue of bioequivalence is a frequent cause for misinformation, leading to considerable inconsistent and inaccurate assertions about the difference in the levels of the active ingredient that is present in the brand and the generic drug, resulting in claims that vary by more than a 40% difference, from –20% to +25%. The reason for this, the OGD Deputy Director suggests, is the complexity of the statistical analyses involved in the evidence for bioequivalence; an intriguing observation that merits consideration, yet his own explanation of generic bioequivalence to the public relied on this very same study as the basis for the FDA’s articulation of this phenomenon.

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Indeed, in an ideal world, simpler calculations and explanations may help a greater number of stakeholders to accept or reject the bioequivalence of these 2 similar yet competing groups of products that theoretically have a unified goal of helping patients. Complexity is not too helpful when seeking the understanding of consumers, especially with regard to drug therapy, of which payers and providers are well aware. Convincing patients to use medications is often a long and arduous task, with which pharmaceutical companies, too, have been struggling for years. Yet the makers of brand-name products have found innovative ways to illustrate to consumers why using pharmaceuticals can often help improve their health and well-being. Using simple and clear language that does not require high-level education is crucial.

The FDA, and perhaps the makers of generic products, must also find innovative and more patient-focused ways of simplifying the complex issues of bioequivalence to consumers, who are after all, the ultimate target of the drug companies but are often the ones who do not buy into the very idea of generics (“cheap” is not always a positive and is often peculiarly suspect, especially when it comes to the American consumer). Lack of understanding of the true benefits of drug therapy is among the well-known causes of patient lack of adherence.

Although the FDA’s effort to explain bioequivalence is commendable, its very way of explanation and choice of communication with the public leave much to be desired. Improved channels of communication and clearer messages are needed to clarify a complex issue in simple but convincing words.

References