Before

THE FOOD AND DRUG ADMINISTRATION

on

THE PRESCRIPTION DRUG USER FEE ACT

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Presented by:

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four Americans. Blue Cross and Blue Shield Plans have extensive experience in providing prescription drug coverage to American consumers through a variety of products. Thank you for the opportunity to appear before the Food and Drug Administration at today's public meeting on the Prescription Drug User Fee Act (PDUFA).

I am here to address the following question posed in the *Federal Register* notice for today's meeting: *Should PDUFA allow the use of user fee funding to monitor safety after new drug or biologic approval?*

Summary of BCBSA Recommendations on PDUFA:

BCBSA believes that an integral part of delivering new drug therapies to physicians and consumers is assuring consumer safety after the drug has penetrated the market. By funding only the premarket review of new drugs, PDUFA speeds access to new therapies but does not provide FDA with the necessary resources to conduct critical postmarket surveillance activities that keep patients safe.

In addition, BCBSA believes that the rapid flow of new drugs to market must be accompanied by health outcomes information that allows consumers to make value-driven decisions. BCBSA also supports continued increases in federal appropriations for FDA to provide resources for agency programs that impact public health.

To ensure consumer safety at each stage of the drug product life cycle, BCBSA recommends:

- Expanding PDUFA's definition of user fee-funded activities to include:
  - Postmarketing surveillance of adverse events; and
  - The monitoring of the risk and benefit information in direct-to-consumer (DTC) advertising.
- Supporting FDA initiatives to require manufacturers to provide information that allows evaluation of the benefits, costs and risks of new drugs compared to the benefits, costs and risks of drugs already on the market; and
- Increasing federal appropriations for FDA to provide resources for agency programs that impact public health.

Background on PDUFA

In 1992, Congress passed the Prescription Drug User Fee Act, which authorized the FDA to collect user fees from prescription drug manufacturers seeking marketing approval for new products. Under PDUFA, the FDA collected $327 million in user fees during the five-year implementation period. It used these funds to hire 600 additional reviewers and upgrade the management systems in the premarket review program for branded

prescription drugs in the Center for Drug Evaluation and Research (CDER) and biologics products in the Center for Biologics Evaluation and Research (CBER).

In exchange for this new funding, PDUFA required the FDA to meet rising annual performance targets. These targets were designed to ensure that the agency would upgrade its efficiency significantly between 1993 and September 1997, when a sunset provision terminated the program. The FDA faced the prospect of losing this important source of new funding unless it performed well enough to motivate Congress to reauthorize user fees in 1997. However, in 1997 Congress renewed user fee funding for five more years as part of the FDA Modernization Act (FDAMA). It is set to expire in September 2002.

Since the enactment of PDUFA, total approval time — the time from the initial submission of a marketing application to the issuance of an approval letter — has dropped from a median of 23 months to 12 months. Total approval time for priority applications (applications for those products providing significant therapeutic gains) has dropped from a median of over 12 months in the early PDUFA years to six months.

In addition, because FDA has put greater effort into communicating what it expects applicants to submit, a higher percentage of applications are being approved. Before PDUFA, only about 60 percent of the applications submitted were ultimately approved. Now, about 80 percent are approved.

As a result, more new drugs are coming to the market faster than ever before. However, resources for important activities that ensure these new products are safe and effective for consumers have not kept pace with resources for drug review. PDUFA provides funding only for tasks that lead up to a decision on whether to approve or deny a new drug application. Postmarketing regulatory activities that are critical for all new drugs — such as tracking and responding to reports of adverse drug reactions and monitoring drug advertisements for compliance with agency regulations — are not covered by user fees. Thus, these vital consumer safety responsibilities must be paid for out of congressional appropriations.

However, PDUFA currently requires that FDA spend as much appropriated money on drug review each year as it did in 1997, adjusted for inflation. If the FDA fails to meet this requirement, its legal authority to collect and spend user fees that year becomes void. As a practical matter, the FDA must spend slightly more from appropriations each year on drug review than it spent in 1997 so that the statutory threshold is met when its accounting is complete.

Last week, Congress and the President signed a record budget for FDA for fiscal year 2002. This represents the first increase in appropriations for drug reviews since 1992. BCBSA applauds Congress and the Administration for their recognition of the agency's key role in protecting public health and for their support of a broad range of FDA programs that protect the public health. We are encouraged that the appropriations

measure also enables the agency to meet the statutory "triggers" for collection and use of PDUFA fees without diverting resources from other key agency programs.

However, there is an ongoing need for funding for critical agency responsibilities. Despite the welcome infusion of appropriated money for fiscal year 2002, Congress must commit to long-term funding for FDA.

BCBSA Recommendations

BCBSA has three recommendations as the FDA evaluates PDUFA in anticipation of its reauthorization: (1) Expand PDUFA's definition of user fee-funded activities to include postmarketing surveillance of adverse events and monitoring of risk and benefit information in direct-to-consumer (DTC) advertising; (2) Support agency initiatives to require manufacturers to provide information that allows evaluation of the benefits, costs and risks of new drugs compared to the benefits, costs and risks of drugs already on the market; and (3) Increase federal appropriations for FDA to provide resources for agency programs that impact public health.

Postmarketing Surveillance

We recommend that Congress amend PDUFA to include postmarket monitoring adverse drug events under section 379(g)(6) in the statutory definition of "process[es] for the review of human drug applications." This new statutory language will give FDA the resources to speed consumer access to new therapies *and* conduct critical postmarket surveillance activities that keep patients safe.

Not all of a drug's potential side effects and interactions are known at the time of market entry. Instead, these events manifest themselves gradually as the drug is accepted into clinical practice and used in a large patient population for the first time. Currently, the FDA relies on voluntary reporting of drug adverse events by consumers and health care professionals. As new products flood the market under PDUFA, the volume of adverse event reports (AERs) is growing substantially.

According to *CDER 2000 Report to the Nation*, the FDA received 245,750 reports of drug-related adverse events in calendar year 2000. This level is more than twice the 118,000 AERs that the FDA received in 1992, and almost four times as many as the 68,000 received in 1989.[i] The General Accounting Office (GAO) in its report *Major Management Challenges and Program Risks* released in January 2001 stated the FDA estimates it receives reports for only 1% to 10% of serious adverse events.

As the FDA conceded in announcing this meeting, the agency lacks sufficient resources to adequately monitor reports of adverse events and conduct timely safety interventions. FDA also believes that the current system for detecting adverse drug and biologics events does not provide sufficient data on the actual incidence of problems. When BCBSA last testified on this issue before FDA in September 2000, we cited the withdrawal of several drugs as examples of the need for PDUFA funding for postmarket surveillance: the antihistamine Seldane; two obesity drugs, Pondimin and Redux (better known as "fen-phen"); Duract, a prescription medication for pain; and Rezulin, a medication for

diabetes. Since that time, two more drugs have been withdrawn from the market for safety reasons — Lotronex for irritable bowel syndrome, and Baycol, a cholesterol-lowering drug — further illustrating this point.

We believe Congress should provide funds and require the FDA to develop and implement a comprehensive protocol to monitor adverse reactions related to new drugs entering the market. BCBSA supports a proactive role for FDA in collecting adverse event data.

BCBSA applauds Congress and the President for approving last week the FDA's fiscal year 2002 budget request for $10 million to monitor marketed products and safeguard patients against adverse events associated with the use of drugs, biologics and medical devices. However, there is an ongoing need for funding of this critical task. Under the user fee statute, FDA must spend at least as much from appropriated funds for the review of human drug applications as it spent in fiscal year 1997, adjusted for inflation. Thus, despite the welcome infusion of appropriated money for fiscal year 2002, Congress must commit to long-term funding for postmarket surveillance of drugs.

DTC Advertising

BCBSA believes that consumers faced with a barrage of advertisements for new drugs entering the market as a result of user-fee funded reviews must receive clear and understandable information about their benefits and risks. As such, BCBSA recommends that Congress also amend PDUFA to include monitoring of DTC advertising compliance

under section 379(g)(6) in the statutory definition of "process[es] for the review of human drug applications." BCBSA further recommends that Congress require the FDA to establish criteria for the level and type of information that consumers need to make informed choices about advertised drugs.

As more new drugs reach the market faster under PDUFA, they are marketed directly to consumers. In 2000, pharmaceutical manufacturers spent $2.5 billion on DTC advertising. According to a 2000 study by National Institute for Healthcare Management (NIHCM), increased sales of the 50 most heavily promoted drugs in 2000 accounted for almost half (47.8%) of the $20.8 billion increase in retail spending on prescription drugs from 1999 to 2000.[ii] In total, these 50 drugs had 2000 sales of over $41 billion – accounting for 31.3% percent of all retail drug sales. This use-inducing advertising raises issues with respect to consumer safety in the absence of complete information about product benefits and risks.

Recent surveys raise questions about the effectiveness of DTC advertising in communicating important information about drugs. A survey released last month by the Kaiser Family Foundation found that nearly a third (30%) of adults have talked to their doctor about a drug they saw advertised, and 44% of those who talked to their doctor received a prescription for the medication they inquired about.[iii] This means that one in eight Americans (13%) have received a specific prescription in response to seeing a drug ad. However, when asked for a self-assessment of how much they learned from viewing a specific ad, most respondents (70%) said they had learned little or nothing more about

information." In addition, more than 60% disagreed with the statement, "DTC advertising is an objective source of information."[iv]

By expanding the definition of user fee-funded activities to include this critical regulatory responsibility, Congress will help ensure that consumers have more complete, accurate and understandable information about the risks and benefits associated with prescription drugs.

Health Outcomes Information

BCBSA further recommends that the FDA review PDUFA's role in ensuring that the rapid flow of new drugs to market is accompanied by information that allows consumers, physicians and health plans to make value-driven prescription drug decisions. Specifically, BCBSA recommends that the FDA support initiatives to require manufacturers to provide information that allows a comparison of the benefits, costs and risks of new drugs that replace existing therapies.

Some of the drugs that reach the market faster under PDUFA will truly be breakthrough products – offering treatment where no effective treatment currently exists. These drugs are likely to be the treatment of choice by physicians and their patients, and will bring valuable benefits to consumers. But other newly introduced drugs will simply substitute newer, more expensive drug treatments for existing cost-effective agents.

Because the marketplace is becoming more and more competitive within many therapeutic classes, relative cost-effectiveness information is becoming more important. For example, little is known about the effectiveness of new diabetes drugs compared to older therapies in terms of their ability to reduce incidences of microvascular complication and retinal problems. Similarly, consumers, clinicians, and government and private payers need more information about the relative value of various asthma treatments in terms of symptom-free days, decrease in work loss and any decrease in the use of inpatient services. Quality-of-life data also is an important determinant of value.

By supporting initiatives to require manufacturers to provide information that allows a comparison of benefits, costs and risks of new drugs that replace existing therapies, the FDA will help to ensure that Americans have continued access to breakthrough medical treatments and the right information to make informed choices about their own medical treatment.

Appropriations

Given the critical consumer safety functions the FDA performs with respect to new drugs and under many other important agency programs, sustained increased congressional appropriations are necessary. BCBSA calls on Congress to match the 2002 fiscal year appropriations level each year going forward, adjusted for inflation. We look forward to working with the agency, the pharmaceutical industry and other stakeholders on this initiative to achieve the goal of a fully-funded FDA that has the resources to carry out its public health and safety mission.

Conclusion

BCBSA is very concerned that accelerated drug reviews under PDUFA have not in the past been accompanied by comparable funding for consumer safety initiatives. BCBSA believes that as user fees speed new therapies to consumers, there is a comparable need to ensure that these drugs are safe and effective and that consumers receive complete and accurate information about the risks and benefits associated with their use.

In order to achieve this objective, BCBSA recommends that Congress expand the statutory definition of "process[es] for the review of human drug applications" to include postmarketing surveillance and compliance activities (e.g., monitoring adverse drug events and DTC advertising) (21 USC §379(g)(6)(A)) as "activities necessary for the review of human drug applications and supplements."

In addition, BCBSA recommends that the FDA review PDUFA's role in ensuring that the rapid flow of new drugs to market is accompanied by health outcomes information that allows consumers, physicians and health plans to make value-driven prescription drug decisions.

Finally, we applaud Congress and the Administration for their recent approval of increased appropriations for FDA in fiscal year 2002, and we urge them to propose a larger increase for fiscal year 2003. BCBSA supports continued increases in federal appropriations for FDA to provide resources for agency programs that impact public health.

BCBSA applauds the FDA for addressing this critical health care issue and supports the agency in its endeavor.

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[i] Food and Drug Administration, Center for Drug Research and Evaluation, *CDER 2000 Report to the Nation: Improving Public Health Through Human Drugs*. Accessed May 21, 2000 from http://www.fda.gov.

[ii] National Institute for Health Care Management, *Prescription Drugs and Mass Media Advertising, 2000*, (November 2001).

[iii] Henry J. Kaiser Family Foundation, *Understanding the Effects of Direct-to-Consumer Prescription Drug Advertising*, (November 2001).

[iv] "Half of Rx drug consumer ad spending goes to TV, Scott-Levin reports." Cf. also "IMS Health Reports Direct-to-Consumer Advertising Increases Prescription Pharmaceutical Brand Requests and Awareness: Majority of Physicians have Negative View Toward DTC Advertising."