Report to Senate Committee on Health, Education, Labor, and Pensions and the House Committee on Energy and Commerce

Report on Study Commitment Regarding Inclusion of Toll-Free Adverse Event Reporting Number by FDA

Food and Drug Administration

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Introduction

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85). Section 906 of Title IX of FDAAA amends section 502(n) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 352), by requiring printed direct-to-consumer (DTC) advertisements for prescription drug products to include the following statement printed in conspicuous text: "You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088." Section 906 of FDAAA also requires the Secretary of the Department of Health and Human Services (HHS), in consultation with the Advisory Committee on Risk Communication, to conduct a study not later than 6 months after the date of enactment of FDAAA to determine if this statement is appropriate for inclusion in DTC television advertisements for prescription drug products. As part of this study, the Secretary of HHS is required to consider whether the information in the statement described above would detract from the presentation of risk information in a DTC television advertisement. If the Secretary determines that the inclusion of such a statement would be appropriate for television advertisements, FDAAA mandates the issuance of regulations implementing this requirement, and for the regulations to determine a reasonable length of time for displaying the statement in television advertisements. Finally, FDAAA requires the Secretary of HHS to report the study's findings and any subsequent plans to issue regulations to Congress.

For the reasons discussed below, we estimated the conduct of the required study will take up to 2 years to complete. The Food and Drug Administration (FDA) will complete the study and will report to Congress on the results as soon as it is completed.

Relevant Prior History and Research

Congress has previously passed legislation requiring the addition of a statement to the labeling of drugs about reporting side effects to a toll-free number. FDA's experience with implementing this legislation is relevant to the conduct of the study under section 906 of FDAAA.

Section 17 of the Best Pharmaceuticals for Children Act (the BPCA) (Public Law 107-109, January 4, 2002) required FDA to issue a final rule requiring the addition of a statement to the labeling of each drug product for which an application is approved under section 505 of the Act. Under the BPCA, the statements must include: (1) a toll-free number maintained by FDA for the purpose of receiving reports of adverse events regarding drugs; and (2) a statement that the number is to be used only for reporting purposes, and it should not be used to seek or obtain medical advice (the side effects statement).

On April 22, 2004, FDA published a proposed rule with a proposed side effects statement for certain prescription drug product labeling and a proposed side effects statement for certain over-the-counter drug product labeling.[1] In the proposed rule, FDA solicited comments on a statement that FDA believed comported with the above mandate in the BPCA. FDA received 12 comments suggesting changes to the specific wording proposed. FDA also received several comments suggesting that it engage in research to study how the wording of the proposed side

[1] See 69 *Federal Register* 21778

effects statement is perceived by consumers. Among the reasons cited for testing the statement were:

(1) to determine the best and most precise wording for the statement;
(2) to evaluate consumer comprehension of the proposed statement; and
(3) to address concerns that consumers who read the statement will mistakenly call FDA in search of medical advice rather than seeking appropriate medical treatment.

In addition, during the clearance process for the proposed rule, it was determined that FDA should conduct focus groups or other consumer studies to inform the wording of the side effects statement.

During the spring of 2006, to assist in developing the study on the toll-free number statement, FDA conducted two focus groups that included participants with a high school education or less and participants with some college education to gauge consumer understanding and preferences for a number of proposed side effects statements and to narrow the number of statements to be tested in subsequent experimental research. Focus groups are guided discussions led by a trained moderator. This research method is often used to collect qualitative information on a specific topic. Focus group results are not generalizable. These two focus groups with American consumers produced some helpful findings about the usefulness and clarity of various statements. In addition to the information collected on which versions of the statements participants preferred, major findings included:

- Some of the high school educated or less group thought that the statements instructed them to call FDA for medical help.
- Some participants in both groups understood the statements, but said they were not motivating enough to cause them to call FDA's toll-free number in the event that they might experience an adverse side effect.
- Some participants in both groups understood the statements and said they would call FDA to report adverse side effects if serious enough.
- Many suggested the addition of a Web site to report adverse side effects.

Based on the findings from the focus groups, a small number of statements were selected for quantitative testing. The data from that quantitative test were made available to FDA on March 1, 2008, and are currently undergoing analysis. The results from that study will provide FDA with information about the wording of the toll-free number statement that best communicates to consumers how to contact FDA about side effects. Notwithstanding the ongoing studies, in accordance with FDAAA section 502(f), the toll-free number proposed rule, as modified by FDAAA, became effective by operation of law on January 1, 2008.[2]

Although the process of conducting research on the statements has been lengthy, FDA believes it has obtained worthwhile information about the statement that should be included on drug labeling about reporting adverse events. FDA believes that the study required by FDAAA under section 906 will involve similar research methods and take up to 2 years to complete. A table

[2] See Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products, Interim Final Rule, 73 *Federal Register* 402 (2008).

describing the steps in the conduct of the research and the estimated time to completion is provided below. This is intended to illustrate, based on previous experience, the steps necessary to determine the appropriateness of a toll-free number in a DTC television advertisement.

Table 1: Steps and Associated Timeframes for Conducting Proposed Toll-Free Number Study

Process	Time Required
Develop methodology, draft questionnaire, draft materials and mock ads and consult with Advisory Committee on Risk Communication, as directed by FDAAA. Note that the first available Advisory Committee meeting is May 15-16, 2008.	90 days
Revise research plan based on Advisory Committee comments	30 days
Task order procured	30 days
Draft and publish *Federal Register* (*FR*) notice soliciting public comments on proposed information collection	14 days
60-day *FR* notice soliciting public comments on proposed information collection*	**60 days**
Revise research plan based on public comments	Between 14 and 60 days, depending on complexity of comments
Peer review of revised research plan	30 days
Final revisions based on peer review comments	30 days
Research in Human Subjects Committee review of proposal	30 days
Develop the Office of Management and Budget (OMB) submission package and 30-day *FR* notice	30 days
30-day *FR* notice soliciting public comments on revised proposed information collection. Public comments sent to OMB for review*	**120 days or more**
OMB/FDA's Division of Drug Marketing, Advertising, and Communication discussion of proposed research	1 day
OMB consideration of discussion. OMB may suggest revisions, approve or disapprove proposed information collection	15-30 days or more
Data collection	45 days
Report and data from contractor	30 days after end of data collection phase
Analyze data	60 days
Write report	30 days
Total Minimum Timeframe	*659-720 days*

***Procedures and timeframes in boldface are mandated by the Paperwork Reduction Act and cannot be changed.**

As a public agency, FDA is required by the Paperwork Reduction Act of 1995 to go through multiple steps to allow for public comment on its intent to perform research, and OMB must review the request. Peer review by other researchers in the topic area is also necessary to ensure the scientific validity of the research question and design. Finally, review by FDA's Research in Human Subjects Committee is required before any data can be collected.

Conclusion

FDA shares Congress' goal of encouraging the public to report side effects of prescription drugs directly to FDA, which could augment the agency's ongoing activities to quickly identify postmarketing adverse events associated with a particular prescription drug product and take appropriate action. FDA's current activities in this important area include the collection of individual post-market adverse events by MedWatch and surveillance activities. The MedWatch form for reporting a side effect can now be filled out online, also streamlining the ability of consumers and healthcare providers to report adverse events and medications areas. FDA is also involved in a major transformation of its website to make information about all the products it regulates accessible to consumers and healthcare providers. The consumer information webpage has already been launched.

Because television advertisements reach a broad national audience, it is crucial to ensure that any statement included in these ads encouraging reporting of side effects has the intended effect without impeding the communication of risk information. The best way to credibly accomplish this is to conduct empirical research. FDA appreciates Congress' recognition that empirical research will provide a scientific basis for the appropriate implementation of the statement mandated by section 906 of FDAAA. FDA regrets that it will not be able to conduct the research in the timeframe specified, but intends for this document to explain and describe the appropriate time necessary to complete this important study.