Request for OMB Review

Supporting Statement for

Toll-Free Number for Consumer Reporting of Drug Product Side Effects: Comprehension Experiment

Submitted by
Carol Drew
Office of Regulatory Policy
Center for Drug Evaluation and Research
Food and Drug Administration
Department of Health and Human Services

October, 2006

Revised: June 26, 2007

Supporting Statement for

Toll-Free Number for Consumer Reporting of Drug Product Side Effects: Comprehension Experiment

Submitted by
Center for Drug Evaluation and Research
Food and Drug Administration

A. JUSTIFICATION

1. Circumstances Necessitating Information Collection

Section 17 of the Best Pharmaceuticals for Children Act (the BPCA) (Public Law 107-109) required FDA to issue a final rule mandating the addition of a statement to the labeling of each drug product for which an application is approved under section 505 of the Federal Food Drug and Cosmetic Act (the Act). Under the BPCA the statements must include (1) a toll-free number for consumers to use to report drug product side effects, and (2) a statement that the number is to be used only for reporting side effects and is not intended 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 (69 FR 21778). In the proposed rule FDA solicited comments on the wording of these side effect statements. We received 12 comments suggesting changes to the specific wording of the proposed side effects statements. We also received several comments suggesting that FDA engage in research to study the wording of the proposed side effects statements with consumers. Among the reasons cited for testing the statements were: (1) to determine the best and most precise wording for the statements, (2) to evaluate consumer comprehension of the proposed statements, and (3) to address concerns that consumers who read the statement will mistakenly call FDA in search of medical advice. In addition, during the clearance process for the

proposed rule, both the Office of Information and Regulatory Affairs of the Office of Management and Budget (OMB) and the Office of the Assistant Secretary for Planning and Evaluation (ASPE) of the Department of Health and Human Services suggested that FDA conduct focus groups or other consumer studies to inform the wording of the side effects statements. We did not conduct testing at that time because of the Congressional mandate to issue a rule one year after the enactment of the BPCA. After the publication of the proposed rule and based on the comments received, it was decided to delay the issuance of the final rule in order to conduct research to study the wording of the proposed side effects statements.

FDA conducted two focus groups (OMB Control No. 0910-0497) to narrow the field of potential statement alternatives. The focus groups, representing higher and lower levels of education, suggested the use of four prescription drug side effects statements and three over-the-counter side effects statements (see section 2). Additionally, given the increasing use of the Internet, as mentioned in the focus groups, we would like to test the inclusion of a website address in both prescription drug and over-the-counter drug product arenas. Testing the statements experimentally will provide valuable information on the comprehension, usefulness, and selection of the side effect statements.

2. How, By Whom, Purpose of Collection

This supporting statement describes an experimental study that will enhance the Agency's understanding of which side effects statements most effectively convey appropriate information to consumers, therefore, assisting the Agency in selecting statements to fulfill the BPCA.

The side effects statements to be tested for the prescription drug label are:

1. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

2. Call your doctor for medical advice about side effects. Report serious side effects to FDA at 1-800-FDA-1088.

3. Call your doctor or pharmacist for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

4. Side effects? Call your doctor for medical advice. You may report them at 1-800-FDA-1088.

5. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

As explained in the proposed rule, OTC drug product labeling has a prescribed format designed to assist consumers in reading and understanding OTC drug product labeling (the Drug Facts label) (21CFR 201.66). The agency has incorporated the side effects statement into the Drugs Facts label, therefore the side effects statements to be tested for the over-the-counter label are:

1. Stop use and ask a doctor if side effects occur. You may report side effects to FDA at 1-800-FDA-1088.

2. Stop use and ask a doctor if you have a side effect. You may report side effects to FDA at 1-800-FDA-1088.

3. Stop use and ask a doctor if you have a side effect. Report serious side effects to FDA at 1-800-FDA-1088.

4. Stop use and ask a doctor if side effects occur. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Each participant will be exposed to only one side effects statement, in a "between-subjects" or "monadic" design. Participants will initially see one statement in the context of either a prescription drug bottle or a Drug Facts label, depending on which condition they are in, and will all answer the same series of questions (samples of the stimuli are included in Attachment B). For the remainder of the study, each participant will see the statement as they answer questions specifically about the statement. Again, all participants will answer the same series of questions.

The proposed experimental study data will be collected via the Internet from 1,600 members of a consumer panel maintained by the research firm Synovate. Synovate's Internet panel consists

of approximately 600,000 households that have agreed to participate in research studies conducted through the Internet.

Panel members are recruited by a variety of means designed to reflect all segments of the population. They are required to have a computer with Internet access. Typical panel members receive three or four invitations per month to participate in research projects. Studies begin with an e-mailed invitation to the sampled respondents.

Each panel member has provided demographic data for their household that allows for the selection of samples that resemble closely the distribution of the U.S. population on age, gender, education, and race/ethnicity. Overall, the panel tends to under-represent minorities, low income households, and the elderly.

Conventional statistical techniques for experimental data, such as descriptive statistics, analysis of variance, and regression models will be used to analyze the data. Covariates used in the analysis will include prescription and over-the-counter drug product side effect experience, age, race/ethnicity, gender, and education.

This proposed data collection would be one-time only. No successive related data collections are planned.

3. Consideration Given to Information Technology

This proposed study will use the Internet for data collection. Members of the sample, who are part of a consumer opinion panel, will receive an e-mailed invitation to participate in the experiment. People who choose to participate will respond from their personal computer at a time of their choosing. The respondents will view the product labels and study questions on their computer screen and will register their responses using their keyboard and mouse. The Internet was selected as the means to collect data to minimize burden cost-effectively.

4. Identification of Information

FDA received comments on the wording and development of appropriate side effects statements, including requests to conduct research. The Agency is not aware of previous data collected on the subject.

During the spring of 2006, FDA conducted two focus groups 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 groups results are not generalizable. These two focus groups with consumers produced some helpful findings about the usefulness and clarity of various statements. In addition to the top statements in terms of participant preference, other findings were:

- Some people in the lower education group thought that the statement instructed them to call FDA for medical help.
- Some people in both groups understood the statement but said that it was not motivating enough to cause them to call the number.
- Some people in both groups understood the statement and said they would call FDA to report side effects if they were serious enough.
- Some people suggested the addition of a website to report side effects.

Based on the findings from the focus groups, we have selected a small number of statements for quantitative testing. The proposed experimental study will provide quantitative data to help choose the best side effects statements to fulfill the BPCA.

5. Small Businesses

No small businesses will be involved in this data collection.

6. Less Frequent Information Collection

The proposed data collection is one-time only. There are no plans for successive data collections.

7. Information Collection Circumstances

This collection of information fully complies with 5 CFR 1320.5. There are no special circumstances.

8. Consultations with Persons Outside FDA

See section one (Circumstances Necessitating Information Collection). Aside from public comments received after the publication of the Federal Register notice for the proposed rule (69 FR 21778), FDA has not consulted with persons outside the Agency.

9. Payment or Gift

Members of Synovate's Internet panel will not be paid specifically for their participation in this study. However, as part of the firm's incentive to recruit and maintain membership, panelists are offered rewards by the firm for their general participation in surveys sent out by the panel. The reward takes the form of entries into the panel's monthly sweepstakes. Each time a member completes a study, the individual is automatically entered into the current month's drawing to win one of the following cash prizes: one cash prize of $1000, 10 prizes of $100, 15 prizes of $50, 30 prizes of $25, and 150 prizes of $10.

10. Confidentiality Provisions

All respondents will be provided with the assurance of confidentiality. The experiment will include information explaining to respondents that their information will be kept confidential. An independent contractor for the FDA will collect these data and will not provide FDA identifying information on the respondents.

The contractor, Synovate, has procedures in place to prevent unauthorized access to respondent information. The firm stores members' personal identifiable information on separate servers from survey response data, uses firewalls to secure its servers, maintains audit records of log-ins, file accesses and other security incidents, and conducts its work in a high security building.

Synovate reassesses security protocols each month. Access to all data collected by Synovate is limited to the internal Chief Privacy Officer and designated staff members only. Synovate staff members are trained in their privacy policy. Each staff person who requires access to system data must sign a confidentiality agreement each year.

All electronic data will be maintained in a manner which is consistent with the Department of Health and Human Services ADP Systems Security Policy as described in DHHS ADP Systems Manual, Part 6, chapters 6-30 and 6-35. All data will also be maintained in consistency with the FDA Privacy Act System of Records #09-10-0009 (Special Studies and Surveys on FDA Regulated Products).

11. Privacy

This data collection will not include sensitive questions. The complete list of questions is included in attachment A.

12. Burden of Information Collection

The total annual estimated burden imposed by this collection of information is 257 hours for this one-time collection (Table 1).

Table 1. Estimated Annual Reporting Burden[1]

Activity	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Screener	1,684	1	1,684	0.01	17
Experiment	1,600	1	1,600	0.15	240
Total					257

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

These estimates are based on FDA's experience with previous consumer studies. The screener will be administered to the entire 600,000 Internet panel, with an expected 1,684 responses. The screener is estimated to take no more than one minute to complete.

The experiment will be conducted with 1,600 panel members. The experiment is estimated to take each respondent no longer than 15 minutes to complete.

13. Costs to Respondents

There are no costs to respondents.

14. Costs to Federal Government

The estimated cost to the federal government is $24,658. This includes the costs paid to the contractor to program the study, draw the sample, collect the data, and create a database of the results. This cost also includes FDA staff time to design and manage the study, to analyze the resultant data, and to draft a report.

15. Reason for Change

This is a new data collection.

16. Statistical Reporting

Conventional statistical techniques for experimental data, such as descriptive statistics, analysis of variance, and regression models will be used to analyze the data. Covariates used in the analysis will include prescription and over-the-counter drug product side effect experience, age, race/ethnicity, gender, and education.

The Agency anticipates disseminating the results of the study and selecting a side effects statement for prescription drug labels and another for over-the-counter labels after the final analyses of the data are completed, reviewed, and cleared. The exact timing of such an application has not been determined, but will occur as quickly as possible to allow for the finalization of the rule.

17. Display of OMB Approval Date

No exemption is requested.

18. Exceptions to "Certification for Paperwork Reduction Act Submissions"

No exceptions are requested.

B. Collections of Information Employing Statistical Methods

1. Potential Respondent Universe and Sampling Selection

The universe for this experimental study is members of the Synovate Internet panel. Synovate's Internet panel consists of 600,000 households that are recruited by a variety of means to reflect all segments of the U.S. population and have agreed to participate in Internet research studies. Typical panel members receive three or four invitations per month to participate in research projects.

The 1,600 participants for this study would be drawn from the pool of over 5,614 panel members. Quotas will be used so that the overall sample is in proportion to the U.S. adult population on age, gender, education, and race/ethnicity.

The Agency does not intend to generate nationally or locally representative results or precise estimates of population parameters from this study. The sample used is a convenience sample, rather than a probability sample. Despite the attempt to match between the study's sample and known population characteristics, matching is used solely to produce samples with a reasonable degree of diversity in key demographic characteristics. Furthermore, no legitimate weights can be constructed from non-probability samples such as the one used here. Hence, the Agency does not construe this sample or the results generated from this sample as nationally or locally representative. Rather, the strength of the experimental study lies in its internal validity, on which meaningful estimates of differences across conditions can be produced and generalized.

Power

The sample size per condition is 175 respondents. This figure is based on (1) 0.05 alpha, (2) 0.80 power, (3) two-tailed mean tests, and (4) an estimated effect size between small and medium, roughly 0.25. Based on this figure, the total sample size required for the analysis is 1,575 (the

product of multiplying 175 by each of nine conditions).[1] We will test 1,600 individuals to account for rounding errors as well as incomplete interviews and missing data.

2. Procedures for the Collection of Information

Participants will see one statement in the context of a prescription bottle or a Drug Facts label. They will respond to survey questions about their intended actions when side effects occur and then respond to more specific questions about the statement itself. This method will allow FDA to compare the responses of participants who saw nine (9) different statements. Main dependent variables are: comprehension of the side effects statements, as measured by reasons for calling a physician and/or the FDA; the likelihood of calling FDA, to appreciate prospective workload burden; and the clarity of each statement. The complete questionnaire is included as Attachment A.

3. Methods to maximize response rates and to deal with issues of non-response

This experimental study will use an existing Internet panel to draw a sample. The panel includes people who have expressed interest in sharing their opinions via the Internet and do so regularly. The expected participation rate for the Internet panel is 55 percent when responding to a specific study. To help ensure that the participation rate is as high as possible, the Agency will:

- Design an experimental protocol that minimizes burden (short in length, clearly written, and with appealing graphics);
- Administer the experiment over the Internet, allowing respondents to answer questions at a time and location of their choosing;
- Administer the experiment to individuals who have expressed interest in participating in Internet studies;

1 Cohen, J., & Cohen, P. (1983). *Applied multiple regression/correlation analysis for the behavioral sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates.

- Email a reminder to the respondents who do not complete the protocol four days after the original invitation to participate is sent;
- Provide contact information on where to get help for respondents who may have questions as they complete the experiment.

4. Test Procedures

Pretests will be completed before the actual study to clarify the questionnaire wording and to control glitches in procedure. After OMB clearance is received, pretests of the questionnaire shall be conducted in two waves with 30 members of Synovate's Internet panel in each wave, representing a reasonable degree of demographic diversity. These pretests are designed to ensure that questionnaire wording is clear and that procedures for viewing stimuli and proceeding through the experiment are as planned.

5. Individuals Involved in Statistical Consultation and Information Collection

The contractor, Synovate, will collect the information on behalf of the FDA as a task order under the Quick-Turn-Around Research Services contract. Leigh Seaver, Ph.D., is the Senior Study Director for Synovate, telephone (703) 790-9099. Analysis of the information will be conducted primarily by the Research Team, Division of Drug Marketing, Advertising and Communications, Office of Medical Policy, CDER, FDA, and coordinated by Amie C. O'Donoghue, Ph.D., 301-796-0574 and Kathryn J. Aikin, Ph.D., 301-796-0569.