Study of Clinical Efficacy Information in Professional Labeling and Direct-to-Consumer (DTC) Print Advertisements for Prescription Drugs

0910-Number

SUPPORTING STATEMENT A

Submitted by

Division of Drug Marketing, Advertising, and Communications
Center for Drug Evaluation and Research

Food and Drug Administration

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A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes the Food and Drug Administration (FDA) to conduct research relating to health information. Section 903(d)(2)(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(b)(2)(c)) authorizes FDA to conduct research relating to drugs and other FDA regulated products in carrying out the provisions of the FD&C Act.

FDA regulations require that an advertisement that makes claims about a prescription drug include a "fair balance" of information about the benefits and risks of the advertised product, in terms of both content and presentation (21 CFR 202.1(e)(5)(ii)). In past research FDA has focused primarily on the risk component of the risk-benefit ratio. In the interest of thoroughly exploring the issue of fair balance, however, the presentation of effectiveness, or benefit, information is equally important.

The Federal Food, Drug, and Cosmetic Act (the Act) requires that manufacturers, packers, and distributors (sponsors) who advertise prescription human and animal drugs, including biological products for humans, disclose in advertisements certain information about the advertised product's uses and risks.[1] By its nature, the presentation of this risk information is likely to evoke active trade-offs by consumers, i.e., comparisons with the perceived risks of not taking treatment, and comparisons with the perceived benefits of taking a treatment.[2] Since FDA has an interest in fostering safe and proper use of prescription drugs, an activity that engages both risks and benefits, an in-depth

[1] For prescription drugs and biologics, the Act requires advertisements to contain "information in brief summary relating to side effects, contraindications, and effectiveness" (21 U.S.C. 352(n)).

[2] See Schwartz, L., Woloshin, S., Black, W., & Welch, H.G. (1997). The role of numeracy in understanding the benefit of screening mammography. *Annals of Internal Medicine, 127(11),* 966-72.

understanding of consumers' processing of this information is central to this regulatory task.

Research and guidance to sponsors on how to present benefit and efficacy information in prescription drug advertisements is limited. For example, "benefit claims," broadly defined, appearing in advertisements are often presented in general language that does not inform patients of the likelihood of efficacy and are often simply variants of an "intended use" statement.[3] In a content analysis of DTC advertising,[4] the researchers classified the "promotional techniques" used in the advertisements. Emotional appeals were observed in 67% of the ads while vague and qualitative benefit terminology was found in 87% of the ads. Only 9% contained data. For risk information, however, half the advertisements used data to describe side-effects, typically with lists of side-effects that generally occurred infrequently.

FDA regulations require that prescription drug advertisements that make (promotional) claims about a product also include risk information in a "balanced" manner (21 CFR 202.1(e)(5)(ii)), both in terms of the content and presentation of the information. This balance applies to both the front (aka "display") page of an advertisement, as well as the brief summary page. However, beyond the "balance" requirement limited guidance and research exists to direct or encourage sponsors to present benefit claims that are informative, specific, and reflect clinical effectiveness data.

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[3] Woloshin, S., & Schwartz, L. (2001). Direct to consumer advertisements for prescription drugs: What are Americans being told. *Lancet, 358*, 1141-46.

[4] Woloshin, S., & Schwartz, L. (2001). Direct to consumer advertisements for prescription drugs: What are Americans being told. *Lancet, 358*, 1141-46.

The purpose of this project is to 1) understand how physicians process clinical efficacy information and how they interpret approved product label information;[5] 2) determine physician preferences for alternative presentations of clinical efficacy information in direct-to-consumer (DTC) advertising; and 3) examine how different presentations of clinical efficacy information in DTC advertising affect consumers' perceptions of efficacy and safety. Specifically, we are interested in how physicians and consumers evaluate benefit information and particularly, how consumers make such judgments in response to variations in the efficacy presentations in the "display" (first) page of a DTC print ad. A particular concern is whether certain presentations cause consumers to form skewed perceptions or unfounded risk/benefit tradeoffs. Therefore, we will investigate to what extent consumers, when provided with efficacy information, form perceptions that correspond with clinically-based physicians' assessments of the benefits, risks, and benefit/risk tradeoffs of the same drugs. These studies will inform FDA's thinking regarding how manufacturers may provide useful and non-misleading efficacy information in DTC print advertisements.

2. **Purpose and Use of the Information Collection**

This project will involve one web-based experiment with consumers and one web-based study with physicians. The purpose of this two-part project is to gather data to address 1) how physicians process approved product label information; 2) what physician preferences for alternative presentations of clinical efficacy information in direct-to-consumer (DTC) advertising are; and 3) how different presentations of clinical efficacy information in DTC advertising affect consumers' perceptions of efficacy and safety.

[5] As part of this effort, a qualitative mental models procedure was completed that helped us determine how physicians think about the efficacy of potential pharmaceutical options (OMB Control No. 0910-0649).

Part of FDA's public health mission is to ensure the safe use of prescription drugs; therefore it is important to communicate the risks and benefits of prescription drugs to physicians and consumers as clearly and usefully as possible. Parts of this study explore areas that have not been investigated to date and, as such, is designed to be the first in a series of potential studies—sponsored by FDA and others—to investigate complex issues of physician understanding of the approved label and consumer understanding of placebo information in different frames. Although this study may inform initial policy decisions, we propose this study as the first step in a longer series of studies which will eventually provide stronger evidence for science-based Agency policies.

3. **Use of Improved Information Technology and Burden Reduction**

Automated information technology will be used in the collection of information for this study. The contracted research firm will collect data through Internet administration. The participant will self-administer the Internet survey via a computer, which will record responses and provide appropriate probes when needed. In addition to its use in data collection, automated technology will be used in data reduction and analysis. Burden will be reduced by recording data on a one-time basis for each respondent, and by keeping surveys to less than 20 minutes.

4. **Efforts to Identify Duplication and Use of Similar Information**

There is a body of research on the topic of framing[6] but we are not aware of published studies that have examined this approach in DTC ads. Little research exists on the public's understanding of placebo, despite evidence that some people do not

[6] Moxley, A., O'Connell, D., McGettigan, P., & Henry, D. (2003). Describing treatment effects to patients: How they are expressed makes a difference. *Journal of General Internal Medicine, 18*, 948-959; Peters, E., Vastfjall, D., Slovic, P., Mertz, C.K., Mazzocco, K., & Dickert, S. (2006). Numeracy and decision making. *Psychological Sciences*, *17*, 407-413.

understand the concept.[7] Finally, we know of no studies that have examined how physicians use and read the current format of the prescribing information for prescription drugs.

5. **Impact on Small Businesses or Other Small Entities**

No small businesses would be involved in this data collection.

6. **Consequences of Collecting the Information Less Frequently**

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

7. **Special Circumstances Relating to the Guidelines of 5 CFR 1320.5**

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

8. **Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency**

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of June 16, 2010 (Vol. 75, No. 115; see Appendix A). FDA received no comments.

In addition to public comment, DDMAC sent materials to three individuals for external peer review. These individuals are:

• Jeremy Kees, Ph.D., Assistant Professor of Marketing, Villanova University

• Erika Waters, Ph.D., MPH, Assistant Professor of Surgery, Washington University

[7] As part of the studies conducted during development of the OTC Drug Facts box label, FDA asked participants to define several health terms, including placebo "as if you saw it in a dictionary." The results showed that over 50% of participants could not correctly define placebo. Aikin, K.J. (1998). Consumer comprehension and preference for variations in the proposed Over-the-Counter drug labeling format: Final report. Food and Drug Administration, Center for Drug Evaluation and Research.

• Jennifer Harlow, M.S., Associate Partner, Gallup

9. **Explanation of Any Payment or Gift to Respondents**

Internet panel participants receive points for completing a survey. Two thousand points (approximately monetary equivalence of $3) will be awarded. Members are allowed to use their points to exchange for vouchers and gifts from a partner network.

10. **Assurance of Confidentiality Provided to Respondents**

No personally identifiable information will be sent to FDA. All information that can identify individual respondents will be kept by the independent contractor in a form that is separate from the data provided to FDA. The information will be kept in a secured fashion that will not permit unauthorized access. Confidentiality of the information submitted is protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)), and by part 20 of the agency's regulations (21 CFR part 20). These methods will all be approved by FDA's Institutional Review Board (Research Involving Human Subjects Committee, RIHSC) prior to collecting any information.

All respondents will be provided with an assurance of confidentiality. The Internet Panel includes a Panel Privacy Policy that is easily accessible from any page on the site. A link to the Privacy Policy will be included on all survey invitations. The Panel complies with established industry guidelines and states that members' personally identifiable information will never be rented, sold, or revealed to third parties except in cases where required by law. These standards and codes of conduct comply with those set forth by American Marketing Association, the Council of American Survey Research Organizations, and others.

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' ADP Systems Security Policy as described in the 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. **Justification for Sensitive Questions**

This data collection will not include sensitive questions. The complete list of questions for consumers is available in Appendix B. The complete list of questions for physicians is available in Appendix C.

12. **Estimates of Annualized Burden Hours and Costs**

The total annual estimated burden imposed by this collection of information is 1,099 hours for this one-time collection (Table 1).

Table 1. Estimated Annual Reporting Burden[a]

Activity	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Screener, Physicians	2,272	1	2,272	1/60	38
Pretest, Physicians	50	1	50	20/60	17
Questionnaire, Physicians	500	1	500	20/60	167
Screener, Consumers	10,590	1	10,590	1/60	177
Pretest, Consumers	100	1	100	20/60	33
Questionnaire,	2,000	1	2,000	20/60	667

Consumers					
Total					1,099

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

These estimates are based on FDA's and the contractor's experience with previous consumer and physician studies.

Table 2. Estimated Annual Recordkeeping Burden

Activity	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
N/A	N/A	N/A	N/A	N/A	N/A

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

13. **Estimates of Other Total Annual Costs to Respondents and Record Keepers**

There are no costs to respondents. There are no record keepers.

14. **Annualized Cost to the Federal Government**

The estimated cost to the Federal Government for the collection of data is $378,099.81. This includes the costs paid to the contractors to create stimuli, to program the study, draw the sample, collect the data, and create a database of the results. The cost also includes FDA staff time to design and manage the study, to analyze the resultant data, and to draft a report.

15. **Explanation for Programs Changes or Adjustments**

This is a new data collection.

16. **Plans for Tabulation and Publication and Project Time Schedule**

Conventional statistical techniques for experimental data, such as descriptive statistics, analysis of variance, and regression models, will be used to analyze the data. The Agency anticipates disseminating the results of the study after the final analyses of the data are completed, reviewed, and cleared. The exact timing and nature of any such dissemination has not been determined, but may include presentations and articles at trade and academic conferences, publications, and Internet posting.

Table 3. Project Timetable

Task	**Estimated Completion Date**
External Peer Review	October, 2010
RIHSC Review	November, 2010
30-day FR notice publication	November, 2010
OMB Review of PRA package	March, 2011
Data Collection	April, 2011
Receipt of Data and Methods Report from Contractor	July, 2011
Data Analysis	September, 2011
Draft Report	November, 2011
Internal Review of Draft Report	December, 2011
Revisions	January, 2012
Final Report	February, 2012

17. **Reason(s) Display of OMB Expiration Date is Inappropriate**

No exemption is requested.

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

No exceptions are requested.