Experimental Study: Disease Information in Branded Promotional Material

0910-New

SUPPORTING STATEMENT

Submitted by

Office of Prescription Drug Promotion
Center for Drug Evaluation and Research

Food and Drug Administration

[June, 2012]
[Revised September, 2012]
[Revised October, 2012]

A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

Regulatory background. 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 prescription drug advertisements to contain accurate information about the benefits and risks of the drug advertised. Generally, the advertising must not be misleading about the effectiveness of the drug. Specifically, the ad must not contain a representation or suggestion that the drug is better than has been shown by substantial evidence or useful in a broader range of patients.[1] The regulations prohibit sponsors from, for example, disseminating promotional information that may broaden the indications of medications beyond the indication for which they have been approved.

Rationale: As a public health agency, FDA encourages the communication of accurate health messages about medical conditions and treatments. One way in which broad disease information is communicated to the public is through disease awareness communications.

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1 See 21 CFR 202.1(e)(6): "An advertisement for a prescription drug is false, lacking in fair balance, or otherwise misleading, or otherwise violative of section 502(n) of the act, among other reasons if it: (i) Contains a representation or suggestion, not approved or permitted for use in the labeling, that a drug is better, more effective, useful in a broader range of patients (as used in this section, *patients* means humans and in the case of veterinary drugs, other animals), safer, has fewer, or less incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience (as described in paragraphs (e)(4)(ii)(b) and (c) of this section) whether or not such representations are made by comparison with other drugs or treatments…"

> "Disease awareness communications are communications disseminated to consumers or health care practitioners that discuss a particular disease or health condition, but do not mention any specific drug or device or make any representation or suggestion concerning a particular drug or device. Help-seeking communications are disease awareness communications directed at consumers. FDA believes that disease awareness communications can provide important health information to consumers and health care practitioners, and can encourage consumers to seek, and health care practitioners to provide, appropriate treatment. This is particularly important for under-diagnosed, under-treated health conditions, such as depression, hyperlipidemia, hypertension, osteoporosis, and diabetes. Unlike drug and device promotional labeling and prescription drug and restricted device advertising, disease awareness communications are not subject to the requirements of the Federal Food, Drug, and Cosmetic Act (the act) and FDA regulations."[2]

Some research has shown that disease awareness advertising is viewed by consumers as more informative and containing less persuasive intent than full product advertising.[3]

Sponsors may choose to include disease information in their full product promotions. Such information is designed to educate the patient about his or her disease condition. However, in some cases a full description of the medical condition may include information about specific health outcomes that are not part of a drug's approved indication. The current project is designed to determine if providing such information in branded full product advertisements affects perceptions of the product.

When broad disease information accompanies or is included in an ad for a specific drug, consumers may mistakenly assume that the drug will address all of the

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2 See *Draft Guidance for Industry: "Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms* (pg. 1). Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070068.pdf. Last accessed June 8, 2012.

3 Lee-Wingate, S. & Xie, Y. (2010). Consumer perceptions of product-claim versus help-seeking direct-to-consumer advertising. *International Journal of Pharmaceutical and Healthcare Marketing*, *4*(3), 232-246.

potential consequences of the condition mentioned in the ad by making inferences that go beyond what is explicitly stated in an advertisement.[4] For example, the mention of diabetic retinopathy in an advertisement for a drug that lowers blood glucose may lead consumers to infer that the drug will prevent diabetic retinopathy, even if no direct claim is made. The advertisement may imply broader indications for the promoted drug than are warranted, leading consumers to infer effectiveness of the drug beyond the indication for which it was approved. If consumers are able to distinguish between disease information and product claims in an ad, then they will not be misled by the inclusion of disease information in a branded ad. If consumers are unable to distinguish these two, however, then consumers may be misled into believing that a particular drug is effective against long-term consequences. The current study will explore perceptions that result from including both disease information and promotional information about a specific drug in the same advertising piece.

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

This project will investigate the effects of adding disease information to branded prescription drug promotional materials on consumer perceptions and understanding. 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 consumers in a way that is clear, useful and non-misleading. The results from this project will be used by FDA to inform its understanding of DTC advertising, inform regulatory policy, and may also help to identify areas for further research.

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4 Burke, R. R., DeSarbo, W. S., Oliver, R. L., & Robertson, T. S. (1988). Deception by implication: An experimental investigation. *Journal of Consumer Research, 14(4)*, 483-494; Harris, R. J. (1977) Comprehension of pragmatic implication in advertising. *Journal of Applied Psychology, 62*, 603-608; Jacoby, J., & Hoyer, W. (1987). *The comprehension and miscomprehension of print communications.* New York: The Advertising Educational Foundation.

Data will be collected by an independent contractor and shared with FDA electronically. No personally identifiable information will be sent to FDA. All information that can identify individual respondents will be maintained by the independent contractor in a form that is separate from the data provided to FDA. The data shared with FDA will be used to answer the research questions. The proposed data collection should have no impact on privacy.[5]

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. Participants will self-administer the survey instrument via a computer, which will record responses and provide appropriate probes when needed. FDA estimates that 100% of the respondents will use electronic means to fulfill the agency's request. 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**

We conducted a literature search to identify duplication and use of similar information. We conducted a systematic review of the scientific literature by locating relevant articles through keyword searches using five different databases, including PubMed and PsycInfo. We also identified relevant articles from the reference list of articles found through keyword searches. As noted above, we did not find duplicative

5 This paragraph satisfies sections D.b.2 and D.b.3 of the OMB Guidance for Implementing the Privacy Provisions of the E-Government Act of 2002.

experimental work on the communication of disease outcome information combined with product information in direct-to-consumer prescription drug advertisements.

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

No small businesses will 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 August 16, 2011, Volume 76, Number 158 (Docket No FDA-2011-N-0568). A copy of the 60-day Federal Register notice is included in Appendix 1. FDA received one public submission. In the following section, we outline the observations and suggestions raised in the submission and provide our responses.

(Comment 1) One statement suggested we add a multiple choice question to obtain a baseline of how consumers research information about their disease in other forms and if they are actively engaged in healthcare decisions.

(Response) We agree this question is interesting, but feel it is outside the scope of the current study. The purpose of the study is to examine how disease outcome and

product information contained within the same piece influences perceptions of product benefit.

(Comment 2) One comment stated that the inclusion of the MedWatch reporting statement discloses the prescription status of the product and suggested rewording the question about the type of product being tested.

(Response) We have reworded the question, removing the choice options "household cleaner" and "herbal supplement" and added a "don't know" option.

(Comment 3) Two statements said that open-ended questions would result in subjective data interpretation and suggested either replacing them with closed-ended questions or deleting. These statements also suggested that procedures for coding, categorizing and analyzing verbatim responses be established in advance, and that comparable questions about both benefits and risks be included.

(Response) We have established baseline codes for the open-ended questions and included parallel questions to assess perceptions of benefits and risks (see draft questionnaire). Other codes will be established through pretesting. We will have two independent raters for coding and we will calculate inter-rater reliability. Disagreements between coders will be resolved through discussion. In addition, our open-ended questions are accompanied by closed-ended questions.

(Comment 4) One comment stated that those previously diagnosed with the medical condition may respond differently than the newly diagnosed.

(Response) We agree that length of diagnosis could impact responses to information. We are recruiting a general population sample and plan to use medical

condition as a covariate. We have added a question to assess time since diagnosis among those who self-identify as having the condition of interest.

(Comment 5) The submission suggested deleting items: 1) attitudes about the product, 2) multiple items measuring the same construct (risk, benefit), and 3) perceptions of the risk/benefit tradeoff.

(Response) We have addressed these suggestions in the following ways. We have deleted the questions measuring product attitudes. We believe that two questions measuring risk and benefits are necessary to assess the reliability[6] of each construct and so have kept both questions. With regard to the final point, we agree that the risk/benefit ratio is different for each patient, but we also think that the perceived risk/benefit ratio for a product is influenced by the information presented in the ad. It is relevant here in that the risk/benefit assessment may be influenced by the perception that the disease outcome information is a product characteristic.

(Comment 6) One statement suggested deleting the questions related to behavioral intention, while another statement suggested expanding these questions.

(Response) As these statements are contradictory, we offer our reasoning behind including these questions. In an ideal situation, we would be able to measure actual behaviors that may result from exposure to a particular promotional campaign. Because we cannot do that, we propose to measure participants' intended behavior; that is, the likelihood that they would engage in specific outcome behaviors that may occur as a result of exposure to the product and disease information. This is in concordance with the recommendations of the November 17, 2011 meeting of the Risk Communication

6 Guidance for Industry: Patient Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071975.pdf. Last accessed November 16, 2011.

Advisory Committee, which suggested behavioral intention as an important variable to measure in research studies on promotion.[7]

(Comment 7) One comment stated that the questions assessing recall included false benefit items but were not balanced with statements to recall true/factual disease awareness information and suggested including true statements from the disease awareness information.

(Response) Our use of the term "false benefit" in the questionnaire notes may have caused confusion. In the draft questionnaire, "false benefit" simply refers to disease characteristics that are not part of the product's indication. The purpose of this question is to first determine which, if any, of the outcome claims are being interpreted by the participant as product benefits. Following this question is an open-ended question intended to measure what it was about the ad that suggested that (see questionnaire). We have revised the questionnaire notes to read "outcome" and "non-outcome" for clarity.

(Comment 8) One statement asked for more detail about the study design and stimuli layout and offered specific suggestions on variables to include in the study: vary the presentation of the disease information using headers with and without disclaimers, use a control test ad with no headers, use branded colors, non-branded colors, etc. to maximize understanding of whether consumers are able to distinguish between disease information and product claims and whether the format enhances understanding.

(Response) We have included a description of the study design in both the 60-day and 30-day Federal Register notices. We are exploring a number of different options for implementing the layout of the stimuli. For example: alternating paragraphs of product

7 Transcript available at http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/RiskCommunicationAdvisoryCommittee/UCM283132.pdf. Last accessed January 4, 2012.

and disease information, disease information on one page and product information on another page, use of identical or different colors and fonts for disease and product information, and different visuals for disease and product information. Final format variations will be determined through pretesting. This is the first study of this issue and therefore we are focusing on a small number of variations. It is not feasible to include every possible variation. We appreciate the layout suggestions provided.

(Comment 9) One statement addressed the recruitment process, requesting that we disclose how participants will be recruited and recommending mall intercept recruitment because recruiting participants online may not be reflective of the consumer likely to observe print advertising.

(Response) We plan to recruit and conduct the study online to use our resources most efficiently.

(Comment 10) One statement asked for a rationale for our sample size.

(Response) We have provided a rationale for our sample size in the Power Analysis.

(Comment 11) One statement requested details on the assignment to conditions, saying it was unclear if the study will include a sufficiently stratified sample based on language abilities, preexisting knowledge/disease awareness, age, gender, etc.

(Response) Participants will be randomly assigned to conditions. An attempt will be made to have an equal number of males and females in each experimental cell. Approximately 20% of participants in each cell will have a high school education or less, with a range of education and race/ethnicity represented in each condition. The following screening criteria will be employed: participants must be age 18 and over, must not work

for a pharmaceutical company, an advertising agency, a market research company, or be healthcare professionals.

(Comment 12) One statement asked that the screener specify if only those previously diagnosed with the condition will be eligible to participate, saying those previously diagnosed with the medical condition may engage differently than those who are recently diagnosed.

(Response) We agree that those who have the medical condition may react differently than those who do not. We plan to use diagnosis as a covariate in our analyses.

External Reviewers

In addition to the comments above, FDA requested that several outside experts review the study design and methodology. The following individuals reviewed the study design, methodology, and questionnaires in 2012:

- Lisa Bolton, Ph.D., Associate Professor of Marketing, The Pennsylvania State University.
- Jeremy Kees, Ph.D., Assistant Professor of Marketing, Villanova University.
- Sooyeon Nikki Lee-Wingate, Assistant Professor of Marketing, Fairfield University.

9. Explanation of Any Payment or Gift to Respondents

Participants will be offered a minimal incentive for participation. Internet panel participants are enrolled into a points program that is analogous to a 'frequent flyer' card: respondents are credited with sweepstakes entries or bonus points in proportion to their

regular participation in surveys (for the households provided Internet appliances and an Internet connection, their incentive is the hardware and Internet service. They are not provided with sweepstakes entries or bonus points). Traditionally, panelists earn sweepstakes entries on some surveys (including surveys more than 15 minutes in length) and bonus points for surveys that are longer or require special tasks by the panel member. Panelists may elect to redeem their points for checks (1,000 points = $1) or raffle entries as they accrue them. Participants receive points from the online panel so the incentive is not a separate cost to the Government. No cash incentive will be offered.

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 maintained 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. Privacy 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 20.63).[8] These methods have been approved by FDA's Institutional Review Board (Research Involving Human Subjects Committee (RIHSC)) prior to collecting any information. A Privacy Impact Assessment (PIA) will be required for this information collection.

8 This section states: "(a) The names or other information which would identify patients or research subjects in any medical or similar report, test, study, or other research project shall be deleted before the record is made available for public disclosure. (b) The names and other information which would identify patients or research subjects should be deleted from any record before it is submitted to the Food and Drug Administration. If the Food and Drug Administration subsequently needs the names of such individuals, a separate request will be made."

2[1] This satisfies section D.b.4.1 and D.b.4.2 of the OMB Guidance for Implementing the Privacy Provisions of the E-Government Act of 2002.

All respondents will be provided an assurance of privacy to the extent allowable by law. 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 the American Marketing Association, the Council of American Survey Research Organizations, and others. In addition, a consent form will be displayed before participants begin the survey (Appendix D). The consent form states that participation is voluntary.[9]

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.[10] All data will also be maintained consistent with the FDA Privacy Act System of Records #09-10-0009 (Special Studies and Surveys on FDA-Regulated Products).[11]

11. Justification for Sensitive Questions

This data collection will not include sensitive questions. The complete list of questions is available in Appendix 2.

12. Estimates of Annualized Burden Hours and Costs

The total annual estimated burden imposed by this collection of information is 1,873 hours for this one-time collection (Table 1).

9 This satisfies section D.b.4.1 and D.b.4.2 of the OMB Guidance for Implementing the Privacy Provisions of the E-Government Act of 2002.
10 This satisfies section D.b.4.3 of the OMB Guidance for Implementing the Privacy Provisions of the E-Government Act of 2002.
11 This satisfies section D.b.4.4 of the OMB Guidance for Implementing the Privacy Provisions of the E-Government Act of 2002.

The response burden chart is listed below.

Table 1.—Estimated Burden[1]

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Respondents	Hours per Response[2]	Total Hours
Sample outgo (pretests and main survey)	27,679	==	==	==	==
Number of screener completes (35%)	9,688	1	9,688	2/60	323
Number eligible (80%)	7,750	==	==	==	==
Number of completes, Pretests (60%)	900	1	900	20/60	300
Number of completes, Study (60%)	3,750	1	3,750	20/60	1,250
Number of pretest/study completes	4,650				
Total					1,873

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

Table 2. Estimated Annualized Burden Costs

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
General public	1,873	$18.90[a]	$35,400
Total			$35,400

[a]Based on the 2011 median weekly income of $756 for both sexes, as reported by the Department of Labor, http://www.bls.gov/news.release/pdf/wkyeng.pdf.

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 total estimated cost to the Federal Government for the collection data is $1,500,000 (approximately $500,000 per year for three years). This includes the costs

paid to the contractors to create stimuli, program the study, draw the sample, collect the data, and create a database of the results. The task order was awarded as a result of competition. Specific cost information other than the award amount is proprietary to the contractor and is not public information. The cost also includes FDA staff time to design and manage the study, to analyze the resultant data, and to draft a report ($120,000; 15 hours per week for 3 years).

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. See Section B below for detailed information on the design, hypotheses, and analysis plan. 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 at trade and academic conferences, publications, articles, and posting on FDA's website.

Table 4: Estimated Project Timetable

Task	Estimated Completion Date
60-day FR notice publication	August, 2011
External peer review	February, 2012
RIHSC review	June, 2012
Cognitive testing	July, 2012
30-day FR notice publication	July, 2012

OMB Review of PRA package	August, 2012
Pretesting	September, 2012
Data Collection	October, 2012-November, 2012
Receipt of Data and Methods Report from Contractor	December, 2012
Data Analysis	January-March, 2012
Draft Report	April, 2013
Internal Review of Draft Report	June, 2013
Revisions and Internal Clearance	July, 2013-August 2013
Final Report	September, 2013

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

No exemption is requested.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.