Examination of Online Direct-to-Consumer Prescription Drug Promotion

0910-Number

SUPPORTING STATEMENT A

Submitted by

Office of Prescription Drug Promotion
Center for Drug Evaluation and Research

Food and Drug Administration

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A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

Pharmaceutical products are launched and marketed in a number of new modalities and venues that did not exist a short time ago. Increasingly, prescription products are promoted to consumers online in such formats as banners, websites, and videos. The interactive nature of the internet allows for features not possible with traditional media (i.e., print, radio, and television), such as scrolling information, pop-up windows, linking to more information, and embedded videos. FDA regulations require that prescription drug advertisements include a "fair balance" of information about the benefits and risks of advertised products, both in terms of the content and presentation of the information (21 CFR 202.1(e)(5)(ii); Appendix A). All prescription drug promotion that makes claims about a product must, therefore, also include risk information in a "balanced" manner. Currently, there are a number of questions surrounding how to achieve "fair balance" in online direct-to-consumer (DTC) promotion.

A few content analyses have examined how well online DTC websites communicate benefit and risk information. Although content analyses demonstrate that most websites include information on side effects and contraindications (Ref. 1), risk information is often presented less prominently and in fewer locations on the website (Refs. 2, 3, and 4). Content analyses also suggest that risk information on DTC prescription drug websites is often incomplete (Ref. 5) and written at very high literacy levels (Ref. 6). Content analyses can describe what branded prescription drug websites currently look like, but cannot examine how factors such as the placement of risk information affects consumer understanding.

One experimental study examined how users interact with prescription drug websites (Ref 7). This study found that the placement of risk and benefit information on a website is an

important factor in whether it achieves "fair balance." Specifically, participants' ability to find and accurately recall risk information was enhanced when risk and benefit information were presented separately and when risk information was presented on a higher order page (i.e., on a second-level page clearly linked from the homepage, or on the homepage).

This project is designed to test different ways of presenting prescription drug risk and benefit information on branded drug websites. This project will build on the previous research by examining placement of the risk information (Study 1), but will also examine different formats for presenting the information (Study 1), the prominence of risk information with personal testimonials and animated visuals (Study 2), and links from branded prescription websites to disease awareness websites (Study 3). To our knowledge these additional issues have not been studied previously. Although we have an active research program examining DTC promotion, none of our other studies examine *online* DTC promotion. Instead, our other studies have examined issues such as the addition of quantitative information to print and television ads ("Presentation of Quantitative Effectiveness and Risk Information to Consumers in Direct-to-Consumer (DTC) Broadcast and Print Advertisements for Prescription Drugs" [FDA-2009-N-0263]; "Study of Clinical Efficacy Information in Professional Labeling and Direct-to-Consumer Print Advertisements for Prescription Drugs" [FDA-2010-N-0266]); "Experimental Study of Format Variations in the Brief Summary of Direct-to-Consumer (DTC) Print Advertisements" [FDA-2010-N-0417]), the addition of a toll-free number for reporting adverse events to FDA to television ads ("Experimental Study: Toll-Free Number for Consumer Reporting of Drug Product Side Effects in Direct-to-Consumer Television Advertisements for Prescription Drugs" [FDA-2008-N-0595]), and the addition of super-imposed text and the effects of distracting visuals in television ads ("Experimental Evaluation of the Impact of Distraction on

Consumer Understanding of Risk and Benefit Information in Direct-to-Consumer Prescription Drug Broadcast Advertisements" [FDA-2007-N-0451).

This research is relevant to current policy questions and debate (for example, see "Public Hearing on Promotion of FDA-Regulated Medical Products Using the Internet and Social Media Tools":http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm184250.htm) and will complement qualitative research we plan to conduct on issues surrounding social media ("Examination of Online Direct-to-Consumer Prescription Drug Promotion"; OMB Control No. 0910-0677). The series of studies described in this notice will provide data that, along with other input and considerations, will inform the development of future guidance.

2. Purpose and Use of the Information Collection

This project will involve three web-based experiments with consumers. The first experiment will examine the format and visibility of risk information on branded drug websites. The second experiment will examine the prominence of risk information in special features (such as testimonials) on branded drug websites. The third experiment will examine links from a branded drug website to a site with general disease information. The purpose of this project is to gather data for the FDA to address issues surrounding the presentation of risk information and links to general disease information websites on branded drug websites. 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 as clearly and usefully as possible.

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. One hundred percent (100%) of participants 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 25 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 six different databases, including PubMed and Web of Science. We also identified relevant articles from the reference list of articles found through keyword searches. As noted above, we found little experimental work on the communication of risk and benefit information on direct-to-consumer prescription drug websites.

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

A 60 day Federal Register Notice was published in the *Federal Register* on April 28, 2011, vol. 76, No. 82; pp. 23821-23823 (Appendix B). FDA received seven public statements, some of which included several comments. In the following section, we outline the observations and suggestions raised in the comments and provide our responses.

(Comment 1) One comment expressed the opinion that DTC advertising will never present risk and benefit information in a balanced manner and therefore the government should take a stronger stand against DTC advertising.

(Response) This is outside the scope of this project, but we note that the overall purpose of the research is to improve consumer understanding of prescription drug advertising.

(Comment 2) The comment describes web archiving technology and how it can be used to capture information from websites. They recommended we use their company's web archiving services for regulatory activities and to conduct the study.

(Response) The sections of this comment that relate to how the company's services can be used for regulatory activities are beyond the scope of this project. The sections that relate to the research suggest that we could use web archiving technology to create websites for the study; however, we plan to create new, unique, fictitious websites for the study to ensure familiarity with a particular website or brand does not have any influence on our findings.

(Comment 3) Two statements suggested additional information should be collected from participants. One statement suggested we use some of this additional information (prescription drug use) as a covariate.

(Response) Some of the additional information suggested is already included in the questionnaire (e.g., age, ethnicity, education level, and prescription drug use for the medical condition of interest). Although native language and whether participants are hearing or vision impaired are not directly assessed, participants must be capable of completing an intake questionnaire and core adult profile survey, both of which are written at an eighth grade reading level. Other additional information suggested will be included. Specifically, we will include level of internet use and length of time from diagnosis with the medical condition of interest. In addition, we will use prescription drug use for the medical condition of interest as a covariate in our analyses.

(Comment 4) One comment addressed the recruitment process, requesting that we disclose how participants will be recruited and recommending online recruitment.

(Response) We plan to recruit and conduct the study online.

(Comment 5) One comment recommended that caregivers also be included as participants.

(Response) To ensure that our participants are motivated to consider the information presented in the study and to conserve resources, we will limit our sample to people who have the medical condition of interest.

(Comment 6) One comment requested that we not apply the results of these studies to social media and mobile technology, as websites differ in a number of ways from other online contexts.

(Response) These studies are designed to address questions surrounding branded prescription drug websites and therefore the results will not be applied to social media and mobile technology.

(Comment 7) One comment requested that FDA publish the study design for the qualitative study mentioned in the Federal Register notice.

(Response) FDA plans to conduct ten focus groups to investigate how consumers, patients, and caregivers use online health communities and social media sites to make health decisions, especially regarding prescription drugs. These focus groups received OMB approval on April 28, 2011 ("Examination of Online Direct-to-Consumer Prescription Drug Promotion"; OMB Control No. 0910-0677). FDA will share the results of these focus groups when they become available.

(Comment 8) One comment suggested that the proposed samples sizes may not result in adequate statistical power.

(Response) We have conducted power analyses and will have sufficient sample to detect small to medium size effects with an alpha level of .05 and power of .90.

(Comment 9) One statement suggested that the proposed 2 x 2 + 1 design in Study 2 may limit an objective assessment of the effect of the variables in the control group. Another questioned the presence of the control group in Study 2, suggesting that it may confound the interpretation of results regarding the "prominence" manipulation. This statement suggested evaluating prominence in a separate part of the study.

(Response) Study 2 is designed to test two research questions: (1) to what extent does the presence of special features (e.g., personal testimonials, animated visuals) on a branded drug website influence consumer perceptions of a prescription drug, and (2) to what extent does the prominence of risk information in special features on a branded drug website influence consumer perceptions of a prescription drug? Both research questions can be addressed within the same design without having to evaluate prominence in a separate design. The first research question

will be tested by comparing responses of participants exposed to a website with a special feature to those who were not (the control group). The second research question will be tested by comparing responses of participants exposed to more prominently displayed risk information to those exposed to less prominently displayed risk information (i.e., the control condition would not be included in these analyses).

(Comment 10) One comment stated that the study outcome measures were not clear and recommended using validated measures.

(Response) The key outcome measures are risk comprehension, benefit comprehension, risk perceptions, and benefit perceptions. Where validated measures exist we will use them. Because the comprehension measures by necessity will be based on the information particular to each fictitious drug, these will be new measures; however, they will take the form of similar comprehension measures used by FDA and others in past research.

(Comment 11) One comment noted that we planned to conduct the studies with participants diagnosed with medical conditions like high cholesterol, seasonal allergies, depression, acid reflux, and high blood pressure, but suggested we also include participants with other medical conditions such as HIV and cancer and replicate the studies across different therapeutic areas.

(Response) As noted in the comment, we plan to conduct the studies with patients diagnosed with a range of medical conditions that differ in diagnosis, symptomatology, patient population, and treatment options. Because it is difficult to recruit participants from low-incidence samples such as those recommended, we do not plan to include these other medical conditions in the study. However, we will consider this for future studies and encourage replication across medical conditions by other researchers.

(Comment 12) One comment recommended that FDA not delay issuing draft internet guidance until the results of the studies are known.

(Response) FDA does not intend to delay issuing draft guidance because of this research.

(Comment 13) One comment suggested that FDA policy should not categorically prohibit the use of hyperlinks to provide risk information.

(Response) Because this comment addresses issues of policy and not the current research, this comment is outside the scope of this project.

(Comment 14) One comment suggested that, rather than focus on a single branded drug website, the studies should take into account the multiple executional elements of internet drug promotion and how online promotional executions are affected by the broader health information environment. The comment argues that this is necessary because risk and benefit comprehension is affected not only by the specifics of one branded drug website but also by other health information found online and elsewhere.

(Response) The regulations these studies address do not apply to the broader online health information environment; rather, each individual branded drug website needs to achieve fair balance. The fictitious branded drug websites used in the studies will include multiple executional elements; however, only one variable will be manipulated at a time in order to maintain experimental control.

(Comment 15) One comment recommended we take advantage of other researchers who can help revise the study design.

(Response) We obtained comments from peer reviewers and incorporated their suggestions in the new design (see list of External Reviewers at the end of this section).

(Comment 16) One comment noted that there are numerous issues that this research does not address, including online data mining by pharmaceutical companies, techniques of personalization for targeted digital pharmaceutical and health marketing, and pharmaceutical marketing's "exploitative" approach to social media. The comment criticized the focus on branded drug websites, as the online marketing environment encompasses newer technology.

(Response) Although there are several other issues surrounding prescription drug advertising online, such as privacy concerns, this is not the purview of the current research. This research is not designed to "assess the full impact of digital drug marketing" or document pharmaceutical marketing practices but rather to address specific issues regarding implementation of "fair balance" regulations for branded prescription drug websites. We note that no one study can address all relevant questions and encourage others to pursue research in this area to supplement the proposed research.

Although the online landscape is much broader than websites, websites continue to be a major source of information for consumers (e.g., a recent survey found that 49% of respondents who went online for prescription drug information reported seeking this information on a specific brand's website; Ref 8) and, as noted above, there is not much relevant research on branded prescription drug websites.

(Comment 17) One comment suggested that the study use eye tracking and neuromarketing methods.

(Response) Because the comment does not specify why eye tracking and neuromarketing should be used in this research beyond noting that the pharmaceutical industry employs these methods, it is difficult to understand how the current research would benefit from these methods. Neuromarketing, for instance, may tell us that participants prefer one website over another.

While this is relevant information from a marketing perspective, from a regulatory perspective it is comprehension, and not preference, that is the important outcome to assess.

(Comment 18) One comment requested additional information on the study. Issues not already addressed above include hypotheses, how the risk information will be portrayed, whether the website will be viewed under controlled conditions, how the participants' perceptions and understanding of the risks and benefits will be assessed, and the statistical analyses to be performed.

(Response). As noted in the 60-day Federal Register Notice, the questionnaire is available upon request; this demonstrates how participants' perceptions and understanding will be assessed. We intend to manipulate how the risk information will be portrayed; please see the study design. Participants will complete the study online, not under controlled conditions. We will ask about the type of device they are using to view the website and can control for this if necessary. Hypotheses and statistical analyses are included below (see Section B.2).

(Comment 19) One comment recommends testing the use of hyperlinks to risk information in the first study. The comment states that this would be useful in developing guidance for social media as well.

(Response) We have revised the design in Study 1 so that the risk visibility manipulation now tests the use of hyperlinks to risk information. We note that this study focuses on prescription drug websites aimed at consumers. As discussed in a previous comment, the results of these studies will be applied in this context only and not to social media.

(Comment 20) One comment asks for more detail regarding the checklist and animated spokesperson to be used in the first study.

(Response) The Study 1 risk formats were chosen based on the risk communication literature. Risk communication studies have found that making risk information less dense (e.g., bulleted lists), more visual (e.g., checklists), and audible (e.g., spokesperson) might increase comprehension. Thus, we want to test formats that are consistent with risk communication best practices. The checklist will be more visual and pronounced than a typical bulleted list. The animated spokesperson will include an audio component.

(Comment 21) One comment recommended that FDA follow FDA's 2009 Draft Guidance on Presenting Risk Information when deciding which risk information should be included in the special features in Study 2.

(Response) FDA will consider this guidance when designing the study stimuli.

(Comment 22) One comment questioned the usefulness of the Study 3 design.

(Response) We have redesigned the third study to ensure it addresses relevant questions in online prescription drug promotion. Please see the revised study design below (see Section B.2).

External Reviewers

In addition to public comment, OPDP sent materials and received comments from three individuals for external peer review. These individuals are:

- Joel Davis, Ph.D., School of Journalism and Media Studies, San Diego State University
- Jisu Huh, Ph.D., School of Journalism and Mass Communication, University of Minnesota
- Michael Wogalter, Ph.D., Department of Psychology, North Carolina State University

9. Explanation of Any Payment or Gift to Respondents

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.

10. Assurance of Confidentiality Provided to Respondents

All respondents will be provided with the assurance of confidentiality to the extent provided by law. The study instructions will include information explaining to respondents that their information will be kept confidential.

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. These methods will all be approved by FDA's Institutional Review Board (Research Involving Human Subjects Committee, RIHSC) prior to collecting any information.

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 is available in Appendix C (Appendices C, D, and E are now separate files and are available in the Information Collection (IC) List). Mock-ups of the informed consent form and one question are provided in Appendix D so that it is clear how the OMB control number and other pertinent information will be shown to participants on each screen of the program.

12. Estimates of Annualized Burden Hours and Costs

The total annual estimated burden imposed by this collection of information is 4,683 hours for this one-time collection (Table 1).

Table 1.--Estimated Annual Reporting Burden[1]

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response (in hours)[2]	Total Hours
Screener	16,000	1	16,000	2/60	533
Pretests	1,200	1	1,200	30/60	600
Study 1	6,000	1	6,000	25/60	2,500
Study 2	2,000	1	2,000	25/60	833
Study 3	1,000	1	1,000	25/60	417
Total					4,883

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

[2] Burden estimates of less than 1 hour are expressed as a fraction of an hour in the format "[number of minutes per response]/60".

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

Table 3. --Estimated Annualized Burden Costs

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs

General public	4,883	$18.68[1]	$91,214
Total			$91,214

[1]Based on the 2010 median weekly income of $747 for both sexes, as reported by the Department of Labor, ftp://ftp.bls.gov/pub/special.requests/lf/aat39.txt

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 of data is $2,019,620 ($673,207 per year for three years). This includes the costs paid to the contractors to conduct a literature review, create measurement instruments and stimuli, program the study, draw the sample, collect the data, and create and analyze a database of the results ($1,899,620). The contract 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 Internet posting.

Table 4. – Project Timetable

Task	Estimated Completion Date
External Peer Review	August, 2011
RIHSC Review	July, 2011
30-day FR notice publication	December, 2011
OMB Review of PRA package	June, 2012
Data Collection	August, 2012
Receipt of Data and Methods Report from Contractor	October, 2012
Data Analysis	December, 2012
Draft Report	January, 2013
Internal Review of Draft Report	February, 2013
Revisions	March, 2013
Final Report	April, 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 certifications.