Market Claims in Direct-to-Consumer (DTC) Prescription Drug Print Ads

OMB Control No. 0910- NEW
Supporting Statement Part A

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 FDA to conduct research relating to health information. Section 1003(d)(2)(c) of the Federal Food, Drug, and Cosmetic Act (the 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.

The marketing literature divides product attributes ("cues") into intrinsic and extrinsic. Intrinsic cues are physical characteristics of the product (e.g., size, shape), whereas extrinsic cues are product-related but not part of the product (e.g., price and brand name). [1],[2] Research has found that both intrinsic and extrinsic cues can influence perceptions of product quality.[3] Consumers may rely on product cues in the absence of explicit quality information. The objective quality of prescription drugs is not easily obtained from promotional claims in DTC ads; thus consumers may rely upon extrinsic cues to inform their decisions. Market claims such as "#1 prescribed" and "new" may act as extrinsic cues about the product's quality, independent of the product's intrinsic characteristics. Prior research has found that market leadership claims can affect consumer beliefs about product efficacy, as well as their beliefs about doctors' judgments about product efficacy.[4] One limitation of these prior studies is the lack of quantitative information about product efficacy in the information provided to respondents. Research indicates that providing consumers with efficacy information generally improves understanding and facilitates decision-making.[5],[6] Efficacy information may moderate the effect of the extrinsic cue by providing insight into characteristics that would otherwise be unknown. Other research has shown that consumers are able to use information about efficacy to inform judgments about the product.[6,7] The

[1] Lee, M., & Lou, Y.-C. (2011). Consumer reliance on intrinsic and extrinsic cues in product evaluations: a conjoint approach. *Journal of Applied Business Research (JABR), 12*(1), 21-29.
[2] Teas, R. K., & Agarwal, S. (2000). The effects of extrinsic product cues on consumers' perceptions of quality, sacrifice, and value. *Journal of the Academy of marketing Science, 28*(2), 278-290.
[3] Rao, A. R., & Monroe, K. B. (1989). The effect of price, brand name, and store name on buyers' perceptions of product quality: an integrative review. *Journal of marketing Research*, 351-357.
[4] Mitra, A., Swasy, J.L., Aikin, K.J. (2006). How do consumers interpret market leadership claims in direct-to-consumer advertising of prescription drugs? *Advances in Consumer Research, 33*, 381-387.
[5] O'Donoghue, A., Sullivan, H., Aikin, K., Chowdhury, D., Moultrie, R., & Rupert, D., (2014). Presenting efficacy information in direct to consumer prescription drug advertisements. *Patient Education Counsel*, 95(2), 271-80.
[6] Schwartz, L. M., Woloshin, S., & Welch, H. G. (2009). Using a drug facts box to communicate drug benefits and harmstwo randomized trials. *Annals of Internal Medicine, 150*(8), 516-527.
[7] Sullivan, H. W., O'Donoghue, A. C., & Aikin, K. J. (2013). Presenting quantitative information about placebo rates to patients. *JAMA Internal Medicine*, -. doi: 10.1001/jamainternmed.2013.10399.

Office of Prescription Drug Promotion (OPDP) plans to investigate, through empirical research, the impact of market claims on prescription drug product perceptions with and without quantitative information about product efficacy. This will be investigated in direct-to-consumer (DTC) print advertising for prescription drugs.

2. Purpose and Use of the Information Collection

The purpose of this study is to examine the impact of market claims and quantitative efficacy information on prescription drug product perceptions in DTC print advertising for prescription drugs. The long-term objective is to improve the communication of accurate and non-misleading information in DTC ads. 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. 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 participant, and by keeping surveys to less than 30 minutes in both the pretests and main study.

4. Efforts to Identify Duplication and Use of Similar Information

We conducted a literature search to identify duplication and use of similar information by locating relevant articles through keyword searches using two databases, PubMed and EBSCO Academic. We also identified relevant articles from the reference list of articles found through keyword searches. We found one study examining the impact of market leadership claims in DTC advertising on product perceptions.[4] We have cited this work above and are expanding upon it to examine the role quantitative effectiveness information may have in modifying the impact of these claims. We did not find any duplicative work on the relative importance of quantitative efficacy information and market claims in DTC ads in driving product choice.

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

There are no special circumstances for this collection of information.

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

In the Federal Register of July 20, 2015 (80 FR 138, 42823-42825), FDA published a 60-day notice requesting public comment on the proposed collection of information. Six submissions were received; three from biopharmaceutical companies (AbbVie, Eli Lilly, Merck), two that were anonymous, and one from Danny Weiss, PharmD. The comments from the two anonymous submitters and Dr. Weiss requested the United States ban DTC advertising for pharmaceuticals. This is outside the scope of this project. We summarize and respond to the other comments below.

Comments 1 from AbbVie: Respondents may view "benefits" and "risks" more generally versus "side effects" as a specific inquiry. For example, "side effects" could be interpreted as adverse effects or adverse events, and as such, elicit a much more specific response than "risks" which could be seen more broadly. We suggest that "side effects" be eliminated from Q4 to keep Questions 3 and 4 as both general in nature.

Response: We are interested in recall of both risks and side effects, and so we inquire about both. Inquiring about risks only may artificially reduce the quantity of recall. Moreover, we counterbalance the presentation of Q3 and Q4 in efforts to account for any influence of question ordering. It would be feasible to instead inquire about risks and side effects in separate questions; however, in our experience, we find that consumers tend to think about risks and side effects together, which makes sense given the typical presentation of risks and side effects in direct-to-consumer promotional materials.

Comment 2 from AbbVie: The answers to questions 7 through 12 may be biased by attitudes toward advertising in general and may go well beyond the pharmaceutical ad they are shown.

Response: By asking these questions, we hope to detect any differences in perceived effectiveness and risk between those exposed to different experimental conditions. For example, those exposed to an ad with a #1 prescribed market claim may perceive the product to be more effective than those in the control condition. We acknowledge participants may bring their own opinions about advertising to the study. However, these opinions tend to be evenly distributed across experimental conditions based on random assignment procedures. Thus, any differences result from the experimental manipulations.

Comment 3 from AbbVie: We acknowledge we have not seen the test ad; but we wish to point out that questions 13 and 17 rely on the ad presenting numeric efficacy and safety information that can be interpreted by respondents.

Response: Prior research has shown that consumers can reach numeric judgments about efficacy and risk despite no numeric information being presented.[8] As described in our study design (see Exhibit 1 in section B.2), we are not manipulating quantitative safety information and not all test ads contain quantitative efficacy information. We have worked with an expert reviewer in OPDP to produce efficacy claims that are realistic for this drug product class.

Comment 4 from AbbVie: Question 18 relies on the ad presenting information about the seriousness of one or more "side effects" that the respondent could rank. We do not usually see print ads that present details about the extent of the seriousness of one or more side effects. In the absence of this presentation, how are respondents to answer this question?

Response: We find that consumers are generally able to differentiate between the seriousness of various risks and side effects, and also that they can make judgments about the overall (gist) seriousness of the risks and side effects. We ask this question with the intention to detect whether or not exposure to market claims and efficacy information impacts risk perceptions.

Comment 5 from AbbVie: The answers to questions 21-26 may reflect a patient's perception of their doctor rather than the ad. Therefore, the answers may not reflect what was communicated in the ad but rather reflect the patient-doctor relationship (e.g. patient perception of their doctor).

Response: We are endeavoring to replicate the results of Mitra et al (2006), who found that market leadership claims affected consumer beliefs about doctor's judgments.

Comment 6 from AbbVie: In the table headers for questions 27 and 28, please change "claim" to "statement" so that it matches the text in the question.

Response: We will make this change.

Comment 7 from AbbVie: It is beneficial to rotate the order of response choices in questions 27 and 28 as is done in prior questions. Some of the features a-h are broad (b. pictures and images) while some are specific (e. percentages). It would be better to compare the very general features in a question and group the very specific features into another question to compare like features.

Response: We will make this change.

[8] O'Donoghue, A.C., Sullivan, H.W., Aikin, K.J., Chowdhury, D., Moultrie, R.R. & Rupert, D.J. (2014). Presenting efficacy information in direct-to-consumer prescription drug advertisements. *Patient Education and Counseling*, 95, 271-280.

Comment 8 from AbbVie: For questions 35-38, rather than rank from Strongly Disagree to Strongly Agree, which are absolutes, it would be better to rank by frequency from Never to Always; this moves the response to how often patients perceive this and away from absolutes.

Response: We acknowledge that it is difficult to rank agree/disagree on all drugs. However, a scale range of always-never is uni-polar; we can't assess whether respondents think the opposite, e.g., that new drugs tend to be *more* risky or that the #1 prescribed drug is *more* risky. Our intention is to use these items as a moderator when examining the impact of the experimental manipulations (i.e., market claims, efficacy claims) on benefit and risk perceptions, intentions to take the product, and other outcomes. We believe the most relevant scale for this analysis is the current strongly disagree to strongly agree scale. Although it would be interesting to assess participant responding using both scales, doing so may not add significant value relative to the additional burden it would pose for participants.

Comment 9 from AbbVie: We suggest that all the features of Q43a-h be stated in the affirmative/positive. For example, h. should be worded as, "the drug has few side effects," to be consistent with features a-g that are positively stated.

Response: The proposed item, "the drug has few side effects," assesses a different outcome than our current question, "the drug has serious side effects." We have also added items assessing "drug cost and/or copay" and "doctor's recommendation." For consistency, we will change the wording so that all features are neutral. For instance: the drug's side effects, opinions of people I know, how often the drug is prescribed

Comment 10 from Lilly: Given the proposed FDA research questions, Lilly believes the design is appropriate and the sample size will allow for breakouts by each cell. In advertising A/B tests, in which this is similar to, all aspects of the stimulus not being tested are held the same in order to reduce bias and isolate the feature being tested. We strongly recommend that this guideline is followed in this study.

Response: We intend to hold all features other than the manipulations constant in the stimuli.

Comment 11 from Lilly: One research objective for the main study suggests that the study will measure perceptions of the doctors' acceptance of the drug by respondents. Since respondents will only be seeing a print ad and not interacting with a doctor, we believe the research setting will be too artificial to gain meaningful insights into this topic. We recommend removing the section (Questions 21-26).

Response: Please see response to Comment 5 from AbbVie.

Comment 12 from Lilly: The details of the follow-up study are less clear than the main study. What are the techniques and what are the dependent measures on which the respondent will be asked to decide?

Response: The follow up study assesses the relative weighting of a market claim and efficacy in decision-making. Participants are asked to choose a drug out of two options that vary in (a) the presence of a market claim and (b) efficacy. We will examine product preference as a function of efficacy using logistic regression. The difference in efficacy between the two drugs on each choice set will be a continuous predictor variable and drug choice will be a binary outcome variable. Critically, we will examine whether, and to what extent, the efficacy-choice relationship varies as a function of an added market claim; thus, market claim presence will be an interaction term. The experiment uses a discrete choice approach common in psychology and economics.[9]

Comment 13 from Lilly: We suggest FDA stratify the sample for both studies across demographic variables to ensure it is representative of the US diabetic population.

Response: We are applying demographic quotas to achieve a representative sample.

Comment 14 from Lilly: The questionnaire employs a number of different Likert scales that differ on the number of scale values and definition of values. Lilly suggests using a standard 5-point scale with a mid-point and definitions for each value for all scalar questions.

Response: We have changed the Likert scales to be internally consistent.

Comment 15 from Lilly: For questions 9 and 16, by asking the respondents to perceive overall quality of the drug, the survey risks introducing perceptions outside of experimental control into the study. Overall quality is a very broad topic and might be dependent on the graphics, wording, and personal biases that are outside of the market claims and efficacy levels being tested. We suggest removing these questions, or changing the question to "Overall efficacy."

Response: By asking these questions, we hope to detect any differences in perceived quality between those exposed to different experimental conditions. For example, those exposed to an ad with a #1 prescribed market claim may perceive the product to be of higher quality than those in the control condition. By keeping all ad elements beyond the experimental manipulations (market claims, efficacy claims) constant, we can ensure that significant differences between conditions are a result of the manipulations rather than any extraneous factors. Random assignment to conditions should also distribute any random variance equally across all cells.

Comment 16 from Lilly: We recommend removing questions 13 and 17 as they have the potential to be misinterpreted or simply difficult for the respondent to answer if the stimulus is not communicating prevalence of the drug's side effects or benefits using precise numbers.

Response: Please see answer to Comment 3 from AbbVie.

[9] See, for example, Train, K. E. (2009). *Discrete choice methods with simulation*. Cambridge University Press.

Comment 17 from Lilly: For questions 27 and 28, we recommend slightly changing the wordings for the possible answer choices to "Yes/No, claim is/is not mentioned as a benefit in the ad" for Q27, and "Yes/No, claim is/is not mentioned as a side effect or risk in the ad" for Q28.

Response: We agree that more specific wording would be helpful and have revised the answer choices to read "Yes, statement is mentioned in the ad" and "No, statement is not mentioned in the ad."

Comment 18 from Lilly: Recommend removing Q31 as the question is an inverse of Q30 to avoid confounding data.

Response: We have removed Q31 (skepticism).

Comment 19 from Lilly: The instructions for the Q35 through 38 section seems to have an omitted word. We recommend revising to "how much do you agree or disagree with the following statements?"

Response: Thank you for pointing this out. We will correct this.

Comment 20 from Lilly: We agree with placement of demographic questions (Q39-) at the end but recommend re-evaluating them and consider removing them so as to avoid lack of response due to respondent fatigue.

Response: The comment about respondent fatigue is well taken. However, we are adhering to good questionnaire design in putting our most important dependent measures first and are willing to accept the potential tradeoff in missing demographic data.

Comment 21 from Lilly: We suggest providing a more complete list of choices for Q43 and placing this question earlier in the study.

Response: We appreciate this suggestion and have added questions about cost.

Comment 22 from Merck: Merck supports the importance of communicating information that can be understood by consumers so that they can make better decisions about prescription drugs. We believe that FDA should focus their efforts and research first on improving the health literacy of approved patient labeling, and then on DTC print advertising. In addition, FDA should consider exploring the inclusion of benefit information in patient labeling, which may help improve consumer understanding and comprehension of patient labeling.

Response: We share the goal of improving communications about prescription drugs. There are efforts underway within FDA examining ways to improve patient labeling (see Boudewyns et al., 2015). Although this comment is outside the scope of this project, we will share this information internally.

Comment 23 from Merck: Merck believes the current study design limits the practical utility of the information collected. The study proposes presenting efficacy information in the form of simple quantitative information. Prior OPDP research acknowledged the limitations of studying simple quantitative information. For many prescription drugs, clinical trial outcomes are often more complicated than simple frequencies, which limit the applicability of this research. Numeracy challenges are common in people with inadequate health literacy. Numeracy challenges are not well represented in online research, and hence the proposed methodology may not detect a lack of comprehension.

Response: We are pleased Merck has read FDA's prior research in the area of communicating quantitative information. As this is the first study examining the impact of quantitative efficacy information on the perception of market share claims, we felt it was better to start with relatively straightforward, though not simplistic, quantitative efficacy information. We have worked with an expert reviewer in OPDP to product efficacy claims that are realistic for this drug product class. The efficacy claim communicates both the level of expected benefit and the likelihood of experiencing that benefit. We encourage additional research on this topic utilizing increasingly complex quantitative information.

We have included a measure of numeracy in our questionnaire. We acknowledge that online panels may underrepresent individuals with extremely low health literacy. Thus, any differences we find as a function of numeracy in our sample may be magnified in the general population.

Comment 24 from Merck: Merck recommends a mixed-method approach to reach limited-literacy respondents. The phone or web approach allows for a broad, diverse geographic sample. Respondents with low health literacy are not typically represented in these databases, and may need to be recruited in less traditional places, such as literacy centers, senior centers, and health clinics. Additionally, if a desktop computer is required, this may inadvertently eliminate respondents from low socioeconomic status, who are less likely to have a desktop computer and more likely to have internet only on their mobile device.

Response: We acknowledge that internet administration is not perfect and have chosen this method to maximize our budget. We will permit the survey to be taken on a variety of devices. We are excluding phones because the stimuli cannot be fully viewed on a very small screen.

Comment 25 from Merck: For the follow-up study, we recommend reducing the number of trials for respondents across health literacy levels, as respondent fatigue can occur, resulting in reduced focus and unreliably responses. Refining the methodology to present fewer choices to each respondent, and assuring the clarity of the information presented, would help to enhance comprehension.

Response: We agree that minimizing respondent burden is a priority. We estimate that the 48 trials and instructions would require less than 8 minutes, on average. Pretest data may reveal that the experiment can be shortened without loss to validity, in which case we will reduce the number of trials.

Comment 26 from Merck: Questions 6, 32, and 50 include percentages. According to Health Literacy Missouri, natural frequencies (1 out of 10) may be more useful than percentages. Research suggests that less literate readers may interpret numbers as more risky when in frequency form (1 out of 10) versus percentage form (10%).

Response: We have worked with an expert reviewer in OPDP to product efficacy claims that are realistic for this drug product class.

Comment 27 from Merck: We suggest adding the following screener question to increase the odds of recruiting limited-literacy respondents: "How confident are you in filling out medical forms by yourself?"

Response: We acknowledge that internet panels underrepresent individuals with very low literacy. Thus, it is important to acknowledge that our findings may not apply to very low literacy individuals. It would be prohibitively expensive for us to screen for literacy up front in order to establish quotas. We will measure health literacy and included it in analyses.

External Reviewers

In addition to public comment, OPDP solicited peer-review comments on potential measures and study methodology from a panel of experts. These individuals are:

Sujity Sansgiry, Ph.D., Associate Professor of Pharmaceutical Health Outcomes and Policy, University of Houston.

Christine Skubisz, Ph.D., Assistant Professor, School of Communications, Emerson College.

9. Explanation of Any Payment or Gift to Respondents

Ipsos's i-Say panelists participate in two main incentive programs: sweepstakes drawings and a per-survey point system. For the sweepstakes component, drawings are held several times a year among panelists who have participated in surveys, with various prizes offered worth up to $5,000. Panelists are entered for each survey in which they participate. Points can be redeemed for electronic gift cards, prepaid cards, PayPal payments and charitable donations. Participants in the Main Study and Pretests 1 and 2 will receive 180 i-Say points (the equivalent of $1.80) in compensation for the 30-minute studies. Participants in Pretest 3 and the Follow-Up study will receive 90 i-Say points (the equivalent of $0.90) in compensation for the 15-minutes studies. All participants are entered in the sweepstakes.

10. Assurance of Confidentiality Provided to Respondents

All participants will be provided with an assurance of privacy to the extent allowable by law. See Appendix A for the consent form.

Survey data is collected via Ipsos Interactive Services, a secure online survey platform. Each respondent uses a unique login and password to access the survey. Public facing servers such as those hosting online surveys are separate from servers with project and protected data. The system is regularly inspected for FISMA compliance.

Physical and digital access is restricted throughout Ipsos's offices. Access to servers and data can only be achieved through a legitimate network account and requires a network logon and password. Also, only employees specifically assigned to the project can access project material and data. Hard or paper materials, such as printed materials and questionnaires, are kept in access-restricted locations and under lock and key.

No personally identifiable information will be sent to FDA. All information that can identify individual participants will be maintained by the independent contractor in a form that is separate from the data provided to FDA. For all data, alpha numeric codes will be used instead of names as identifiers. These identification codes (rather than names) are used on any documents or files that contain study data or participant responses.

The information will be kept in a secured fashion that will not permit unauthorized access. Throughout the project, any hard-copy files will be stored in a locked file cabinet in the Project Manager's office, and electronic files will be stored on the contractor's password-protected server, which allows only project team members access to the files. The 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). These methods have been approved by FDA's Institutional Review Board (Research Involving Human Subjects Committee, RIHSC).

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' Security Policy. 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 B.

12. Estimates of Annualized Burden Hours and Costs

The first two pretests and main study are expected to last no more than 30 minutes. The third pretest and follow-up study are expected to last no more than 15 minutes. This will be a one-time (rather than annual) collection of information. FDA estimates the burden of this collection of information as follows:

Table 1: Estimated Burden[1]

Activity	No. of respondents	No. of responses per respondent	Total annual respondents	Avg. burden per response	Total hours
Sample outgo (pretests and main survey)	16,384	==	==	==	==
Screener completes	1,638	1	1,638	.03 (2 mins.)	49.1
Eligible	1,556	==	==	==	==
Completes, Pretest 1	252	1	252	0.5 (30 mins.)	126.0
Completes, Pretest 2	252	1	252	0.5 (30 mins.)	126.0
Completes, Main Study	495	1	495	0.5 (30 mins.)	247.5
Completes, Pretest 3	108	1	108	0.25 (15 mins.)	27.0
Completes, Follow-up Study	216	1	216	0.25 (15 mins.)	54.0
Total	==	==	==	==	629.6

[1] 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 studies.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

The total estimated cost to the Federal Government for the collection of data is $529,742 ($176,581 per year for three years). This includes the costs paid to the contractors to create the stimuli, program the study, draw the sample, collect the data, and create and analyze a database of the results. 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 manuscript ($85,800; 10 hours per week for three years).

15. Explanation for Program 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 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 2. – Project Time Schedule

Task	**Estimated Number of Weeks after OMB Approval**
Pretest data collected	6 weeks
Pretest data completed	14 weeks
Main study data collected	26 weeks
Final methods report completed	38 weeks
Final results report completed	48 weeks
Manuscript submitted for internal review	56 weeks
Manuscript submitted for peer-review journal publication	64 weeks

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.