U.S. Food and Drug Administration

Disclosures in Professional and Consumer Prescription Drug Promotion

OMB Control No. 0910-NEW

SUPPORTING STATEMENT **Part 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.

FDA regulates prescription drug advertising and promotional labeling directed to healthcare professionals (HCPs) and consumers (section 502(n) and section 502(a) of the FD&C Act (21 U.S.C. 352(n) and 21 U.S.C. 352(a)). In the course of promoting their products, pharmaceutical sponsors (sponsors) may present a variety of information including the indication, details about the administration of the product, efficacy information, and clinical trial data. In an effort to present often complicated information concisely, sponsors may not include relevant information in the body of the text or visual display of the claim. Additionally, sponsors may not always present limitations to the claim in the main body of the text or display. In these cases, sponsors typically include disclosures of information somewhere in the promotional piece.

There is limited published research on disclosures in prescription drug promotion, either directed to consumers or to HCPs. The use of disclosures is one method of communicating information to HCPs and consumers about scientific and clinical data, the limitations of that data, and practical utility of that information. These disclosures may influence HCP and consumer comprehension and decision-making, and may affect how and what treatment HCPs prescribe for their patients. Previous research on the effectiveness of disclosures has been conducted primarily in the dietary supplement arena (Refs. 1-4). Thus, the proposed research will examine the effectiveness of clear and conspicuous disclosures in prescription drug promotion directed to both of these populations. The purpose of our study is to determine how useful disclosures regarding prescription drug information are when presented prominently and adjacent to claims.[1] Specifically, are HCPs and consumers able to use

[1] The Federal Trade Commission (FTC), which regulates the advertising of non-prescription drug products as well as other non-FDA regulated products (e.g., package goods, cars, etc.), issued a specific position on disclosures for the advertising it regulates (https://www.ftc.gov/system/files/documents/public_statements/410531/831014deceptionstmt.pdf). Specifically, FTC explains that disclosures must be "clear and conspicuous"; in other words, in understandable language, located near the claim to be further clarified, and not hidden or minimized by small font or other distractions.

disclosures to effectively frame information in efficacy claims in prescription drug promotion?

2. Purpose and Use of the Information Collection

The purpose of this project is to investigate how HCPs and consumers understand additional context provided in pharmaceutical promotion in the form of disclosures. 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 HCPs and to consumers as clearly and usefully as possible. This study will inform FDA of the usefulness of disclosures as a way to present important contextual information to professional and lay audiences.

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 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 the written parts of surveys to less than 25 minutes in both the pretests and main study.

4. Efforts to Identify Duplication and Use of Similar Information

Although the literature revealed a rich background on which to base the current research, we found no studies that have examined the specific issues we propose to study.

OPDP is also currently proposing research that will investigate the use of disclosures in professional promotion of oncology prescription drugs (82 FR 27845). Although the two studies both investigate disclosures as a method for conveying important contextual information, the two studies examine different types of disclosures in different populations. OPDP has also completed or proposed two other studies which utilize disclosures but for which disclosures themselves are not the focus of the research (79 FR 26255 and 82 FR 855). We believe these studies will collectively provide FDA with valuable information about the use of disclosures as a method for ensuring the safe and effective use of prescription drugs.

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 June 14, 2017 (82 FR 27268), FDA published a 60-day notice requesting public comment on the proposed collection of information. Four comments were received. Responses to those comments follow. For brevity, some public comments are paraphrased and therefore may not reflect the exact language used by the commenter. We assure commenters that the entirety of their comments was considered even if not fully captured by our paraphrasing in this document. The following acronyms are used here: DTC = direct-to-consumer; HCP = healthcare professional; FDA and "The Agency" = Food and Drug Administration; OPDP = FDA's Office of Prescription Drug Promotion.

The first public comment responder (*regulations.gov tracking number 1kl-8y39-rtyb*) included 25 individual comments, to which we have responded.

Comment 1a *(summarized)*: FDA is conducting too much research without articulating a clear, overarching research agenda or adequate rationales on how the proposed research related to the goal of further protecting public health. The Agency should publish a comprehensive list of its prescription drug advertising and promotion studies from the past five years and articulate a clear vision for its research priorities for the near future.

Response 1a: OPDP's mission is to protect the public health by helping to ensure that prescription drug information is truthful, balanced, and accurately communicated, so that patients and health care providers can make informed decisions about treatment options. OPDP's research program supports this mission by generating scientific evidence to help ensure that our policies related to prescription drug promotion will have the greatest benefit to public health. Toward that end, we have consistently conducted research to evaluate the aspects of prescription drug promotion that we believe are most central to our mission, focusing in particular on three main topic areas: advertising features, including content and format; target populations; and research quality. Through the evaluation of advertising features we assess how elements such as graphics, format, and disease and product characteristics impact the communication and understanding of prescription drug risks and benefits; focusing on target populations allows us to evaluate how understanding of prescription drug risks and benefits may vary as a function of audience; and our focus on research quality aims at maximizing the quality of research data through analytical methodology development and investigation of sampling and response issues.

Because we recognize the strength of data and the confidence in the robust nature of the findings is improved through the results of multiple converging studies, we continue to develop evidence to inform our thinking. We evaluate the results from our studies within the broader context of research and findings from other sources, and this larger body of knowledge collectively informs our policies as well as our research program. Our research is documented on our homepage, which can be found at: https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/

ucm090276.htm. The website includes links to the latest FRNs and peer-reviewed publications produced by our office. The website maintains information on studies we have conducted, dating back to a survey of DTC attitudes and behaviors conducted in 1999.

Comment 1b *(The commenter provided a summary of their comments followed by a more detailed description of the same comments. For brevity, the summary of comments has been omitted and only the specific comments [1b through 1y] are provided below. The commenter's full comments may be accessed at* www.regulations.gov *via tracking number lkl-8y39-rtyb) (verbatim)*: It is not clear from this description whether the study will yield useful information to evaluate whether disclosures provide appropriate contextual information in certain communications, whether such disclosures can be made more effective, and where the disclosures are necessary to ensure communications are truthful and non-misleading. The Agency should provide significantly more detail regarding the design of the study, the proposed disclosures, the mock promotional pieces, and the information it seeks to collect.

Response 1b: We have provided the purpose of the study, the design, the population of interest, and have provided the questionnaire to numerous individuals upon request. These materials have proven sufficient for others to comment publicly, and for academic experts to peer-review the study successfully. We do not make draft stimuli public during this time because of concerns that this may contaminate our participant pool and compromise the research.

Comment 1c *(summarized)*: After pretesting, the Agency should make available revised questionnaires, data collection methodologies, and stimuli.

Response 1c: In this current notice, we provide the revised design as based on academic peer reviewers, cognitive interviewing, and public comments. The revised questionnaire is also available upon request. Our full stimuli are under development during the PRA process. We do not make draft stimuli public during this time because of concerns that this may contaminate our participant pool and compromise the research. Individuals are welcome to inquire about the progress of the study and any changes from the pretests will be communicated at that time.

Comment 1d *(summarized)*: FDA should base mock promotional stimuli on realistic promotional pieces.

Response 1d: We have done this. Our stimuli are modified from actual promotional pieces in the marketplace to disguise the original product.

Comment 1e *(summarized)*: It is unclear whether such disclosures will contain relevant information ordinarily provided in promotional materials.

Response 1e: The goal of our research is to obtain answers to questions about prescription drug promotion that will inform the Agency and stakeholders. Thus, we strive in all of our

studies to make our mock promotional pieces as realistic as possible. That includes any disclosures that we may include in testing. Also, please see response to comment 1d.

Comment 1f *(verbatim)*: FDA seems to have an overly broad conception of the need for disclosures for "scope of treatment" communications. In the Notice, FDA describes this type of communication as "a disease-awareness claim; that is, a broader discussion of a medical condition that may include disease characteristics beyond what the promoted drug has been shown to treat." Where a disease awareness communication discusses a disease in a manner beyond what the promoted drug has been shown to treat, but does so in a balanced manner without implying any particular treatment benefits from the associated drug, it should be viewed as providing helpful general background information on the disease, and not as making an off-label claim for the drug. In those circumstances, there should be no need for any disclosure about the limits of use of the drug. FDA should clarify its understanding of "scope of treatment" claims and make its proposed claims and disclosures available for public comment.

Response 1f: Previous research has demonstrated that presenting study participants with information about the consequences of a disease, particularly when the information was integrated into one print ad with information about a particular drug, resulted in false beliefs that the advertised drug prevented those consequences (Ref. 5). The "scope of treatment" claims that are included in this research are embedded in mock promotional materials, juxtaposed with specific efficacy information about the mock drug products. As such, they will likely imply "particular treatment benefits from the associated drug." This research will help us to evaluate the usefulness of a disclosure in relation to this type of information when it is found in promotional pieces. Also, please see response to comment 1c.

Comment 1g *(verbatim)*: FDA states that the "ease of use" claim "is a simple claim of easy drug administration that omits specific important details that contribute to a more difficult drug administration than suggested." This statement appears to imply that all ease of use claims are misleading, where the Agency perhaps intends to clarify that validated and non-misleading "ease of use" claims may require a disclosure or more context. FDA should clarify its understanding of "ease of use" claims, and, in testing, ensure it does not test overly misleading base claims for "ease of use" that would be difficult to contextualize with a disclosure statement and hence would bias the results of its study. Such claims should be made available for public comment.

Response 1g: FDA did not intend to imply that all ease of use claims are misleading or that all ease of use claims would necessarily require a disclosure. FDA agrees that some ease of use statements require a disclosure or more context and intends to evaluate one such example with this research. We have revised the description of the study in this notice to clarify. Also, please see response to comment 1c.

Comment 1h *(verbatim)*: FDA states that the "statistical significance" claim "will be one in which the disclosure reveals that the presented analyses were not statistically significant, and thus must be viewed with considerable caution." It is not clear what content FDA intends to test for this type of claim. We encourage FDA to clarify how it intends to present "not

statistically significant" analyses for testing in order to ensure such claims are presented with appropriate contextual information. Such claims should be made available for public comment.

Response 1h: Please see responses to comment 1c, 1d, and 1e.

Comment 1i *(summarized)*: The Agency should clarify what distinctions will be made between HCP and consumer pieces.

Response 1i: As our mock promotional pieces have been adapted from existing materials in the public domain, the materials directed to HCPs and to consumers vary in similar ways to what can currently be seen in the public domain. For example, materials directed to HCPs tend to have more data, more technical medical language, and more text in general. Consumer pieces are generally written in plainer language and generally do not include as much data and statistical information. Our pieces are highly realistic as they were developed from actual promotional pieces.

Comment 1j *(verbatim)*: The Agency proposes that consumer and HCP subjects will be recruited from Internet panels, indicating that the study will be conducted using an electronic format. Because the proposed research topic is not dependent on an electronic medium, FDA should consider testing non-electronic media as well, including printed promotional pieces.

Response 1j: Although our study will be conducted via the Internet, we will show participants mock print materials in .pdf format.

Comment 1k *(verbatim)*: The Agency proposes to use eye tracking studies to complement the self-reported items on the questionnaire and to improve the main studies. [The commenter] encourages the Agency to use this technology in conjunction with other inputs (for example, qualitative research) to understand why subjects are looking at a portion of the proposed materials, rather than to draw conclusions that such portions were viewed. Additionally, an explanation of the use of eye tracking technology should also be included during the subject enrollment process.

Response 1k: FDA plans to collect and analyze eye tracking (physical measures of attention) data in conjunction with other measures, including cognitive interviews. To avoid the potential for priming effects, the eye-tracking component of the study will not be explained to recruited individuals before they report for their in-person sessions. However, participants will be made aware of the eye-tracking component during the informed consent process.

Comment 1l *(summarized)*: The commenter recommends increasing the sample size of the eye tracking components to ensure more robust data.

Response 1l: Our primary method of analysis of the eye-tracking data will be examination of gaze plots coupled with self-report data provided by participants. Thus, eye-tracking results will be examined on an individual, rather than aggregate, level. Furthermore, the eye-tracking studies included in this research are intended as qualitative, formative studies; they will be

used to inform any necessary changes to the stimuli before the main studies. Formative eye-tracking studies such as these are often executed with sample sizes as small as five participants Ref. 6). In our experience, a sample of 20 participants in each population ensures that we will collect fully useable data from a minimum of 15 participants in each population. Used as an observation tool, eye-tracking complements the other data collected to increase discoverability of specific events and confidence in our qualitative findings.

Comment 1m *(summarized)*: The commenter recommends limiting the participant sample to disease sufferers rather than a general population sample.

Response 1m: We carefully consider the type of sample to use in each of our studies. In the current study, the population of sufferers for the conditions addressed by our stimuli (i.e., Chronic Obstructive Pulmonary Disease [COPD], chronic iron overload, and high blood pressure) are varied. Because we are showing participants more than one ad, we chose not to select diagnosed populations or specialists.

Comment 1n *(summarized)*: FDA should recruit a demographically and geographically diverse sample.

Response 1n: We agree and we plan to recruit individuals with a range of gender, race, ethnicity, and, as much as possible within an Internet sample, socioeconomic status. For the consumer sample, we aim for a sample with 60% of people who have some college or less. An advantage of sampling via Internet panel is that we have access to individuals in all parts of the U.S.

Comment 1o *(verbatim)*: FDA should capture whether subjects comprehend certain information disclosed in the mock promotional pieces, even if the subject does not recall information on the specifics. Currently, open-ended and recall questions (e.g., Consumer Questionnaire Q2-Q3; HCP Questionnaire Q2-Q3) ask test subjects to identify certain information regarding the featured drug products (what a mock drug product is specifically "used for" or "not approved for"). It is not clear why such an open-ended format or questions are necessary for the research purpose of the study, as subjects could recognize a limit to the efficacy being presented even if they do not follow or recall all of the details of a disclosure.

Response 1o: We do intend to capture what information has been observed in the mock promotional pieces, and we do this through the open-ended and recall questions. It is common practice to include open-ended and closed-ended questions in one research study, as they tend to complement each other. Open-ended questions allow responses that have not been prompted by particulars, which is not the case with closed-ended questions. Closed-ended questions provide a more efficient way of obtaining information.

Comment 1p *(summarized)*: FDA should ensure that terms used in the consumer pieces are consumer-friendly.

Response 1p: We agree and always review our mock consumer pieces for lay language. The terms mentioned by the commenter (e.g., chronic iron overload, COPD, lung function, scientific evidence, effectiveness, statistically significant) will be used in the HCP materials. However, we also strive to make our materials as realistic as possible, and in this case, we have modified existing DTC pieces for consumers. If they used a term (e.g., COPD), and OPDP reviewers agreed that this is common and acceptable, we maintained it in our mock pieces.

Comment 1q *(summarized)*: FDA should consider changing the sliding scale format of Q4.

Response 1q: We carefully develop each question of our questionnaires, taking into account language and response options. No cognitive interview participant reported confusion with this sliding scale question. Without scientific justification for changing the response format of this question, we will maintain the current format.

Comment 1r *(verbatim)*: In a study setting, subjects may be prone to pay attention to more or all of the information presented throughout the study, including claims designed to be intentionally misleading. As a result, subjects are more likely to be biased based on the strength or weakness of the claims and disclosures presented. The Agency should address what efforts it will take to avoid response bias by presenting these varying degrees of disclosures.

Response 1r: The study is designed so that participant will be randomly assigned to condition. Moreover, the only aspect of the participants' experiences that will be varied in the study will be the manipulations that we have described. Any individual differences in attention or ability or potential biases should be spread across experimental conditions. Thus, if we find differences between and among conditions, we can be reasonably sure that the manipulations caused the differences. We have not found in the past that our participants spend an inordinate amount of time viewing stimuli, but we will be careful to place the research in context when we interpret the data.

Comment 1s *(verbatim)*: The Consent Text introduction should not state that the survey is being conducted "on behalf of the U.S. Food and Drug Administration." This statement could potentially influence subjects' responses to study questions. Instead, this information might be provided at the conclusion of the study.

Response 1s: In previous studies, we took this same view and typically used "Department of Health and Human Services." We will incorporate this change.

Comment 1t *(verbatim)*: Questions regarding statements in ads (Consumer Questionnaire Q10, Q20, Q30; HCP Questionnaire Q12, Q22, Q33) should be the first questions presented following the subjects' viewing of a promotional piece. A subject will likely recall the statements that appeared in the promotional piece most accurately immediately after reviewing the piece and before answering other questions that could influence their selection of answers.

Response 1t: As with all other aspects of study design, we carefully develop questionnaires with order effects in mind. Therefore, we chose to include questions regarding perception of efficacy or ease of use, information seeking, and behavioral intention first because it is important that participant responses to these items be based solely on the information presented in the ads. The questions referenced by the commenter also include incorrect recall items, which could potentially bias responses to later questions if the order was changed. Additionally, repeated exposures to the correct recall items in the above-referenced questions could have a reinforcing effect that could confound results.

Comment 1u *(verbatim)*: In the Consumer Questionnaire, an "FDA employee" category, similar to S7 and S8, should be added to the Screener Survey. These individuals should also be terminated from the study.

Response 1u: We will revise question S8 to read, "Do you work for a pharmaceutical company, an advertising agency, a market research company, or the U.S. Department of Health and Human Services?" to capture these individuals, as suggested.

Comment 1v *(verbatim)*: In the Consumer Questionnaire, Q8-Q9 should be presented prior to Q6-Q7 in order to prevent bias in favor of non-HCP sources. Similarly, Q19 should appear before Q18, and Q28 should appear before Q27.

Response 1v: We will reorder the questionnaire as the commenter suggested.

Comment 1w *(summarized)*: We recommend that Q8-Q9, Q19, and Q28 be expanded to more fully evaluate the role of the prescriber in aiding consumers' understanding of disclaimers in promotional materials.

Response 1w: HCPs are often a very important source of information about prescription drugs. However, when prescription drugs are promoted directly to consumers, they may be more likely to look for information on their own before taking steps to consult their HCPs. We have taken this into account in this study by examining the responses of both consumers and HCPs.

Comment 1x *(verbatim)*: In the HCP Questionnaire, Q5, Q7, and Q29 should be omitted. Comparative efficacy is highly dependent on the particular HCP subject's experience outside the experiment setting; this question thus may lead to highly variable results. Further, how the drug featured in the mock promotional communication compares to other prescription medications has no relevance to FDA's stated study goals. Questions regarding comparative efficacy should thus be omitted from the proposed HCP Questionnaire.

Response 1x: Comparative efficacy questions are another way to assess how HCPs respond to prescription drug promotion. Any subjective experiences outside the experiment setting should fall out because HCPs will be randomly assigned to conditions. The questions are relevant to our study because HCPs make comparative decisions each time they make a prescribing decision.

Comment 1y *(verbatim)*: In the HCP Questionnaire, Q34 does not appear to provide appropriate programming instructions for the scenario in which Q33_A=01 and Q33_D=01. FDA should confirm that Q33 may be asked if subjects select both Q33_A and Q33_D, and provide that this question may be repeated for both responses. The variable label text for Q34 should also be rewritten as follows: "How much did the statement [disclosure] influence your assessment of the scientific evidence for [D]esyflux?"

Response 1y: Q33 asks whether participants have seen any of the listed statements. Q34 is asked for each of Q33_A and Q33_D when they respond affirmatively to that statement in Q33. Thus, participants who chose option 01 for both items will see two separate questions. We will make the suggested changes to Q34.

The second public comment responder (www.regulations.gov *tracking number lkl-8y11-169c)* included four individual comments, to which we have responded.

Comment 2a *(summarized)*: FDA should give consideration to the representativeness of online study volunteers to the general public who will view print ads.

Response 2a: This is an excellent point and one to which we have given much thought. As with all research, there is a tradeoff of efficiencies when it comes to collecting information from volunteers. Recruiting from internet panels is a relatively economical way to achieve large sample sizes from all across the U.S., making it possible to achieve geographic and urban/rural diversity in a way that was not previously possible. However, it is true that members of lower socioeconomic classes do not have the same access to computers and the Internet, and therefore our sample may be skewed toward individuals who have higher education and/or income. We have attempted to mitigate this issue by aiming for recruitment of 60% of individuals with some or no college and 40% of individuals with a college degree or more.

While it is important to note that random assignment of respondents to experimental conditions provides us the ability to make causal claims about our findings, we do note that truncating the population from which we sample is a limitation of the study and will describe this in any publication or presentation that results from the data.

Comment 2b *(verbatim)*: We suggest that the study include electronic advertisements in addition to print advertisements to account for and reflect changes in consumer consumption of media, including the increase of electronic promotion and advertising of products by sponsors.

Response 2b: We agree that more information and promotion is moving to electronic presentations, including the internet, mobile applications, and other communication formats. However, the questions we ask in this current study are fundamental questions that should not differ based on presentation format. Moreover, our print ads are similar to what might be shown on a website, which is a prominent electronic format. We have other studies ongoing that are examining other electronic presentation modes (e.g., 81 FR 78163).

Comment 2c *(summarized)*: If the three levels of disclosure are to be strong, weak, and none, we recommend considering the following levels of disclosure:

-Additional concluding information makes it strong
-Less additional information makes it weak
-No additional information makes it none

Response 2c: Thank you for clearly investing time and energy in responding to this study design. The suggested levels of disclosure are effectively the same as what we have included in our study design. The weak disclosure provides some additional information, while the strong disclosure provides both the additional information and an explicit conclusion based on the information.

Comment 2d *(summarized)*: FDA should keep in mind that stronger disclosures may be longer, therefore eye tracking time may reflect length, not necessarily effectiveness.

Response 2d: The commenter is correct in that a longer block of text will generally result in a longer gaze fixation. We have taken steps to keep the stronger disclosures as close as possible in length to the weaker disclosures. However, as noted previously, eye tracking outcomes will be analyzed qualitatively. Our primary interest is whether the disclosure was attended to—the length of attention is of less interest in this case.

The third public comment responder (www.regulations.gov *tracking number lkl-8y16-bf58*) included five individual comments, to which we have responded.

Comment 3a *(summarized)*: The commenter assumes that stimuli will conform to FDA regulations and requirements in non-study aspects and will not over-dramatize claims versus disclosures.

Response 3a: All stimuli will conform to FDA regulations, as reviewed by OPDP reviewers. Additionally, we have designed the materials to fall within realistic parameters, thus the claims and disclosures are representative of what we may see in the marketplace.

Comment 3b *(summarized)*: The commenter includes a section titled "Comments on the Brief Summary and Provision of Risk Information in Advertising" wherein they encourage FDA to continue to consider the purpose and practical limits of advertising.

Response 3b: FDA agrees that a consideration of the purpose and practical limits of prescription drug promotion will guide the development of research projects. Otherwise, the comment appears to fall outside the scope of this particular proposed research.

Comment 3c *(summarized)*: Add "Don't Know" options for questions about perceived effectiveness in the consumer questionnaire.

Response 3c: Questions about perceived effectiveness by definition involve subjective rather than objective assessments of effectiveness. Participants have the option to skip these questions if they wish.

Comment 3d *(verbatim)*: We suggest also including questions to capture whether respondents have a general understanding that there are limitations to the data and information being presented, even if they do not recall specific information and disclosure statements.

Response 3d: This is a good suggestion, but it is important to phrase such questions appropriately. For example, simply asking participants if they believe the data is thorough and complete or that the data has limitations is not likely to yield useful information. However, there are several validated skepticism scales that approach this idea of trusting the validity of presented information. Although these items are not tied to data specifically, they will provide some information for us about how much individuals rely on the data. We have added two questions near the end of the survey to address this issue.

Comment 3e *(summarized)*: The commenter recommends deleting "…from a source other than your healthcare provider" from questions 6 and 7.

Response 3e: Because we ask about seeking information from a HCP in other questions, we will retain this distinction in Q6 and Q7 for clarity.

The fourth public comment responder (www.regulations.gov *tracking number lkl-8y38-n0p8, also duplicated at lkl-8y38-smx8)* included eight individual comments, to which we have responded.

Comment 4a *(summarized)*: The commenter is supportive of the research.

Response 4a: Thank you for your support.

Comment 4b *(summarized)*: The commenter suggests carefully selecting medical conditions to ensure a range of therapeutic areas. Specifically, they suggest one life-threatening condition (e.g., cardiovascular conditions leading to stroke), one chronic condition (e.g., atopic dermatitis), and one non-life-threatening and non-chronic condition (e.g., urinary tract infection).

Response 4b: FDA believes this proposed range of medical conditions is a great way to choose therapeutic categories. For the current study, however, we limited ourselves to medical conditions that have existing promotional pieces that include a variety of limitations that can be feasibly explained in a disclosure. We will keep the commenter's approach in mind and apply it in future research when possible.

Comment 4c *(summarized)*: The commenter suggests selecting a diversity of participants, including gender, race, ethnicity, socioeconomic status, etc., to better represent the population at large. Also, the FDA should consider inclusion and exclusion criteria for HCPs and consumers carefully.

Response 4c: We agree that these characteristics are important and strive to obtain representativeness across a variety of personal demographics. Although we will aim to recruit a diverse group of participants with sufficient variation on demographic characteristics such as gender, race, age, and education, we note that this study features random assignment to condition, whereby these demographic characteristics should have an equal chance of occurring. In terms of HCPs, we will include them if they are a primary care physician, and will work to recruit a sample with sufficient diversity on demographic characteristics as noted above.

Comment 4d *(verbatim)*: It is critical that FDA evaluates the merits of unbiased introduction by not presenting a promotional piece to HCPs with specialty in the same therapeutic category.

Response 4d: For this study, we will be recruiting only primary care physicians and not specialists. Thus, while any given participant may have experience treating one or more of the conditions represented by our stimuli, none should have specialties in the respective therapeutic categories.

Comment 4e *(summarized)*: The commenter encourages the use of a health literacy competency tool such as a readability calculator to ensure consumers can understand the language.

Response 4e: We agree that the plain-language communication of information is critical for the best public health outcomes. Nevertheless, our aim in this study is to test promotional materials that are available in the public domain. Although we have disguised the products and campaigns in our mock stimuli, all pieces are derived directly from promotion in the marketplace. We feel this is important to ensure that our study is relevant.

Comment 4f *(summarized)*: The commenter recommends recruiting through hospitals, doctor offices, and clinics rather than via the Internet. The commenter suggests that this will expand on the pool of participants, help minimize potential bias, and ensure the entire population of the U.S. is represented as not everyone has access to or uses the internet.

Response 4f: Please see our response to comment 2a.

Comment 4g *(summarized)*: The commenter recommends conducting subgroup analyses, such as with older adults.

Response 4g: We will examine covariates including age, race, and education level to determine whether these variables have any effect on our findings. This study is not designed to conduct between-subgroup analyses. If we detect relevant trends, such subgroup analyses may become good candidates for future studies.

Comment 4h *(verbatim)*: [The commenter] recommends that the FDA communicate the actions they will take based on the study results and analysis. We also encourage FDA to

provide further communication about when FDA will publish the study results, how the study results will be applied, and how this will impact the work of FDA.

Response 4h: Please see our response to comment 1a.

External Reviewers

In addition to public comment, OPDP solicited peer-review comments from researchers in fields relevant to the communication of DTC prescription drug information. We received responses and incorporated the thoughts of the following individuals:

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9. Explanation of Any Payment or Gift to Respondents

After completing the surveys, participants will receive an incentive as a token of appreciation for participating. As participants often have competing demands for their time, incentives are used to encourage participation in research. When applied in a reasonable manner, incentives are not coercive but rather they serve as an approach that acknowledges respondents for their participation (Ref. 7). The use of incentives treats participants justly and with respect by recognizing and acknowledging the effort that they expend to participate. In this particular research study, we are asking participants to provide feedback on concepts that require a high level of engagement.

Incentives must be high enough to equalize the burden placed on respondents with respect to their time and cost of participation (Ref. 8), as well as provide enough motivation for them to participate in the study rather than another activity. If the incentive is not adequate, participants may agree to take the survey and then drop out early. An additional consideration for use of incentives is the potential increased cost due to low participation. Low participation can cause a difficult and lengthy recruitment process that, in turn, can cause delays in launching the research, which leads to increased costs.

For the survey portion of the consumer study, participants will receive proprietary internal currency through Research Now. Although it does not equate to an exact dollar-for-dollar value, it does hold monetary value. For the purposes of this study, participants will earn approximately $5.00 in e-rewards currency. Following completion of the survey, participants will be redirected to their profile on Research Now, where they will receive their incentive.

Physician survey participants will receive a $50 honorarium. SERMO offers its panelists a variety of options for honoraria disbursement, including checks, prepaid Visa cards, charity donations, and Amazon.com vouchers. Following completion of the survey, participants will be redirected to SERMO, where they can select their disbursement method.

For the eye-tracking studies, consumer participants will receive an incentive of $100, and physician participants will receive an incentive of $250. These incentives reflect the increased amount of time—including travel time—that participants must devote to the study. In addition to increased time burden, eye-tracking studies place an increased cognitive burden on participants, further justifying the incentive amounts. Incentives for eye tracking will be disbursed as a Visa gift card at the completion of each participant's session.

10. Assurance of Confidentiality Provided to Respondents

All data will be collected with an assurance that the participants' responses will remain private to the extent allowable by law. The consent form (see Appendix C) contains a statement emphasizing that no one will be able to link a participant's identity to his/her responses and that each participant will only be identified by a unique ID. Researchers will not tie respondents' personally identifiable information (PII) to their answers. All analyses will be done in the aggregate, and respondent information will not be appended to the data file used. Further, no identifying information will be included in the data files delivered by FMG to FDA.

The following procedures will be used to ensure participant confidentiality before, during, and after fielding: (1) data transfer between Research Now and FMG and between SERMO and FMG will be conducted via a secure password-protected File Transfer Protocol (FTP) site; (2) all screening-related information will not be tied to any PII but will be identified and matched by the assigned unique ID; (3) data sets and reports will not contain any PII; and (4) respondents will not be tied to their individual responses, and all analyses will be conducted in the aggregate (i.e., any data used in reporting will not be attributed to specific participants).

Any data sets and reports delivered to FDA will not include PII. All identifying information will be kept on a separate password-protected computer and/or in locked cabinets for a period of three years and will only be accessible by FMG. After three years, FMG will destroy the information by securely shredding documents or permanently deleting electronic information. In the case of a breach of confidentiality, appropriate steps will be taken to notify participants.

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

For both the pretests and main study, the questionnaire is expected to last no more than 25 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 Annual Reporting Burden[1]

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response (in Hours)	Total Hours[2]
Consumers					
Pretest Screener	833	1	833	.03 (2 min.)	25
Pretest	500	1	500	0.33 (20 min.)	165
Eye-Tracking Screener	80	1	80	.08 (5 min.)	7
Eye-Tracking Study	20	1	20	1 (60 min.)	20
Main Study Screener	2,500	1	2,500	.03 (2 min.)	75
Main Study	1,500	1	1,500	0.33 (20 min.)	495
Physicians					
Pretest Screener	735	1	735	.03 (2 min.)	22
Pretest	500	1	500	0.33 (20 min.)	165

Eye-Tracking Screener	80	1	80	.08 (5 min.)	7
Eye Tracking Study	20	1	20	1 (60 min.)	20
Main Study Screener	2,206	1	2,206	.03 (2 min.)	67
Main Study	1,500	1	1,500	0.33 (20 min.)	495
Total					1,563

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Rounded to next full hour

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 $669,354 ($223,118 per year for three years). This includes the costs paid to the contractors to manipulate 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 report ($97,000; 8 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 Part 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 completed	16 weeks
Main study data collected	80 weeks
Final methods report completed	80 weeks
Final results report completed	102 weeks
Manuscript submitted for internal review	106 weeks
Manuscript submitted for peer-review journal publication	110 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.

References

1. Dodge, T. and A. Kaufman. "What Makes Consumers Think Dietary Supplements Are Safe and Effective? The Role of Disclaimers and FDA Approval." Health Psychology, 26(4), 513-517. (2007).

2. Dodge, T., D. Litt, and A. Kaufman. "Influence of the Dietary Supplement Health and Education Act on Consumer Beliefs About the Safety and Effectiveness of Dietary Supplements." Journal of Health Communication: International Perspectives. 16(3), 230-244. (2011).

3. Mason, M. J., D. L. Scammon, and X. Feng. "The Impact of Warnings, Disclaimers and Product Experience on Consumers' Perceptions of Dietary Supplements." Journal of Consumer Affairs, 41(1), 74-99. (2007).

4. France, K. R. and P. F. Bone. "Policy Makers' Paradigms and Evidence from Consumer Interpretations of Dietary Supplement Labels." Journal of Consumer Affairs, 39(1), 27-51. (2005).

5. Aikin, K.J., Sullivan, H.W., & Betts, K.R. (2016). Disease information in direct-to-consumer prescription drug print ads. *Journal of Health Communication, 21(2)*, 228-239.

6. Pernice, K., and Nielsen, J. (2009). How to Conduct Eye Tracking Studies. https://media.nngroup.com/media/reports/free/How_to_Conduct_Eyetracking_Studies.pdf

7. Halpen, S. D., Karlawish, J. H., Casarett, D., Berlin, J. A., & Asch, D. A. (2004). Empirical assessment of whether moderate payments are undue or unjust inducements for participation in clinical trials. *Archives of Internal Medicine*, *164*, 801–803.

8. Russell, M. L., Moralejo, D. G., & Burgess, E. D. (2000). Participants' perspectives. *Journal of Medical Ethics*, *26*, 126–130.