Experimental Study: Effect of Promotional Offers in Direct-to-Consumer Prescription Drug Print Advertisements on Consumer Product Perceptions

0910-Number

SUPPORTING STATEMENT A

Submitted by

Office of Prescription Drug Promotion
Center for Drug Evaluation and Research
Office of the Commissioner

Food and Drug Administration

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A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

Regulatory Background - Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes FDA to conduct research relating to health information. Section 1003(d)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(d)(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.

Section 502(n) of the FD&C Act (21 U.S.C. 352(n)) requires all advertisements for prescription drugs to include, among other things, "such information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations." Pursuant to this authority, FDA has promulgated regulations to require most prescription drug advertisements to provide a "true statement of information in brief summary relating to side effects, contraindications, and effectiveness." (21 CFR 202.1(e)(1). To satisfy this requirement, an advertisement that makes claims about a prescription drug must also include a "fair balance" of information about the benefits and risks of the advertised product, in terms of both content and presentation (21 CFR 202.1(e)(5)(ii)). In part,

> [a]n advertisement for a prescription drug is false, lacking in fair balance, or otherwise misleading, or otherwise violative of section 502(n) of the act, among other reasons, if it [c]ontains a representation or suggestion, not approved or permitted for use in the labeling, that a drug is better, more effective, useful in a broader range of conditions or patients… safer, has fewer, or less incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience…whether

> or not such representations are made by comparison with other drugs or treatments, and whether or not such a representation or suggestion is made directly or through use of published or unpublished literature, quotations, or other references."

(21 CFR 202.1(e)(6)(i)).

FDA's current regulations provide a limited exception to the requirement in 202.1(e)(1), of presenting a true statement of information in brief summary, for "reminder advertisements" ("reminder ads") -- advertisements that draw attention to the name of the product but do not make representations about the product's indication(s) or dosage recommendations. 21 CFR 202.1(e)(2)(i). (Certain drugs are not permitted to qualify for the reminder advertisement exemption.) To meet the terms of this exemption, reminders ads must in general be limited to the proprietary and established name of the product and the established name of each active ingredient in the drug product. Reminder ads may also (optionally) contain information about the product's quantitative ingredients, dosage form, quantity, price, and manufacturer, as well as other written, printed, or graphic matter containing no representation or suggestion relating to the product. Further, reminder ads that are intended to provide consumers with information concerning the price charged for a prescription drug product need not meet the terms of 21 CFR 202.1(e)(2)(i) in order to be exempt from 202.1(e)(1) if they meet all of the conditions in 21 CFR 200.200. That regulation, in turn, applies to prescription drug reminders ads that are intended solely to provide consumers with information concerning the price charged for a prescription for a particular drug product, and the reminder ad contains no representation or suggestion concerning the drug product's safety, effectiveness, or indications for use. (21 CFR 200.200(a)(1), (b)).

Rationale. A topic of ongoing interest for consumer product manufacturers and retailers is the use of consumer-oriented sales promotions such as free trial offers, discounts, money-back guarantees, and rebates. Such promotions are widely used in many product categories, including prescription drugs.

Prior research has demonstrated that the type of promotion offered can affect how consumers respond to the promotion.[1] Price incentives may act as cues about product quality. For example, a price incentive may not only act as an economic incentive to buy the product, it may also artificially enhance consumers' perceptions of the product's quality.[2] In the case that consumers can readily test the performance of some products (termed "experience" goods[3]), this misperception is quickly corrected through the consumer's use of the product. In situations where little information about the product is available or when consumers are unmotivated to seek further information, consumers may use price as a heuristic cue to ascertain the quality of a product. Rao (2005)[4] has referred to the use of price as a cue to quality as the "price-quality heuristic," where heuristics are conceptualized as mental shortcuts that minimize cognitive effort to process information and are used either when individuals are unable or unwilling to engage in more analytical processing of information.[5] For example, if length of warranty is strongly believed to be a good predictor of quality, then consumers may perceive a product as higher quality when a long

1 See for example, deGroot, I.M., Antonides, G., Read, D. et al. (2009). "The Effects of Direct Experience on Consumer Product Evaluation," Journal of Socio-Economics, 38(3), 509-519; DelVecchio, D., Henard, D.H.& Freling, T.H. (2006). "The Effect of Sales Promotion on Post-Promotion Brand Preference: A Meta-analysis, Journal of Retailing, 82(3), 203-213; Mico, C.C.& Chowdhury, T.G. (2010). "The Effect of Message's Regulatory Focus and Product Type on Persuasion., Journal of Marketing Theory and Practice, 18(2), 181-190.

2 LeClerc, F.& Little. J.D.C. (1997). "Can Advertising Copy Make FSI Coupons More Effective?" Journal of Marketing Research, 34(4), 473-484.

3 Wolk, A.& Ebling, C. (2010). "Multi-channel Price Differentiation: An Empirical Investigation of Existence and Causes.," International Journal of Research in Marketing, 27(2), 142-150.

4 Rao, A. R. (2005). The quality of price as a quality cue. Journal of Marketing Research, 42, 401-405.

5 Chaiken, S., Liberman, A.& Eagly, A. H. (1989). Heuristic and systematic information processing within and beyond the persuasion context. In J. S. Uleman. & J. A. Bargh (Eds.), Unintended thought (pp. 212-252). New York: Guilford Press.

warranty is present than when one is not present.[6] Thus, price incentives may have the potential to act as an "inference rule" (or heuristic[7]) and, when present, they may preempt consumers from thinking carefully about the product information contained in the advertisement (i.e., fully elaborating on the information). This could result in either favorable or unfavorable beliefs about the product.[8] If a price incentive offer acts as a mental heuristic in such a way as to result in an unbalanced or misleading impression of the product's safety or efficacy, however, this would raise concerns for FDA.

Consumers vary in their reactions to price incentive promotions[9] and researchers and economists have proposed a number of explanations for why some consumers are sensitive to these tactics. Two such traits are "price consciousness" and "belief in the price-quality relationship." Price consciousness is defined as the degree to which the consumer focuses exclusively on paying low prices. Belief in the price-quality relationship is defined as the degree to which one believes a higher price indicates superior quality.[10] A broader trait of "value consciousness" has also been used. This trait involves assumptions about the construct of perceived value and its relationship (a ratio) with the constructs of perceived quality and perceived price.

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6 Johar, G.V, & Simmons, C.J. (2000). "The Use of Concurrent Disclosures to Correct Invalid Inferences." Journal of Consumer Research, 26(4), 307.

7 Chaiken, S., Liberman, A.,& Eagly, A. (1989). "Heuristic and Systematic Processing Within and Beyond the Persuasion Context,". In J.S. Uleman and J.A. Bargh (Eds.), Unintended Thought (chapter 7, p. 212-252), Guilford Press: New York; Bettman; J.R., Luce, M.F., & Payne, J.W. (1998). "Constructive Consumer Choice Processes." Journal of Consumer Research, 25(3), 187-217.

8 Alba, J.W.& Marmorstein, H. (1987). "The Effects of Frequency Knowledge on Consumer Decision Making." Journal of Consumer Research, 14(1), 14-25 Inman, J.J., McAlister, L. & Hoyer, W.D. (1990). "Promotion Signal: Proxy for a Price Cut?", Journal of Consumer Research, 17(1), 74-81.

9 In this document, we will use the terms "price incentive" and "coupon" interchangeably to refer to the types of promotional offers to be addressed in our study.

10 Garretson, J.A. & Burton, S. (2003). "Highly Coupon and Sale Prone Consumers: Benefits Beyond Price Savings." Journal of Advertising Research, 43, 162-172.

While price incentive promotions have been extensively studied in the context of package goods, information on their effects in DTC prescription drug ads is limited. One relevant study[11] found that a free-trial offer in a DTC ad for a high cholesterol drug resulted in more favorable perceptions of the product and the ad (both rated as good/bad, favorable/unfavorable, and pleasant/unpleasant), and greater intentions to ask about the product. No differences were found in terms of perceived product risk. However, the study did not measure perceptions of product risk and benefit separately, or comprehension of risk and benefit information. Additionally, no attempt was made to control for factors that may predispose individuals toward use of price incentives nor was the study conducted with the target population (high cholesterol sufferers). We propose to expand on this initial study by measuring perceived product risk and benefit separately, measuring risk and benefit comprehension, investigating a variety of price incentive promotional offers, recruiting a wider range of the target audience from malls and online, and by measuring traits that may predispose individuals toward use of price incentives.

The current study will examine what effect, if any, the presence of price incentive promotional offers in DTC prescription drug ads have on the following: (1) Consumers' perceptions of product risks and benefits, (2) recall of product risks and benefits, and (3) strongly held beliefs that may act as potential moderators. This information collection is not related to the American Recovery and Reinvestment Act of 2009 (ARRA).

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

This project will involve a two-part experiment with consumers, to 1) assess the effect of promotional offers in DTC prescription drug print ads on consumers' perceptions and recall of

11 Bhutada, N.S., Cook, C.L.& Perri, M. (2009). "Consumer Responses to Coupons in Direct-to-Consumer Advertising of Prescription Drugs." Health Marketing Quarterly, 26, 333-346.

product risks and benefits, 2) examine how strongly held beliefs may act as potential moderators, and 3) compare findings across different modes of data collection. This project will also examine potential differences that may occur as a result of the mode of administration (mall intercept versus web-based). Part of FDA's public health mission is to ensure the safe use of prescription drugs; therefore it is important to communicate the risks and benefits of prescription drugs to consumers in a way that is clear, useful and non-misleading. The results from this project will be used by FDA to inform its understanding of DTC advertising, inform regulatory policy, and may also help to identify areas for further research.

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 and via mall intercepts. In both methods, the participant will self-administer the survey instrument via a computer, which will record responses and provide appropriate probes when needed. FDA estimates that 100% of the respondents will use electronic means to fulfill the agency's request. In addition to its use in data collection, automated technology will be used in data reduction and analysis. Burden will be reduced by recording data on a one-time basis for each respondent, and by keeping surveys to less than 20 minutes.

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

A literature search identified one study[12] that examined a price incentive promotion, specifically a free trial offer, within a DTC prescription drug print ad. As noted above, the current study will address this initial study's omissions by measuring perceived product risk and benefit separately

12 Bhutada, N.S., Cook, C.L. & Perri, M. (2009). "Consumer Responses to Coupons in Direct-to-Consumer Advertising of Prescription Drugs." Health Marketing Quarterly, 26, 333-346.

and measuring risk and benefit comprehension. It will also expand the scope of that study by investigating a variety of price incentive promotional offers, recruiting a wider range of the target audience from malls and online, and by measuring traits that may predispose individuals to be susceptible to influence by price incentive offers.

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

No small businesses will be involved in this data collection.

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

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

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

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

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

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of September 22, 2010, Volume 75, Number 183 (Docket No FDA-2010-N-0456). A copy of the 60-day Federal Register notice is included in Appendix 1. FDA received five comments. In the following section, we outline the observations and suggestions raised in the comments and provide our responses.

Two comments wrote in support of the study. We thank those who commented for their support of this research.

One comment spoke against FDA conducting the research, saying (in part), "[T]his survey

is so unnecessary and such a waste of tax dollars… [W]e all know already how consumers take this information… [Y]ou can see from teh (sic) way the ads are presented what the big money big pharma con men are up to."

Response: We thank the citizen that took the time to comment on this study. The purpose of this study is to examine the potential impact on perceptions of product safety and efficacy of promotional price incentives included in the body of a prescription drug advertisement. We disagree that the field has definitively answered the question of how consumers will "take this information." As described in section A.1 (above), one study that examined the impact of a price incentive promotion in a prescription drug print advertisement found that consumers who saw an ad with the price incentive promotion had favorable perceptions of the product and the ad and had greater intentions to ask about the product. No differences were found in terms of perceived product risk. However, the study did not measure perceptions of product risk and benefit separately, or comprehension of risk and benefit information. In addition, we note that the findings of other academic studies in this field point in two different directions; research shows the presence of coupons (price incentives) can foster beliefs about product quality or diminish beliefs about product quality. Therefore, the lack of information about the potential influence of price incentive promotions on risk and benefit comprehension and the conflicting findings in the current literature make this an opportune area in which to conduct an empirical study.

Two comments included multiple points about the study justification and design. We thank those who provided the comments for taking the time to provide detailed comments on our study and respond to their points below.

One comment suggested that the proposed study is not necessary for the proper performance

of FDA's functions because no evidence of a serious or widespread problem with price incentive promotions has been identified.

Response: FDA disagrees with the comment. While no "serious or widespread problem" has been previously identified, the agency has observed increasing use of a variety of price incentive promotional offers in DTC print advertisements for prescription drugs. The proposed study is intended to help the agency better understand what effect, if any, these price incentive promotions have on consumer perceptions of risk and benefit information about the advertised prescription drugs. Improving FDA's understanding of these effects will assist the agency in proactively meeting its responsibility to implement the FD&C Act. As already noted, both the Act and existing regulations promulgated to implement it are concerned with ensuring that prescription drug advertisements, including DTC print ads, provide appropriate risk and benefit information and are not otherwise misleading. (See, e.g., 21 USC 352(n) & 321(n); 21 CFR 202.1(e);) The study will provide information to help the agency assess how these mandates can be met where price incentives are employed, and is and therefore "necessary for the proper performance of FDA's functions . . ." (44 U.S.C. 3508).

Another comment suggested that the inclusion of a truthful price incentive in an otherwise compliant DTC advertisement cannot render the advertisement false, misleading or lacking fair balance under the FDCA regardless of the psychological theories implicated. The comment further asserted that the inclusion of a truthful price incentive into an otherwise compliant DTC ad cannot serve as the basis for FDA to initiate regulatory action against the ad under the Act.

Response: FDA believes that if the inclusion of a "truthful" price incentive in promotional

material results in an unbalanced net impression of the drug product, that this would create a misleading impression of risk and benefit. As explained in FDA's draft Guidance for Industry, "Presenting Risk Information in Prescription Drug and Medical Device Promotion"[13] (emphasis in original):

> It is important to emphasize that when FDA evaluates the risk communication in a promotional piece, FDA looks not just at specific risk-related statements, but at the ***net impression*** – i.e., the message communicated by all elements of the piece as a whole. The purpose of the evaluation is to determine whether the piece ***as a whole*** conveys an accurate and non-misleading impression of the benefits and risks of the promoted product. Manufacturers should therefore focus not just on individual claims or presentations, but on the promotional piece as a whole. A promotional communication that conveys a deceptive net impression of the product could be misleading, even if specific individual claims or presentations are not misleading.

Thus, even if a price incentive included in an advertisement is in fact "truthful," the net impression of the promotional piece as a whole can be unbalanced or misleading, which may in turn violate existing regulations. FDA proposes this study to help determine whether or not including a price incentive in a DTC print advertisement for a prescription drug can result in an unbalanced or otherwise misleading net impression of the drug product.

One comment stated that the study may provide interesting information about the effect of price incentives on consumer attitudes toward a brand and useful information on optimal advertising practices, but it cannot provide information relevant to the statutory and regulatory requirements applicable to DTC advertising.

Response: FDA disagrees with the assertion that the study cannot provide information relevant to the statutory and regulatory requirements applicable to DTC advertising. As noted above, this study will examine issues that are well within our regulatory authority – whether the

13 Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM155480.pdf. Last accessed May 26, 2011.

inclusion of price incentives in prescription drug ads impacts a consumer's understanding of the risk and benefit information of the drug. In particular, we are interested to learn whether the inclusion of price incentives can interfere with the fair balance of information and cause a misleading net impression. Knowing whether or not misleading impressions result is a prerequisite to considering how any such misleading effects should be addressed.

One comment contends that the citation to 21 CFR 202.1(e)(6)(i) included in the agency's prior Federal Register notice is inaccurately truncated, and further asserts that the only indirect claims and representations subject to this regulation are those made through use of literature, quotations, or other references. The comment argues that because price incentives do not involve the use of published or unpublished literature, quotations or other references, this provision does not provide a legal basis for the proposed study or for the agency to regulate the heuristic effects (if any) of price incentives.

Response: To ensure that the regulation is adequately represented, FDA includes a fuller excerpt of 21 CFR 202.1(e)(6) in this document, and in the 30-day notice, than was included in the prior notice. However, in its conclusion about the justification for the proposed study, the comment focuses too narrowly, and incorrectly, on certain elements in 21 CFR 202.1(e)(6)(i).

As an initial matter, as noted, under 502(n), FDA has authority to specify by regulation how to present the brief summary of risk and benefit information required in prescription drug advertisements. This authority, together with FDA's authority for research, amply supports the proposed study. FDA need not establish that it would bring enforcement actions under 202.1(e)(6)(i) or any other specific provisions of the present regulations in order to justify conducting a study that is intended to provide a better empirical understanding of the impact, if any, on risk and benefit

information communication where price incentives are included in DTC print advertisements for prescription drugs. The results of this study will help to inform FDA's review of, and regulatory policies for, prescription drug advertising subject to section 502(n) of the Act.

Turning specifically to 21 CFR 202.1(e)(6), we disagree with the comment's construction of that regulation. As indicated in the prefatory text of 202.1(e)(6), the specifics that follow are "among other reasons" that an advertisement for a prescription drug is be false, lacking in fair balance, or otherwise misleading, indicating that these are examples and not an exclusive list as the comment assumes. In the same vein, 21 CFR 202(e)(6)(i) states that an advertisement may not contain:

> a representation or suggestion, not approved or permitted for use in the labeling, that a drug is better, more effective, useful in a broader range of conditions or patients… safer, has fewer, or less incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience … whether or not such representations are made by comparison with other drugs or treatments, and whether or not such a representation or suggestion is made directly or through use of published or unpublished literature, quotations, or other references.

(emphasis added). This phrasing prohibits "a representation or suggestion, not approved or permitted for use in the labeling" even if the representation or suggestion is not made via the means given as examples in the regulation. Thus, FDA has consistently, and appropriately, examined both direct and indirect representations and suggestions when examining the net impression presented in a prescription drug advertisement.[14]]

One comment asserts that the citation to 21 CFR 202.1(e)(6)(xviii) is inappropriate because this regulation concerns only the presentation of heading and subheadings and FDA is studying the

14 See Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM155480.pdf. Last accessed May 26, 2011.

mere fact that a price incentive has been made, not the way in which headline, subheadline, or pictorial or other graphic matter are used to communicate that price incentive.

Response: FDA does not need to rely on 21 CFR 202.1(e)(6)(xviii) to justify the proposed study, therefore, we have removed the reference to this regulation.

One comment contends that the scientific research identified does not provide justification for conducting the study nor does it provide support for the proposition that promotional offers have the capacity to act as a cue or a heuristic with respect to prescription drugs.

Response: We acknowledge that there is little research on the impact of price incentive promotional offers in prescription drug advertising. The paucity of existing research is a primary motivation for the proposed research. The question of whether or not a price incentive can affect perceptions of and recall of prescription drug efficacy and risk is an empirical one and will be tested in the proposed study.

One comment directly questioned the need to conduct this study in light of the results found by Bhutada et al. (2009). Specifically, the comment asserts that the study found no effect of a price incentive on consumer comprehension of risks or benefits of the prescription drug.

Response: As noted in our background section, the Bhutada et al. study did not measure perceptions of product risk and benefit separately. Perceptions of product risk and benefit were measured on a scale with risk at one end and benefits at the other, so it was not possible to assess the effects of the price incentive on risks and benefits separately. Further, comprehension of risk and benefit information was not measured at all, so it is impossible to determine from this study if there was an effect on comprehension. The current proposed study will extend this initial study by measuring perceived product risk and benefit separately, measuring risk and benefit

comprehension, investigating a variety of promotional offers, recruiting a wider range of the target audience from malls and online, and by measuring traits that may predispose individuals to be susceptible to influence by a price incentive.

One comment asserts that heuristic effects are not claims, either expressed or implied, and since reminder ads do not include any safety or effectiveness information, there is no basis even to argue that they may preempt consumers from thinking carefully about the product information contained in the reminder ad.

Response: It is an empirical question whether price incentives operate as a heuristic cue and further, whether those cues impact perceptions of product characteristics (in this case, the product's efficacy and risk). As the literature on heuristic judgment demonstrates, individuals are frequently faced with situations in which they are required to make judgments using incomplete information and are able to do so.[15] Therefore, it is reasonable to test whether an incentive can influence this judgment in the context of both a full-product and a reminder DTC prescription drug advertisement.

One comment asserts that the regulation explicitly permits companies to include information about price within reminder ads. The comment argues that because price incentives pertain to price, this regulation provides no legal basis for the proposed study or for the agency to regulate price incentives contained in reminder ads.

Response: FDA acknowledges that current regulations permit reminder ads to include price information under defined conditions, while remaining exempt from the requirement for a "true

15 See, for example, Kivetz, R.& Simonson, I. (2000). The effects of incomplete information on consumer choice. Journal of Marketing Research, 37, 427-448. For a review, see Kardes, F.R., Posavac, S.S. & Cronley, M.L. (2004). Consumer inference: A review of processes, bases, and judgment contexts. Journal of Consumer Psychology, 14(3), 230-256.

statement of information in brief summary." FDA does not intend to use the results of this study to regulate drug prices. In this study, FDA is only seeking to assess the effects, if any, of the presence of various offers in DTC advertisements on consumers' perceptions of product risks and benefits. As stated above, we will use "reminder ads" in this study to understand the effect of offers on consumer perceptions of safety and efficacy. Reminder ads present a useful tool in determining this effect as broad safety and efficacy information is not otherwise provided in such advertisements. Results of this preliminary study will help FDA in its assessment of drug ads and in broader assessment of its regulatory policy for effectuating section 502(n) of the FD&C Act and other legal authorities governing drug promotion.

One comment said that FDA has not established standards by which to judge the results of the study. This comment asserted that even if consumers have a more positive view of the safety or effectiveness of a product with a price incentive compared to one that does not, this does not automatically deem the ad false, lacking in fair balance, or otherwise misleading.

Response: To judge the results of our study, we take our cue from the related field of research conducted on potentially misleading claims and employed frequently by the Federal Trade Commission in their investigations of advertising claims.[16] In this research, an ad with the content at issue removed serves as an appropriate experimental control. Based on this precedent, an ad without a price incentive is an appropriate control in this study.

One comment stated that unless FDA can establish that differences in perceptions of safety or efficacy are not due to differences in price and/or the size of the price incentive, any restrictions or requirements on price incentives will require FDA to regulate prescription drug pricing.

16 See, for example, Murphy, D., Hoppock, T.H., & Rusk, M.K. (1998). Generic Copy Test of Food Claims in Advertising. Joint Staff Report of the Bureaus of Economics and Consumer Protection, Federal Trade Commission. Available at http://www.ftc.gov/os/1998/11/netfood.pdf. Last accessed January 14, 2011.

Response: As previously acknowledged, the FD&C Act does not provide FDA with authority to regulate prescription drug pricing and that is not the purpose or intended outcome of this study. The purpose of the currently proposed study is to investigate how different purchase incentives, including ones that may affect the actual price of the product, may operate in the context of a DTC ad. If we find that some types or all types of offers do influence viewers' comprehension and perceptions of safety or effectiveness, then, as suggested by this comment, the next logical step may be to conduct further study to disentangle the effects of the presence of the offer itself and the magnitude of the price incentives. In one research study we do not have the ability to examine all variables of interest, however, and we believe the variables we have chosen for the proposed study are reasonable.

One comment asserted that by equating cues and inference rules with product claims, FDA risks imposing restrictions on DTC advertising based on potential deception rather than actual deception, which the comment argues is fraught with risk under the First Amendment. This comment cites the following from *Washington Legal Foundation v. Henney* (56 F. Supp. 2d 81, 85 (D.D.C. 1999)), "FDA may not restrict speech based on its perception that the speech could, may, or might mislead." The comment urges FDA to carefully consider First Amendment issues before proceeding with the study.

Response: We have carefully considered First Amendment issues in designing this study. The *WLF* case cited by the comment notes that "the government must demonstrate that the restricted speech, by nature, is more likely to mislead than to inform" (*Id*. at 85). It is the goal of the proposed study to investigate whether a price incentive may or may not be "more likely to mislead than to inform." Our participants will view a fictitious but realistic DTC print ad and

answer questions about that ad. From their answers we will be able to determine their responses to the information in the ad. Thus, we will measure whether the ad is actually misleading and not potentially misleading. The experimental control afforded by participants' random assignment to different experimental conditions ensures that we will be able to pinpoint the source of any differences in responses to ad variations by comparing responses of participants who see the variables of interest (in this case, the offer) versus those who do not.

One comment stated that the proposed study appears to be designed more to assess the effect of coupons on brand attitudes and consumer impressions and does not appear to be tailored to assess the effect of price incentives on statutory and regulatory requirements. In other words, the comment argues that FDA has no regulatory authority to manage or regulate consumer attitudes or impressions toward a brand.

Response: As noted previously, the study is designed to determine whether price incentive offers embedded in prescription drug ads can result in a misleading net impression of risk and benefit, which may in turn violate existing regulations under the FD&C Act. We will measure the effect of the offer on consumer's understanding of the product's efficacy and safety and the net impression of the product created by a promotional piece in regards to that piece alone, which will inform our review of DTC prescription drug advertising generally. FDA does not intend to regulate or manage consumer attitudes or impressions towards a particular brand.

One comment questioned the utility of including the reminder and OTC test arms in the study as these advertisements do not include both safety and effectiveness information.

Response: As stated previously, individuals are frequently faced with situations in which they are required and able to make judgments using incomplete information. As detailed in the

background section, the inclusion of a prescription reminder ad and an OTC ad provides experimental control. We will compare perceptions of the product attributes among participants who see 1) full risk and efficacy information (full ad), 2) only efficacy information (OTC ad), and 3) neither risk nor efficacy information (prescription reminder ad). The question of whether an incentive can influence this judgment in the context of a DTC prescription drug advertisement is the empirical question we are addressing in the proposed study.

Two comments requested FDA provide more information on the study population and study design including the primary research questions, stimuli, endpoints, and action standards.

Response: The proposed questionnaire has been and continues to be available upon request. We refer to pages 57800 and 57801 of the 60-day notice where the study design was described. We have described the primary research questions in more detail in the 30-day notice. Specific hypotheses and the analysis plan are included in this document.

One comment requested that FDA specify the types of advertisements to be used in the study (i.e., spread, gatefold, 1/3 page ad). Another comment requested that FDA engage the services of an advertising agency that specializes in the development of DTC print advertisements. Further, the comment asserted that the location of the promotional offer may have an impact on consumer perceptions of product risks and benefits and requested FDA define the location of the offer and clarify if it will be varied in the test ads.

Response: The full product DTC ad will be two pages, including a brief summary. The OTC ad and reminder ad will each be one page. We have contracted with an organization that produces realistic ads and stimuli to ensure that we will show respondents realistic materials. The location of the promotional offer will be standardized as much as possible across all test conditions

and will be incorporated in such a way as to not obscure the description of either the risks or benefits in the full product ad.

One comment requested FDA identify and study more general disclosures that are not directly related to safety or effectiveness info, such as "consult with a physician to discuss whether this drug is right for you."

Response: We appreciate the comment about widening the scope of the disclosures to be studied. Based upon the suggestion of our peer reviewers, we have changed the focus of the second study to examine a second medical condition and will not be investigating disclosures as part of this initial study. We encourage other interested entities to engage in research on disclosures.

One comment requested that the study population be limited to individuals who have been diagnosed with the medical condition of interest and exclude those merely 'at risk' of developing the condition because those who do not have the medical condition may be much less attentive to the information in the ad and thus skew the study results. In another paragraph, the same comment questioned the need to conduct the proposed study in the target population since doing so would not yield different results from Bhutada et al. (2009) who did not use diagnosed individuals.

Response: As these two suggestions are contradictory, we offer our reasoning behind selecting participants in Study 1 who are either diagnosed or fit the criteria for diagnosis of insomnia (formerly referred to as "at risk"). One purpose of a purchase incentive is to encourage new users to try a product.[17] Similarly, the first of the Pharmaceutical Research and Manufacturers of America's (PhRMA) guiding principles on direct to consumer advertising[18] state that "… DTC

17 RxMarketMetrics Series. Savings offers: Effectively reaching the right audience? (2011). DTC Perspectives, 10(1), 14-16.
18 PhRMA Guiding Principles: Direct to Consumer Advertising about Prescription Medicines (2005). Available at http://www.phrma.org/files/attachments/2005-11-29.1194.pdf. Last accessed January 5, 2011.

advertising of prescription medicines can benefit the public health by … motivating patients to contact their physicians and engage in a dialogue about health concerns…" Inclusion of an incentive might encourage a consumer who recognizes the symptoms described in the advertisement to discuss the condition with a doctor or other healthcare professional. Thus, we believe that both diagnosed patients and those individuals who self-report as meeting the diagnostic criteria for the advertised medical condition but have not yet been diagnosed, are a valid sample for Study 1. We are limiting our Study 2 sample to individuals who have been diagnosed with high blood pressure by a healthcare professional.

One comment requested that demographic information such as age, education, income, ethnicity, race, a baseline assessment of health literacy, and whether the consumer is currently being treated with a prescription drug for the condition being studied be included in the information collection.

Response: Demographic and health literacy information will be collected (see questionnaire).

One comment requested that FDA use prudence when broadly interpreting the results from this study and developing subsequent guidance based on these study results, and requested that the results of the study not be applied beyond print ads or, alternatively, to expand the study to include internet promotion.

Response: At this time, we cannot expand the study to encompass internet promotion. We concur that there are media-specific factors that influence information processing between static (e.g., print) and dynamic (e.g., video) platforms, and will note that our study was conducted with print ads in our interpretation of the results. However, we contend that the cognitive processes used

in understanding and interpreting incentive information are likely to apply across promotional platforms.

Two comments mentioned that the study does not assess how consumer perceptions of product risks and benefits are translated into a discussion with their health care provider. One comment stated that because these products can only be purchased after a discussion with a healthcare provider, the study be redesigned so that consumer perceptions are measured after a discussion with a healthcare provider.

Response: We concur that this study does not address behaviors, such as how ad perceptions are translated into a discussion with a health care provider. As noted previously, one purpose of DTC advertising is to motivate consumers to engage in a discussion with their healthcare provider about health concerns. Another purpose, supported by research findings,[19] is to increase awareness of available treatments. DTC advertising does not exist solely in the confines of a doctor's office; rather, DTC advertising targets consumers outside of a doctor's office, with the goal of prompting consumers to ask their physicians about the product. In deciding whether or not to discuss a particular product with their healthcare provider, consumers presumably are engaging in some sort of judgment about the product being promoted. Therefore, clear communication of risks and benefits is needed for consumers before a consultation with a physician, and it is valid to measure these impressions.

One commenter requested that FDA provide clarity on the timing of this study vis a vis other FDA DTC studies and make available the results of previous DTC studies on the DDMAC

19 See, for example, Aikin, K.J., Swasy, J.S., & Braman, A.C. (2004). Patient and Physician Attitudes and Behaviors Associated with Direct-to-Consumer Promotion of Prescription Drugs: Summary of FDA Survey Research Results. Final Report. Technical Research Report. Available at: http://www.fda.gov/downloads/Drugs/ScienceResearch/ResearchAreas/DrugMarketingAdvertisingandCommunicationsResearch/UCM152860.pdf (Last accessed May 26, 2011); Prevention Magazine (2010). 13th Annual Survey of Consumer Reactions to DTC Advertising of Prescription Medicines. Emmaus, PA: Rodale, Inc.

Research webpage.

Response: The timing of this study is not dependent on other research currently underway. We have taken steps to publish reports from our previous research on the DDMAC webpage.[20] When the current project is concluded, we will report on the study.

External Reviewers

In addition to the comments above, FDA requested that several outside experts review the study design and methodology. The following individuals reviewed the study design, methodology, and questionnaires in 2011:

- Daniel Ariely, Ph.D., James B. Duke Professor of Psychology and Behavioral Economics, Duke University
- Karen France, Ph.D., Chairperson, Department of Marketing, West Virginia University
- Michael Norton, Ph.D., Associate Professor of Business Administration, Harvard Business School.
- Jeremy Kees, Ph.D., Assistant Professor of Marketing, Villanova University.

9. <u>Explanation of Any Payment or Gift to Respondents</u>

The data collection contractor for this project is Synovate. Internet panel participants receive points for completing a survey. One thousand points (approximate monetary equivalence of $1) will be awarded. Members are allowed to use their points to exchange for vouchers and gifts from a partner network. We propose to offer mall-intercept participants a small token of appreciation for their participation (approximate value of $1).[21]

20 http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090276.htm

21 Numerous experiments and two meta-analyses have demonstrated that incentives motivate survey participation over multiple administration modes (e.g., online, face-to-face, mail, mall-intercept). Nonmonetary token incentives

10. Assurance of Confidentiality Provided to Respondents

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

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

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' ADP Systems Security Policy as described in the DHHS ADP Systems

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increase response rates over no incentive (Willimack et al, 1995), whereas monetary incentives are the most effective at increasing response rates (Church, 1993; Ryu et al., 2005; Singer et al., 1999).
Church, A. (1993). Estimating the effect of incentives on mail survey response rates: A meta-analysis. Public Opinion Quarterly, 57, 62-79; Ryu, E., Couper, M.P. & Marans, R.W. (2005). Survey incentives: Cash vs. in-kind; face-to-face vs. mail; response rate vs. nonresponse error. International Journal of Public Opinion Research, 18(1), 89-106; Singer, E., Van Hoewyk, J., Gebler, N., Raghunathan, T., & McGonagle, K. (1999). The effect of incentives on response rates in interviewer-mediated surveys. Journal of Official Statistics, 15(2), 217-230; Willimack, D.K., Schuman, H., Pennell, B-E., & Lepkowski, J.M. (1995). Effects of a prepaid nonmonetary incentive on response rates and response quality in a face-to-face survey. Public Opinion Quarterly, 59(1), 78-92.

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 questionnaires are available in Appendix 2.

12. Estimates of Annualized Burden Hours and Costs

The total annual estimated burden imposed by this collection of information is 2,561 hours for this one-time collection (Table 1).

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	Hours per Response[2]	Total Hours
Screener	8,500	1	8,500	2/60	283
Pretests	994	1	994	20/60	328
Study 1: online	1,950	1	1,950	20/60	650
Study 1: mall intercept	1,950	1	1,950	20/60	650
Study 2	1,950	1	1,950	20/60	650
Total	15,344				2,561

[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".

Table 3. Estimated Annualized Burden Costs

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
General public	2,561	$18.68[a]	$47,839
Total			$47,839

[a]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 data is $924,365 (approximately $308,122 per year for three years). This includes the costs paid to the contractors to create stimuli, program the study, draw the sample, collect the data, and create a database of the results. The task order was awarded as a result of competition. Specific cost information other than the award amount is proprietary to the contractor and is not public information. The cost also includes FDA staff time to design and manage the study, to analyze the resultant data, and to draft a report ($120,000; 15 hours per week for 3 years).

15. Explanation for Programs Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

Conventional statistical techniques for experimental data, such as descriptive statistics, analysis of variance, and regression models, will be used to analyze the data. See section B below for detailed information on the design, hypotheses, and analysis plan. The Agency anticipates disseminating the results of the study after the final analyses of the data are completed, reviewed, and cleared. The exact timing and nature of any such dissemination has not been determined, but may include presentations at trade and academic conferences, publications, articles, and posting on FDA's website.

Table 4: Project Timetable

Task	Estimated Completion Date
External Peer Review	February, 2011
RIHSC Review	June, 2011
30-day FR notice publication	September, 2011
OMB Review of PRA package	May, 2012
Pretesting	June, 2012
Data Collection	July, 2012-November, 2012
Receipt of Data and Methods Report from Contractor	December, 2012
Data Analysis	January-May, 2013
Draft Report	June, 2013
Internal Review of Draft Report	August, 2013
Revisions and Internal Clearance	September, 2013-February 2014
Final Report	March, 2014

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.