Supporting Statement for

Experimental Evaluation of the Impact of Distraction on Consumer Understanding of Risk and Benefit Information in Direct-to-Consumer Prescription Drug Broadcast Advertisements

Submitted by

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

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes the Food and Drug Administration (FDA) to conduct research relating to health information. Section 903(b)(2)(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(b)(2)(c)) authorizes FDA to conduct research relating to drugs and other FDA regulated products in carrying out the provisions of the FD&C Act.

FDA regulations require that advertisements that make claims about a prescription drug include a "fair balance" of information about the benefits and risks of advertised products, in terms of both content and presentation. Ads can present information in ways that can optimize or skew the relative balance of risks and benefits. Both healthcare providers and consumers have expressed concerns to FDA about the effectiveness of its regulation of manufacturers' prescription drug advertising directed to consumers (DTC), especially as it relates to assuring balanced communication of risks compared with benefits.

One characteristic of DTC television broadcast ads that has raised continuing concerns is the use of compelling visuals. Many assert that the visuals present during the product risk presentation are virtually always positive in tone and often depict product benefits.[1] A consistently raised question is whether advertising visuals depicting benefits interferes with consumers' understanding and processing of required risk information in the ad's audio or text disclosures about where to obtain additional information.

The manner in which required risk information is presented in DTC ads has been recently addressed in the Food and Drug Administration Amendments Act of 2007 (FDAAA). Sec.

[1] See, for example, Wolfe, Sidney (2002). Direct-to-consumer advertising: Education or emotion promotion? *New England Journal of Medicine*, *346*(7), 524-526.

901(3) states that the major statement in DTC broadcast ads "shall be presented in a clear, conspicuous and neutral manner." Further, the Secretary "shall establish standards for determining whether the major statement is presented in such a manner." FDAAA does not define how the objective of "clear, conspicuous, and neutral" is to be achieved.

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

The purpose of the proposed study is, in part, to gather empirical evidence to address concerns that the use of competing, compelling visual information about potential drug benefits in DTC advertising interferes with viewers' processing and comprehension of risk information about drugs. Concerns have been raised that positive visual images could influence the processing of risk-related information and consumers' final understanding of the risks and benefits of the advertised drug in multiple ways. First, compelling visuals could simply distract consumers from carefully considering and encoding the risk information. To the extent that compelling visuals cause them to attend to or to process risk information less, participants exposed to risk information with simultaneous compelling positive visuals should recall fewer risks than do participants exposed to the risk information without the positive visuals. Second, compelling visuals may affect initial impressions of the brand and the way consumers think about the brand, specifically their attitudes toward the advertised brand.[2] An attitude is an association between an object and a degree of positivity or negativity. Thus, the impact of varying visual displays during the presentation of audio risks may be manifested in varying attitudes toward the brand. This is important because brand attitudes may be an important determinant of future behavior toward the brand. In contexts where product information is complex, initial impressions based on more subtle processes may have as significant an impact

[2] Payne, B.K., Cheng, C.M., Govorun, O., and Stewart, B.D. (2005). An Inkblot for Attitudes: Affect Misattribution as Implicit measurement. *Journal of Personality and Social Psychology*, *89*(3) 277-293.

on behavioral tendencies as impressions based upon more "cognitively-effortful" factual information. Since visual cues are typically easier to process than verbal information (Houston et al., 1987), initial attitudes for this group are likely to be greatly influenced by these cues.[3] Under many circumstances, people rely much less on facts that they know, such as the number of risks associated with, for example, ibuprofen, and much more on general feelings they have, such as strong positivity toward a brand, such as the Advil brand of ibuprofen. Compelling visuals during the audio risk portion of DTC advertisements have the potential to lead a consumer to form a positive opinion of a drug for no other reason than that it is presented in the same context as positive images.

Another purpose of the present study is to examine the role of textual elements in the processing of risk information. Sponsors often place superimposed text ("supers") onto the screen to clarify spoken information or to provide extra information that is not included in the audio. For example, information that fulfills certain disclosure requirements[4] ("See our ad in…") and limits claims of product use may appear. Providing verbatim text repetition of the risks required to be in the audio portion in broadcast ads may facilitate processing the risks, but only if viewers pay attention to the text. Viewers' attention may be affected by both the prominence of the textual information and the combined effects of text prominence and different visual information. The proposed study examines these associations.

A final purpose of this study is to provide FDA with information on defining the presentation of the major statement as "clear, conspicuous, and neutral" as required by FDAAA. We have limited data about how consumers perceive risk and benefit information in DTC

[3] Houston,M,J., Childers, T.L., and Heckler, S.E. (1987) Picture –Word Consistency and the Elaborative Processing of Advertisements, *Journal of Marketing Research 24 (Nov)*, 359-69.
Sengupta, J. and Fitzsimons,G.J. (2004). The effect of analyzing reasons on the stability of brand attitudes: A Reconciliation of Opposing Predictions, *Journal of Consumer Research, 31(3)*. 705-711.
[4] For a discussion, see Guidance for Industry: Consumer-Directed Broadcast Advertisements. Available at http://www.fda.gov/cder/guidance/1804fnl.htm. Last accessed March 18, 2008.

broadcast ads as a function of exposure to different content and presentations. Therefore, we do not fully understand the influence of visual and textual factors on the conveyance of a balanced or "neutral" picture of the product.

This study will investigate the impact of visual distraction and the interplay of different sensory modalities (audio, visual) used to present risk and benefit information during a television prescription drug advertisement. Data from this study will provide useful information for FDA as it considers whether it is appropriate to develop guidance to help improve how broadcast ads present a prescription drug's risks and benefits. This study will also provide preliminary data on how FDA might interpret the "clear, conspicuous, and neutral" standard. The data should help us plan whether additional research is needed to develop the standards called for in the FDA Amendments Act of 2007.

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. The participant will self-administer the Internet survey via a computer, which will record responses and provide appropriate probes when needed. In addition to its use in data collection, automated technology will be used in data reduction and analysis. Burden will be reduced by recording data on a one-time basis for each respondent, and by keeping surveys to less than 15 minutes.

4. Efforts to Identify Duplication and Use of Similar Information

Although some previous studies have investigated various aspects of print DTC ads,[5] little published research has been conducted on television DTC ads. Published research has typically used content analysis and not rigorous experimental investigation.[6] Such research does not permit extrapolation to understanding consumers' perceptions or intended behavior. Moreover, even after a recent sponsored rigorous review of the literature, FDA is not aware of previous research investigating the role of distraction in broadcast DTC ads.

5. Impact on Small Businesses or Other Small Entities

No small businesses would be involved in this data collection.

6. Consequences of Collecting the Information Less Frequently

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

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

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

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

The 60-day public comment notice was published in the Federal Register on August 22, 2007, Volume 72, Number 162 (Docket No 2007N-0321).

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[5]See, for example:
Holmes, E.R. & Desselle, S.P. (2004). Evaluating the balance of persuasive and informative content within product-specific print direct-to-consumer ads. *Drug Information Journal, 38*, 83-98.
Munce, S.E., Robertson, E.K., Sansom, S.N., & Stewart, D.E. (2004). Who is portrayed in psychotropic drug advertisements? *The Journal of Nervous and Mental Disease, 192*, 284-288.

[6]See, for example:
Kaphingst, K.A., DeJong, W., Rudd, R.E., & Daltroy, L. (2004). A content analysis of direct-to-consumer television prescription drug advertisements. *Journal of Health Communications, 9*, 515-528.
Kaphingst, K.A., Rudd, R.E., DeJong, W., & Daltroy, L. (2005). Comprehension of the information in direct-to-consumer television prescription drug advertisements among adults with limited literacy skills. *Journal of Health Communications, 7*, 609-619.
Sumpradit, N., Ascione, F.J., & Bagozzi, R.P. (2004). A cross-media content analysis of motivational themes in direct-to-consumer prescription drug advertising. *Clinical Therapeutics, 26*, 135-154.

FDA received comments from 30 groups or individuals in response to our initial federal register notice, published on August 22, 2007. In total, this amounted to approximately 29 distinct comments that specifically referenced the study. Of these, 12 were not PRA related. Many other comments did not require specific responses, as they were either outside the scope of the project (e.g., "Ban DTC advertising") or simply provided statements of support. We thank the three commenters who took the time to document their support for FDA's research in this area.

Number of Comments	Source	Specific Commenters	Notes
12	Individual Consumers		Outside scope
3	Organizations	• Breast Cancer Action • American Medical Association • Families USA	Statements of support and nothing more
6	Industry	• PhRMA • AstraZeneca • Eli Lilly & Co. • Merck • Pfizer • Sanofi-Aventis	
5	Academia	• Centers for Education and Research in Therapeutics (CERTs) • Jon Schommer, University of Minnesota • Jon Krosnick, Stanford University • Josh Murray, SUNY Stonybrook • Lewis Glinert, Dartmouth University	
4	Organizations	• Prescription Access Litigation (PAL) • Davidson & Company • American Academy of Pediatrics • Joint comment[7]	More than simple statements of support, although AAP did not attach their submission, despite additional contact

30	**TOTAL**		

In thinking about and responding to the comments, FDA made extensive modifications to the study's methodology and design. As reflected in these modifications, we agreed to: change from a mall-intercept to an internet administered procedure; limit use of the AMP (Attitude Misattribution Procedure) to a sub-experiment consisting of only 5 of the experimental conditions; add questions addressing the advertised (fictitious) drug's benefits; and make certain changes to the wording of the questions. Changing the administration procedure also allows us to double our sample size and test more conditions. In response to comments received both by the comment and by our peer reviewers, we also decided to do significantly more pretesting than originally planned to address the suggestion that the test ad should be embedded in a clutter reel of other ads and to test the validity of the stimulus manipulations (the mocked up advertisements). We disagreed, primarily because of time and complexity constraints, with suggestions to: add more independent variables; recruit a different set of participants; change the use of Chinese characters in the (now more limited) AMP-measured conditions; add certain additional dependent measures; increase (or decrease) the number of behavioral intention questions; control for baseline attitudes (because this is not needed in an experimental design and we are using a fictitious drug for the stimulus materials); and get industry approval and public comment on the mocked up ads.

Due to the high volume of comments and the fact that many commenters had similar suggestions, FDA's detailed responses to the comments is divided below into sections. The first section addresses comments that appeared in multiple submissions. Because these comments

[7] Joint comment by the National Association of Advertising Agencies, Association of National Advertisers, Coalition for Healthcare Communications, National Association of Broadcasters, and National Cable and Telecommunications Association.

were mentioned by more than one entity, it is likely that they represent elements of interest to a wide audience. The second section addresses the remaining individual comments, broken down as a function of source (academic or industry).

Responses to Comments Appearing in Multiple Submissions

1. *Addition of other factors to study*

Many commenters suggested additional factors that we might study in our investigation of distraction in broadcast ads. Some of these suggestions were quite good and we agree that they would be worthwhile studying. For example, commenters suggested studying the music in the background of the ads or varying the number of times participants are exposed to the ad. One specific comment repeated in many submissions was the idea that we should study more than one medical condition.

All of these suggestions, particularly the addition of another medical condition, would represent valuable contributions to the literature and to regulatory policy. Nonetheless, FDA has a limited budget and a limited number of resources. We have defined the study in such a way to address major questions of interest to stakeholders. Future studies conducted by FDA or others should indeed expand the research by investigating additional factors. At the present time, however, we have revised the design to be more comprehensive while maintaining research vigor. We have no reason to suspect, for instance, that any of the distraction characteristics we find would be different across medical conditions. We invite others to conduct research studies to look at additional factors and to replicate the results of our research when we obtain them.

2. *Recruitment issues*

FDA proposed in the initial submission to recruit individuals 40 years of age or over, a population that will approximate those at risk for high blood pressure. FDA selected high blood pressure as the medical condition that the fictitious drug would treat because it is an under-reported and under-treated condition in the population. Moreover, there is little current DTC advertising in this category, so prior experience with such ads will be less of a factor in our analysis and interpretation of the data. FDA decided not to restrict the sample to those who had been diagnosed with high blood pressure by a healthcare provider because it is likely that many people are at risk without knowing it. Furthermore, this strategy will allow FDA to determine whether individuals can accurately select in or out of the target market, thereby reducing the burden on physicians from customers who are not appropriate for a given drug product. Finally, ads broadcast on television are seen by individuals with a wide range of characteristics, so exposure is not limited to those diagnosed with the disease. For these reasons, although we respect the suggestions to limit the recruitment process, we will maintain our original recruitment strategy.

3. *Asking about benefits as well as risks*

FDA originally proposed that the Attitude Misattribution Procedure (AMP), which is expected to take approximately 5-7 minutes, was to be administered in all experimental conditions, thus limiting the number of other questions that could be administered within the 15-minute time limit negotiated with the contractor. Based partially on public comments as well as further internal discussion, FDA has altered the design of the study such that the main 13 cells of the design will not include the AMP. The AMP will be administered in 5 additional cells with approximately 50 persons per cell, as a supplementary investigation. Eliminating the AMP from

the main part of the experiment allows FDA to include additional questions not in the original proposal. Questions addressing the benefits of the drug have been added to the questionnaire.

4. *Embedding the ad in a clutter reel to enhance external validity*

FDA originally proposed to show one ad twice to each participant at the beginning of the interview. Several commenters suggested that FDA embed the ad within a clutter reel of other ads to make the protocol more similar to an actual viewing environment. The research team took this comment very seriously and discussed this suggestion at length. In addition, two peer reviewers cited to research where stimuli were tested in both a clutter reel and solo situation, showing that effects were only seen in the clutter-reel situation. In the end, the research team decided to engage in pretesting to determine the best way to address this issue. FDA will pretest the stimuli in a clutter-reel and stimuli-only situation. The final disposition of the stimuli will be determined by the results of this pretest.

5. *Existence of an* a priori *analysis plan.*

Several comments asked for more description of the analysis plan. This is presented in Section B1 (Hypotheses).

6. *Pretesting stimuli*

Several comments inquired about pretesting. FDA proposes to conduct multiple rounds of pretesting to assess 1) validity of manipulations in the stimuli, and 2) whether the stimuli should be presented in a clutter reel or not.

7. *Explicit and Implicit attitude*

Several comments mentioned questions about the brand attitude. Basically, these involved the relevance of brand attitude (explicit or implicit) as a construct in this research and the reliability of AMP. The comments suggested that whether someone has a positive or negative view of the drug is not related to the comprehension of risks. Others argued that the method has not been validated in a DTC setting and we should not be using our resources on an untested method.

It is important to clarify that portions of this study involve our understanding of the determinants of attitude *change* -- change is the focus here and not an absolute level of positive or negative attitude (likewise for risk and benefit perceptions).

FDA is not looking at the AMP as a measure of whether participants "liked the ad" or not. The AMP provides a method for specifically investigating whether affect (positive/negative valence) from certain visuals in an ad (those during the audio risk) transfer to feelings about the drug brand. This effect, in turn, bears directly on whether corresponding change is observed in perceptions of product risks (and benefits). This issue is at the heart of the question of tonal distraction and has not been studied in a DTC setting the past. If scenes of joy and positive activity during the presentation of the audio risk information interfere with the processing of the audio risk information (as evidenced by decreased risk comprehension scores), then, in essence, this risk information has not been fully conveyed. FDA may find that this affect transfer does not occur—that positive images during risk information have no influence on comprehension of risk information.

What represents a reasonable "baseline" comparison or "control" for the visual conditions? One suggestion was a "radio" spot. For the purposes of this study, images of the brand name and logo will be used in order to maintain the integrity of the broadcast ad and are

considered to be "neutral" in affect and meaning. This baseline provide a reasonable point for assessing causes by other visual images on viewer processing of the audio (risk) information, integration of that information and the formation of brand perceptions.

Because this is an open question and has relevance for revisiting broadcast ads and also to be responsive to critics' concerns, FDA must conduct empirical research to investigate this domain. In summary, this research is not looking at whether people have a certain positive (or negative) view of the brand as a dependent variable in itself. Rather, differences in affect toward the brand across conditions provide a way to further our understanding of the potential influence of positive visuals during risk information.

The second argument, that the AMP has not been validated in this sort of research, is more germane. Indeed, FDA is extending the use of the AMP by including an additional step; participants will watch a mock ad before seeing the images and symbols they will judge. FDA has spoken with the creator of the AMP (Keith Payne, Ph.D., University of North Carolina) on several occasions and received assurance that this seems like a reasonable extrapolation of the method. Again, this is an empirical question. Nonetheless, it is important that research funded and produced by the government rely on the most cutting-edge science rather than using old and outdated methods.

FDA agrees that it was perhaps ambitious to include the AMP in all cells of the design given the novel application of the method, but continues to feel the contribution of the procedure is worthwhile. Thus, FDA has revised the design of the project such that the main part of the study will not include the AMP. An additional five cells, with 50 participants each, will repeat some of the crucial cells in the design using the AMP. This strategy will enable FDA to validate the AMP against more traditional explicit measures. The AMP is not identical to these

measures, so we do not expect findings to replicate each other exclusively, thus obviating the need for additional methods, but we will have data to suggest whether this is a viable method for investigating such designs. If it indeed translates well to this situation, this study will then open up a large area of study on which other researchers can capitalize. The social psychology field and, particularly, the study of DTC and broadcast DTC, would be much strengthened by this contribution.

Given these reasons, FDA has modified the design to include the AMP in some of the cells of the design, but maintains that its placement in the design is critical and useful.

8. *Use of Chinese characters in Attitude Misattribution Procedure* **(***AMP)*

Several commenters expressed concern that using Chinese characters as pictographs during the AMP may no longer be wise given the recent recalls of food and toys from China. Although this is a logical concern, there are several reasons why we will maintain the Chinese characters as pictographs. Primarily, we want to maintain the integrity of the testing stimuli as we apply the AMP to our novel project. The pictographs used in previous research have been validated successfully multiple times. Developing new stimuli to match the properties of the existing pictographs would require extensive time and pretesting.

There are two reasons why the validation of the pictographs outweighs the concerns of the reviewers. First, the research we propose is experimental, and all individuals in all conditions will be exposed to the same pictographs. Thus, any bias that might occur from current news reports would be spread evenly across conditions. There is no reason to suspect that the bias would differ in direction in different conditions. Second, the instructions for the AMP have been refined in prior research to reflect comparative responses. In other words, participants will be asked to rate how positive or negative each character is *in comparison to*

other Chinese characters. Thus, any negativity should be eliminated because this becomes a task between Chinese characters in general, and not a question of the positivity of each character in an absolute sense. For the complete revised instructions, please view the questionnaire.

9. *The role of FDAAA*

More than one commenter mentioned the passing of the Food and Drug Administration Amendments Act (FDAAA). They suggested that based on the provisions in the act, the need for the current research had changed and/or that the current research should be molded to address the concerns in the bill. First, FDA does not believe that FDAAA alters the need for the current proposed research, particularly as modified in this document. DTC continues to exist on television, and as such, the current issues of informational and tonal distraction remain.

The current study, as modified, will, however, provide some preliminary information to FDA on how it should interpret the "clear, conspicuous, and neutral" requirement for risk disclosure in DTC broadcast ads.

Responses to Individual Comments

From Academic Sources

1. *FDA should abandon the idea of a mall-intercept protocol in favor of a projectable Internet survey.*

Ideally, we would adopt this suggestion entirely and use one of the two truly projectable survey vendors available. Nevertheless, we do not have the funds required to secure a contract with one of those entities and we are currently limited to existing contractors. FDA has, however, decided to alter the administration of the survey to an Internet format. Although the panel we will use is not projectable as are the suggested vendors' panels, the experimental nature of the design makes Internet administration at least as representative as a mall-intercept (with

different limitations). Moreover, given cost considerations, the new administration allows us to double our sample size and test more conditions, thus arriving at a more sophisticated design with which to test our theories. FDA could not have improved the design as it has without these further participants, due to statistical power concerns.

2. *Behavioral intention measures are not necessary for our study.*

This comment is in direct contrast to several industry comments requesting that we *increase* the number of behavioral intention questions in our study. We believe that behavioral intention questions do represent another way to approach the issue of what consumers take away from DTC ads and intend to maintain the four questions we have included. On the other hand, we do not feel that we should increase the number of behavioral intention questions, given constraints and priorities.

3. Specific comments about questionnaire wording

Please see wording changes in the revised questionnaire.

<u>From Industry Sources</u>

1. *How will FDA control for differences in respondents between conditions?*

The proposed design is experimental in nature. One of the cornerstones of experimental research is random assignment. That is, each respondent has an equal chance of being assigned to a given condition. With this random assignment, particular individual differences should cancel out across conditions.

2. *FDA should provide more detail before proceeding.*

The current notice provides extensive detail about the revised experimental design. In addition, we have included the revised questionnaire and our analysis plan.

3. *Our company now integrates risk information into the characters in our ads, so the need for studying visual distraction as proposed has passed.*

We applaud this company for attempting to improve the communication of risk information in their ads, however, this is by no means a universal approach. Many ads still exist that make use of visuals and storylines that have the potential for distraction during the risk information. Bob Ehrlich of DTC Perspectives recently predicted that given the quieting of recent Congressional activity, companies will again move away from doctor portrayals or other integrated approaches.[8]

4. *Having positive scenes during risk information will not lead to positive product beliefs.*

First, this is an empirical question that deserves study. Second, we are not directly interested in the outcome of positive product beliefs, but in fact whether these beliefs lead to an alteration of the perceived risk benefit tradeoff.

5. *Should control for baseline attitudes.*

FDA respects this suggestion, but has utilized a fictitious drug to control for this issue. Moreover, we have selected a medical condition (high blood pressure) for which there is little DTC advertising, particularly on television, thus reducing the chance of spillover influence from existing advertising in this class.

6. *FDA should consult the Risk Communication Advisory Committee before proceeding.*

It is not clear that this committee is the appropriate place to receive feedback about this study. FDA has consulted an internal group of social scientists and also solicited peer review from a number of outside experts in the fields of psychology, advertising, and communications.

[8] DTC Perspectives blog, January 4, 2008. Last accessed at http://dtcperspectives.com/blog/?p=54 on April 8, 2008.

Moreover, FDA has seriously considered the public comments received to date and has incorporated many of the suggestions included. In the interest of expediting the process of the research, we do not feel that the committee is the best venue for feedback in this case.

7. *Only looking at creative elements rather than communication principles.*

This comment is a bit abstract and difficult to decipher. It is true that FDA is operationalizing informational and tonal visual distractions in terms of creative elements. Moreover FDA has not designed a study to investigate message communication (as has been done extensively in the social psychology literature[9]). FDA is applying existing theories of communication to the specific arena of DTC television advertising.

8. *Proposed alternative to create protocol for evaluating DTC ads.*

While FDA agrees that it could be useful to have a validated protocol for investigating DTC television ads, that fact does not alleviate the need for pioneering research to investigate the factors at play in the proposed study. The current study may inform the development of such a protocol.

9. *Regarding AMP, respondents not likely to be motivated to correct for biased attitudes.*

FDA agrees that prescription drug ads do not raise the same social desirability issues as race or gender, previously investigated by the AMP. Nevertheless, we do not feel that this difference diminishes the usefulness of the AMP. In previous research, the AMP has been found to show valid results using images such as coffee or alcohol brands, also areas that are not considered especially fraught with social or political meaning. FDA's modified design may

[9] See, e.g., Petty, R.E., & Cacioppo, J.T. (1986). The Elaboration Likelihood Model of persuasion. In L. Berkowitz (Ed.), *Advances in experimental social psychology* (Vol. 19, pp. 123-205). New York: Academic Press;.Petty, R.E., & Cacioppo, J.T. (1986). *Communication and persuasion: Central and peripheral routes to attitude change.* New York: Springer/Verlag.

alleviate the concerns of this commenter somewhat, as we have reduced the role of the AMP in the study, as discussed above.

Research involving implicit attitude measures is not limited to topics concerned with just "social desirability" effects (c.f., brand preference (Maison, Greenwald and Bruin 2004; Friese and Wanke, 2005); genetically modified foods (Spence and Townsend (2006)).[10] The modified design does reduce the role of the AMP in the study, as discussed above.

10. *Study does not address the issue of the risk of non-treatment.*

FDA acknowledges that this study does not address this risk. Nevertheless, this is outside the scope of the current investigation.

11. *Should focus more on action.*

The act of visiting the doctor to ask about a prescription drug or filling a prescription is obviously an important consideration for members of industry who fund DTC ads. This commenter presents four components of action: awareness, comprehension, conviction, and action. FDA is interested in these components to a certain extent, also, as reflected in the four behavioral intention questions that we have included in the design. Ultimately, a consumer's understanding of the benefit-risk profile of a drug will influence the actions that a consumer does or does not take. FDA's main focus, in this study is comprehension and understanding of the risks and benefits of the drug. We are interested in whether a patient can make an informed decision about whether or not talking with a doctor would be the right approach. It may be that

[10] Friese, M. & Wanke, M. (2005) Implicit consumer preferences attitudes and their influence on product choice (manuscript cited in Bluemke, M. and Friese, M. (2006) "Do features of stimuli influence IAT effects?" *Journal of Experimental Social Psychology, 42,* (2006) 163-176); Maison, D., Greenwald, A.G., and Bruin, R.H. (2004). "Predictive validity of the Implicit Association Test in studies of brands, consumer attitudes, and behavior. *Journal of Consumer Psychology, 14(4),* 405-415; Spence, A. and Townsend, E. (2006). "Implicit attitudes towards genetically modified (GM) foods: A comparison of context-free and context –dependent evaluations." *Appetite, 46,* 67-74.

the appropriate decision in one case is no action because for some reason the drug does not apply to a certain individual. We welcome further studies by other organizations that may build on what we find in the current proposed study.

12. *Need definition of fair balance and when and when it is not achieved.*

FDA agrees that it would be extremely useful and ideal to have a concrete definition of fair balance. In many ways, the currently proposed research is designed to inform this question. As a science-based agency, FDA relies on its research to make policy decisions and definitions that are then used by the Agency.

13. *FDA is overlooking existing copy testing procedure.*

For this study, it is true that FDA is not interested in standard industry questions that drive marketing decisions. FDA instead is interested in uncovering a deeper understanding of the factors and motivations behind the communication of risk information in television advertising. One of the strengths of the current design is that there are no studies, to our knowledge, that approach the issues we will investigate in a DTC arena.

14. *FDA should vet the mock ads with industry and allow public comment on them.*

Logistically, FDA does not have the resources to create professional ads and submit them for public comment, which could lead to major changes requiring additional resources. FDA is also unable to accept donations of work from outside agencies, even advertising agencies, to create these ads. FDA has contracted with a professional multimedia company to create ad stimuli. In addition, FDA has instituted a procedure of extensive pretesting of the ad stimuli to be used (see above). Our extensive pretesting and collaboration with the contractor should ensure reasonable ads that will enable us to successfully investigate our experimental variables.

15. *Response rates are likely to be lower than 50%.*

FDA acknowledges the reality that despite its best efforts, response rates may be lower than 50%. There are procedures in place to maximize the response rate. This experimental study will use an existing Internet panel from which we will draw a sample. The panel includes people who have expressed interest in sharing their opinions via the Internet and do so regularly. The expected participation rate for the Internet panel is 55 percent when responding to a specific study. To help ensure that the participation rate is as high as possible, the Agency will:

- Design an experimental protocol that minimizes burden (short in length, clearly written, and with appealing graphics);
- Administer the experiment over the Internet, allowing respondents to answer questions at a time and location of their choosing;
- Administer the experiment to individuals who have expressed interest in participating in Internet studies;
- Email a reminder to the respondents who do not complete the protocol four days after the original invitation to participate is sent;
- Provide contact information on where to get help for respondents who may have questions as they complete the experiment.

Additionally, FDA notes that this study is experimental in nature, which alleviates this problem in two ways. First, FDA is primarily interested in differences between experimental conditions. We are not interested in overall values or absolute values of factors but in how these factors differ between cells. Second, because we are interested in the experimental manipulations, we are not attempting to create a representative, projectable sample to apply to the entire nation. The focus of this study is in its experimental control, allowing us to determine what factors have a causal role in the comprehension of risk information.

16. *One ad is unprojectable to all ads.*

FDA agrees that one ad cannot be projected to all ads and is not attempting to suggest it would be. FDA is merely operationalizing some experimental variables of interest in a particular ad execution and many variations. The current study is not designed to be a survey of what people think about ads in general, or what kind of information they think they obtain or retain from DTC ads. There is a place for that research, but not in the current project. FDA's interest in this study is to look at what consumers actually understand from a DTC ad given a number of manipulations of informational and tonal visual information and the presence or absence of superimposed text.

17. *A different study with different objectives is necessary.*

FDA notes that many different studies can be conducted on endless variations of the communication of risk information in DTC ads. We invite others to join in the scientific endeavor to determine the parameters of this communication. As such, however, this comment is unhelpful without more specific recommendations.

External Reviewers

The Agency requested that several outside experts review the revised study design and methodology. The comments of these reviewers were also considered in modifying the study design and methodology, and especially in increasing the extent of the pretesting of the stimulus materials and whether they should be included in a clutter reel. The following individuals reviewed the study design, methodology, and questionnaire.

- Jon Krosnick Professor in Humanities and Social Sciences, Stanford University.
- Paula Bone, Professor of Marketing, College of Business and Economics, West Virginia University.

- B. Keith Payne, Assistant Professor, Department of Psychology, University of North Carolina.
- Dena Cox, Professor of Marketing, Kelley School of Business, Indiana University.
- Anthony Cox, Professor of Marketing, Kelley School of Business, Indiana University.

9. Explanation of Any Payment or Gift to Respondents

Members of the Internet panel who agree to participate in this study will not be paid specifically for their participation. However, as part of the firm's incentive to recruit and maintain membership, panelists are offered rewards by the firm for their general participation in surveys sent out by the panel. The reward takes the form of entries into the panel's monthly sweepstakes. Each time a member completes a study, the individual is automatically entered into the current month's drawing to win one of the following cash prizes: one cash prize of $1000, 10 prizes of $100, 15 prizes of $50, 30 prizes of $25, and 150 prizes of $10. FDA will not contribute to this lottery.

10. Assurance of Confidentiality Provided to Respondents

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

No personally identifiable information will be sent to FDA. All information that can identify individual respondents will be kept by the independent contractor (Synovate, Inc.) in a form that is separate from the data provided to FDA. The information will be kept in a secured fashion that will not permit unauthorized access. These methods will all be approved by FDA's Institutional Review Board (Research Involving Human Subjects Committee, RIHSC) prior to collecting any information.

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' ADP Systems Security Policy as described in the DHHS ADP Systems Manual, Part 6, chapters 6-30 and 6-35. All data will also be maintained in consistency with the FDA Privacy Act System of Records #09-10-0009 (Special Studies and Surveys on FDA Regulated Products).

11. Justification for Sensitive Questions

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

12. Estimates of Annualized Burden Hours and Costs

The total annual estimated burden imposed by this collection of information is 920 hours for this one-time collection (Table 1).

Table 1. Estimated Annual Reporting Burden [a]

Activity	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Screener, pretesting	1,600	1	1,600	.03	48
Questionnaire, pretesting	800	1	800	.16	128
Screener, study	4,800	1	4,800	.03	144
Questionnaire, study	2,400	1	2,400	.25	600
Total					920

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

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

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 estimated cost to the Federal Government for the pretesting is $22,000 and the estimated cost to the Federal Government for the main study is $145,000, for a total of $167,000. This includes the costs paid to the contractors to create stimuli, to program the study, draw the sample, collect the data, and create a database of the results. The cost also includes FDA and DHHS staff time to design and manage the study, to analyze the resultant data, and to draft a report.

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. 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 and articles at trade and academic conferences, publications, and Internet posting.

Project Timetable

Task	Estimated Completion Date
External Peer Review	June, 2008
RIHSC Review	July, 2008
30-day FR notice publication	August, 2008
OMB Review of PRA package	October/November, 2008

Pretesting	December, 2008
Data Collection	December, 2008
Receipt of Data and Methods Report from Contractor	February, 2009
Data Analysis	May, 2009
Draft Report	September, 2009
Internal Review of Draft Report	October, 2009
Revisions	November, 2009
Final Report	December, 2009

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

No exemption is requested.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions are requested.

B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

1. Respondent Universe and Sampling Methods

The universe for this experimental study is members of the Synovate Internet panel. Synovate's Internet panel consists of 600,000 households that are recruited by a variety of means to reflect all segments of the U.S. population and have agreed to participate in Internet research studies. Typical panel members receive three or four invitations per month to participate in research projects.

The 2,400 participants for this study would be drawn from the pool of over 6,000 panel members. Quotas will be used so that the overall sample is in proportion to the U.S. adult population on gender and race/ethnicity. A range of participants over the age of 40 will be selected to approximate a reasonable sample of individuals for whom high blood pressure may be a concern. At least 30% of the sample will have achieved a high school education or less.

FDA does not intend to generate nationally or locally representative results or precise estimates of population parameters from this study. The sample used is a convenience sample, rather than a probability sample. Despite the attempt to match between the study's sample and known population characteristics, matching is used solely to produce samples with a reasonable degree of diversity in key demographic characteristics. Furthermore, no legitimate weights can be constructed from non-probability samples such as the one used here. Hence, the Agency does not construe this sample or the results generated from this sample as nationally or locally representative. Rather, the strength of the experimental study lies in its internal validity, on which meaningful estimates of differences across conditions can be produced and generalized.

Overview

Our goal is to investigate the overall and interactive role of visual images and text presentations during the audio presentation of risk information in television DTC ads. We will create a variety of ads for a new (fictitious) brand of high blood pressure medication. The ads will vary only in the type of information shown on screen during the presentation of required risk information (the "major statement"). Participants will view one version of the ad two times. They will then answer questions about the ad, including information about product risks and benefits, whether they intend to ask the doctor about the product, basic comprehension of the risk and benefit information, and their general attitudes toward the product. This experimental design will allow for comparisons between conditions in a controlled presentation where only the visual information varies.

Design

• Independent Variables

To operationalize our investigation of distraction in television ads, two proposed designs incorporate three independent variables. The first variable is the *visual consistency with audio risks* (VCAR). The description of product risks in the ad's audio (required by law and regulation), is the section of the ad that details the most serious and/or frequent side effects (see 21 C.F.R. 202.1(e)(1)). We define VCAR as visual information that either reinforces the product's risks (*consistent* conditions) or reinforces the product's benefits (*inconsistent* conditions). In two "*consistent*" ("very" and "somewhat") VCAR conditions, participants will see the words of the risks on the screen as they are being spoken. In "*inconsistent*" conditions, participants will see blood pressure numbers decreasing from a high, dangerous number (e.g., 200/112), to an ideal number within a normal range (e.g., 120/80). The degree or magnitude of consistency or inconsistency will be manipulated by including fewer pieces of any information,

interspersed with images of the fictitious drug logo. A comparison or "*neutral*" condition will be created in which the brand logo is the only thing displayed during the entire risk presentation.

The second independent variable we will investigate is *tonal consistency with audio risks* (TCAR). In many DTC ads, scenes of patients "living their lives," including socializing with family and friends and enjoying recreational activities are shown during the audio presentation of risk information. Critics of DTC complain that these scenes are inappropriate. However, FDA is not aware of empirical data demonstrating that these images distract viewers from processing the risk information. This independent variable is designed to examine this question. It is unrealistic to show visual images of patients experiencing side effects. Instead, we propose to compare visuals that evoke a mildly positive tone to visuals that evoke a strongly positive tone. These conditions will be contrasted with the neutral ad showing simply the logo of the drug (identical to the neutral VCAR manipulation).

The third independent variable is the presence of superimposed text (SUPERs) during the risk presentation. Specifically, we are interested in whether the presence of a super that reinforces the audio risk information will alleviate any potential distraction from tonally inconsistent visual images. We will compare a less prominent SUPER condition with more prominent and control (no SUPER) conditions.

Because of resource constraints, potential confounds, and differential interest in the importance of certain interactions of these variables, we have designed the study to look at the independent variables in the following manner:

VCAR 5 cells

Very Consistent
Somewhat Consistent
Neutral (Control)
Somewhat Inconsistent
Very Inconsistent

3 x 3 (TCAR x SUPER)

……..**SUPER**…….				
		None	Level 1	Level 2
TCAR	Neutral (Control)			
	Mildly Positive			
	Strongly Positive			

• Dependent Variables

The primary dependent variables are recall and comprehension of risk and benefit information. We will also investigate behavioral intention and attitudes toward the fictitious brand. These variables can be seen in the proposed questionnaire, Attachment 2.

Comprehension of risk information in comparison to the comprehension of benefit information is the key to understanding whether an ad meets the requirement that it presents a "fair balance" of information about risks and information about benefits. Therefore, we will include questions about both risks and benefits.

Behavioral intention is not our primary measure but can help inform us of the nature of the decision process that viewers undergo when watching this television ad. If the comprehension measures do not display variability but the behavioral intention measures do, either our comprehension questions are not sufficiently sensitive, or there is some other factor

influencing intent to act. As this is initial research, we will not be able to parse these explanations, but we hope to glean additional information from these variables.

Attitudes toward the brand are investigated here to determine their relationship to comprehension variables. Although brand attitude is not our primary dependent variable, we discuss attitudes here because this measure prompted the most comment during the first public comment period. Critics of DTC charge that positive scenes during the risk information may detract from the serious risk-benefit analysis required for a patient to consider whether it is appropriate to have a conversation with the doctor about a given medication. If we find that some experimental conditions reduce comprehension, we can compare this finding to participants' attitudes about the brand in each condition. If very positive attitudes correlate strongly with poor comprehension of risks, then there is reason to suspect that positive images may have a negative impact. The FDA Amendments Act of 2007 (FDAAA) directs FDA to ensure that the major statement is conveyed in a clear, conspicuous and neutral manner. A better understanding of how attitude may transfer from the images in the ad to the brand itself will inform us about the relationship of visuals' presentation to the messages about the product's risks and benefits.

Our primary method of investigating this variable will utilize traditional explicit attitude measures (see Attachment 2). In an effort to make use of cutting-edge cognitive research, however, we will conduct a sub-experiment with additional participants, using an implicit measure called the Attitude Misattribution Procedure (AMP, Payne, et al., 2005). Explicit measures involve asking questions directly, which might be subject to social desirability biases. In contrast, implicit attitude measures infer attitudes through measurement of behavior toward the attitude exemplars. In this case, the AMP will measure affective reactions to images of the

fictitious brand, which will then allow us to infer a respondent's attitude, rather than asking directly about the attitude, which leaves open the possibility of social desirability biases related to willingness to admit to drug brand attitudes. These brand images will be paired with abstract symbols during the measurement procedure. Participants will be told that the images are simply warning signals for the symbols, and that their task is to rate how positive or negative the symbols are (see Attachment 3 for exact wording of instructions to participants). Previous research has shown that participants are influenced by the images even when warned specifically not to pay attention to them. Because we are extending the use of the AMP to a novel application (i.e., the viewing of an ad that includes the brand images paired with the abstract symbols), we have responded to the concerns in the public comments by making this exploration supplemental rather than the cornerstone of the study.[11] Our intent is to see whether the AMP is validated in this context for use in future studies.

Hypotheses

Visual Consistency with Audio Risks (VCAR)

- Participants in visually consistent conditions will score higher on recall of product information than participants in visually inconsistent conditions;
- Participants in visually consistent conditions will score higher on comprehension of product information than participants in visually inconsistent conditions;
- Participants in visually consistent conditions will report more negative attitudes toward the brand than participants in visually inconsistent conditions;

[11] We will use the AMP in the following five conditions (see page 30): In the VCAR design, in the Very Consistent and Very Inconsistent conditions; in the TCAR x SUPER design, in the Neutral, Mildly positive, and Strongly positive conditions with no SUPER.

• Direction of influence of visual consistency on behavioral intention is exploratory. We have no specific hypotheses.

Tonal Consistency with Audio Risks (TCAR)

• Participants in tonally positive conditions will score lower on recall of product information than participants in the tonally neutral condition. Participants in the strongly positive condition will score lower on recall of product information than participants in the mildly positive tonal condition;

• Participants in tonally positive conditions will score lower on comprehension of product information than participants in the neutral condition;

• Participants in the strongly positive condition will show a more positive attitude toward the brand than participants in the neutral and mildly positive conditions;

• Participants in tonally positive conditions will report higher intention to act on the ad than participants in neutral condition. Participants in the strongly positive condition will report higher intention to act on the ad than participants in the mildly positive tonal condition.

Superimposed Text (SUPER)

• Participants in the prominent SUPER condition will score higher on recall of product risks than participants in the less prominent SUPER condition, who in turn will score higher on recall of product information than participants in the control SUPER condition;

• Participants in the prominent SUPER condition will score higher on comprehension of product information than participants in the less prominent SUPER condition, who will score higher on recall than participants in the control SUPER condition;

• Participants in prominent SUPER condition will report more negative attitudes toward brand than participants in the less prominent SUPER condition, who will report more negative attitudes toward the brand than participants in the control SUPER condition;

• Direction of influence of SUPER on behavioral intention is exploratory. We have no specific hypotheses.

Tonal Consistency with Audio Risks (TCAR) x Superimposed Text (SUPER)

• Participants in the neutral (control) condition with a prominent SUPER will score highest on recall of product information. Participants in the strongly positive tonal condition with no SUPER will score lowest on recall of product information;

• Participants in the neutral (control) condition with a prominent SUPER will score highest on comprehension of product information. Participants in the strongly positive tonal condition with no SUPER will score lowest on comprehension of product information;

• Participants in the strongly positive tonal condition with no SUPER will report the most positive attitudes toward the brand. Participants in the neutral (control) tonal condition with a prominent SUPER will report the least positive attitudes about the brand.

Power

This section illustrates the power levels provided by equal cell sizes of 150.

For the main effects, some planned comparisons involve two proportions (2 cells). For a test of two proportions (p1, p2) such that is greater than p1 with $\alpha = .05$ and equal sample sizes n; 150 per cell), the power to detect various effect sizes (differences in proportions) follows:

p1	p2	Power
.55	.60	.21
.50	.60	.43

.45	.60	.83
.40	.60	.97

Again for the main effects, some planned comparisons involve two proportions where one proportion is based on two cells (e.g., neutral tone (no SUPER) vs both tone (TCAR) conditions (no SUPER)).

For a test of two proportions such that p2 is greater than p1 with α = .05 and unequal sample sizes n; 150 for p1 and 300 for p2), the power for these proportions is as follows:

p1	p2	Power
.55	.60	.26
.50	.60	.64
.45	.60	.91
.40	.60	.99

We will look at interaction effects for a 3x3 fixed-effects factorial with cell sizes of 150 (N=1350; interaction df = 4).

For the interaction term, the "adjusted" sample size (n) for the interaction (given two main effects in the model) for table entries in a primary power handbook (n', Cohen, 1988, pg. 365) [12] is 269 ([1350-9]/[4+1] + 1). Rounding to 270 with *df* = 4, the power of the F test at α(alpha) = .05, for various "small" effects is estimated to be:

	f		
	.05	.10	.15
Power	.27	.85	.99

…where effect size is given by f, standard deviation of standardized means, or

[12] Cohen, Jacob (1988). *Statistical Power Analysis for the Behavioral Sciences, Second Edition*. Hillsdale, NJ: Lawrence Erlbaum Associates.

. $f^2 = [\Sigma(\alpha\beta_{ij})^2] / [(a)(b)] / [\sigma^2_{S/AB}]$

Given cell sizes of 150, these reveal very high power for smallish effects in ANOVAs and reasonable power levels for medium effects in tests of proportion.

Pretesting of Stimuli

Key to our study is the reasonableness and appropriateness of the stimuli we use to approximate television DTC prescription drug ads. Because the particular images are subjective, we will conduct extensive pretesting with consumers similar to our main target audience. This pretesting will involve 800 individuals in four waves. The purpose of the pretesting is to ensure that the images evoke the meaning that the research team has assigned to them. For example, we want to make sure that consumers report more positive emotions after viewing our strongly positive tonal condition compared to our mildly positive condition. During the pretesting stage, the primary dependent variable will be the success of the particular manipulation. The pretesting will allow us to make changes in the ad stimuli before the actual study commences, thus making participants' time more valuable.

Pretesting of Methodology

We received comments from both the public and peer reviewers that our stimuli should be shown in a clutter-reel, rather than as a stand-alone piece. We believe there are good reasons to present the stimuli as a stand-alone piece, just as there are good reasons for presenting the stimuli as part of a clutter-reel. To empirically address this issue, we propose to test the stimuli in both a clutter-reel and stand-alone environment. This will serve as a test of the methodology. We anticipate this pretesting will involve up to 800 consumers in four waves.

2. <u>Procedures for the Collection of Information</u>

Respondents will participate in the study via the Internet (see sampling criteria above). They will initially watch one version of the advertisement two times. In the main study (without the AMP), participants will then answer questions, as shown in Attachment 2. In the supplemental study (with the AMP), participants will respond to an abbreviated set of questions, shown in Attachment 3. The whole procedure, regardless of AMP administration, will take no more than 15 minutes.

3. Methods to Maximize Response Rates and to Deal with Issues of Non-Response

This experimental study will use an existing Internet panel to draw a sample. The panel includes people who have expressed interest in sharing their opinions via the Internet and do so regularly. The expected participation rate for the Internet panel is 55 percent when responding to a specific study. To help ensure that the participation rate is as high as possible, FDA will:

- Design an experimental protocol that minimizes burden (short in length, clearly written, and with appealing graphics);
- Administer the experiment over the Internet, allowing respondents to answer questions at a time and location of their choosing;
- Administer the experiment to individuals who have expressed interest in participating in Internet studies;
- Email a reminder to the respondents who do not complete the protocol four days after the original invitation to participate is sent;
- Provide contact information on where to get help for respondents who may have questions as they complete the experiment.

4. Test Procedures

The contractor will run nine participants through the procedure to assess questionnaire wording, basic glitches in the programming and execution of the study. This pretest is designed to ensure that questionnaire wording is clear and that procedures for viewing stimuli and proceeding through the experiment are as planned. The stimuli will be tested in waves of 300 participants to ensure that the images evoke the meaning that the research team has assigned to them.

5. Individuals Involved in Statistical Consultation and Information Collection

The contractor, Synovate, will collect the information on behalf of FDA as a task order under the Quick-Turn-Around Research Services contract. Leigh Seaver, Ph.D., is the Senior Study Director for Synovate, telephone (703) 663-7240. Data analysis will be conducted primarily by the Research Team, Division of Drug Marketing, Advertising, and Communications (DDMAC), Office of Medical Policy, CDER, FDA, and coordinated by Nancy Ostrove, Ph.D., of the Office of the Commissioner, 301-827-9279, and Kathryn J. Aikin, Ph.D., 301-796-0569 and Amie C. O'Donoghue, Ph.D., 301-796-0574, of DDMAC.

Attachment 1

Screener and questionnaire, main study

Questionnaire, Distraction Study (Main Study)

Interview Protocol.

{Programming notes}
Questionnaire will be administered by computer.

Section I. Instructions

Thank you for agreeing to participate in this study today.

This study is about advertising for a new product. You will see an ad for a new product and answer some questions about it. Your answers are anonymous, which means that no one will ever connect your name with your answers. So please answer as openly and honestly as you can.

Now you will see an ad for a new product. You will see the ad twice and then move on to the next part of the study.

[PROGRAMMER: Show ad twice]

Now please answer the following questions.

Q1. Based on this ad, what are your initial feelings about Zintria?

[PROGRAMMER: *randomize order of a,b,c*]

a. Do you feel…
    1. very good … about Zintria,
    2. somewhat good,
    3. neither good nor bad,
    4. somewhat bad, or
    5. very bad …about Zintria?
    6. DK/RF

b. Do you feel…
    1. very negative … about Zintria,
    2. somewhat negative,
    3. neither negative nor positive,
    4. somewhat positive, or
    5. very positive …about Zintria?
    6. DK/RF

c. Do you feel…
    1. very unpleasant … about Zintria,
    2. somewhat unpleasant,
    3. neither unpleasant nor pleasant,

4. somewhat pleasant, or
5. very pleasant…about Zintria?
6. DK/RF

Q2. (Behavioral Intention) How likely or not likely you are to do each of the following behaviors?

	Not at all likely	Somewhat likely	Very likely	Extremely likely
a. Look for more information about Zintria				
b. Talk to your doctor about Zintria				
c. Ask your doctor about getting a sample of Zintria				
d. Ask your doctor to prescribe Zintria				

[PROGRAMMER: COUNTERBALANCE Q3a and Q3b]

Q3a. (Comprehension of risks)
Select the best answer.

[PROGRAMMER: *randomize*]

i. Why should you *NOT* stop taking Zintria suddenly?

a. This can lead to unusual changes in behavior
b. Your eyes will have trouble adjusting to the immediate change in pressure
c. You may have a temporary loss of coordination
d. You may experience chest pain

ii. When you first take Zintria, why should you avoid activities that require you to be alert?

a. You may have a temporary loss of coordination
b. A common side effect of Zintria is dizziness
c. A common side effect of Zintria is nervousness
d. You may have a temporary loss of consciousness

iii. Why might you have blurry vision when taking Zintria?

a. Zintria lowers the pressure in the eye
b. Zintria increases the likelihood of chronic dry eye
c. Zintria lowers the concentration of red blood cells in the eye
d. Zintria increases sensitivity to light

Q3b. (Comprehension of benefits)
Select the best answer.

[PROGRAMMER: *randomize*]

i. What advantage does Zintria have over other treatments for this condition?

a. Zintria helps lower blood pressure
b. Zintria is approved to treat more types of high blood pressure
c. Zintria helps lower cholesterol
d. Zintria helps prevent heart attacks

ii. Why is high blood pressure bad?

a. High blood pressure increases the risk of liver damage
b. High blood pressure increases the likelihood of anxiety
c. High blood pressure increases the risk of strokes
d. High blood pressure increases the likelihood of joint pain

iii. Why might your doctor prescribe Zintria over other treatments for this condition?

a. Zintria lowers blood pressure faster
b. Zintria is approved for all age groups
c. Zintria is safer acting
d. Zintria helps prevent strokes

[PROGRAMMER: COUNTERBALANCE Q4a and Q4b]

Q4a. Answer the following questions as best you can.
(Take-away risk beliefs)

[PROGRAMMER: *randomize*]

	Yes	No	Not Sure
a. Taking some kinds of over-the-counter cough medicines at the same time as taking Zintria increases your risk of having a heart attack.			
b. Zintria may cause excitability.			

c. If you have a very slow heart rate, you should not take Zintria.			
d. Zintria may cause you to have blurry vision.			
e. Patients with a history of liver disease can take Zintria if they are monitored by a doctor.			
f. Antibiotics may not work as well if you use Zintria at the same time.			
g. You should have regular eye exams when you take Zintria.			
h. Zintria is approved to treat children.			

Q4b. Answer the following questions as best you can.
(Take-away benefit beliefs)
[PROGRAMMER: *randomize*]

	Yes	No	Not Sure
a. Your high blood pressure can increase your risk of having a stroke.			
b. High blood pressure can damage the lining of the liver.			
c. Zintria is given by IV injection.			
d. Zintria is proven to help prevent strokes.			
e. Zintria is a fast-acting treatment.			
f. Zintria is proven to help prevent heart attacks.			
g. Zintria is approved to treat all age groups			

Q5. (Risk/benefit tradeoff) Please indicate your level of agreement or disagreement with the following statements.

	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
a. The side effects of Zintria are worse					

than having high blood pressure.					
b. If I lowered my blood pressure *a lot* with Zintria, I would be willing to deal with the side effects of the drug.					
c. If I lowered my blood pressure *a little* with Zintria, I would be willing to deal with the side effects of the drug.					

Q6. (Manipulation checks) Answer each question as best you can based on the information in the ad.

[PROGRAMMER: *randomize*]

	Excellent	Good	Fair	Poor
a. How well do the words on the screen match up with the risks that are spoken out loud?				
b. How well do the images shown match up with the words on the screen during the risk information?				
c. How well do the images shown match up with the risks that are spoken out loud?				

Q7. (Manipulation checks)

a. Overall, how would you rate the images in the ad?

Very Happy	Somewhat Happy	Neither Happy nor Sad	Somewhat Sad	Very Sad
1	2	3	4	5

b. This ad had many happy scenes.

Strongly Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Strongly Agree
1	2	3	4	5

Q8. Are you currently taking a prescription medicine for high blood pressure?

A) Yes
B) No (*do not ask Q9*)
C) Don't know or uncertain

Q9. Before you started treatment, how severe was your high blood pressure? Would you describe it as:

A) Very mild
B) Mild
C) Moderate
D) Serious
E) Very serious

Q10. How severe is your high blood pressure now? Would you describe it as:

A) Very mild
B) Mild
C) Moderate
D) Serious
E) Very serious

Q11. In general, how much do you feel you know about high blood pressure? Would you say you know:

A) A lot
B) A good bit
C) Some
D) Only a slight amount
E) Nothing at all

Q12. Have you ever seen any advertising for Zintria before today?

A) Yes
B) No
C) Don't Remember

[Q13. Are you:

- Hispanic or Latino
- Not Hispanic or Latino

Q14. Which of these best represents your ethnic group? You may choose one or more. Would you say that you are:

- American Indian or Alaska Native
- Asian

- Black or African-American
- Native Hawaiian or Other Pacific Islander
- White

--In screener]

Q15. Gender

1 Male 2 Female

[End time: _____]

You have been very helpful. Thank you very much for your participation!

ATTACHMENT 3

Questionnaire with AMP instructions

AMP Sub-study

Section I. Instructions

This study is about how people make simple but quick judgments. Your answers are anonymous, which means that no one will ever connect your name with your answers. So please answer as openly and honestly as you can. Any questions?

Now you will see an ad for a new product. You will see the ad twice and then move on to the next part of the study.

[PROGRAMMER: Show double ad series]

TO BE UPDATED: Remember, the study is about how people make simple but quick judgments. You will watch a series of pairs of pictures flashed one after the other. The first one will be a real-life picture and the second will be a Chinese character. The real-life picture is just a warning signal for the Chinese character, so you don't need to do anything with the real-life picture. Your job is to judge the visual pleasantness or unpleasantness of each Chinese character. The pictures will go by very quickly because we only want your first impression—don't put too much thought into it. After each character appears, press the # key if you think it was visually *pleasant* or the # key if you think it was visually *unpleasant*. Then the next symbol will appear, and the next. You will do this 30 times.

[PROGRAMMER: Run AMP program.]

Q1. Based on this ad, what are your initial feelings about Zintria?

[PROGRAMMER: *randomize*]

d. Do you feel…
   1. very good,
   2. somewhat good,
   3. neither good nor bad,
   4. somewhat bad, or
   5. very bad …about Zintria?
   6. DK/RF

e. Do you feel…
   1. very negative,
   2. somewhat negative,
   3. neither negative nor positive,
   4. somewhat positive, or
   5. very positive …about Zintria?
   6. DK/RF

f. Do you feel…

1. very unpleasant,
2. somewhat unpleasant,
3. neither unpleasant nor pleasant,
4. somewhat pleasant, or
5. very pleasant…about Zintria?
6. DK/RF

Q2. (Behavioral Intention) Please rate how likely or not likely you are to do each of the following behaviors based on the scale on this sheet

[PROGRAMMER: *randomize*]

	Not at all likely	Somewhat likely	Very likely	Extremely likely
a. Talk to your doctor about Zintria				
b. Ask your doctor about getting a sample of Zintria				
c. Look for more information about Zintria				
d. Ask your doctor to prescribe Zintria				

Q6. (Manipulation checks) Answer each question as best you can based on the information in the ad.

[PROGRAMMER: *randomize*]

	Excellent	Good	Fair	Poor
a. How well do the words on the screen match up with the risks that are spoken out loud?				
b. How well do the images shown match up with the words on the screen during the risk information?				
c. How well do the images shown match up with the risks that are spoken out loud?				

Q7. (Manipulation checks)

c. Overall, how would you rate the images in the ad?

Very Happy	Somewhat Happy	Neither Happy nor Sad	Somewhat Sad	Very Sad
1	2	3	4	5

d. This ad had many happy scenes.

Strongly Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Strongly Agree
1	2	3	4	5

Q8. Are you currently taking a prescription medicine for high blood pressure?

A) Yes
B) No (*do not ask Q9*)
C) Don't know or uncertain

Q9. Before you started treatment, how severe was your high blood pressure? Would you describe it as:

A) Very mild
B) Mild
C) Moderate
D) Serious
E) Very serious

Q10. How severe is your high blood pressure now? Would you describe it as:

A) Very mild
B) Mild
C) Moderate
D) Serious
E) Very serious

Q11. In general, how much do you feel you know about high blood pressure? Would you say you know:

A) A lot
B) A good bit
C) Some
D) Only a slight amount
E) Nothing at all

Q12. Have you ever seen any advertising for Zintria before today?

A) Yes
B) No
C) Don't Remember

Q13. Are you:

- Hispanic or Latino
- Not Hispanic or Latino

Q14. Which of these best represents your ethnic group? You may choose one or more. Would you say that you are:

- American Indian or Alaska Native
- Asian
- Black or African-American
- Native Hawaiian or Other Pacific Islander
- White

[Q13 and Q14 are also in screener]

Q15. Gender

1 Male 2 Female

[End time: _____]

You have been very helpful. Thank you very much for your participation!