Request for OMB Review

Supporting Statement for

Experimental Evaluation of Variations in Content and Format of the Brief Summary in Direct-to-Consumer (DTC) Print Advertisements for Prescription Drugs

Submitted by
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Department of Health and Human Services

February, 2007

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A. JUSTIFICATION

1. Circumstances Necessitating Information Collection

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes 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. Under the FD&C Act, a drug is misbranded if its labeling or advertising is false or misleading. Generally, the display text of an advertisement should present a fair and balanced disclosure of the product's indication and benefits and the product's side effects and contraindications. In addition, Section 502(n) of the Act specifies that advertisements for prescription drugs and biological products must provide a true statement of information "in brief summary" describing the advertised product's "side effects, contraindications and effectiveness." The prescription drug advertising regulations (21 CFR 202.1(e)(3)(iii)) specify that the information about risks must include *each specific side effect and contraindication* from the advertised drug's approved labeling. The regulation also specifies that the phrase *side effect and contraindication* refers to all of the categories of risk information required in the approved product labeling written for health professionals, including the Warnings, Precautions, and Adverse Reactions sections. Thus, every risk in an advertised drug's approved labeling must be addressed to meet these regulations.

More recent research and feedback suggests that listing all possible risks may not be the best way to communicate information to consumers and has caused FDA to investigate better ways to do so. For example, in January 2006, the Agency revised the regulations governing the content and format of prescribing information for human prescription drug and biological products (21 CFR 201.56 and 201.57). Revisions included creation of a section detailing highlights of the prescribing information (Highlights), a table of contents (Contents), reordering and minor content changes, and minimum graphical requirements.[1] In addition to the formatting changes, one goal of the new labeling rule is to streamline labeling by only including adverse events for which there is likely a causal relationship between the event and the use of the drug.

Just as this new rule incorporates new standards of presenting information, the draft Brief Summary Guidance published in 2004 does the same. The guidance suggests that listing all minor side effects may detract from the understanding of more serious risks. Two alternatives to the traditional risk

1 A summary of the changes mandated by the rule are available at http://www.fda.gov/cder/regulatory/physLabel/summary.htm. Last accessed 11/2/2006.

section of the prescribing information for physicians (PI) are suggested: an approved patient package insert (PPI) which may have a question and answer format, and a highlights format derived from the content and format rule. Because the body of academic literature on consumer processing of the brief summary is limited, this guidance cannot be finalized until further research is conducted to inform our understanding of how best to present medical information to consumers in this arena.

In light of this guidance, FDA has designed three studies to examine how consumers interact with the brief summary. The first study was approved by OMB in April of 2006 (OMB Control number 0910-0591) and involved how people use the current brief summary. The next two studies are the focus of the current OMB proposal. The first study in this proposal involves the content of the brief summary. Although aspects of a drug risk profile may always be included in a brief summary due to sheer importance (e.g., warnings), there may be information about the common side effects that enhance consumer understanding of these common side effects and also possibly enhance processing of other risk information. For example, consider the current practice of simply listing all common side effects. The simple listing alone does not help consumers distinguish relative importance, and may cause consumers to "over weight" these common side effects vis a vis other information contained in the brief summary. The addition of information such as the frequency of minor but common side effects may enable consumers to put these risks into perspective. A reasonable counter hypothesis is that such information may not facilitate risk processing. For example, chance (likelihood) information may create an information overload that causes consumers to scramble concepts relevant to more serious risks.

A second type of information that may facilitate consumer processing of the brief summary by helping consumers to further distinguish the common side effects is their duration. Specifically, some participants will see side effects separated into two lists: one list of side effects that will last only a few days as the body adjusts to the drug, and another list of side effects that will last the duration of treatment. Other participants will not receive this differentiating information. We expect that participants who receive the duration information will be able to put the side effects into perspective, devote more cognitive resources to comprehending more serious risks than those who receive an undistinguished list of minor side effects. Alternately, as with side effect frequency, it is possible that duration information instead detracts from the processing of more serious risk information.

A third type of information that may enhance consumer understanding of the "whole picture" is clinical efficacy. Without this context, consumers may be either less motivated to engage in detailed processing and/or feel they are unable to fully assess the risk profile of the drug. Conversely, consumers may be more motivated to ignore minor but common side effects if clinical efficacy is high but scrutinize product risks more thoroughly in cases where clinical efficacy is low.

In addition to the content of the brief summary, the format of that information can also influence the comprehensibility of the risk information contained within it. In the second study of the current proposal, FDA will look at four different formats of information. Based on the draft guidance, we will examine the current PI risk information format using consumer-friendly language, the approved PPI format in a question and answer layout, and a consumer-friendly highlights format from the new content and format rule. In addition, based on extensive research with the OTC medication label, we will examine a "Prescription Drug Facts" format. We anticipate that all altered versions will perform better than the traditional format, but we are unclear as to which of the new formats will be most easy to understand relative to one another. It is possible that they are equally

comprehensible. In order to tease out differences among these new formats, we will also investigate the roles of behavioral intention, self-efficacy, and consumer preference.

2. Consideration Given to Information Technology

Automated information technology will be used in the collection of information for this study. The contracted research firm will collect data through face-to-face personal interviews involving computer administration. The participant will self-administer the questionnaire 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 interviews to less than 30 minutes.

3. Identification of Information

Stakeholders have expressed interest in improving the current brief summary.[2] Although some research has been conducted on the format of the brief summary[3] FDA is not aware of previous research investigating the content of the brief summary, nor the specific formats of the brief summary proposed here.

4. Small Businesses

No small businesses would be involved in this data collection.

5. Less Frequent Information Collection

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

6. Information Collection Circumstances

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

7. Consultations with Persons Outside FDA

The 60-day public comment notice was published in the Federal Register on April 25, 2006, Volume 71, Number 79 (Docket No 2006N-0133). A copy of the 60-day Federal Register notice is included as Attachment 1.

FDA received seven comments on this proposed data collection. Five comments were from individual citizens, one comment was from AstraZeneca, a member of industry, and one comment

2 http://www.fda.gov/cder/ddmac/dtc2005/default.htm

3 Stotka, J.L., Rotelli, M.D., Dowsett, S.A., Elsner, M.W., Holdsworth, S.M., Pitts, P.J., & McAvoy, D.R. (2007). A new model for communicating risk information in direct-to-consumer print advertisements. *Drug Information Journal, 41*, 111-127.

was from a healthcare coalition, the Clear Language Group. Most of the comments addressed the proposed content study.

The five comments from individual citizens were identical. They stated, "Deny the drug industry petition. Show all side effects." These comments show a lack of understanding of the relevant issues. This proposed information collection is not a pharmaceutical industry petition; it is a research project supported by funds received from the Office of Medical Policy within the Center for Drug Evaluation and Research (CDER), part of FDA. The goal of this research is to further the public health by improving the readability and functionality of the brief summary in print ads, an easily accessed forum for information. Research in cognitive psychology overwhelmingly suggests that people have limited capacity for information and cannot process endless lists.[4] Recent research has suggested that providing a small number of the more minor side effects may actually improve the understanding of the benefit-risk tradeoff of the drug as a whole.[5] FDA wants to ensure that the presentation of risk information is in the best interests of consumers. This research will provide empirical evidence to support the optimal presentation of side effects.

In the sixth comment, AstraZeneca supported the proposed research as a method to create more consumer-friendly brief summaries. They requested that the research be delayed, however, until the data from study 1 is collected. If this were not possible, they requested that the comment period remain open until commenters have the ability to look at the questionnaire materials. Study 1 is currently in the field and we expect to have data available by the end of the year. These results will be analyzed in the next several months. Given the interest in the finalization of the brief summary guidance,[6] which in part relies on information from these studies, we cannot delay the development of studies 2 and 3 until data from study 1 are analyzed and interpreted. Questionnaire materials are available for public comment through FDA's Office of Information Review Management. Comments may be submitted to the docket at any time, even after the docket has closed.

The final comment was submitted by Sarah Furnas as a representative of the Clear Language Group, a consortium of plain language consultants, and involved two primary concerns. The first concern regarded our plan to recruit and divide respondents into education groups of *completed college* or *some college or less*. This division may limit our ability to make finer distinctions among educational groups. Moreover, Furnas suggests that people who struggle with obesity fall disproportionately into the lower education groups. If we choose a division point that represents a fairly high level of education, we may recruit more people from the highest education group, thus leaving out an appropriate proportion of lower education individuals. Furnas suggests using the educational breakdown used by the American Obesity Association: 4+ years of college, some college, high school grad, and some high school. We agree and will incorporate this suggestion into our questionnaire.

This commenter also expressed concern that the options in our research design require high numeracy and document literacy skills. Furnas suggested that we omit some of the design options and perhaps add other, easier options. First, although we share the goal of making documents easier

4 Lavie, N. (2001). Capacity limits in selective attention: Behavioral evidence and implications for neural activity. In Braun, J., Koch, C., et al. (Eds.), *Visual attention and cortical circuits*. Cambridge, MA: The MIT Press (pp.49-68); Shapiro, K. (Ed.) (2001). *The limits of attention: Temporal constraints in human information processing*. London: Oxford University Press.

5 See footnote 4.

6 See, e.g., www.fda.gov/ohrms/dockets/dockets/05n0354/05N-0354-EC444-Attach-1.pdf; www.wlf.org/upload/DDMBenicarResponse.pdf

to read and we would like to make the brief summary accessible to the greatest number of people possible, at some level, people who have difficulty reading will not seek out a *written* explanation of risks. In its guidance *Consumer Directed Broadcast Advertisements,*[7] the Agency suggested a number of ways complete risk information could be obtained by consumers, including a toll-free telephone number, making this option a good choice for those who have difficulty reading health information.

Consumers who have difficulty reading may not seek out medical information in a print ad, especially in its current form. However, the very nature of the information in the brief summary is the communication of risk information which is at its heart probability-based. By limiting our options, we not only fail to empirically determine the best option for the greatest number of people, but we may fail to appropriately inform the people who are most likely to read the ad and the brief summary. Therefore we are testing ways to better communicate this information.

Second, we do not agree that table formats are more difficult to read than lists of information in paragraph format. The OTC labeling change of 1999 (21 CFR 201.66), requiring a presentation of Drug Facts in a table format, has received positive reviews for its improvement over older labels.[8] Moreover, the Nutrition Facts label required as part of the Nutrition Labeling and Education Act of 1990 has also received praise for its easier-to-understand format.[9] These two table-based formats have been in the public domain for several years now, making them familiar to consumers. Nonetheless, we have changed our design based on other factors and will not be examining a chart or table format.

We acknowledge that *placebo* may be a fairly complex concept for many people. One of our research goals is to determine whether the addition of context may improve the understandability or usefulness of the brief summary as a whole. The value of an experimental design is that we will be able to empirically test whether or not our manipulations have an effect. Therefore we have chosen two other forms of context, the frequency of side effects, and the temporal nature of side-effects, in place of placebo rate. We will be able to determine which groups have more or less difficulty with each condition. It is likely that at least some people will value the addition of this information.

In the interest of communicating to as many people as possible, we have changed the format of the rate information. Instead of providing this information in percentages, we will provide this information as, "x out of 100." We thank this commenter for bringing these issues to our attention.

External Reviewers

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

• Nancy Ostrove, Ph.D., Office of the Commissioner, FDA

7 Available at http://www.fda.gov/cder/guidance/1804fnl.htm. Last accessed August 29, 2006.
8 For example, the Association of Clinicians for the Underserved states, "These new labels should assist consumers in the selection of Over the Counter (OTC) products by enabling them to assess drugs' risks and benefits more easily." http://www.clinicians.org/programsandservices/rxfiles/patient_education_safety.shtml
9 Marietta, A.B., Welshimer, K.J., & Anderson, S.L. (1999). Knowledge, attitudes, and behaviors of college students regarding the 1990 Nutrition Label Education Act food labels. *Journal of the American Dietetic Association, 99,* 445-449.

• Jordan Lin, Ph.D., Division of Social Sciences, Center for Food Safety and Applied Nutrition, FDA
• Paula Bone, Ph.D., University of West Virginia
• Mariea Hoy, Ph.D., University of Tennessee
• Matthew Perri, Ph.D., Pharm.D., University of Georgia

In addition to the outside experts listed above, John L. Swasy, Ph.D., Associate Professor of Marketing in the Kogod School of Business at American University, is a member of the survey development team and has reviewed the questionnaires extensively.

8. Payment or Gift

We are proposing to offer respondents $5 for their participation.

9. Confidentiality Provisions

All respondents will be provided with the assurance of confidentiality. The experiment will include information explaining to respondents that their information will be kept confidential. An independent contractor for the FDA will collect these data and will not provide FDA identifying information on the respondents.

No personally identifiable information will be sent to the agency. All information that can identify individual respondents will be kept by the contractor in a form that is separate from the data provided to FDA. All information will be kept by the contractor in a secured fashion that will not permit unauthorized personnel to examine any of the collected information.

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

10. Privacy

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

11. Burden of Information Collection

The total annual estimated burden imposed by this collection of information is 468 hours for this one-time collection (Table 1).

Table 1. Estimated Annual Reporting Burden[1]

Activity	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Screener, content study	1,800	1	1,800	.03	54
Questionnaire, content study	900	1	900	.33	297
Screener, format study	600	1	600	.03	18
Questionnaire, format study	300	1	300	.33	99
Total					468

[1]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.

12. Costs to Respondents

There are no costs to respondents.

13. Costs to Federal Government

The estimated cost to the federal government for these two studies is $225,000. This includes the costs paid to the contractor to program the study, draw the sample, collect the data, and create a database of the results. This cost also includes FDA staff time to design and manage the study, to analyze the resultant data, and to draft a report.

14. Reason for Change

This is a new data collection.

15. Statistical Reporting

Conventional statistical techniques for experimental data, such as descriptive statistics, analysis of variance, and regression models, will be used to analyze the data. Covariates used in the analysis will include scores of literacy and numeracy.

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.

16. Display of OMB Approval Date

No exemption is requested.

17. Exceptions to "Certification for Paperwork Reduction Act Submissions"

No exceptions are requested.

B. Collections of Information Employing Statistical Methods

1. Potential Respondent Universe and Sampling Selection

For both studies, eligible participants will be recruited for participation in eight or more geographically dispersed malls serving a variety of socioeconomic classes. Recruited subjects will be screened for: ability to read English, presence of the medical condition of excess weight or obesity, ability to visually process the label (have reading glasses available if necessary), age (18 years of age or older) and education level. They will be asked to participate in a study of consumer product advertising that lasts no more than 20 minutes.

Research has shown that motivated participants tend to engage in more effortful information processing[10] Individuals who suffer from the medical condition are expected to be more motivated to read the advertisement and the brief summary than individuals who do not suffer from the medical condition. Participants will be randomly assigned to clinical efficacy, side effect frequency, and risk frame conditions. Each participant will see only one experimental advertisement/brief summary.

All respondents will be over 18 years of age and be primary English speakers. A Spanish-language questionnaire will not be developed for this study as virtually all DTC advertising is in English. FDA will conduct the research through an existing contract by FDA's Center for Food Safety and Nutrition with Synovate, Inc. Approximately 900 interviews will be conducted for the content study and approximately 300 interviews will be conducted for the format study. This constitutes approximately 112 interviews at each of 8 geographically disperse shopping malls in the U.S for the content study and 38 interviews at each of 8 geographically disperse shopping malls in the US for the format study. There will be an equal number of males and females interviewed at each location. Malls will be selected to assure that the respondent universe represents varying degrees of education and other socioeconomic and ethnic variables.

Content Study

The traditional small-print, PI-based brief summary is not the best way to present information to consumers, yet somehow important risk information must be conveyed. One way to improve the current brief summary is to provide context for some of the risk information on the page. Contextual information may help consumers process the information that FDA has determined must appear in the brief summary. For example, in some cases, information about the controllability of an adverse event may be useful. In other cases, information about how adverse events are managed may provide important contextual information. In the current study, we focus on three types of context: the frequency of adverse events, the duration of side effects, and clinical efficacy.

10 See, for example, Lord, C.G., Lepper, M.R. & Preston, E. (1984). Considering the opposite: A corrective strategy for social judgment. *Journal of Personality and Social Psychology*, *47*, 1231-1243; Neuberg, S.L. (1989). The goal of forming accurate impressions during social interactions: Attenuating the impact of negative expectancies. *Journal of Personality and Social Psychology*, *56*, 374-386; Tetlock, P.E. & Kim, J.I. (1987). Accountability and judgment processes in a personality prediction task. *Journal of Personality and Social Psychology*, *52*, 700-709.

FDA has determined a hierarchy of information that must be placed in the brief summary, including warnings and precautions, contraindications, and drug interactions. Because of the importance of these categories and the work that each review division devotes to their wording, it is unlikely that changes to these sections would have practical significance. The brief summary draft guidance of 2004 does not mention these sections. Conversely, the section formerly titled "adverse events" seems appropriate for manipulation. This section details minor but possibly commonly occurring side effects that patients may experience when taking the drug. In fact, the 2004 draft guidance mentions this section as perhaps too long as currently used, suggesting that large lists of information may detract from more important risk sections.

Thus, in the content study, we will manipulate the minor side effect section, varying the presence of frequency information and, separately, the presence of duration information. We are interested in how these changes influence the understanding of the risks of the product as a whole, particularly the more serious risk sections. If these changes enhance or, at the very least, do not detract from the major risks, then these additions of context may be something to include in future brief summaries. In the best case scenario, we find context that enhances the total picture of the drug and does not interfere with the processing of the major risks.

Additionally, information on the clinical efficacy of the product may influence how consumers process the major risks of the product. By providing information on the "whole picture" of the product, consumers may be more motivated to process the risk profile of the drug. The level of efficacy may also play a role; it is likely that the consideration of the risks will vary depending on whether clinical efficacy is high or low.

Our primary dependent variable is the comprehension of the major risks (i.e., warnings and precautions, contraindications). The major risks are essential to understanding the risk profile of the drug and therefore comprehension of these risks is important for future action or inaction. Secondarily, we are interested in the comprehension of the minor side effects and behavioral intentions of consumers after they read one of the brief summaries. If comprehension of major risks is not impeded and minor side effects are better understood, then contextual information can be considered in future research or regulation.

Primary Research Questions

a. Will the presence of information on the frequency of minor side effects influence the readers' comprehension of the major risks? Will the comprehension of major risks vary depending on whether the frequencies are high or low?
b. Will the presence of information on the temporal duration of minor side effects influence the comprehension of the major risks?
c. Will the presence of clinical efficacy information influence readers' comprehension of the major risks? Will the comprehension of the major risks vary depending on whether clinical efficacy is high or low?
d. Will clinical efficacy and frequency of minor side effects interact to influence comprehension of major risks? Will clinical efficacy and temporal duration interact to influence comprehension of major risks?

Planned design and analysis

Independent Variables and Design

3 x 3 (clinical efficacy x frequency of side effects)

		Frequency of Side Effects		
		None	High	Low
Clinical Efficacy	None			
	High			
	Low			

3 x 2 (clinical efficacy x presence of duration information)

		Duration of Side Effect Information	
		Present	Absent
Clinical Efficacy	None		
	High		
	Low		

Covariates:

- Education
- Age
- Gender
- Disease severity
- Baseline ratings of side effect riskiness
- Reading speed
- Health literacy
- Numeracy

Covariates will be used to account for differences in responses related to the characteristics of the respondent and prior attitudes about the inherent riskiness of individual side effects.

Dependent Variables

Primary

- Comprehension of major risks

Secondary

- Comprehension of minor risks
- Behavioral intention

Hypotheses

1. Including frequency information about minor side effects will enhance the comprehension of major risks. Readers who see high frequencies of minor side effects will show lower comprehension of the major risks than readers who see low frequencies.

2. Including temporal duration information about side effects will enhance the comprehension of major risks. Readers who see such information will be more likely to comprehend the major risks than readers who do not see duration information.
3. Including clinical efficacy information will influence the comprehension of major risks. Readers who see clinical efficacy information will show greater comprehension of major risks than readers who are not given any clinical efficacy information. Readers who see low clinical efficacy information will show greater comprehension of major risks than those who see high clinical efficacy information.

Power

The primary dependent variable, comprehension of major risks, will be assessed using a continuous composite score based on four dichotomous items (true/false); recall of the major risks will be based on ten dichotomous items (yes/no). These scores will be used in ANOVA to test for main and interaction effects. To test main effect and interaction hypotheses, the following assumptions were made in deriving the sample size: (1) 0.05 alpha and at least 0.80 power, (2) 1 degree of freedom for the numerator, and (3) an effect size between small and medium.

The power to detect a (conventional) *medium* effect size (f= .25) for the main effect in a 3 by 3 factorial having equal cell sizes of n=60 per cell and an alpha of .05 is .99. Similarly, the power to detect a medium sized interaction is also excellent (.99).[11]

The power to detect a (conventional) *small* effect size (f= .15) for the main effect in a 3 by 3 factorial having equal cell sizes of n=60 per cell and an alpha of .05 is .88. Similarly, the power to detect a similarly sized interaction is .80.

Thus, based on these assumptions we are confident that we have sufficient power to conduct our planned analyses.

Format Study

In addition to the content of the brief summary, an important component of the readability of the document is its format. Traditionally, sponsors have reproduced the risk-related sections of the physician-directed PI and inserted them onto the adjacent page of the print ad, regardless of the amount of information or the size of the font. This traditional format usually resulted in a document with tiny font written in medical language.

In the current study, we propose three formats as alternatives to the traditional format. Two of these formats were suggested in the draft brief summary guidance of 2004: the FDA-approved PPI version and the highlights version from the content and format rule of 2006. Another format, the Prescription Drug Facts box, was suggested by extensive research conducted on the OTC Drug Facts label. We expect that all three of these formats will result in greater comprehension of risks and the risk/benefit tradeoff as compared with the traditional brief summary format.[12] Given that we know of no research that directly compares these alternative formats in terms of comprehension

11 See Table 8.4.4, "n to detect f by F test at a = .05"; p. 384 in Cohen, Jacob (1988). *Statistical Power Analysis for the Behavioral Sciences, Second Edition*. Hillsdale, NJ: Lawrence Erlbaum Associates.
12 See footnote 3.

of risk information, we do not have a hypothesis as to the version that will result in the greatest comprehension.

As in the content study, we will also measure other dependent measure. The format study differs, however, because here all four dependent variables are primary. Comprehension of risk information is valuable, but when examining format differences, we expect that other issues such as self-efficacy, behavioral intention, and even preference will also play a role in the use of the brief summary.

To a larger extent than content, format plays a role in the "stopping-power" of a page, or the degree to which a person decides to read something or not. Part of this power potentially comes from the amount of confidence the person has that they will be able to successfully understand the concepts, thus achieving something from their efforts. Therefore, we will also measure readers' self-efficacy. Based on work by Bandura[13], self-efficacy is participants' beliefs about, or confidence in, their own ability to exercise personal control over their learning about the product. These questions measure participants' self-confidence to perform the tasks necessary to use the information in the brief summary (e.g., recognize adverse effects, identify who should not take the drug). In this case, since readers will be familiar with the Prescription Drug Facts format due to current OTC labels, we expect this format to show the greatest self-efficacy.

It is possible that while all three formats mark an improvement over the traditional brief summary, none of them can themselves be distinguished with regard to comprehension, behavioral intention, or self-efficacy. Another variable that might further distinguish these formats is consumer preference. All of the previous measures will be examined in the context of one format. In other words, each participant will see only one format and we will compare responses across participants (often called "between-subjects"). After these variables have been measured, we will show participants all four versions and ask them to rank the versions from most to least preferable. Although comprehension is our key dependent measure, consumer preference is also an important variable to assess for this reason. Little comprehension will occur if people are turned off enough by format factors to avoid the brief summary altogether. We expect consumer preference to correlate with self-efficacy.

It is important to note, however, that in previous studies the Nutrition Facts Label format most preferred by consumers was not the one that resulted in the best comprehension[14]. If this is the case with the brief summary, comprehension factors will prevail. If not, consumer preference will provide additional differentiating information in the case that several of the formats show similar comprehension.

Primary Research Questions

a. Will alternative formats influence the comprehension of major risks, behavioral intentions, and/or self-efficacy?
b. Which format will consumers prefer?

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13 Bandura, Albert (1986). *Social Foundations of Thought and Action: A Social Cognitive Theory*. Englewood Cliffs, NJ: Prentice Hall.

14 Levy, Alan S., Fein, Sara B., and Schucker, Richard E. (1992). More effective nutrition label formats are not necessarily more preferred. *Journal of the American Dietetic Association*, 92(10), 1230-1234.

Planned design and analysis

Independent Variables

Type of Format (4 levels)
- Traditional
- Highlights
- Prescription Drug Facts
- Question and Answer (Q&A; from Patient Package Insert)

Covariates
- Education
- Age
- Gender
- Health literacy

Covariates will be used to account for differences in responses related to the characteristics of the respondent.

Dependent Variables

- Comprehension of major and minor risks
- Self-efficacy
- Behavioral intention
- Consumer preference

Hypotheses

1. Readers will show higher comprehension of major risks in the highlights format, the PPI format, and the Prescription Drug Facts format compared with the traditional brief summary format. The particular differences within the alternative formats are exploratory.
2. Readers will show higher self-efficacy in the highlights format, the PPI format, and the Prescription Drug Facts format compared with the traditional brief summary format. The highest self-efficacy will be shown in the Prescription Drug Facts format.
3. Readers will exhibit different behavioral intentions in the highlights format, the PPI format, and the Prescription Drug Facts format compared with the traditional brief summary format. The particular differences within the alternative formats are exploratory.
4. The alternative brief summary formats will be preferred to the traditional brief summary format. Which format is most preferred is exploratory.

Power

To test a main effect hypothesis in a 4 x 1 ANOVA, the following assumptions were made in deriving the sample size: (1) 0.05 alpha and at least 0.80 power, (2) 3 degrees of freedom for the numerator, and (3) an effect size between small and medium. For a (conventional) *small* to *medium*

effect size (f= .20), the per cell sample size required to detect a difference should be 69.[15] Taking into consideration uncommon but unavoidable technical glitches in data collection, we are confident that a sample size of 75 per cell will provide us with adequate power (0.83).

2. Procedures for the Collection of Information

In both the content and the format studies, participants will see one brief summary in the context of an ad for a new (hypothetical) prescription weight loss drug. They will respond to survey questions about their understanding of the risks intended actions when side effects occur and then respond to more specific questions about the statement itself. This method will allow FDA to compare the responses of participants who saw nine (9) different statements. Main dependent variables are: comprehension of the side effects statements, as measured by reasons for calling a physician and/or the FDA; the likelihood of calling FDA, to appreciate prospective workload burden; and the clarity of each statement. The complete questionnaire is included as Attachment A.

3. Methods to maximize response rates and to deal with issues of non-response

Respondents will be recruited and interviewed at 8 shopping malls. Participants will be told they will be evaluating a new product concept. This procedure has been reviewed and approved by FDA's human subject protection committee (RIHSC).

4. Test Procedures

See Procedures for Collection of Information, above.

5. Individuals Involved in Statistical Consultation and Information Collection

The contractor, Synovate, will collect the information on behalf of the 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) 790-9099. Analysis of the information will be conducted primarily by the Research Team, Division of Drug Marketing, Advertising and Communications, Office of Medical Policy, CDER, FDA, and coordinated by Kathryn J. Aikin, Ph.D., 301-796-0569 and Amie C. Braman, Ph.D., 301-796-0574.

15 See Table 8.4.4, "n to detect f by F test at a = .05"; p. 384 in Cohen, Jacob (1988). *Statistical Power Analysis for the Behavioral Sciences, Second Edition*. Hillsdale, NJ: Lawrence Erlbaum Associates.

ATTACHMENT 1

60-Day FR Notice

[Federal Register: April 25, 2006 (Volume 71, Number 79)]
[**Notices**]
[Page 23921-23924]
From the Federal Register Online via GPO Access [wais.access.gpo.gov]
[DOCID:fr25ap06-80]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2006N-0133]

Agency Information Collection Activities; Proposed Collection; Comment Request; Experimental Evaluation of Variations in Content and Format of the Brief Summary in Direct-to-Consumer Print Advertisements for Prescription Drugs

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (**FDA**) is announcing an opportunity for public comment on a proposed collection of certain information by the agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal agencies are required to publish notice in the Federal Register concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on two studies of consumer evaluations of variations in content and format of the brief summary in direct-to-consumer (**DTC**) prescription drug print advertisements.

DATES: Submit written or electronic comments on the collection of information by June 26, 2006.

ADDRESSES: Submit electronic comments on the collection of

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information to: http://www.**fda**.gov/dockets/ecomments. Submit written

comments on the collection of information to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Karen Nelson, Office Management Programs (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1482.

SUPPLEMENTARY INFORMATION:

I. Backround

Under the PRA (44 U.S.C. 3501-3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. ``Collection of information'' is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the Federal Register concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, **FDA** is publishing notice of the proposed collection of information set forth in this document.

With respect to each of the following collection of information, **FDA** invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of **FDA**'s functions, including whether the information will have practical utility; (2) the accuracy of **FDA**'s estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Experimental Evaluation of Variations in Content and Format of the Brief Summary in **DTC** Print Advertisements for Prescription Drugs

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 903(b)(2)(c) of the Federal Food, Drug, and Cosmetic Act (the 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 act. Under the act, a drug is misbranded if its labeling or **advertising** is false or misleading. In addition, section 502(n) of the act (21 U.S.C. 352(n)) specifies that advertisements for prescription drugs and biological products must provide a true statement of information ``in brief summary'' about the advertised product's ``side effects, contraindications, and effectiveness.'' The prescription drug **advertising** regulations (Sec. 202.1(e)(3)(iii) (21 CFR 202.1(e)(3)(iii))) specify that the information about risks must include ``each specific side effect and contraindication'' from the advertised drug's approved labeling. The regulation also specifies that the phrase ``side effect and contraindication'' refers to all of the categories of risk information required in the approved product labeling written for health professionals, including the warnings, precautions, and adverse reactions sections. Thus, every risk in an advertised drug's approved labeling must be included to meet these regulations.

In recent years, **FDA** has become concerned about the adequacy of the brief summary in **DTC** print advertisements. Although **advertising** of prescription drugs was once primarily addressed to health professionals, increasingly consumers have become a target audience, as **DTC advertising** has dramatically increased in the past few years. Results of **FDA**'s 2002 survey on **DTC advertising** (available at http://www.**fda**.gov/cder/ddmac/researchka.htm

) show that 41 percent of

respondents in 2002 reported they do not usually read any of the brief summary that accompanies the main print ad. Use of the brief summary was a function of whether they have an interest in the condition; about 45 percent of those having a particular interest in the advertised drug read all or almost all of the brief summary. Despite their interest, about half of these individuals described the brief summary as somewhat or very hard to understand.

Because the regulations do not specify how to include each risk, sponsors can use discretion in fulfilling the brief summary requirement under Sec. 202.1(e)(3)(iii). Frequently, sponsors print in small type, verbatim, the risk-related sections of the approved product labeling (also called the package insert, professional labeling, or prescribing information). This labeling is written for health professionals, using medical terminology. **FDA** believes that while this is one reasonable way to fulfill the brief summary requirement for print advertisements directed toward health professionals, this method is difficult for consumers to understand and therefore may not be the best approach to communicate this important information to them.

In 2004, **FDA** published a draft guidance entitled ``Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements'' (available at http://www.**fda**.gov/cder/guidance/5669dft.htm). This

guidance outlined possible options for improving the communication of risk information to consumers in specific promotional pieces. When discussing the current professional prescribing information format, the guidance states that the ``volume of the material, coupled with the format in which it is presented... discourages its use and makes the information less comprehensible to consumers.'' The draft guidance suggested three possible presentations for the brief summary, including the current prescribing information format, an approved patient package insert, or highlights from the physician labeling rule.

In the content study, **FDA** plans to investigate the role of context in providing useful risk information to consumers. It has been theorized that long lists of minor risks may detract from the understanding of more serious risks, as stated in the draft guidance. Nonetheless, if the risk information is presented with proper supporting context, people may find the information facilitates rather than distracts from the understanding of the risk information. One of the two proposed studies in this notice will investigate the context that may contribute to this facilitation.

In addition to context, format also plays a role in the clarity and understanding of the brief summary. **FDA** proposes to collect information on the usefulness of different formats suggested in the draft guidance. In addition to the patient package insert, which is usually presented in a question and answer format, **FDA** proposes to test a consumer-friendly highlights format, as well as a format based on the drug facts labeling used for over-the-counter drugs.

Data from these two studies will converge to allow a better assessment of various ways to present risk information

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in a print advertisement for a prescription drug.

II. Studies

A. Content Study

1. Design Overview

This study will employ a between-subjects crossed factorial design using a mall-intercept protocol. Ten print advertisements will be created using two levels of drug side effect information and five levels of context. Thus, the factors will be the amount of side effect information (short; long) and amount of supportive context for the side effect information (paragraph only; paragraph rate; paragraph rate plus placebo rate; chart rate; chart rate plus placebo rate). Other information will be constant across conditions. Respondents who self-identify as being in the target market for the condition will be asked to read a single print advertisement for a new prescription drug. After reading the advertisement, they will be asked questions about their comprehension and evaluation of the information presented in the advertisement.

2. Factors

a. Participants. Consumers will be screened and recruited by the contractor to be self-identified as being moderately overweight or more. We chose to limit our investigation to this one disease condition (weight loss) because it has a high prevalence rate in the population (http://www.cdc.gov/nccdphp/dnpa/obesity/faq.htm) and is likely to

occur both in males and females. We chose to accept this decrease in generalizability to maximize our ability to detect subtle differences in content variation. Participants will be screened to represent a range of education levels (some college or less; completed college or more). Because the task presumes basic reading abilities, all screened participants will speak English as their primary language and, as appropriate, have reading glasses available when participating in the study.

b. Amount of side effect information. The number of side effects will be varied to create ``short'' and ``long'' levels as follows:

Short: ``Side effects include a, b, and c. This is not a complete list. Talk to your doctor for more information.''

Long: ``Side effects include a, b, c, d, e, f, g, and h. Talk to your doctor for more information.''

c. Context. The context for the side effect information will be varied to create five levels ranging from least supportive to most supportive as follows:

Paragraph only: Listing of side effects in paragraph form.

Paragraph rate: Listing of side effects and their rate of occurrence in paragraph form.

Paragraph rate plus placebo rate: Listing of side effects, their rate of occurrence, and the rate of placebo effects in paragraph form.

Chart rate: Listing of side effects and their rate of occurrence in table form.

Chart rate plus placebo rate: Listing of side effects, their rate of occurrence, and the rate of placebo effects in table form.

3. Procedure

Participants will be shown one ad. Then a structured interview will be conducted with each participant to examine a number of important perceptions about the brief summary, including perceived riskiness of the drug, comprehension of information in the brief summary, and perceived usefulness of brief summary information. Finally, demographic and health care utilization information will be collected. Interviews are expected to last approximately 20 minutes. A total of 900 participants will be involved. This will be a one-time (rather than

annual) collection of information.

B. Format Study

1. Design Overview

This study will employ a between-subjects crossed factorial design using a mall-intercept protocol. Three print advertisements will be created using three different formats: Question and answer, highlights (71 FR 3922, January 24, 2006), and drug facts (21 CFR 201.66 and Appendix A). The information in the formats will be constant across conditions. Participants who self-identify as being in the target market for the condition will be asked to read a single print advertisement for a new prescription drug. After reading the advertisement, they will be asked questions about their comprehension and evaluation of the information presented in the advertisement.

2. Factors

a. Participants. Consumers will be screened and recruited by the contractor to be self-identified as being moderately overweight or more. As in the content study described previously in this document, we chose to limit our investigation to one disease condition-weight loss. Participants will be screened to represent a range of education levels (some college or less; completed college or more). Because the task presumes basic reading abilities, all screened participants will speak English as their primary language and, as appropriate, have reading glasses available when participating in the study.

b. Type of format. The format of the information in the brief summary will be varied as follows: Question and answer, highlights, and drug facts. Please refer to Appendix A for examples of the different format variations.

3. Procedure

Participants will be shown one ad. Then a structured interview will be conducted with each participant to examine a number of important perceptions about the brief summary, including perceived riskiness of the drug, comprehension of information in the brief summary, and perceived usefulness of brief summary information. Finally, demographic and health care utilization information will be collected. Interviews are expected to last approximately 20 minutes. A total of 300 participants will be involved. This will be a one-time (rather than annual) collection of information.

FDA estimates that 1,800 individuals will need to be screened to obtain a respondent sample of 900 for the content study and that 600 individuals will need to be screened to obtain a respondent sample of 300 for the format study. The screener is expected to take 30 seconds, for a total screener burden of 41 hours. The 1,200 respondents in the two studies will then be asked to respond to a series of questions about the advertisement. We estimate the response burden for each of the two studies to be 20 minutes, for a burden of 396 hours. The estimated total burden for this data collection effort is 437 hours. The respondent burden is listed in table 1 of this document.

FDA estimates the burden of this collection of information as follows:

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Table 1.--Estimated Annual Reporting Burden \1\

No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
1,800 (content study: screener)	1	1,800	.017	31
900 (content study: questionnaire)	1	900	.33	297
600 (format study: screener)	1	600	.017	10
300 (format study: questionnaire)	1	300	.33	99
Total				437

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

Dated: April 18, 2006.
Jeffrey Shuren,
Assistant Commissioner for Policy.
[FR Doc. E6-6142 Filed 4-24-06; 8:45 am]
BILLING CODE 4160-01-S

ATTACHMENT 2

Questionnaires

Participant Screener for Content AND Format Studies

Participants.
Adult consumers will be solicited and pre-screened for suitability and presence of condition (excessive weight). Initially, during the screening, participants will be told that the study concerns their opinions about new products. Following the data collection, all participants will be debriefed regarding the study purpose and the fictitious nature of the brand rated.

SCREENER

Hello, my name is _____ and I work for _____, a research firm…[Standard introduction including confidentiality.]

We would like to get your opinion about some new products on the market. The interview will take about 20 minutes and you will be paid $5 if you qualify. Can I ask you some questions?

S1. Can you read English?

___Yes
___No [eliminate, thank politely]

DO NOT READ Don't Know 8 [eliminate]
DO NOT READ Refused 9 [eliminate]

S2. In what year were you born? _____

If Year is > 1988 [eliminate, thank politely]
DO NOT READ Don't Know 8 [eliminate]
DO NOT READ Refused 9 [eliminate]

[Interviewer: Recruit range of ages]

S3a. Do you usually wear glasses or contact lenses for reading or watching television?
A) Yes (ask 3b)
B) No

S3b. Do you have your glasses or contact lenses with you today?

A) Yes
B) No [eliminate]

S4a. Do you consume any of the following products on a regular basis?

_____Fruit juice
_____Coffee
_____Soymilk

S4b. Do you use any of the following products on a regular basis?

_____A dishwasher
_____Swiffer dusting products
_____A microwave oven

S5. Has a doctor or other healthcare provider ever said you have any of the following health problems?

a. Asthma _____Yes _____No [filler]

b. Diabetes _____Yes _____No [filler]

c. You are overweight or you need to lose more than 15 pounds?

_____Yes _____No

d. High blood pressure _____Yes _____No [filler]

[INTERVIEWER: If "no" to c, eliminate]

S6. What was the last grade of school that you completed? (READ CODES IF NECESSARY)

1 Grade school or less
2 Some high school
3 Completed high school
4 Some college
5 Completed college
6 Graduate school or more
7 Other education beyond high school (business, technical, etc)
9 Refused

[Interviewer: recruit range of education level, 30% to be HS education or less]

S7. Are you:

Hispanic or Latino	1
Not Hispanic or Latino	2
DK/Ref	9

S8. Which of these best represents your ethnic group? You may choose one or more. Would you say that you are:

1 American Indian or Alaska Native
2 Asian
3 Black or African-American
4 Native Hawaiian or Other Pacific Islander
5 White
9. (Don't Read) Ref / DK /NA

S9. [DO NOT READ] Gender: _____Male _____Female

Thank you. I would like to invite you to participate in this study. Please follow me…

Questionnaire, Content Study

Interview Protocol.

{Programming notes}
Questions will be self-administered by participants.
Professional interviewers will be on hand to assist where necessary.
Answers to open-ended questions will be audio recorded.
Computer will track/record reading times and page-switching sequences for all pages.
Test ad will always be in last position.

(Present and explain Informed Consent Form. Participants will be blind to FDA's sponsorship).

Section I. Interview.

Thank you for agreeing to participate in this study today. Before we start I need to check that the microphone and recording equipment are working properly. Please speak into the microphone and read the sentence that appears on the computer screen. READ THIS OUT LOUD: "The quick brown fox jumps over the lazy dog."

Make sure you are comfortable and can read the screen from where you sit. The screen will show some instructions. Please use the Back and Continue buttons to move backwards and forwards through the instructions at your own pace. When you are ready to begin, simply press the "continue" key and follow the instructions. Any questions?

Q1. Please rate how risky or not risky these physical symptoms are using the scale provided. (randomize)

	Not at all risky	Somewhat risky	Moderately risky	Very risky	Extremely risky
Fainting					
Mood swings					
Diarrhea					
Rash					
Nausea					
Vomiting					
Weakness					
Difficulty swallowing					

Next you will see some magazine ads for consumer products on the computer screen. We are interested in finding out your opinions on some new products and some you may have seen before. Remember that all of your responses are confidential so please answer as honestly as possible. After you have finished reading these instructions, we will show you the magazine ads. Even though they are on a computer screen, please read them as you would in a magazine if you saw ads for products that you might be interested in for yourself or someone in your family.

You can take as much time as you want to look over this material and you can flip back and forth between pages if that is how you would usually read these ads. When you reach the end of the ads, you will come back to a blank screen.

[show ads]

Q3a. What products do you recall seeing ads for? You may select more than one.
A) Westinghouse
B) Sony
C) Lactaid
D) Oncazil
E) Femara

Q3b. Do you recall seeing an ad for ONCAZIL?
[*This only gets asked if respondent does not choose D above*]

A) Yes
B) No (*show 3c*)

Q3c. (display Oncazil ad on screen) Do you recall seeing this ad?
[*This only gets asked if respondent chooses NO in 3b*]
A) Yes
B) No [TERMINATE]

Q4. What condition does ONCAZIL treat?
A) Asthma – breathing difficulties
B) Weight condition – weight control
C) High Cholesterol – control cholesterol
D) Fungus – athlete's foot
E) Osteoporosis – brittle bones

Q5. What type of product is ONCAZIL? Please choose one answer. Is this:
A) An herbal supplement that you can buy in a drug or grocery store
B) A medicine that you can only get with a prescription from a doctor, or
C) An "over-the-counter" drug that you can buy without a prescription from a doctor

Q9. For each item, please rate how likely or not likely you are to do each of the following behaviors (*randomize*)

	Not at all likely	Somewhat not likely	Neither likely nor unlikely	Somewhat likely	Extremely likely
a. Talk to my doctor about ONCAZIL					
b. Ask my doctor about getting a sample of ONCAZIL					
c. Look for more information about ONCAZIL					
d. Ask my doctor to prescribe ONCAZIL					

Q10. As best you can, answer each of these questions *based on the information presented in the advertisement for Oncazil.* For each item, indicate whether the statement is true or false or if you are not sure. (*randomize*)

	True	False	Not Sure
a. You cannot take ONCAZIL if you have had a stroke.			
b. If you take some kinds of over-the-counter cough medicines at the same time you take ONCAZIL, your blood pressure may go up			
c. Your blood pressure can go down to dangerous levels if you take antifungal medicines with ONCAZIL			
d. Seizures are a known side effect of taking ONCAZIL.			
e. You can take ONCAZIL if you are pregnant			
f. Patients with a history of kidney disease can take ONCAZIL if they are monitored by a doctor.			
g. Antibiotics may become less effective if you use ONCAZIL at the same time.			
h. You can take ONCAZIL if you have narrow-angle glaucoma			
i. You must be at least 18 years old to take ONCAZIL			
j. ONCAZIL is for people with a body mass index (BMI) of 25 or greater			

Q11. Answer each question as best you can based on the information in the ad. [*randomize*]

	Yes	No	Not Sure

a. The ad tells me how likely I am to experience a benefit from using ONCAZIL			
b. Rash is a more frequent side effect of ONCAZIL than nausea			
c. The ad tells me how likely I am to experience a side effect from using ONCAZIL			
d. All side effects will go away within one week of taking ONCAZIL			
e. All side effects will last the entire time I am taking ONCAZIL			

Q12. Please indicate your level of agreement or disagreement with the following statements. [*randomize*]

	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
a. The information in the ad is believable					
b. The risks and negative effects seem reasonable compared with the benefits and positive effects of ONCAZIL					
c. The benefits and positive effects of ONCAZIL outweigh the risks and negative effects					
d. I could deal with the side effects if I lost weight with ONCAZIL					
e. Even losing a lot of weight would not be enough to balance the risks and negative effects from ONCAZIL					

INTERVIEWER: Hand page 2 of print ad to participant.

Q13. Imagine you have taken ONCAZIL. Think about each situation presented below. Answer each question as best you can based on the information on this page of the ad. [*randomize*] [*this section should be timed*]

	Yes	No	Not Sure
a. Since you have been on ONCAZIL, you have felt that your thinking skills are slowed. Based on what you read, could this be a side effect of ONCAZIL?			
b. You have been taking medicine for kidney disease. Can you take ONCAZIL?			
c. Based on what you read, is it ok to take Tylenol (acetaminophen) while taking ONCAZIL?			
d. You have just learned you have Hepatitis-C (a disease that affects your liver). Should you take ONCAZIL?			

Q16. Are you currently taking a prescription medicine for weight control?

A) Yes
B) No (*do not ask Q19*)
C) Don't know or uncertain

Q17) What is your height? Your best guess is fine.

A) Feet _____
B) Inches _____

Q18. What is your weight in pounds? Your best guess is fine.

A) Weight _____

Q19. Before you started treatment, how severe was your weight condition? Would you describe it as:

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

Q20. How severe is your weight condition now? Would you describe it as:

A) Very mild

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

Q21. In general, how much do you feel you know about your medical condition? Would you say you know:
A) A lot
B) A good bit
C) Some
D) Only a slight amount
E) Nothing at all

Q22. Have you ever...

had liver damage?	Yes	No	Don't Know
had a heart attack or stroke?	Yes	No	Don't Know
had kidney disease?	Yes	No	Don't Know
had the flu recently?	Yes	No	Don't Know

Q23. Have you ever seen any advertising for Oncazil before today?
A) Yes
B) No

The respondent's response will be digitally recorded in their own words.

INTERVIEWER: Now I'm going to ask you to say some words out loud that sometimes appear on medicines. The list contains some "easy to read" words, and some "hard to read" words, so just do your best to say as many of these words as you can. Remember, almost everyone will have trouble reading many of these words so don't be upset if some words are difficult -- just do your best! If a word is too difficult, just say "blank" and go on to the next word in the list. I want to hear you read as many words as you can from these lists. Speak directly into the microphone. Begin with the first word on this page and read aloud. When you come to a word you cannot read, do the best you can or say "blank" and go on to the next word.

Q24) fat flu pill dose eye stress smear nerves germs meals disease cancer caffeine attack kidney hormones herpes seizure bowel asthma rectal incest
The respondent's response will be digitally recorded in their own words.

Q25) fatigue pelvic jaundice infection exercise behavior prescription notify gallbladder calories depression miscarriage pregnancy arthritis nutrition menopause appendix abnormal syphilis hemorrhoids nausea directed
The respondent's response will be digitally recorded in their own words.

Q26) allergic menstrual testicle colitis emergency medication occupation sexually alcoholism irritation constipation gonorrhea inflammatory diabetes hepatitis antibiotics diagnosis potassium anemia obesity osteoporosis impetigo

Q27. Imagine that you flip a fair coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips?
___ times out of 1,000

Q28. In the BIG BUCKS LOTTERY, the chance of winning a $10 prize is 1%. What is your best guess about how many people would win a $10 prize if 1,000 people each buy a single ticket to BIG BUCKS LOTTERY?
____ person(s) out of 1,000

Q29. In ACME PUBLISHING SWEEPSTAKES, the chance of winning a car is 1 in 1,000. What percent of tickets to ACME PUBLISHING SWEEPSTAKES will win a car?
____ %

Q30. Gender (Record by observation; **do not read**)

1 Male 2 Female

[End time: _____]

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

Questionnaire, Format Study

Interview Protocol.

{Programming notes}
Questions will be self-administered by participants.
Professional interviewers will be on hand to assist where necessary.
Answers to open-ended questions will be audio recorded.
Computer will track/record reading times and page-switching sequences for all pages.
Test ad will always be in last position.

(Present and explain Informed Consent Form. Participants will be blind to FDA's sponsorship).

Section I. Interview.

Thank you for agreeing to participate in this study today. Before we start I need to check that the microphone and recording equipment are working properly. Please speak into the microphone and read the sentence that appears on the computer screen. READ THIS OUT LOUD: "The quick brown fox jumps over the lazy dog."

Make sure you are comfortable and can read the screen from where you sit. The screen will show some instructions. Please use the Back and Continue buttons to move backwards and forwards through the instructions at your own pace.

You will see a magazine ad for a new consumer product on the computer screen. Remember that all of your responses are confidential so please answer as honestly as possible. After you have finished reading these instructions, we will show you the magazine ad. Even though it is on a computer screen, please read it as you would in a magazine if you saw an ad for a product that you might be interested in for yourself or someone in your family.

The ad is two pages long. You will have XX minutes to read the ad. The computer will automatically shut off the picture if you are not finished in that time. When you are ready to begin, simply press the "continue" key and follow the instructions. Any questions?

Q3a. What product do you recall seeing an ad for? You may select more than one.
A) Westinghouse
B) Sony
C) Lactaid
D) Oncazil
E) Femara

Q3b) Do you recall seeing an ad for ONCAZIL?
[*This only gets asked if respondent does not choose D above*]
A) Yes
B) No (*show 3c*)

Q3c (display Oncazil ad on screen) Do you recall seeing this ad?
[*This only gets asked if respondent chooses NO in 3b*]
A) Yes
B) No [TERMINATE]

Q4. What condition does ONCAZIL treat?
A) Asthma – breathing difficulties
B) Weight condition – weight control
C) High Cholesterol – control cholesterol
D) Fungus – athlete's foot
E) Osteoporosis – brittle bones

Q5. What type of product is ONCAZIL? Please choose one answer. Is this:
A) An herbal supplement that you can buy in a drug or grocery store
B) A medicine that you can only get with a prescription from a doctor, or
C) An "over-the-counter" drug that you can buy without a prescription from a doctor

Q9. For each item, please rate how likely or not likely you are to do each of the following behaviors (*randomize*)

	Not at all likely	Somewhat not likely	Neither likely nor unlikely	Somewhat likely	Extremely likely
a. Talk to my doctor about ONCAZIL					
b. Ask my doctor about getting a free sample of ONCAZIL					
c. Look for more information about ONCAZIL					
d. Ask my doctor to prescribe ONCAZIL					

Q10. As best you can, answer each of these questions *based on the information presented in the advertisement for Oncazil*. For each item, indicate whether the statement is true or false or if you are not sure. (*randomize*)

	True	False	Not Sure
a. You cannot take ONCAZIL if you have had a stroke.			
b. If you take some kinds of over-the-counter cough medicines at the same time you take ONCAZIL, your blood pressure may go up			
c. Your blood pressure can go down to dangerous levels if you take antifungal medicines with ONCAZIL			
d. ONCAZIL should only be used by people with a BMI of 25 or higher			
e. You can take ONCAZIL if you are pregnant			

f. Patients with a history of kidney disease can take ONCAZIL if they are monitored by a doctor.			
g. ONCAZIL may become less effective if you use antibiotics at the same time.			
h. You can take ONCAZIL if you have narrow-angle glaucoma			
i. You must be at least 18 years old to take ONCAZIL			
j. ONCAZIL is for people with a body mass index (BMI) of 25 or greater			

INTERVIEWER: Hand print ad to participant.

Q11. Imagine you have taken ONCAZIL. Think about each situation presented below. Answer each question as best you can based on the information on this page of the ad. [*randomize*] [*this section should be timed*]

	Yes	No	Not Sure
a. Since you have been on ONCAZIL, you have felt that your thinking skills are slowed. Based on what you read, could this be a side effect of ONCAZIL?			
b. You have been taking medicine for kidney disease. Can you take ONCAZIL?			
e. Based on what you read, is it ok to take Tylenol (acetaminophen) while taking ONCAZIL?			
f. You have just learned you have Hepatitis-C (a disease that affects your liver). Should you take ONCAZIL?			

Q12. Please indicate your level of agreement or disagreement with the following statements. [*randomize*]

	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
a. I am very willing to read the information on this page.					
b. The information on this page is believable					
c. This page is not at all useful in helping me decide to talk with my doctor about ONCAZIL					
d. The risks and negative effects seem reasonable compared with the benefits and positive effects of ONCAZIL					
e. It is very hard to find information on this page.					
f. The benefits and positive effects of ONCAZIL outweigh the risks and negative effects					
g. The side effect section is presented in an easy-to-read format					
h. I could deal with the side effects if I lost weight with ONCAZIL					
i. The format and layout of this page is very clear					
j. I do not like the way the information on the page is presented.					
k. Even losing a lot of weight would not be enough to balance the risks and negative effects from ONCAZIL					
l. I would be unsure relying on the information in this page.					
m. The important information on this page stood out very well.					
n. The way the information was presented on this page was useful.					

Based on your reading of the information on this page, please tell me how confident you are that you could do the following tasks from 0 (no confidence at all) to 10 (complete confidence). [*random start*]

Q13a. Recognize any bad reactions.
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13b. Identify which drugs interact with this one.
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13c. Remember the warnings.
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13d. Know when to stop taking the drug
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13e. Know what condition is treated by this drug
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13f. Tell the difference between a minor side effect and a major reaction.
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13g. Identify who should not take this drug.
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

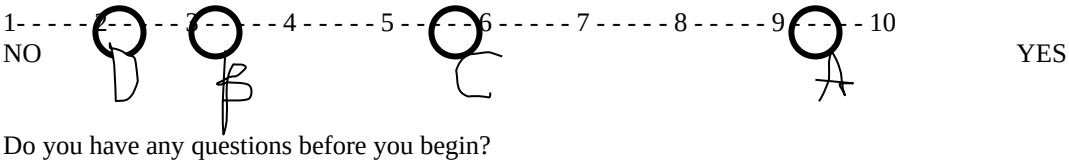
Q13h. Know when you should ask a doctor or health professional about a side effect you might have.
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q13i. Feel confident you can discuss the side effects with your doctor
0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
no confidence complete confidence

Q14. Next you will see four versions of the page you have just rated (*hand out paper copies of all versions*). Please rank the versions by lining them up on the table, starting with the one you prefer most and ending with the one you prefer least. [*Respondent rank orders the four versions. After the respondent has finished ranking, hand respondent a pen.*] Please mark the order of your choices A, B, C, and D. [*Observe respondent marking versions A, B, C and D on the copy.*]

Q15. Now I'm going to ask you a few questions about all the versions. For each question you're going to use the scale on this paper. [*hand out paper answer sheets*] After each question, I'd like you to circle on the line where you think each version should score and write the letter of that version below it.

SAMPLE
The information on this page is too small to read.



Do you have any questions before you begin?

{Either present questions on pre-printed paper RANDOM ORDER or see if ION has touch-screen pen writing capability}

a. I am very willing to read the information on this page.

b. The format and layout of this page is attractive.

c. The format and layout of this page looks easy to read.

d. It is very hard to find information on this page.

e. I do not like the way the information on the page is presented.

f. The important information on this page stood out very well.

Q16) Are you currently taking a **prescription** medicine for weight control?
A) Yes
B) No
C) Don't Know or uncertain

Q17) What is your height? Your best guess is fine.
A) Feet
B) Inches

Q18) What is your weight in pounds? Your best guess is fine.
A) Weight

Q19) Before you started treatment, how severe was your weight condition? Would you describe it as:
A) Very mild
B) Mild
C) Moderate
D) Serious
E) Very serious

Q20) How severe is your weight condition now? Would you describe it as:
A) Very mild
B) Mild
C) Moderate
D) Serious
E) Very serious

Q21. In general, how much do you feel you know about your medical condition? Would you say you know:
A) A lot
B) A good bit
C) Some
D) Only a slight amount
E) Nothing at all

Q22) Have you ever...

had liver damage?	Yes	No	Don't Know
had a heart attack or stroke?	Yes	No	Don't Know
had diabetes?	Yes	No	Don't Know
had the flu recently?	Yes	No	Don't Know

Q23) Have you ever seen any advertising for Oncazil before today?

A) Yes
B) No

INTERVIEWER: Now I'm going to ask you to say some words out loud that sometimes appear on medicines. The list contains some "easy to read" words, and some "hard to read" words, so just do your best to say as many of these words as you can. Remember, almost everyone will have trouble reading many of these words so don't be upset if some words are difficult -- just do your best! If a word is too difficult, just say "blank" and go on to the next word in the list. I want to hear you read as many words as you can from these lists. Speak directly into the microphone. Begin with the first word on this page and read aloud. When you come to a word you cannot read, do the best you can or say "blank" and go on to the next word. Press START when you are ready to begin.

Q24) fat flu pill dose eye stress smear nerves germs measles disease cancer caffeine attack kidney hormones herpes seizure bowel asthma rectal incest
The respondent's response will be digitally recorded in their own words.

Q25) fatigue pelvic jaundice infection exercise behavior prescription notify gallbladder calories depression miscarriage pregnancy arthritis nutrition menopause appendix abnormal syphilis hemorrhoids nausea directed
The respondent's response will be digitally recorded in their own words.

Q26) allergic menstrual testicle colitis emergency medication occupation sexually alcoholism irritation constipation gonorrhea inflammatory diabetes hepatitis antibiotics diagnosis potassium anemia obesity osteoporosis impetigo
The respondent's response will be digitally recorded in their own words.

Q27. Gender (Record by observation; **do not read**)

1 Male 2 Female

[End time: _____]

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

ATTACHMENT 3

Stimuli.

Please see accompanying documents:

For content study:
• Study2 brief summary versions.pdf

For format study:
• Study3 brief summary stimuli.pdf