TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
208.20	25	1	25	320	8,000
208.24(e)	59,000	5,000	295,000,000	0.05	14,750,000
208.26(a)	1	1	1	4	4
314.70 (b)(3)(ii) and 601.12(f)	5	1	5	72	360
Total					14,758,364

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

Dated: November 19, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–28064 Filed 11–25–08; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2008–N–0595]

Agency Information Collection Activities; Proposed Collection; Comment Request; Experimental Study: Toll-Free Number for Consumer Reporting of Drug Product Side Effects in Direct-to-Consumer Television 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 a study examining the impact on consumer comprehension of inclusion of a toll-free number to report side effects in direct-to-consumer (DTC) prescription drug television advertisements.

DATES: Submit written or electronic comments on the collection of information by January 26, 2009.

ADDRESSES: Submit electronic comments on the collection of information to *http://www.regulations.gov*. 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: Elizabeth Berbakos,Office of Information Management (HFA–710), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–796–3792.

SUPPLEMENTARY INFORMATION: 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 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.

Toll-Free Number for Consumer Reporting of Drug Product Side Effects in Direct-to-Consumer Television Advertisements for Prescription Drugs

The Federal Food, Drug, and Cosmetic Act (the act) requires that manufacturers, packers, and distributors (sponsors) who advertise prescription human and animal drugs, including biological products for humans, disclose in advertisements certain information about the advertised product's uses and risks. For prescription drugs and biologics, the act requires advertisements to contain ''information in brief summary relating to side effects, contraindications, and effectiveness'' (21 U.S.C. 352(n)). FDA is responsible for enforcing the act and implementing regulations.

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act (FDAAA) (Public Law 110–85). Title IX of FDAAA amends section 502(n) of the act (21 U.S.C. 352) by requiring printed DTC advertisements for prescription drug products to include the following statement printed in conspicuous text: ''You are encouraged to report negative side effects of prescription drugs to the FDA. Visit *www.fda.gov/medwatch*, or call 1–800–FDA–1088.'' Title IX of FDAAA also requires the Secretary of Health and Human Services (the Secretary), in consultation with the Risk Communication Advisory Committee (RCAC), to conduct a study not later than 6 months after the date of enactment of FDAAA to determine if this statement is appropriate for inclusion in DTC television advertisements for prescription drug products. As part of this study, the Secretary shall consider whether the information in the statement described previously in this paragraph would

detract from the presentation of risk information in a DTC television advertisement. If the Secretary determines that the inclusion of such a statement would be appropriate for television advertisements, FDAAA mandates the issuance of regulations implementing this requirement, and for the regulations to reflect a reasonable length of time for displaying the statement in television advertisements. Finally, FDAAA requires the Secretary to report the study's findings and any subsequent plans to issue regulations to Congress.

In accordance with the requirements of FDAAA, FDA convened a meeting of the RCAC on May 15 and 16, 2008. A draft design for studying this issue was proposed at that time and discussed by the Advisory Committee. Based on comments received at that meeting, changes were made to the proposed study design. The transcripts and materials from that meeting can be found online at *http://www.fda.gov/ohrms/dockets/ac/oc08.html#RCAC*.

Relevant Prior History and Research

Section 17 of the Best Pharmaceuticals for Children Act (the BPCA) (Public Law 107–109, January 4, 2002) required FDA to issue a final rule mandating the addition of a statement to the labeling of each drug product for which an application is approved under section 505 of the act (21 U.S.C. 355). Under the BPCA, the statements must include: (1) A toll-free number maintained by FDA for the purpose of receiving reports of adverse events regarding drugs; and (2) a statement that the number is to be used only for reporting purposes, and it should not be used to seek or obtain medical advice (the side effects statement).

On April 22, 2004, FDA published a proposed rule with a proposed side effects statement for certain prescription drug product labeling and a proposed side effects statement for certain over-the-counter drug product labeling (69 FR 21778). In the proposed rule, FDA solicited comments on a proposed statement that FDA believed comported with the previously mentioned mandate in the BPCA. The agency received 12 comments suggesting changes to the specific wording proposed. The agency also received several comments suggesting that FDA engage in research to study the wording of the proposed side effects statement with consumers. Among the reasons cited for testing the statement were to: (1) Determine the best and most precise wording for the statement, (2) evaluate consumer comprehension of the proposed statement, and (3) address concerns that consumers who read the statement will mistakenly call FDA in search of medical advice rather than seeking appropriate medical treatment. In addition, during the clearance process for the proposed rule, both the Office of Information and Regulatory Affairs of OMB and the Office of the Assistant Secretary for Planning and Evaluation of the Department of Health and Human Services suggested that FDA conduct focus groups or other consumer studies to inform the wording of the side effects statement.

During the spring of 2006, to assist in developing this study, FDA conducted two focus groups to gauge consumer understanding and preferences for a number of proposed side effects statements and to narrow the number of statements to be tested in subsequent experimental research. In addition to the information collected on which versions of the statements participants preferred, discussions showed that people varied in their understanding of when to call FDA or their health care practitioners and that some people would not call FDA even if they experienced a serious side effect. Several people in the focus groups suggested the addition of a Web site to report adverse side effects.

Based on the findings from the focus groups, nine statements were selected for quantitative testing. A labeling comprehension experiment was conducted with 1,674 men and women ranging in age from 21 to 95 with varying levels of education (OMB Control No. 0910–0497). The results from that quantitative test found that only one of the versions tested was rated as significantly less clear than the others, which were all rated as generally clear and understandable. The results also showed that participants reported they would not call FDA seeking medical advice. Further, among those participants who said they would call the FDA, the majority indicated they would call their doctor for medical advice, rather than FDA, regardless of the severity of the side effect. Finally, participants indicated they could distinguish between serious and non-serious side effects, reporting that they would seek emergency medical care in the case of serious side effects. The report of the study is available in the docket for the final rule, Docket No. FDA–2003–N–0313. The final rule, Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products (TFNR) (73 FR 63886, October 28, 2008), is available online at *http://www.fda.gov/OHRMS/DOCKETS/98fr/E8–25670.pdf*.

Proposed Research

This study will examine the placement of the toll-free statement and the length of time the statement is presented on-screen in a DTC television advertisement for a prescription drug. The primary dependent measure of interest is consumer comprehension of the risk information in the advertisement. This study will also examine potential differences in comprehension based on the wording of the toll-free statement and the prominence of the statement.

The application of a new piece of information for viewers of DTC ads presents logistical challenges. From a research perspective, the primary issue under investigation is how to impart additional information without increasing ''cognitive load,'' thus leading to information overload. Cognitive load is an index of the memory demands necessary to process a set of information. As cognitive load increases, more mental resources are necessary to process and understand the information.[1] DTC ads are already quite dense when compared to ads for other products. The risk information in the major statement of the ad should not be compromised by the addition of the toll-free statement. At the same time, it is preferable that the risk information and the toll-free statement information are presented in such a way that both are understandable. We have chosen a set of variables in the current study to investigate issues of cognitive load. They are described briefly in the following paragraphs before examining the details of the research design.

1. Placement

The location of the toll-free statement may facilitate or detract from the risk information in the major statement. We have chosen three locations for this information to test which location results in the greatest communication of the risks of the drug and the concept that side effects can be reported. It is possible that locating the toll-free statement before the major statement provides a ''prime'' for the risk information that follows; that is, the mention of side effects in the toll-free statement will cause consumers to start thinking about side effect-related information, which facilitates comprehension of the risk information that follows. In this case, the two conceptual pieces of information may flow together easily. Conversely, it is possible that locating the toll-free statement here confuses consumers or provides no information for them

[1] Chandler, P. and J. Sweller, ''Cognitive Load Theory and the Format of Instruction.'' *Cognition and Instruction*, 8(4), 293–332, 1991.

because they have not yet heard any risk information. Thus, without context, the statement lacks applicability.

Placing the toll-free statement during the major statement likely reduces the comprehension of the risk information for the drug because it divides viewer's attention between two competing pieces of information. It is possible, however, that the juxtaposition of these two informational concepts are complimentary and therefore do not conflict.

The toll-free statement may serve the best role if it is located after the risk information has been presented. In this case, participants have been told about the risks and side effects of the drug before they are told they may report this information. This essentially primes the toll-free statement with the major statement. We do not expect this placement to interfere with the comprehension of risk information, as it is not present during the voicing of risks and has not been introduced to viewers at this point. The usefulness of the toll-free statement, however, may improve in this condition relative to those discussed above because viewers have been provided with context.

Over time, it is likely that the toll-free statement will become part of the background of the ads as people become accustomed to seeing this statement in all DTC ads. In this respect, people will have the statement as an option if needed but will be able to disregard it to focus on the risk information when desired. Thus, we are testing a condition in which the toll-free statement will be present during the entire ad. This test condition will control for the effect of novelty arising from the fact that consumers have not previously seen this type of statement in TV ads. Presence of the statement during the entire ad may increase noticeability of the toll-free statement initially, but will be unlikely to interfere with risk information in the long run.

2. Statement Wording

The second variable, *statement type*, will have two executions of statement language: The language from FDAAA versus the language used in the TFNR and previously tested by FDA. The wording from these two statements is as follows:

- ''You are encouraged to report negative side effects of prescription drugs to the FDA. Visit *www.fda.gov/medwatch*, or call 1–800–FDA–1088.'' (FDAAA)
- ''Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA–1088 or *www.fda.gov/medwatch.''* (TFNR)

We think it is important to test both the toll-free statement version in FDAAA and the version that we have previously tested with actual consumers. The most obvious reason for this is to make sure that the statement is maximally readable and understandable. It may be valuable, however, to test two statements for another reason.

If the toll-free statement is enacted in broadcast ads, it is possible that because of the boilerplate language, some amount of ''burnout'' will occur. That is, after viewers have seen the same language in multiple ads for multiple products, they may ''tune out'' and not pay attention to the toll-free statement at all. If we test two versions of the statement and find both acceptable, it would be possible to either allow sponsors to choose one statement versus another or to suggest some alternating of the two statements. This is a long-term idea, however, and finding appropriate wording is the primary goal of investigating this variable.

3. Duration

Congress specifically mandates that we investigate the duration of the display of the toll-free statement. As with placement, the length of time the toll-free statement is presented on-screen may influence the cognitive load in the ad. For experimental control, we will look at the duration of the statement while holding placement in the ad (after the major statement of risks) constant. Although this placement should not interfere with the processing of the risk information, it is possible that the duration influences the take away message from the ad. For example, having the statement on for a short amount of time may not give consumers enough time to read and process the message, resulting in lower comprehension of the message but no impact on the comprehension of the risk information. Alternatively, displaying the toll-free statement for a longer period of time may wipe away memory traces of the risks from the major statement, resulting in lower risk comprehension. Whether this longer duration increases the usefulness of the toll-free statement itself is an empirical question. We will compare these short and long durations to instances where the toll-free statement is present during the entire ad and where there is no toll-free statement at all.

4. Prominence

In addition to superimposing the toll-free statement on the screen during the ad, there are other methods available to increase the prominence of the statement. In particular, having the statement read aloud in the ad voiceover while the statement is on the screen may be considered particularly prominent. Does the additional prominence of the statement compromise the comprehension of the risk information in the major statement? If not, does the additional prominence result in a greater understanding of the toll-free statement itself? It is likely that there is a tradeoff between the gains of emphasizing the toll-free statement and the comprehension of the risk information, given the limited cognitive capacity of viewers. In examining this variable, we are exploring the parameters of this tradeoff.

Design Overview

The design will consist of three parts. Part one will be a between-subjects factorial design examining the placement of the toll-free statement by the type of statement. The first variable, placement, will have four levels: (1) Before the major statement of risks, (2) during the major statement of risks, (3) after the major statement of risks, or (4) continuously throughout the whole ad.

In each condition the toll-free statement will appear in the ad as superimposed text at the bottom of the screen. We will also include a control condition in which the statement does not appear.

PART ONE: PLACEMENT BY STATEMENT TYPE

4 x 2 + 1

	Statement Type	
Placement	FDAAA	TFNR
Before major statement of risks		
During major statement of risks		

PART ONE: PLACEMENT BY STATEMENT TYPE—Continued

4 x 2 + 1

	Statement Type	
Placement	FDAAA	TFNR
After major statement of risks		
During the whole ad		

Plus:

Control (no toll-free statement)

Part two of the study will examine four variations in the duration of the toll-free statement using the language from FDAAA: (1) Short (approximately 3 seconds after the major statement), (2) long (approximately 6 seconds after the major statement), (3) during the whole ad, and (4) the control condition of no toll-free statement included. These times were adopted by calculating how long it would take a person reading at an average reading speed to read the statement. As in the first part of this study series, the toll-free statement will appear as superimposed text and a control condition in which the toll-free statement does not appear will be included.

PART TWO: DURATION*

4 x 1

Short (Approximately 3 seconds)
Long (Approximately 6 seconds)
During the whole ad
Control (no toll-free statement)

*Using FDAAA statement

Part three of the study will examine two variations in the prominence of the toll-free statement using the language from FDAAA: Spoken with only the Web site and telephone number in superimposed text; or spoken with the full statement superimposed in text. Both variants in part three will place the toll-free statement after the major statement of risks. There will also be a control condition in which the statement does not appear at all.

PART THREE: PROMINENCE*

3 x 1

Audio Only (spoken after major statement of risks, website and phone number on screen)
Extra Prominent (spoken after major statement of risks, entire toll-free statement on screen)
Control (no toll-free statement)

*Using FDAAA statement

We will investigate these issues in one disease condition, high blood pressure, because high blood pressure has a high incidence rate in the population, is a public health concern, and is likely to occur in both males and females. Further, because there is little promotion for prescription treatment of high blood pressure, participants should be less familiar with DTC television ads for this type of drug, reducing the potential influence of prior experience.

Our primary dependent variable is comprehension of the risk information mentioned in the major statement. In addition to this variable, we will also examine comprehension of benefit information. We will also examine the noticeability and comprehension of the toll-free statement.

Procedure

Participants will see an advertising pod of four ads: Two non-DTC ads (fillers), a DTC ad for a fictitious high blood pressure medication, and a DTC ad for an unrelated medical condition with the same toll-free statement included. We include two DTC ads with the toll-free statement in our protocol because this better approximates what will happen if this statement is required to be implemented in DTC TV ads. That

is, viewers will see the statement in all DTC ads for all products. In this study, we want to avoid the suggestion that there is something particular about the high blood pressure drug class that causes the statement to be mandated. Thus, we will show multiple DTC ads but ask questions regarding only the ad which has been manipulated to test our hypotheses. To maximize response information, the test ad will always be the last ad participants see.

After viewing the ads, a structured interview will be conducted. Participants will answer questions about the high blood pressure DTC test ad they have seen. Questions will examine a number of important perceptions about the advertised product, including risk comprehension, risk recall, benefit comprehension, benefit recall, behavioral intention, noticeability of the toll-free statement, and comprehension of the toll-free statement.

Finally, demographic and health care utilization information will be collected. The entire procedure is expected to last approximately 15 minutes. A total of 1,600 interviews will be completed. This will be a one-time (rather than annual) information collection.

Participants

Data will be collected using an Internet protocol. Consumers over the age of 18 will be screened and recruited by the contractor to represent a range of education levels. Because the task presumes basic reading abilities, all selected participants must speak English as their primary language.

FDA proposes to conduct 2 rounds of pretesting with 200 consumers in each round to refine the questionnaire and the stimuli before fielding the main study.

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

FDA estimates that 2,400 individuals will need to be screened to obtain a respondent sample of 400 for the pretests and 1,600 for the study. The screener is expected to take 30 seconds, for a total screener burden of 20 hours. The ad viewing and questionnaire are expected to take 15 minutes for the participants in the pretest and the main study, for a cumulative study burden of 500 hours. The estimated total burden for this data collection effort is 520 hours. The respondent burden is provided in table 1 of this document:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
2,400 (screener)	1	2,400	.008	20
400 (pretest)	1	400	.25	100
1,600 (study)	1	1,600	.25	400
Total				520

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

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA only through FDMS at *http://www.regulations.gov*.

Dated: November 19, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2008–D–0597]

Draft Guidance for Industry: Small Entities Compliance Guide for Renderers—Substances Prohibited From Use in Animal Food or Feed; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry #195, entitled ''Draft Guidance for Industry: Small Entities Compliance Guide for Renderers—Substances Prohibited From Use in Animal Food or Feed.'' This small entities compliance guide aids renderers in complying with the requirements of the final rule published in the **Federal Register** of April 25, 2008 (73 FR 22720). FDA's goal is to strengthen existing safeguards to prevent the spread of bovine spongiform encephalopathy (BSE) in U.S. cattle and to reduce the risk of human exposure to the BSE agent.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit written or electronic comments on the draft guidance by January 26, 2009.

ADDRESSES: Submit written requests for single copies of the guidance to the Communications Staff (HFV–12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.regulations.gov*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Shannon Jordre, Division of Compliance, Center for Veterinary Medicine (HFV–230), Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–276–9229, *Shannon.jordre@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry #195, entitled ''Draft Guidance for Industry: Small Entities Compliance Guide for Renderers—Substances Prohibited From Use in Animal Food or Feed.'' In the **Federal Register** of April 25, 2008 (73 FR 22720), FDA published a final rule entitled ''Substances Prohibited From Use in Animal Food or Feed.'' This