

B. Statistical Methods (used for collection of information employing statistical methods)

1. Respondent Universe and Sampling Methods

Recruiting and screening procedures will be similar for the two pretests and two main studies. We will recruit adult participants with rheumatoid arthritis or overactive bladder. We will exclude individuals who are trained as healthcare professionals, or who work in pharmaceutical, advertising, or marketing settings or at HHS because their knowledge and experiences may not reflect those of the typical consumer. We will also apply exclusion criteria related to eye tracking, including: excluding individuals who have photosensitive epilepsy, cataracts, amblyopia (lazy eye/blind in one eye), strabismus (cross-eyed), mydriasis (permanent pupil dilation), nystagmus (involuntary eye movements), an ocular prosthesis (glass eye), or who are designated as legally blind; use a medical device that is sensitive to infrared light; or wear bifocals, hard contact lenses, or colored contact lenses (see Screener in Appendix A). For the pretests, participants will be recruited from the metropolitan Washington DC area. The sessions will be conducted at Westat's main office in Rockville, MD. The participants for the main studies will be recruited across five testing locations. These locations include Chicago, IL, Tampa, FL, Phoenix, AZ, Houston, TX, and Marlton, NJ.

In order to recruit the needed participants for the pretests and main studies, we plan to primarily use the two following methods:

1. Recruit participants through local health care providers who specialize in treating rheumatoid arthritis or overactive bladder; and
2. Recruit participants by networking with local or online support groups for individuals who have rheumatoid arthritis or overactive bladder.

Since the conditions are of low prevalence in the population, these methods are our best avenues to reach a reasonable number of study candidates within the project schedule. If these methods described above do not immediately yield enough response, we will (1) contact a recruiting vendor to assist in filling out the pool of potential participants, (2) advertise the criteria for participation in local newspapers, and/or (3) post a Craigslist ad for the specific problematic testing location.

2. Procedures for the Collection of Information

Design Overview

Part A of the supporting statement described the rationale for conducting the project. We propose to test two levels of the ISI (short versus long) and the presence of a consumer brief summary (absent versus present) in two different medical conditions (overactive bladder (OAB) and rheumatoid arthritis). The consumer brief summary will follow the draft recommendations for language, readability, content, and format described in "Brief Summary and Adequate Directions for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs:

Guidance for Industry, Revised Draft Guidance" . The "long" ISI is a selection of risks from the brief summary and is typical of what would appear in current DTC ads for each condition. The "short" ISI was created by applying the ideas from recent FDA work on the major statement in broadcast ads. Figures 1 and 2 describe the study design. This will be investigated in DTC print ads for prescription drugs.

Our research questions are descriptive in nature, not explanatory. For example, we are not asking *why* DTC advertising influences reader understanding of risks or benefits of prescription drugs or why certain DTC advertising features influence readers' behaviors and perceptions. Rather, we are primarily asking where and how questions, such as: *Where* do readers look when they are exposed to DTC print advertising and how is this affected by the length of the ad? *How* did exposure to DTC advertising impact the participants' reaction to the drug and how do reactions differ by the length of the ad? Accordingly, we plan to investigate the following:

- Compare participants' attention (measured by both self-report and eye tracking data), risk information retention, and drug risk perceptions after they read DTC drug ads that vary these conditions:
 - The length of the ISI section (which includes repetition of information presented), and
 - The presence or absence of the brief summary page.
- Assess whether attention mediates the relationship between ad design and participants' retention and perceptions of information about the drug's risks.
- Compare additional outcomes -- such as perceived drug efficacy, behavioral intentions, and self-efficacy in understanding the materials -- among the ad conditions.
- Assess the possible effects of moderators (such as personal involvement with the drug) and covariates (such as health literacy and age) on attention, risk retention, and risk perception.

To address these questions, we have two 2x2 designs, one for each medical condition. Both designs vary length of ISI and presence of the Brief Summary as between-subjects factors. Participants will be randomly assigned to view one DTC print ad.

Figure 1: Study 1 Design

Rheumatoid Arthritis	ISI	Brief Summary	
		No	Yes
	Short		
	Long		

Figure 2: Study 2 Design

Overactive Bladder	ISI	Brief Summary	
		No	Yes
	Short		
	Long		

Analysis Plan

During descriptive analysis, we will compute fixation data for each participant while they view a drug ad. By comparing fixation data across participants and ad designs, we aim to describe how the presence and absence of ad features affect attention to the ad overall. In addition to reporting descriptive statistics on fixation outcomes, fixation data may also be used to categorize respondents into low, medium and high levels of attention for the purposes of cross-tabulation.

Heatmaps will be used as a visual tool for analyzing data across multiple participants. Heatmaps provide summaries of the number of fixations and time spent fixating in specific areas for each participant and across participants. For our purposes, we anticipate creating heatmaps to show where participants fixate the most as a measure of the attention they pay to ad elements. We will use them to display the distribution of fixations and fixation durations over the ads and for specific Areas of Interest (AOI) defined within the ads.

Gazeplots are also useful primarily for understanding the sequence of gaze fixation for single individuals; they also indicate how long each fixation lasts. We plan to use gazeplot sequence as an indicator of how participants process the ad and its components. We will examine these to identify general patterns across participants and how those relate to ad type and questionnaire measures.

Frequency distributions will be calculated for our survey questions. We will test hypothesized relationships by conducting chi-square tests and logistic regressions for categorical outcomes and t-tests and ANOVAs for continuous outcomes.

We will define a set of planned contrasts to address specific research questions and hypotheses, conducting these planned comparisons based on hypothesized relationships or post-hoc comparisons to identify significant differences between specific experimental groups. To adjust for multiple comparisons, we will apply a post-hoc family-wise error-rate adjustment, such as a Bonferroni correction. If assumptions are violated for the ANOVA or categorical models mentioned above, nonparametric tests will be employed, such as the Kruskal-Wallis for independent samples or Welch's ANOVA.

Power

We conducted *a priori* power analyses to ensure we obtained a sufficient sample to detect statistically significant differences in the outcome measures of interest across the different experimental conditions. The pretest, assuming the need for power of .80, alpha probability of .05, and a medium effect size ($f = .25$), will require a sample of 40 participants. For the main studies, given the experimental design and assuming a power of .90, alpha of .05, and medium effect size ($f = .25$), we propose obtaining a sample of 200 participants for each study (total $N = 400$).

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

Both the pretest and main studies will be administered in person, with responses recorded electronically. We plan to recruit using \$50 incentives, which are below market-rate (typically \$100 for a 60-minute study). To help ensure that the participation rate is as high as possible, FDA and the contractor will:

- Design a protocol that minimizes burden (reasonable in length, clearly written, and with appealing graphics);
- Send a confirmation email automatically to each participant with details about the study, appointment time/length, contact details, and directions to the test location once an appointment has been scheduled;
- Call to remind each participant of the appointment and to answer any questions or concerns that he or she may have regarding the study a short time before the actual test date;
- Offer some session time slots outside of “regular” business hours, to accommodate attendance for those whose work schedules limit their availability; and
- Provide participants with a call-in number for a study representative, so that if an event occurs that interferes with their scheduled session time, they can call to reschedule.

Participants in the pretest and main studies will be convenience samples, rather than probability-based samples of U.S. adults. The strength of the experimental design used in this study lies in its internal validity, on which meaningful estimates of differences across manipulated conditions can be produced and generalized. This is a counterpoint to observational survey methodologies where estimating population parameters is the primary focus of statistical analysis. The recruitment procedures in this study are not intended to fit the criteria for survey sampling, where each unit in the sampling frame has an equal probability of being selected to participate.

4. Test of Procedures or Methods to be Undertaken

Nine cognitive interviews were conducted per questionnaire to assess questionnaire flow and wording. We plan to conduct one pretest on a larger scale to ensure the main studies will run smoothly.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

The contractor, Westat, Inc., will collect and analyze the data on behalf of FDA as a task order under Contract HHSF223201510001B. Jennifer Crafts, Ph.D., 301-610-4881, is the Project Director for this project. Data analysis will be overseen by the Research Team, Office of Prescription Drug Promotion (OPDP), Office of Medical Policy (OMP), CDER, FDA, and coordinated by Kathryn J. Aikin, Ph.D., 301-796-0569, and Helen W. Sullivan, Ph.D., M.P.H., 301-796-4188.