B. Statistical Methods

1. Respondent Universe and Sampling Methods

The eligible study population is U.S., non-institutionalized adults age 18 and older who have a seasonal allergies diagnosis. The survey sample will be drawn from the databases of two recruitment firms, Shugoll Research (Bethesda, MD) and L&E Research (Raleigh, NC). Shugoll Research maintains a database consisting of over 100,000 residents in the Washington, D.C. area, including suburban Maryland and northern Virginia. L&E Research maintains a database of approximately 57,602 residents in the Raleigh, North Carolina area. The sample will be drawn from members who report having seasonal allergies and will be approximately evenly divided between men and women. It will not be nationally representative of the entire population. This is due to the study design, not a limitation of the sampling frame.

Shugoll Research and L&E Research will generate a list of potential participants based on the study inclusion and exclusion criteria and screen these individuals over the phone. Should insufficient members be available to create a sample of adequate size, the recruitment firms will obtain additional samples by expanding recruitment efforts to include cold calling, networking, referrals, and a variety of social media outlets that include Facebook, Twitter, and LinkedIn.

The current sample design and sample sizes are:

Category	**Number of participants**
Pre-test (2 waves)	210
Main Study	600

2. Procedures for Collection of Information

The main study will be preceded by up to two pretests designed to delineate the procedures and measures used in the main study. Across pretests and the main study, participants will be individuals who have been diagnosed with seasonal allergies. All participants will be 18 years of age or older. We will exclude individuals who work in healthcare or marketing settings because their knowledge and experiences may not reflect those of the average consumer. Participants will be recruited in one of two geographic locations (Washington, D.C. and Raleigh, North Carolina) for in-person administration of protocols. Participants will be invited to come to a 90-minute data collection session.

The experimental design is summarized in Table 1. Participants will be randomly assigned to view a prescription drug ad one, two, or four times as part of clutter reels embedded in 42 minutes of TV programming, for a total of one hour of TV viewing. Clutter reels will not include any other ads for medications, DTC or OTC. In order to ensure sufficient time for potential forgetting of the ad, the final airing of the stimulus ad will occur within the last clutter reel with 1-2 ads following it. We will then show the final few minutes of the television program before the survey questions begin.

Table 1: Study Design

Experimental Arm No.	**Episode #1**			**Episode #2**		
	Clutter Reel 1	**Clutter Reel 2**	**Clutter Reel 3**	**Clutter Reel 4**	**Clutter Reel 5**	**Clutter Reel 6**
1 (views ad 1 time)						Mock DTC ad
2 (views ad 2 times)			Mock DTC ad			Mock DTC ad

3 (views ad 4 times)	Mock DTC ad		Mock DTC ad	Mock DTC ad		Mock DTC ad

After viewing the ad, participants will respond to questions about information in the ad. Measures are designed to assess perception, memory, judgments about the ad, intentions to use the medication advertised, and possible moderators of effects, such as need for cognition and demographics. The questionnaire is available upon request.

Analysis Plan

Our primary research question for the study is whether increasing ad exposure frequency will result in different risk or benefit perceptions than less exposure to the ad. We will also investigate other questions such as whether behavioral intentions, recall or attitudes toward the drug are affected by increased ad exposure. Other exploratory analyses will be conducted as well.

We will conduct ANOVAs (for continuous variables) and chi-squares and logistic regressions (for categorical variables) to examine the impact of increased ad exposure on the outcomes. Before conducting analyses, we will assess whether the inclusion of covariates is justified. If they are, we will conduct the analyses both with and without covariates (e.g., sex, age, race/ethnicity, education) included in the model. If the interaction effect (age x ad exposure frequency) is significant, we will conduct pairwise-comparisons to determine which conditions are significantly different from one another. The primary planned comparison will use a p-value of .05, and the exploratory post-hoc comparison will use Bonferroni-adjusted *p*-values.

Power

For the pretest, power analysis suggests that to have 90% power to detect medium size effects between the three experimental conditions (alpha=0.017; set to adjust for multiple comparisons), we will need to include 105 participants in each of the two pretests. For the same

reason stated above, we will need to overestimate, for the purpose of estimating burden for IRB and OMB packages. For those purposes we estimate 125 total participants in each pretest. We propose conducting the pretests with a smaller sample size than the main study, as we will not plan to test for interaction effects during this phase. The objective is not hypothesis testing but rather to confirm that the entire survey process runs smoothly and that the stimulus will be effective for the study design. The sample size is large enough to thoroughly pretest the stimuli and data collection process.

For the main study, our power analysis suggests a sample size of 200 in each experimental group will allow for the required 90% power (alpha=.017) to test the main effect of exposure on a single dependent variable as well as the joint effect of at least one moderator, such as need for cognition. More specifically, we could detect an effect size of about 0.45 (assuming means across experimental groups ranged from 3.3 to 3.9 with SDs around 1.5 on a 5-point interval scale item) at 90% power. (We assume the use of an interval dependent measure and a single main effect in this study to reduce the total sample needed in light of the need to collect data in person.

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

Response rates can vary greatly depending on many factors including the sample composition, invitation content, time of day and incentive offering. We will calculate response rate as the ratio of the number of surveys completed to the number of screened and eligible participants contacted by invitation. To help ensure that the participation rate is as high as possible, FDA and the contractor will:

- Offer multiple dates and times for data collection so participants can select one based on their availability;

- Provide an incentive of $100 for the 90 minute data collection period, to compensate participants for their time.
- Provide laptops for participants to view the stimulus and complete the questionnaire, allowing respondents to answer questions at their own pace.

4. Test of Procedures or Methods to be Undertaken

Two types of pretesting (qualitative and quantitative) are employed as a test of procedures and methods.[1] The first type of pretesting is qualitative. Cognitive testing has been conducted with a small sample of individuals to refine study questions. Additionally, we intend to conduct up to two rounds of quantitative pretesting. Pretests will be used to refine the design of the experimental stimuli to ensure the validity of the manipulations. These pretests will explore logistical plans for the main study, such as the use of 10 or 15-person data collection sessions. The main study design will not change as a result of the pretests, nor will the results of the pretests increase the burden on respondents in the main study. The pretests are designed to ensure the particulars of the main study are implemented in the best way possible.

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

The contractor, RTI International, will collect and analyze data on behalf of FDA as a task order under Contract HHSF223201310558G. Bridget Kelly, Ph.D., MPH, is the Project Director, 202-728-2098. Review of contractor deliverables and supplemental analyses will be provided by the Research Team, Office of Prescription Drug Promotion (OPDP), Office of Medical Policy, CDER, FDA, and coordinated by Kevin R. Betts, Ph.D., WO BLDG 51, RM 3220, (240) 402-5090, and Kathryn J. Aikin, Ph.D., WO BLDG 51, RM 3240, (301) 796-1200.

1 Pretesting is suggested by OMB as a method to test procedures. See Office of Management and Budget *Standards and Guidelines for Statistical Surveys* (September, 2006). Available at http://www.whitehouse.gov/sites/default/files/omb/assets/omb/inforeg/statpolicy/standards_stat_surveys.pdf. Last accessed January 12, 2012.