UNITED STATES FOOD & DRUG ADMINISTRATION

Accelerated Approval Disclosures on

Direct-to-Consumer Prescription Drug Websites

OMB Control No. 0910-NEW

SUPPORTING STATEMENT **Part B – Statistical Methods:**

1. Respondent Universe and Sampling Methods

   For all phases of this research, we will recruit adult volunteers 18 years of age or older who self-report as cancer survivors or cancer caregivers. For additional screening materials, see the "Participants" section below.

   The samples for the pretests and main studies will be drawn from Kantar's internet panel. Kantar will recruit study participants from its LifePoints consumer panel of more than 5.5 million consumers and from their partner panels by sending invitations to the online study (Appendix D). Kantar's LifePoints panel is composed of people who made a decision to participate in online surveys through a double opt-in registration process. Several methodologies are used by Kantar to recruit panelists to the LifePoints panel, including opt-in email, co-registration, e-newsletter campaigns, as well as both internal and external affiliate networks. Kantar measures recruitment sources on multiple metrics to track both activity and engagement by demographic group, which contributes to the quality of data from panelists. The sample is not intended to be representative of the population.

2. Procedures for the Collection of Information

Design Overview

In Study 1, we will vary the presence, wording (language based on physician-labeling vs. consumer-friendly language), and prominence of the accelerated approval disclosure (e.g., varying the presence, size, color, and location of the disclosure) on a website for a fictitious prescription drug (Table 1). In Study 2, we will use the high-prominence consumer-friendly language disclosure from Study 1 to investigate the content of the disclosure, varying whether information about the unknown outcomes is present and whether information about confirmatory trials is present (Table 2). We have chosen to focus on oncology products because cancer is a life-threatening illness, and many oncology products are granted accelerated approval. Moreover, DTC promotion of oncology drugs is common.

Table 1.--Study 1 Design

	High prominence	Low prominence	Absent
Physician-labeling version	Condition 1	Condition 3	Condition 5
Consumer-friendly version	Condition 2	Condition 4	

Table 2.--Study 2 Design

	Consumer-friendly disclosure elements			
	Approval basis	Approval basis + unknown outcomes	Approval basis + confirmatory trials	Approval basis + unknown outcomes + confirmatory trials
High prominence	Condition 6	Condition 7	Condition 8	Study 1 Condition 2

Procedure

We plan to conduct two pretests (one for each main study) and two main studies not longer than 20 minutes, administered via internet panel. Participants will be randomly assigned to view one version of a website for a fictional oncology prescription drug and then complete a questionnaire (Appendix C) that assesses whether participants noticed the disclosure and their understanding of it, as well as perceptions of the drug's risks and benefits. We will also measure covariates such as demographics and literacy.

Participants

We plan to conduct two pretests (N=100 for Pretest 1 and N=80 for Pretest 2) and two main studies (N=630 in Study 1; N=400 in Study 2). For the pretests and main studies, we plan to recruit two groups: 1) half who are US adults who report a diagnosis with any cancer (except for certain non-melanoma skin cancers) who are not currently undergoing treatment and 2) half who are US adults who report being a caregiver for someone with a diagnosis with any cancer (except for certain non-melanoma skin cancers). We will exclude individuals who work for the U.S. Department of Health and Human Services or work in the health care, marketing, advertising, or pharmaceutical industries. We will also exclude pretest participants from the main studies, and participants will not be able to participate in both Studies 1 and 2. See Appendix B for the study screener.

Hypotheses

For Study 1, we hypothesize that participants will be more likely to notice the disclosure when it is presented more, rather than less, prominently. In turn, we expect that participants' perceptions of the drug are more likely to be affected by the disclosure in the high prominence condition. We also hypothesize that participants will be more likely to notice and understand the disclosure and use it to form their perceptions of the drug if they view the consumer-friendly language. For Study 2, we hypothesize that participants will be more likely to understand each accelerated approval concept (i.e., confirmatory trials, unknown outcomes) when the disclosure directly addresses the concept, compared with when the disclosure does not directly address the concept. Finally, we will explore whether the inclusion of the concepts of confirmatory trials and unknown outcomes in the disclosure affects participants' perceived risk, perceived risk-benefit tradeoff, perceptions of the website, or information-seeking intentions. To test these hypotheses, we will conduct inferential statistical tests such as logistic regression and analysis of variance.

Analysis Plan

We will conduct ANOVAs (for continuous variables) and logistic regressions (for dichotomous variables) with interaction terms and planned comparisons to test the hypotheses outlined above.

Power

We conducted power analyses for each main study, taking into consideration the study's purpose, expected outcome measures, and potential key analyses. Both studies have been powered to detect a small effect size (no smaller than Cohen's f =.15), with a power of .90 and an alpha of .05. Given the achieved effect sizes of previous FDA studies that manipulated aspects of the direct-to-consumer prescription drug websites, we propose an effect size of f =.16, resulting in a total sample size of 630 in Study 1 (with 126 participants per experimental group) and 400 for Study 2 for each study (with 100 participants per experimental group). If a significant main effect is found in Study 1, we will also be able to conduct four planned contrasts using a Bonferroni-adjusted threshold of .0125 with enough sensitivity to detect small to moderate effects. These sample sizes are consistent with Cohen's (1988) definition of small effect size (e.g., f between .10 and .24).

Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Erlbaum.

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

The pretests and main studies will use an existing research panel to draw a sample. The panel comprises individuals who have signed up to participate in online studies. To help ensure that the participation rate is as high as possible, FDA will:

- Design an experimental protocol that minimizes burden (short in length, clearly written, and with appealing graphics);
- Administer the pretests and main studies over the Internet, allowing respondents to answer questions at a time and location of their choosing.

4. Test of Procedures or Methods to be Undertaken

   We will conduct nine hour-long qualitative interviews to cognitively test the study stimuli and materials. For each main study, we will conduct a pretest to test the experimental manipulations and pilot the main study procedures. Finally, we will run each main study as described elsewhere in this document.

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

   The contractor, RTI International, will collect the data on behalf of FDA as a task order under Contract HHSF223201510002B. Mihaela Johnson, 919-990-8365, is the contractor's Project Director for this project. Data analysis will be overseen by the Research Team, Office of Prescription Drug Promotion (OPDP), Office of Medical Policy, CDER, FDA, and coordinated by Helen W. Sullivan, Ph.D., MPH, 301-796-4188, and Amie O'Donoghue, Ph.D., 301-796-1200.