

United States Food and Drug Administration

Study of Disclosures to Health Care Providers Regarding Data that Do Not Support Unapproved

Use of an Approved Prescription Drug

OMB Control No. 0910-NEW

SUPPORTING STATEMENT

Part B. Statistical Methods

1. Respondent Universe and Sampling Methods

For all phases of this research, physician participants will be drawn from an internet panel (Sermo). Sermo is an online panel provider with a national network of practicing physicians from which they draw research respondents, representing diverse specialties, demographics and geographic locations. They have over 60,000 primary care physicians (PCPs) and 5,000 oncologists on their panel. The profile of Sermo's US physician members closely mirrors that of the all U.S. physicians. Sermo validates all panel members and membership is voluntary. Panel members are invited to participate in research by receiving an e-mail invitation (Appendix C) and, if interested, can click on a hyperlink within the e-mail and gain access to the study. All participants in the study will be practicing physicians. For details on screening, see the "Participants" section below. The sample for the current study is not intended to be representative of the physician population.

2. Procedures for the Collection of Information

Design Overview

The purpose of this research is to examine physicians' perceptions and behavioral intentions about an unapproved new use of an approved prescription drug when made aware of other data that are not supportive of the unapproved use. This research will also evaluate the effectiveness of various disclosure approaches for communicating the unsupportive information. Five approaches will be examined: (1) the provision of the unsupportive data in the form of a representative publication; (2) a disclosure that summarizes, rather than provides the unsupportive data and including a citation to the representative publication; (3) a disclosure that does not provide or include a summary of the unsupportive data, but does acknowledge that unsupportive data exist and includes a citation to the representative publication; (4) a general disclosure that that does not provide or include a summary of the unsupportive data, but acknowledges unsupportive data *may* exist, without conceding that such data do exist; or (5) nothing-- the absence of any presentation of unsupportive data or any disclosure about such data (control condition).

Procedure

We plan to conduct two pretests and two main studies not longer than 20 minutes. Physician participants (oncologists, PCPs) will be randomly assigned to one of five experimental conditions (Figure 1) and view one version of a brief study report and then complete a questionnaire (Appendix B) that assesses recall and perceptions of the disclosure, the drug, attitudes, and behavioral intentions. We will also measure covariates such as provider demographics, practice characteristics.

Figure 1: Experimental Study Design

	Accompanied by representative publication with unsupportive data	Accompanied by disclosure with summary of unsupportive data and including a citation for that data.	Accompanied by disclosure that unsupportive data exist and including a citation for that data, but without a summary of the unsupportive data	Accompanied by general disclosure that unsupportive data <i>may</i> exist and no citation	No disclosure or material about unsupportive data
Medical Condition 1 (cancer)					
Medical Condition 2 (insomnia)					

Participants

For all phases of this research, we will recruit adult volunteers 18 years of age or older who are physicians from an Internet panel. For the Pretest and Medical Condition 1, we will recruit board-certified oncologists who report spending at least fifty percent of their time on patient care; and write fifty or more prescriptions per week (N = 30 in the Pretest and N = 510 in Medical Condition 1 study). For the Pretest and Medical Condition 2, we will recruit board-certified family medicine, internal medicine, or general practitioner physicians (primary care physicians, or PCPs) who report spending at least fifty percent of their time on patient care; and write fifty or more prescriptions per week (N = 150 in the Pretest and N = 1,090 in Medical Condition 2 study). We will exclude individuals who work for the Department of Health and Human Services, market research, 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 C for the study screener.

Research Questions

We have four research questions.

RQ1: When considering a presentation of data about an unapproved use of an approved drug product, how does the existence of unsupportive data impact physician perceptions and intentions with regard to that unapproved use?

RQ2: How does the way in which the existence of unsupportive data is communicated, when the specific data is not presented, impact physician perceptions and intentions with regard to an unapproved use of an approved drug product?

RQ3: How are physician perceptions of and intentions toward an unapproved use of an approved drug product affected by the disclosure of specific unsupportive data versus disclosure statements about the unsupportive data or the existence of such data?

RQ4: Do other variables (e.g., provider demographics, practice characteristics) impact physician perceptions of and intentions toward an unapproved use?

Analysis Plan

We will conduct ANOVAs (for continuous variables) and logistic regressions (for dichotomous variables) with interaction terms and planned comparisons to address research questions outlined above.

Power

A power analysis was calculated separately for each medical condition for the main study, with an objective to detect effect sizes between $f = 0.15$ to $f = .20$ (see Cohen, 1988)¹ across the five conditions, with a significance level of 0.05 and power of 0.90 or higher. Our estimates for power are based on the assumption that the variance is as large as possible for proportions and that the sample size is sufficiently large so that the point estimates are approximately normal. At 218 PCP participants per cell, the power is 0.99 for Medical Condition 2. At the same time, we understand that oncologists are a difficult group to recruit. Thus, we have reduced our sample size for Medical Condition 1. At 102 oncologist participants per cell, the power is 0.95.

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

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

¹Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Erlbaum.

- 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 have conducted nine hour-long qualitative interviews to cognitively test the study stimuli and materials. Based on those interviews, we made changes to the questionnaire and study stimuli. 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, Westat Inc., will collect the data on behalf of FDA as a task order under Contract HHSF223201510001B. Simani Price, Ph.D., 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 and Kathryn Aikin, Ph.D., 301-796-1200 and Amie O'Donoghue, Ph.D., 301-796-1200.