

United States Food and Drug Administration

Examination of Secondary Claim Disclosures and Biosimilar Disclosures

in Prescription Drug Promotional Materials

OMB Control No. 0910-NEW

SUPPORTING STATEMENT

Part B. Statistical Methods

1. Respondent Universe and Sampling Methods

For all phases of this research, participants will be drawn from consumer and healthcare internet research panels (Dynata). Dynata's opt-in online consumer panel is demographically balanced, including racial and ethnic minorities, a wide range of age groups, and individuals with relatively less educational attainment. Dynata recruits panel members through a combination of e-mail, online marketing, and by invitation, with over 300 online and offline affiliate partners and targeted website advertising. Panel inclusion is by invitation only, and Dynata invites only pre-validated individuals with known characteristics to participate in the consumer panels.

Health care providers (HCPs) will be recruited through Dynata's Healthcare Panel which uses a multimode approach that combines e-mail, fax, and direct mail to recruit HCPs to participate in online surveys. Additionally, Dynata purchases professional association and governmental databases to verify a HCP's practicing status. These verification resources include the Drug Enforcement Agency number (DEA#) and the American Medical Association Medical Education Number (ME#).

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 build on prior FDA research on the topic of disclosures through two concurrent studies. As described in Part A, Phase 1 will test the influence of three variations of a disclosure statement about a secondary endpoint in the context of a prescription drug website and the presence or absence of a comparative claim about the secondary claim. The test language for Phase 1 is described in Table 1. This design will be replicated for both the HCPs and consumer samples.

Table 1: Phase 1 test language

	Secondary Claim Disclosure 1	Secondary Claim Disclosure 2	Secondary Claim Disclosure 3	Control (No Disclosure)
Comparative Claim Present	“Even though DRUG X is not made for weight loss, it could also help some people lose some weight. In a clinical trial, patients lost more weight with DRUG X compared to DRUG Y.”	”DRUG X could also help some people lose some weight. In a clinical trial, adults with an average starting weight of 197 pounds lost around 12 pounds on DRUG X compared to 4 pounds on DRUG Y.”	“Even though DRUG X is not made for weight loss, it could also help some people lose some weight. In a clinical trial, adults with an average starting weight of 197 pounds lost around 12 pounds on DRUG X compared to 4 pounds on DRUG Y.”	“Drug X could also help some people lose some weight.”
Comparative Claim Absent	“Even though DRUG X is not made for weight loss, it could also help some people lose some weight.”	”DRUG X could also help some people lose some weight. In a clinical trial, adults with an average starting weight of 197 pounds lost around 12 pounds on DRUG X.”	“Even though DRUG X is not made for weight loss, it could also help some people lose some weight. In a clinical trial, adults with an average starting weight of 197 pounds lost around 12 pounds on DRUG X.”	“Drug X could also help some people lose some weight.”

Phase 2 will test the influence of disclosures specifying the product as a biosimilar. Specifically, the study will test: (1) adding a disclosure designating the product as a biosimilar; (2) adding informational statements about biosimilars; and (3) naming a reference product. As a baseline, each of the seven disclosure conditions will include a statement that the drug is a biosimilar. Six of the seven disclosure conditions will include this baseline statement and will vary the amount of additional basic factual information about biosimilar products in the following way: (1) two of the six conditions have the baseline + statement A; (2), two of the six conditions have the baseline + statement A + statement B; and (3) two of the six conditions have the baseline + statement A + statement B + statement C. Moreover, three of the six disclosure conditions will name the

specific reference product while the other three will refer to a reference product generally. The wording of the disclosure will be tailored to the audience; for example, the disclosures for the consumer audience will avoid technical terms. A control condition will also be included in which no biosimilar statement or additional information disclosure is presented. This 8x1 experimental design will be replicated for both the HCPs and consumers samples, with slightly different disclosure language for the HCP and consumer groups. The test language for Phase 2 is described in Table 2.

Table 2: Phase 2 test language

Biosimilar s Disclosure	HCPs	Consumers
1	None	None
2	DRUG Z is a biosimilar.	DRUG Z is a biosimilar.
3	DRUG Z is a biosimilar. This biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.	DRUG Z is a biosimilar. This biosimilar is a safe and effective medication and provides the same treatment benefits as an FDA-approved original biologic.
4	DRUG Z is a biosimilar. This biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from DRUG Q, an existing FDA-approved reference product.	DRUG Z is a biosimilar. This biosimilar is a safe and effective medication and provides the same treatment benefits as DRUG Q, an FDA-approved original biologic.
5	DRUG Z is a biosimilar. This biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. Biosimilars are made from the same types of sources as the FDA-approved reference product.	DRUG Z is a biosimilar. This biosimilar is a safe and effective medication and provides the same treatment benefits as an FDA-approved original biologic. Biosimilars are made from the same types of sources as the FDA-approved original biologic.
6	DRUG Z is a biosimilar. This biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from DRUG Q, an existing FDA-approved reference product. This biosimilar is made from the same types of sources as DRUG Q.	DRUG Z is a biosimilar. This biosimilar is a safe and effective medication and provides the same treatment benefits as DRUG Q, an FDA-approved original biologic. This biosimilar is made from the same types of sources as DRUG Q.
7	DRUG Z is a biosimilar. This biosimilar is a biological product that	DRUG Z is a biosimilar. This biosimilar is a safe and effective

	is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. Biosimilars are made from the same types of sources as the FDA-approved reference product. DRUG Z has the same route of administration, dosage form, and strength as an existing FDA-approved reference product.	medication and provides the same treatment benefits as an FDA-approved original biologic. Biosimilars are made from the same types of sources as the FDA-approved original biologic. DRUG Z is given the same way and has the same strength and dosage as the FDA-approved original biologic.
8	DRUG Z is a biosimilar. This biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from DRUG Q, an existing FDA-approved reference product. This biosimilar is made from the same types of sources as DRUG Q. DRUG Z has the same route of administration, dosage form, and strength as DRUG Q.	DRUG Z is a biosimilar. This biosimilar is a safe and effective medication and provides the same treatment benefits as DRUG Q, an FDA-approved original biologic. This biosimilar is made from the same types of sources as DRUG Q. DRUG Z is given the same way and has the same strength and dosage as DRUG Q.

Procedure

Both study phases will include one pretest and one main study not longer than 20 minutes. Surveys will be administered online. The phases will be conducted concurrently and independently of one another. Potential respondents will participate in only one study phase. In each phase, consumer and HCP participants will be randomly assigned to one experimental condition, view one version of the stimuli, 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 demographics and practice characteristics for potential use as covariates.

Participants

We will recruit participants from Dynata's internet opt-in consumer panel of U.S. adult consumers 18 years of age and older and Healthcare Panel of HCP volunteers. For Phase 1, we plan to conduct one pretest with 252 voluntary adult participants (126 HCPs and 126 general population consumers) and one main study with 900 voluntary adult participants (450 HCPs and 450 general population consumers). For Phase 2, we plan to conduct one pretest with 432 voluntary adult participants (216 HCPs and 216 general population consumers) and one main study with 720 voluntary adult participants (360 HCPs and 360 general population consumers). Sample sizes were determined on the basis of power analysis that will allow us to detect medium effect sizes. Our power analysis is described in below.

In both phases we will seek to recruit a consumer sample of 20% with a high school diploma or less to ensure diversity among educational groups. HCP participants will be physicians, physician assistants and nurse practitioners who engage in patient care at least 50% of the time. We will aim to include a mix of demographic segments to ensure a diversity of viewpoints and backgrounds.

Participants who work for a pharmaceutical company, marketing firm, or the Department of Health and Human Services, or have participated in recent (within the last three months) focus groups will be excluded. Consumer participants who identify as HCPs will also be excluded from the consumer sample. We will also exclude pretest participants from the main studies, and participants will not be able to participate in both Phases 1 and 2. See Appendix C for the study screener.

Research Questions

Phase1 Research Questions:

RQ1a: Does type of secondary claim disclosure affect consumer or HCP outcomes (i.e., recall/recognition of drug benefit, recall/recognition of drug risk, comprehension, perceptions of drug: benefit, risk, efficacy; attitudes toward the drug, and behavioral intentions)?

RQ1b: What factors (e.g., attribution, trust, health literacy, experience with drug) moderate the relationship between secondary claim disclosure and consumer or HCP outcomes?

RQ2a: Does presence of a comparative statement in the disclosure affect consumer or HCP outcomes (i.e., recall/recognition of drug benefit, recall/recognition of drug risk, comprehension, perceptions of drug: benefit, risk, efficacy; attitudes toward the drug, and behavioral intentions)?

RQ2b: What factors (e.g., attribution, trust, health literacy, experience with drug) moderate the relationship between comparative statement in the disclosure and consumer or HCP outcomes?

RQ3: Is there an interaction effect between secondary claim disclosure and comparative statement on consumer and HCP outcomes?

Phase 2 Research Questions:

RQ1a: Does identification of the drug as a biosimilar affect consumer or HCP outcomes (comprehension, perceptions of drug: benefit, risk, efficacy; attitudes toward the drug, and behavioral intentions)?

RQ1b: What factors (e.g., attribution, trust, health literacy, experience with drug, familiarity with or prescribe biosimilars, disease experience) moderate the relationship between biosimilar identification and consumer or HCP outcomes?

RQ2a: Does biosimilar definition affect consumer or HCP outcomes (comprehension, perceptions of drug: benefit, risk, efficacy; attitudes toward the drug, and behavioral intentions)?

RQ2b: What factors (e.g., attribution, trust, health literacy, experience with drug, familiarity with or prescribe biosimilars, disease experience) moderate the relationship between biosimilar definition and consumer or HCP outcomes?

RQ3a: Does naming the reference product in the biosimilar disclosure affect consumer or HCP outcomes (comprehension, perceptions of drug: benefit, risk, efficacy; attitudes toward the drug, and behavioral intentions)?

RQ3b: What factors (e.g., attribution, trust, health literacy, experience with drug, familiarity with or prescribe biosimilars, disease experience) moderate the relationship between naming the reference product in the biosimilar disclosure and consumer or HCP outcomes?

RQ4: Which biosimilars disclosure is preferred for consumers and HCPs?

Analysis Plan

We will conduct ANCOVAs (for continuous variables), logistic regressions (for categorical variables) with interaction terms, and planned comparisons to address the research questions outlined above. To conserve sample in Phase 1 and thus reduce the burden needed to recruit extra participants, we plan combine the control conditions and analyze the design as a 3x2+1.

Power

A power analysis was conducted separately for each phase with an objective to detect effect sizes between $f = 0.15$ to $f = .20$ (see Cohen, 1988)¹ with a significance level of 0.05 and power of 0.90 or higher, taking into consideration the purpose, expected outcome measures, and potential key analyses. The Phase 1 main study includes 450 consumers and 450 HCPs respectively. Given this sample size, we are able to detect moderately small effects for the two factors. Specifically, assuming an alpha of 0.05 and a power level of 0.90, we would be able to detect an effect size of $f = 0.21$ for the main effect of the secondary claim disclosure and an effect size of $f = 0.17$ for the main effect of the comparative claim on proposed continuous outcomes. We would also be able to

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

detect an effect size of $f=.19$ for the interaction effect between the two factors. When comparing the control condition with each of the secondary claim disclosure conditions, we would be able to detect an effect of $f = .22$, assuming an alpha of 0.0167 (adjusted for three pairwise comparisons) and a power level of 0.90. When comparing the control condition with each of the comparative claim conditions, we would be able to detect an effect of $f = .24$, assuming an alpha of 0.025 (adjusted for two pairwise comparisons) and a power level of 0.90. These effect sizes are also consistent with Cohen's (1988) definition of small effect size (e.g., f between .10 and .24; .25 is considered a moderate effect size).

The Phase 2 main study includes 360 consumers and 360 HCPs. With this sample size, and assuming power level of 0.90, we would be able to detect an overall effect size $f=.19$ based on a p-value of .05 and an effect $f=.24$ assuming a Bonferroni adjusted p-value of 0.0018 based on 28 pairwise comparisons (.05/28 pairwise comparisons = .00178).

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

The study will use an 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:

- 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 pretesting to test the experimental manipulations and pilot the main study procedures in each phase. Finally, we will run each phase 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. Jessica DeFrank, 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.