FDA DOCUMENTATION FOR THE GENERIC CLEARANCE OF REQUEST FOR DATA TO SUPPORT SOCIAL AND BEHAVIORAL RESEARCH (0910-0847)

TITLE OF INFORMATION COLLECTION:

Collection of Data to Support "Risk Evaluation and Mitigation Strategy (REMS) Programs to Promote Appropriate Medication Use and Knowledge: Physician Experiences with REMS Programs"

DESCRIPTION OF THIS SPECIFIC COLLECTION

1. **Statement of need:**

The Food and Drug Administration (FDA) has limited data to determine the impact of Risk Evaluation and Mitigation Strategy (REMS) programs. REMS is a drug safety program that FDA can require for certain medications with serious safety concerns to help ensure that the benefits of the medication outweigh its risks. REMS may include one or more of the following such as: (1) A Medication Guide or Patient Package Insert for patients; (2) a Communication Plan for healthcare providers; and (3) Elements to Assure Safe Use (ETASU), which often involve some form of restricted distribution or evidence of safe-use conditions.[1] REMS programs focus on preventing, monitoring, and/or managing a specific serious risk by informing, educating, and/or reinforcing actions to mitigate the frequency and/or severity of an adverse event.

FDA has contracted with Brigham and Women's Hospital affiliated with Harvard Medical School to conduct the REMS Programs to Promote Appropriate Medication Use and Knowledge. They will conduct the study to better understand how REMS programs have operated in practice and to use this information to develop actionable steps for improvement. Specifically, this study seeks to answer: (1) to what degree the terms of REMS programs have been followed; (2) how REMS programs have impacted drug utilization, health outcomes, and physician experiences; and (3) how effectively REMS programs translate important risk-benefit information to physicians. One task to meet these study objectives entails physician surveys about physician experiences with select REMS programs. In addition to this physician survey, we will submit collection of information pertaining to physician interviews for clearance. We have already submitted an information collection request for patient REMS program experiences pertaining to another aspect of the overall study, which OMB has already cleared.

2. **Intended use of information:**

The contractor will analyze the data collected from participants to assess physician experiences with enrolling in REMS programs and complying with REMS program requirements as well as physician knowledge of REMS program rationales and structures. By leveraging interdisciplinary expertise, the results of the findings will be used to better understand real-world experiences with the REMS programs. This information will be

[1]FDA website: Risk Evaluation and Mitigation Strategies, Accessed on Oct. 25, 2021

included with other analyses to recommend actionable steps to support and improve the REMS programs.

3. **Description of respondents:**

The contractor will conduct six surveys, one each for physicians with experience prescribing the following REMS-covered drugs: ambrisentan, bosentan, clozapine, isotretinoin, lenalidomide/pomalidomide/thalidomide (treated as one group), and sodium oxybate. Invited physicians will be randomly selected from a vendor-supplied national sample of prescribers of the drugs over the past year. A total of 200 respondents will be sought for each survey.

4. **Date(s) to be conducted:**

The sponsor will conduct the physician surveys between 1/1/2022 and 12/31/2022 and conduct the full study between 1/1/2022 and 6/30/2023.

5. **How the information is being collected:**

The contractor will send up to four mailings to randomly selected physicians who meet the inclusion criteria and allow survey completion via paper, with an enclosed postage-paid return envelope, or online. The surveys will comprise fewer than 40 questions and take approximately 20 minutes to complete. The contractor will then code the survey data, stripping it of individual identifiers. All participants in the study are expected to benefit from improved risk communication content and strategies of the REMS program.

6. **Confidentiality of respondents:**

The contractor will record personal details of each participant (i.e., name and address) solely for the purpose of collecting initial screening information and providing payment. Once the testing is initiated, the contractor will use a numbering system to protect the identity of each participant and to remove the link between personal details and test data.

At no stage during the recruitment process will the recruiters seek to gain access to any medical records for any participant. The study team will keep personal details and will not circulate them to any third party.

All study personnel interacting with human subjects as part of this research will have completed training on the protection of human subjects.

The contractor will present each participant with a consent form explaining the purpose of the study, what participation entails, the availability of a small gift card as a token of appreciation, the right not to participate, and contact information for the principal investigator and institutional review board. Consent will be presumed based on participation. (See Fact Sheet/Consent Forms).

7. **Amount and justification for any proposed incentive:**

To motivate participation, the contractor will provide prospective participants $20 in the initial mailing and will offer an $80 Amazon gift card to participants who complete a survey as a token of appreciation. The size of the token of appreciation reflects industry best practices and resembles tokens of appreciation for similar type of studies the contractor conducted in past years. Historically, physicians have been one of the most difficult populations to survey, primarily due to busy and often uncertain schedules. Setting appropriate monetary incentives in studies involving physicians is key to ensure a sufficient sample size and minimize the risk of selection bias.

A study that randomly assigned physicians to four compensation groups for a survey—no incentive, $200 lottery, $50 incentive, and $100 incentive—found that response rates were highest in the $100 incentive group at 25.4% (Dykema et al., 2011). Furthermore, they found a meaningful difference in the response rates of the $100 and $50 incentive groups (25.4% v. 15.4%). Past OMB-approved studies have used monetary incentives of varying amounts as a token of appreciation to physicians who complete surveys. For example, in the study "FDA Survey of Physicians' Perceptions of the Impact of Early Risk Communication about Medical Products" (OMB 0910-0615) the standard token was $75 for a telephone survey that included both PCPs and specialists. In another study, titled "Survey of Health Care Practitioners for Device Labeling Format and Content," (OMB 0190-0790), the token of appreciation for physicians was $200.

Because the survey in this project will be distributed to specialist physicians, the contractor would like to offer a $100 token of appreciation. Furthermore, the cohort of drugs that this drug focuses on are prescribed by a smaller number of physicians due to their indications and the REMS certification process required. As a result, the contractor is already planning intensive recruiting cycles to ensure that they obtain the number of interviewees needed. This is better aided by a slightly higher monetary incentive. The contractor also would like to standardize physician payments across the multiple components of this project, one of which calls for physician interviews. The contractor is offering a $100 incentive for the interviews, and the token of appreciation for the surveys matches this amount.

8. **Questions of a sensitive nature:**

We do not expect any questions that would be sensitive in nature. Participants will be allowed to abstain from answering if they are uncomfortable with any questions. Additionally, participants will be notified at the beginning of the study session that they are welcome to end the session at any time for any reason.

9. **Description of statistical methods:**

As noted above, we aim to have at least 200 respondents per survey, anticipating a 50% participation rate. Answers to questions about subjective perceptions of REMS programs and their implementation will be scored on Likert scales. Open-ended questions will provide physicians the opportunity to elaborate on their individual experiences with REMS programs, and multiple-choice questions will be used to assess objective knowledge. At the end of the survey, we will ask demographic questions.

Descriptive statistical analyses will be performed to compare key characteristics of responding physicians to non-responding physicians—including sex, specialty, and ZIP code —and for answers to Likert scale, multiple-choice, and open-field questions grouped into constructed categories. We will explore relations among the covariates through regression analyses. The primary dependent variables will relate to questions about perceptions or knowledge. The independent variables will include demographic data, including the sex, race, ethnicity, specialty, practice setting, and experience of the respondent physician.

BURDEN HOUR COMPUTATION:

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
Survey Respondents	1,200 respondents	20 minutes	400 hours

REQUESTED APPROVAL DATE: November 2021

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