FDA DOCUMENTATION FOR THE GENERIC CLEARANCE,
"TESTING COMMUNICATIONS ON DRUGS PRODUCTS"
(0910-0695)

TITLE OF INFORMATION COLLECTION: Studies to Enhance FDA Communications Addressing Opioids and Other Potentially Addictive Pain Medications

DESCRIPTION OF THIS SPECIFIC COLLECTION

1. Statement of Need:

Opioids are important medications that are widely prescribed for pain. Opioid drugs provide significant pain-relieving benefit for patients when used as directed for their approved indications; however, opioids also carry serious risks. The Food and Drug Administration (FDA) has been actively working to find ways to mitigate the serious risks associated with using opioids, including misuse and abuse, while continuing to ensure that patients in pain have appropriate access to these products that can improve the quality of their lives.

Combating opioid misuse, abuse, and addiction has long been a priority for the Agency. For more than a decade, FDA has worked to pursue a targeted, science-based, multipronged approach that addresses misuse, abuse, and addiction at critical points in the development of an opioid product and in its use throughout the healthcare system.

In addition to the extensive scientific analysis and review of opioids, FDA has focused on efforts to raise awareness and educate the public and healthcare professionals (HCPs) about these drugs and their inherent risks, engaging in public communications and outreach through multiple avenues, such as public meetings, public announcements, discussions with experts, and targeted public outreach. The Agency is committed to ongoing efforts to help enhance the safe and appropriate use of opioids and supports a variety of regulatory, educational, communication, and scientific activities aimed at achieving this goal, both on its own and in collaboration with other agencies and stakeholders.

To fulfill its public health mission, FDA's Center for Drug Evaluation and Research (CDER) Office of Communications (OCOMM) is undertaking research needed to better understand current knowledge, practice, beliefs, behaviors, and perceptions about opioid use, misuse, and abuse among several key stakeholder audiences. To collect the information needed, we are proposing to collect data about these topics through online surveys.

2. Intended Use of Information:

These surveys will be used to collect needed information on a variety of opioid-related issues and topics, including those related to knowledge, attitudes, behaviors and experiences, and training and education. This data will be analyzed, and the results will be used in conjunction with findings from other elements of this project to inform FDA's efforts to most efficiently and effectively educate and communicate about opioids and their safe and appropriate use to various stakeholder audiences, including HCPs and consumers.

3. Description of Respondents:

Two online surveys will be conducted: one of consumers and the other of HCPs who prescribe opioids, each of which is described below. All respondents will be adults aged 18 or older. The questionnaires do not include any sensitive questions, and the questions are designed to be as straightforward as possible for respondents to understand and respond to. The two surveys contain similar question topics; however, the consumer survey was developed to meet a significantly lower literacy level than the HCP survey (Flesch-Kincaid reading level is 9.6).

Consumer Survey

We will conduct an online survey with a target of 1,000 respondents aged 18 or older: 800 general population respondents and 200 chronic opioid users. For the purpose of this survey, a chronic opioid user will be defined as someone who uses opioids daily or most days for the past 3 (or more) months to treat noncancer pain. Respondents who report using opioids but do not meet this definition will be a subset of the general population category (called ever opioid users). On average, the survey will take 15 minutes to complete.

GfK (formerly Knowledge Networks), a market research company, will recruit consumers for this survey. GfK's core capability is the national online panel known as KnowledgePanel (KP). KP is a nationally represented panel consisting of about 55,000 adult members (aged 18 or older). Unlike opt-in panels, individuals can become panelists only after being randomly selected. GfK uses address-based sampling (ABS) for its panel recruitment. Since 2009, recruiting has been conducted entirely with the U.S. Postal Service's Delivery Sequence File, which covers 97% of U.S. households including households that

- have unlisted telephone numbers,
- do not have landline telephones,
- are cell phone only,
- do not have current Internet access (households without Internet access are provided a laptop computer and free Internet service), and
- do not have devices to access the Internet.

Under this recruitment procedure, randomly sampled addresses are invited to join KP through a series of mailings and, in some cases, telephone follow-up calls to non-responders when a telephone number can be matched to the sampled address. Operationally, households invited to participate in KP have the option to join the panel one of several ways: (1) completing and returning a paper form in a postage-paid envelope, (2) calling a toll-free hotline maintained by GfK, or (3) going to a dedicated website and completing an online recruitment form. Once these recruitment procedures are completed, invited respondents become empaneled and are available to begin participating in specific online surveys. All KP panelists complete their surveys online. Only persons sampled through these probability-based techniques are eligible to participate on KP.

GfK's KP recruitment methodology uses the same or similar quality standards as mandated by the Office of Management and Budget in the "List of Standards for Statistical Surveys," which indicates that "Agencies must develop a survey design, including selecting samples using

generally accepted statistical methods (e.g., probabilistic methods that can provide estimates of sampling error)."All consumers for this survey will be part of GfK's KP. When enrolling in KP, respondents complete a background questionnaire that provides information on demographics and other variables of interest. GfK will identify panel members that may be eligible for this study based on our screening criteria (e.g., consumers aged 18 or older; a mix of age, gender, and region). To ensure that we have sufficient representation of opioid users, we will oversample those with chronic conditions that may indicate opioid use.

Potentially eligible consumers will be identified using background questionnaires that they submitted to GfK. A random selection of these consumers will receive an email invitation to the survey (see attached document titled "Email Invitations." Those who are interested in volunteering to complete the survey will click on a link that will take them to introductory information about the study and screening questions to determine eligibility (see attached document titled "Introduction and Screening Questions"). Participants who qualify will be taken to a new screen that shows the informed consent (see attached document titled "Informed Consent"). The informed consent includes information on the risks and benefits of participation, their rights as study participants and other required information. Respondents will be asked to click "yes" or "no" to indicate their decision to participate. Those who click "yes" will be taken to the first screen of the survey that contains brief instructions followed by the full set of survey questions (see attached document titled "Consumer Survey"); those who click "no" will not be able to access the survey.

Note that with online surveys, several respondents may be in the process of completing the survey at the time that the total target sample is reached, and those participants will be allowed to complete the survey. This can result in the number of completes going slightly over the target number. With this in mind, we rounded up the burden hours by 5% over our target number of 1,000 completes to allow for some overage, and based the estimated burden hours in the table below on a sample size of 1,050 respondents.

Healthcare provider (HCP) Survey

We will conduct an online survey to be completed by 300 HCPs who prescribe opioids. This total will include 150 family practice, internal medicine, and other primary care providers (PCPs), including nurse practitioners and physician assistants. We will also include 150 providers consisting of a mix of specialties such as surgeons, emergency room doctors, pain medicine specialists, and dentists, which will also include nurse practitioners and physician assistants in these specialties. All HCPs will have prescribed opioids to at least five patients over the past month. In addition, at least 30 providers (10% of the total) will include those who write at least 10% of their opioid prescriptions for extended release and long-acting (ER/LA) opioids. On average, the survey will take 20 minutes to complete.

The sample for HCPs will be drawn from GfK's national panel of HCPs, the Physicians Consulting Network (PCN). Starting with the American Medical Association Master List, GfK has recruited more than 140,000 respondents to PCN to respond to surveys on a wide variety of health issues that only HCPs can address. The panel can support studies on a variety of general and specialty areas and issues and can be weighted to the national total of physicians using the AMA Master List as the benchmark.

GfK will identify panel members who may be eligible for this study in advance. Potentially eligible HCPs will be identified using background questionnaires they submitted when they joined the PCN. Identified HCPs will receive an email invitation to the survey (see attached document titled "Email Invitations"). If interested in participating, they will click on a link that will take them to introductory information about the study and screening questions to determine eligibility (see attached document titled "Introduction and Screening Questions"). Participants who qualify will be taken to a new screen that shows the informed consent (see attached document titled "Informed Consent"). The informed consent includes information on the risks and benefits of participation, their rights as a study participant, and other required information. Respondents will be asked to click "yes" or "no" to indicate their decision to participate. Those who click "yes" will be taken to the first screen of the survey that contains brief instructions followed by the full set of survey questions (see attached document titled "Healthcare Provider Survey"); those who click "no" will not be able to access the survey.

As with the consumer survey, we will allow for an overage to account for cases where respondents may be completing the survey at the time the target sample is reached, resulting in a sample size of 315, as shown in the burden hours table below.

4. Date(s) to be Conducted:

The opioids-related topic of this survey is a priority for the FDA Commissioner, and we hope to begin collecting data as soon as possible. As a result, invitations for participation will be sent to potential respondents as soon as possible after approvals are received from the Office of Management and Budget (OMB), FDA Research Involving Human Subjects Committee (RIHSC), and the contractor's (RTI) external IRB. It is expected to take 3 to 4 weeks to collect the data from these two populations.

5. How the Information is being Collected:

To ensure data quality, RTI and FDA will test the two survey questionnaires in the online platform before sending them to respondents. This testing will verify that skip patterns in the questions are functioning properly, all survey questions are worded correctly and appear on the screen properly, and the data collection processes flow smoothly.

Randomly selected Individuals will receive an email notification that the survey is available for completion (see attached document titled "Email Invitations"). Those who do not respond to the initial invitation will receive the same email invitation a second time. Additional individuals will be identified and invited to participate on a rolling basis as needed in order to meet our designated sample sizes. The surveys will be self-administered and accessible 24 hours a day for a designated period of time, which is expected to be 3 to 4 weeks. Respondents will be able to complete the survey in more than one sitting if desired as long as the survey remains active. Respondents will be able to complete the survey only once.

As noted above, respondents who choose to initiate the survey process will click on a link that takes them to an introduction and screening questions (see attached document titled "Introduction and Screening Questions"). Participants who qualify will be taken to a new screen that shows the informed consent (see attached document titled "Informed Consent").

Respondents will be asked to click "yes" or "no" to indicate their decision to participate. Those who click "yes" will be taken to the survey. Respondents will complete the survey online and will enter responses in a secure web interface hosted by GfK's secure servers. Secure storage of the data is described below under section 5: Confidentiality of Respondents.

GfK will provide RTI with a completely de-identified data file, which will be stored on RTI's secure servers accessible through password-protected computers. Once the survey has been completed, GfK will provide RTI with the raw data via secure FTP site or electronically via password-encrypted files. However, no identifying information will be included on the data provided to RTI. After the project closes, GfK will archive only the survey data in their secure central processing data center. All study participants will be informed as part of the written consent that no reports or other information will identify participants by name, that all information will be anonymized and reported in aggregate, and that their information will be kept private to the extent possible (see next section for additional information).

Upon receiving the data from GfK, RTI will then clean and process the raw de-identified survey data and will electronically send FDA password-encrypted SPSS and SAS datasets, again with no identifying information included.

6. Confidentiality of Respondents:

We will provide all respondents with an assurance of privacy to the extent allowable by law and will inform them as part of the written consent process that no reports or other information will identify participants by name, that all information will be anonymized and reported in aggregate, and that their personal information will be kept private to the greatest possible extent. When surveys are assigned to KP and PCN panel members, they are notified in their password-protected email accounts that a survey is available for completion.

The KP and PCN recruitment and empanelment process is designed to comply with the law that sets out rules for commercial email and the guidelines of the Council of American Survey Research Organizations. Furthermore, KP and PCN policies conform to participant treatment protocols outlined by OMB. Survey responses are confidential; personally identifying information is never revealed to clients or other external parties without explicit respondent approval and a client-signed nondisclosure agreement. All KP and PCN panel members are given a link to access the privacy terms electronically at all times via the Panel Member website and also are able to review it at any time on the Members Page and in links contained in survey invitations. The Privacy and Terms of Use Policy for GfK panel members is posted at http://www.knpanel.com/participate/privacy2.html. The PCN member page is located at https://www.askpcn.com.

To ensure data security, all RTI and GfK project staff will be required to adhere to strict standards and to sign nondisclosure agreements as a condition to work on this project Completed web questionnaires will be stored on password-protected computer drives at GfK. Survey responses are written in real-time directly to GfK's server and are then stored in a local Oracle database. The database is protected primarily through firewall restrictions, password protection, and 128-bit encryption technology. Individual identifying information will be maintained separately from completed questionnaires and from computerized data files used for analysis.

GfK has developed a secure transmission and collection protocol, including the use of system passwords, encryptions, and firewalls to prevent unauthorized access to the data collection system. Individual identifying information will be maintained separately from completed questionnaires and from computerized data files used for analysis. Individual identifying information is stored only to allow GfK to provide incentives to survey respondents, and no respondent identifiers will be contained in data provided to RTI and to FDA or in any reports or other documents.

Once transferred to RTI, the data and information will be kept in a secured fashion that will not permit unauthorized access. All data will be de-identified prior to receipt at RTI. Electronic files will be stored on RTI's password-protected server, and only the RTI project team members will have access to the files and only upon approval by the RTI project director. The data will be kept on RTI's secure servers for up to 3 years. The privacy of the information submitted is protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)) and by part 20 of the agency's regulations (21 CFR part 20). These methods have been approved by FDA's Institutional Review Board (RIHSC). We will obtain approval of these processes before collecting any data. Similarly, once transferred to FDA, all electronic files will be stored on FDA's password-protected server. It is expected that FDA will keep these files for future data analyses for 5 years.

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' (HHS's) ADP Systems Security Policy as described in the HHS ADP Systems Manual, Part 6, chapters 6-30 and 6-35. All data will also be maintained in consistency with the FDA Privacy Act System of Records #09-10-0009 (Special Studies and Surveys on FDA Regulated Products).

7. Amount and Justification for Any Proposed Incentive:

The incentives are intended to recognize the time burden placed on respondents, encourage their cooperation, and convey appreciation for contributing to this important study, and they are similar to incentives offered for most surveys among respondents in each respective respondent group. Numerous empirical studies have shown that incentives can significantly increase response rates (e.g., Abreu & Winters, 1999; Shettle & Mooney, 1999, Greenbaum, 2000).

Incentives help ensure that sufficient numbers of respondents can be recruited to participate in the data collection. Furthermore, without the incentive as an inducement, it is likely that more people would need to be screened to achieve the desired cooperation rate, thus increasing the burden hours and the cost to the government and U.S. taxpayers. The use of modest incentives is expected to enhance survey response rates without biasing responses. If we are unable to recruit sufficient numbers of respondents to participate in the data collection, the quality of the data will be compromised. GfK has set incentive rates it provides to their panel members, which are described below for each of the two survey respondent groups.

Consumer Survey

GfK typically provides two different types of respondent incentives for KP members: (1) periodic incentives based on the number of surveys completed and (2) survey-specific incentives. Periodic incentives are used to maintain a high degree of panel loyalty and prevent attrition. For households without existing Internet access, GfK provides as an incentive computer hardware and Internet service. For households with Internet service, GfK enrolls panelists in a points program that is analogous to a "frequent flyer" card, and panelists are credited with points based on the number of surveys completed. Panelists receive cash-equivalent checks for these points every 4 to 6 months, typically amounting to $1 to $6 per month. For this survey, respondents will receive 1,000 points for completing the survey, which is the equivalent of $1.00. This incentive is not based on federal guidelines for incentives but rather on GfK policy.

HCP Survey

HCPs who complete the survey will receive each receive $57.50. The incentive will be paid by check, which will be mailed to participants after they complete the survey. This is the fixed, standard amount required as payment for PCN panel members who complete a 20-minute survey.

8. Questions of a Sensitive Nature:

These surveys contain no questions generally to be considered of a sensitive nature; however, one of the topics of this project relates to prescription opioid misuse, abuse, and addiction, which may be unpleasant to some respondents. As part of the written consent, all respondents will be informed they can refuse to answer any question without penalty and doing so will not affect their ability to complete the rest of the survey or the incentive they would receive. To gain a broad understanding of people's knowledge, beliefs, and behaviors related to opioids, the opioid epidemic, and FDA's role in helping to prevent it, the survey will ask consumers questions about their knowledge about, experiences with, and attitudes toward prescription opioids; communication with providers about these medicines; and concerns they may have about misuse and abuse (see attached document titled "Consumer Survey"). In addition to these question topics, HCPs will be asked about their prescribing practices and experiences, and thoughts on education and training (see attached document titled "Healthcare Provider Survey").

9. Description of Statistical Methods:

Data will be analyzed in aggregate. Initially, a contractor (RTI) will conduct initial descriptive statistical analyses (frequencies and cross-tabulations) by major subgroups (consumers versus chronic opioid users and type of HCP –ER/LA versus non-ER/LA providers). The data results will largely be presented in a series of tables (e.g., the percent of respondents who answer knowledge questions correctly, the percent who agree versus disagree to opinion questions, and the percent distribution to the other survey questions) supported by narrative. Weighted survey data will be available for the analysis. Using the raw data it receives from RTI, FDA will do additional higher-level statistical analyses (e.g., regression, ANOVA, ANCOVA) in the future.

BURDEN HOUR COMPUTATION *(Number of responses (X) estimated response or participation time in minutes (/60) = annual burden hours)*:

NOTE: The online survey platform provider, GfK, has preliminarily determined the 2 surveys are about the length proposed (an average of 20 minutes for the HCP and 15 minutes for the consumer survey); however, GfK will conduct timing tests of each before the surveys are fielded. In addition, FDA will conduct some informal internal time testing to ensure that the final questionnaires do not exceed these average times noted in the burden table below by removing questions if needed.

OVERALL TOTAL BURDEN HOURS (see below tables for time specifics associated with each survey)

Consumer Survey Total Hours	352.5
HCP Survey Total Hours	392
Total Consumer + HCP Burden Hours	744.5

Consumer Survey

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
Consumer screener	1,800	3	90
Consumer survey	1,050	15	262.5
Total hours			352.5

HCP Survey

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
HCP screener	4,300	4	287
HCP survey	315	20	105
Total hours			392

REQUESTED APPROVAL DATE: October 27, 2017, or sooner if possible.

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References

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