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. FDA has been actively working to find ways to mitigate the serious risks associated with the use of 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.

FDA plays a critical role in the development, review, and approval of drugs. FDA reviews applications for opioid medical products, requires accurate drug prescribing information, and monitors how these products are used once they go to market—and a balance must be struck between their benefit in treating patients and the risks associated with misuse, abuse, and addiction to those patients and to others.

Combating opioid misuse, abuse, and addiction has long been a priority for the Agency. Over the last decade or so, FDA has worked to pursue a targeted, science-based, multi-pronged approach that addresses misuse, abuse, and addiction at critical points in the development of an opioid product and in its use throughout the health care system. This comprehensive approach includes five broad areas:

- Encouraging scientific work into the development of safe and effective treatments for pain and into the most appropriate uses of pain medicines;
- Encouraging the development of abuse-deterrent drug formulations for opioids;
- Working to improve the appropriate use of opioids to treat pain through prescriber and patient education;
- Evaluating opioid labeling, and
- Improving the availability of products that treat abuse and overdose.

In addition to extensive scientific analysis, FDA has focused on efforts to raise awareness and educate the public and health care professionals about opioids and their inherent safety 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.

2. **Intended use of information:**

FDA has determined further research is needed in order to better understand how to most efficiently and effectively focus resources to educate and communicate about opioids and their safe and appropriate use to various stakeholder audiences.

As a result, this project is designed to provide FDA's Center for Drug Evaluation and Research (CDER) with a better understanding of current knowledge, practice, beliefs, behaviors, and perceptions about opioid use, misuse, and abuse among several key stakeholder audiences, including health care professionals, patients, and other members of the lay public. Gaining this knowledge will assist in more appropriately directed and focused communication efforts aimed at raising awareness and educating the public.

3. **Description of respondents:**

We will conduct 30, 60-minute individual telephone interviews with healthcare providers, including: primary care physicians (e.g., internal medicine doctors and family doctors); advanced practice practitioners in primary care, surgery or pain management (e.g., nurse practitioners and physician's assistants); pain medicine providers and surgeons.

We will also conduct 6 online focus groups via webinar with a total of up to 60 adult members of the general public aged 18 or older. There will be a minimum of 9 participants in each online group. There will be 2 groups each of a) general population consumers, b) people currently using prescribed opioids for treatment of chronic pain, and c) family and/or friends of people using prescribed opioid treatment for chronic pain.

To recruit participants that are well suited for this research project, we have retained the services of two research companies, itracks and Quintiles Healthcare Engagement & Communications, with proven expertise and experience in recruiting the types of participants we are seeking.

1. *itracks*: We will work with itracks (https://www.itracks.com/) for recruitment of healthcare professionals, family/friends of people currently using prescribed opioids for treatment of chronic pain , and general population focus group participants. itracks is a well-established research organization that has created software tools for online and mobile market research since 1996. In addition to hosting online focus groups, they recruit participants for research studies, working with different healthcare provider panels and consumer panels. Individuals volunteer to be added to these panels through itracks' recruitment campaigns via email and online marketing channels with hundreds of diverse online affiliate partners and targeted websites. The itracks project team has recruited and conducted medical and health-related focus groups and interviews across the US on a variety of topics including a study to obtain feedback on a new opioid compound with 330 physicians and patients who use opioids for chronic pain. In addition to assisting with recruitment, itracks will provide the online webinar platform through which the focus groups will be conducted.

To facilitate recruitment efforts and ensure that we include participants who meet our study criteria, we have developed a Healthcare Provider Screening Questionnaire (a copy of which is included separately in the submission package and also contains the text for all email and telephone follow-up contacts for OMB review). This screener includes questions to ensure

that we obtain healthcare providers that meet study needs. To qualify for study participation, providers must be a primary care provider, advanced practice practitioner, surgeon, or pain medicine provider; practice at least 32 hours a week, and regularly prescribe opioids. For PCPs and advanced practice practitioners regularly prescribing opioids is defined as prescribing opioids at least twice in the past 30 days. For surgeons and pain medicine providers, regularly prescribing opioids is defined as prescribing opioids at least once in the past 7 days. We will also seek diversity among participants in gender, race/ethnicity, age, geographic region of residence, those living in rural, urban and suburban areas, number of years in practice (with a minimum of 2 years), and type of practice (e.g., solo, small group practice, large group practice, and whether the practice is part of an academic or healthcare system). Individuals will be disqualified from participation if they have ever worked for the Department of Health and Human Services, FDA, a pharmaceutical company, itracks, or RTI, International.

2. *Quintiles Healthcare Engagement & Communications*: We will also work with Quintiles Healthcare Engagement & Communications for the recruitment of people currently using prescribed opioids for treatment of chronic pain. Quintiles Healthcare Engagement & Communications routinely reaches out to the nearly 3 million members of its patient communities and the broader digital patient universe in support of protocol feasibility, patient recruitment, and observational research programs. With respect to pain management via opioid therapy, Quintiles Healthcare Engagement & Communications has conducted six patient outreach initiatives over the past five years and can identify and target over 30,000 US-based patients taking opioid medications. They will draw from this pool of patients who have expressed a willingness to volunteer to participate in research studies in order to provide pre-screened referrals for the online focus groups.

Participants for the consumer focus groups will be recruited using a two-step process. First, to identify people currently using prescribed opioids for treatment of chronic pain, Quintiles Healthcare Engagement & Communications will send an email to individuals in their system who have indicated that they are willing to participate in research studies and have voluntarily indicated that they are using an opioid medication. The email will explain the study and will include two screening questions to determine suitability for this particular study. These two questions will assess current chronic opioid use and availability to participate in one of the two focus groups conducted among people who are currently using prescribed opioids for treatment of chronic pain. Quintiles Healthcare Engagement & Communications will compile contact information for participants who meet the basic eligibility criteria and who are interested in participating in the focus groups, who will be told they will be contacted by the itracks research firm. This information will be provided to itracks in a password-protected file. Once itracks has obtained this information, they will conduct further screening, using the Chronic Opioid Patients Screening Questionnaire (included in the submission package and also contains the text for all email and telephone follow-up contacts). People currently using prescribed opioids for treatment of chronic pain will be eligible for the focus groups if they are adults 18 and older who self-identify as having used an opioid medication to manage their pain on a regular basis (daily or most days) for the past three months or longer.

itracks will also recruit and screen the friends and family of people currently using prescribed opioids for treatment of chronic pain and general population consumer focus groups by telephone, using the General Population & Friends/Family Screening Questionnaire the to facilitate recruitment (included in the submission package and also contains the text for all email and telephone follow-up contacts). Family and friends of people currently using prescribed

opioids for treatment of chronic pain are those who self-identify as a family member or friend of someone who has used prescription medication to manage their pain on a regular basis (daily or most days) for the past three months or longer. All focus groups participants must be 18 years or older. We will aim to have a mix of education levels within each group, with roughly 1/3 having some or no high school education, 1/3 high school graduates, and 1/3 with some college or more education. We will seek diversity among respondents in gender, race/ethnicity, age, geographic region of residence, and those living in rural, urban and suburban areas. Individuals will be disqualified from participation if they have ever worked for the Department of Health and Human Services, FDA, a pharmaceutical company, itracks, RTI, International or if they have participated in a focus group within the past 6 months.

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

Data collection will take place during an 8 week time frame after OMB and FDA RIHSC approval is received.

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

After written consent is obtained (Healthcare Provider Consent Form is included in the submission package), data will be collected from the various health care providers noted above through 30 in-depth telephone interviews using the Healthcare Provider Interview Guide, a semi-structured interview guide (included in the submission package). Each interview will last no more than 60 minutes. Each interview will use a toll-free conference line into which the interviewer, participant, and a note-taker (which the participants will be informed is in attendance) will call. After verifying signed consent, the interviewer will briefly review the informed consent information with the participant. Semi-structured interview questions will cover topics related to opioids, specifically about current issues related to opioids, prescribing practices, patient-provider communication, education and training, and the role of the FDA in regards to opioids. A note-taker will take notes during each call, and we will also audio-record and transcribe each interview for analysis purposes.

Six, 90-minute online focus groups will be conducted with 3 groups of consumers aged 18 years of age and older as identified above. Participants chosen for participation will be sent two copies of an informed consent form which they will be asked to sign and return one of the forms to itracks. Participants will be given the option of having the consent forms sent to them in the mail, which would include a postage paid return envelope for returning a signed copy to itracks, or they may opt to have the form emailed to them, in which case they could either fax a signed copy to itracks or email a scanned copy to them. Participants will be told that they must return a signed copy of the consent form prior to their participation in the focus group. Participants will be reminded of this as part of a confirmation call that itracks will make after sending an email with call-in/login information for the focus group (included in the Screener Questionnaires that are part of the submission package). The same consent form will be used for all consumer focus groups (Consumer Consent Form is included in the submission package). Each focus group will include no more than 10 participants. At the start of the focus group, the moderator will confirm that all participants returned a signed consent form and will review highlights from the informed consent. Participants will be allowed to ask any additional questions, and asked to confirm their consent. During the group participants will be asked questions pertaining to knowledge, attitudes, and beliefs about and experience with opioids; patient-provider communications about opioids; the role of FDA related to opioids; sources of information about opioids; and reactions

to opioid-related message concepts. The specific questions are included in three separate focus group guides: Chronic Opioid Patients Focus Group Guide, the Family/Friends Focus Group Guide, and the General Population Focus Group Guide (all included in the submission package). The focus groups for family/friends and general population consumers will be video-recorded (video and audio recording). Focus groups with people currently using prescribed opioids for treatment of chronic pain will be audio-recorded only for added participant privacy. Participants will be notified that a member of the research team will take notes during all focus groups, and the recordings will be transcribed for analysis purposes.

In addition to the information collected through the interviews and focus groups, itracks will provide RTI, the external organization conducting the study on behalf of FDA, with data from the screener on the eligible participants, as well as basic demographic information, which will be used for analysis purposes.

6. **Confidentiality of Respondents:**

All study participants will be informed both as part of the written consent and again during the interviews and focus groups 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 given the study methods. Focus group participants will be asked not to share anything that is discussed during the focus group with anyone outside of the group. For an added privacy for the focus groups consisting of people currently using prescribed opioids for treatment of chronic pain , participants will not be able to see one another through the online platform; they will only be able to hear what other participants and the moderator say.

For both the focus groups and the interviews, all notes taken will be kept in a locked file cabinet or on a password-protected computer. Any forms related to the project that have names or other information that could identify individual respondents will be kept by RTI, International separate from the focus group and interview data provided to FDA. The information will be kept in a secured fashion that will permit access only by authorized project staff. All personally identifiable information will be removed from transcripts, audio/video files, reports, and all other materials before RTI provides them to FDA. All files will be stored on password-protected computers at RTI and FDA. These confidentiality methods will be approved by RTI's Institutional Review Board and FDA's Research Involving Human Subjects Committee, (RIHSC) prior to collecting any information.

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

Numerous empirical studies have established that incentives can significantly increase participation rates (Abreu & Winters, 1999; Shettle & Mooney, 1999; Greenbaum, 2000). Incentives are intended to recognize the time burden placed on participants, encourage their cooperation, and convey appreciation for their contributions to the research. Incentives help ensure that sufficient numbers of respondents can be recruited to participate in the data collection. The quality of the data would be significantly compromised without the ability to recruit sufficient numbers of appropriate respondents to participate in the data collection. Research has shown that monetary incentives improve response rates (Martins, 2012), thus it is likely that without the incentive as an inducement, more people would need to be screened to achieve the desired cooperation rate, thus increasing the burden hours.

Experience and research has shown that healthcare providers – particularly specialists – are an extremely difficult population to recruit and retain in research efforts for reasons related primarily to the time burden (VanGeest, Johnson & Welch, 2007; Johnston 2010; Asch, Connor, Hamilton, & Fox, 2000). Providers are typically busy individuals who may work irregular hours, be overcommitted, and need to respond to clinical emergencies. Consequently, research has shown that monetary incentives improve response rates in these groups (Martins, 2012; Dykema, 2011; Van Geest, 2011; Thorpe, 2008). Although research concerning the necessity of incentives is abundant, no studies could be found that discuss the amounts of these incentives for research similar to this study. This is likely because incentive amounts offered vary greatly based on the size and accessibility of the population being studied and the financial requirements to access the population. A Respondent's Fair Market Value [FMV] will rise and fall with the relative scarcity that he or she may represent. In the absence of scientific studies on the topic of incentive amounts for health care providers, we consulted itracks, which has recruited for a wide range of studies involving health care providers, and other research firms, and determined that incentives of $175 for primary care providers and $250 for specialists are necessary to make it worth these prescribers' time to take an hour out of their busy schedules to participate in research studies like this. These amounts are still unlikely to fully compensate them for the resultant losses from their other usual activities, e.g. billing for patient consultations or procedures. The suggested honoraria rates recommended by research firms that RTI has consulted range from $200 to $350 for physicians depending on specialty and geographic location. Our proposed health care provider incentives are in line with other work RTI International has done with health care providers and that we hope will be sufficient to ensure our ability to recruit enough of this group and to have them commit to an hour of time. Based on our interviews and experience, incentives lower than those proposed would have significant ramifications in our ability to complete the interviews needed for this study. Without the ability to do so, we will be unable to gather the information needed from healthcare providers – a key target group in the current U.S. opioid- public health epidemic, combatting which is a top priority for President Obama and the White House, HHS, FDA, and the nation -- and the funding for this study may be wasted.

Each focus group participant will receive the equivalent of a $75 incentive for participation. This is in line with what the research firm, itracks, typically provides to participants in studies of a similar scope, and OMB has approved this incentive amount for focus group participants in prior CDER/OCOMM research. General health consumers and friends/family of people currently using prescribed opioids for treatment of chronic pain will receive 75 e-reward points, where each e-reward point = $1.00. Per its usual practice with which its panel participants are familiar and have agreed, itracks will distribute the e-rewards to consumers via email within approximately 4-6 weeks of participation. These e-rewards can be redeemed at the online sites for such things as gift cards, consumer goods, and magazine subscriptions. Participants currently using prescribed opioids for treatment of chronic pain recruited through Quintiles Healthcare Engagement & Communications will be mailed a $75 check, per its usual incentive process.

8. **Questions of a Sensitive Nature**

None of the questions in the healthcare provider's interview guide are of a sensitive nature. Focus group participants will be informed during the screening process that the research relates to prescription pain medicines and also asked if they are taking any of a list of opioid pain medications, so they so they will know these topics in advance of the focus groups and will have the opportunity to decline to participate. In order to understand people's experiences with opioids, our focus group guides include questions about use of opioids, as well as their

understanding of and/or experiences with topics associated with opioids, including misuse and addiction. As part of the informed consent document, and again at the beginning of the focus group, participants will be informed that they do not need to answer any questions that make them feel uncomfortable. Previous research has shown that online focus groups can be beneficial for obtaining sensitive information because of the anonymity this mode of data collection provides, thus creating a comparatively safer environment that allows for candid contributions of sensitive topics, less inhibition, and less perceive risk among participants (Reid, 2005; Woodyatt, 2016; Murgado-Armenteros et al., 2012).

9. **Description of Statistical Methods**

We will use transcribed interview notes, focus group discussion notes, and participant screener data and demographics when summarizing findings for this study. The screener data and demographics will be summarized in aggregate format with no personally identifiable information in table and text format to describe study participants. Data collected through the interviews and focus groups will all be qualitative data, thus RTI will conduct a thematic analysis of all data.

Analyses will be organized around the major topics included in the interview and focus group guides (e.g., knowledge, attitudes, and beliefs about opioids; role of the FDA; education and training, etc). Project team members trained in qualitative analysis methods will work together to prepare an analysis plan and review the data. To conduct the analyses, data will be organized by data collection method (focus group and interview) and topic (e.g., knowledge of opioids, role of FDA, etc). All analyses will be data-driven. Project team members will each be given primary responsibility for different topics within the interview and focus group guides and will review the transcripts and identify key themes and findings that emerge from the data. The analysis team will meet periodically to discuss findings and overall themes, as well as recommendations for the quantitative work. These will be summarized into a final report with quotations from the interviews and focus groups provided as examples for the key themes.

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

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
Consumer screener	600	5	50
Consumers (focus group)	60	90	90
Healthcare provider screener	400	5	33
Healthcare providers (in-depth interviews)	30	60	30
Totals	1,090	160	203

REQUESTED APPROVAL DATE: June 2016

NAME OF PRA ANALYST & PROGRAM CONTACT: Domini Bean, domini.bean@fda.hhs.gov
FDA CENTER: CDER

References

Abreu DA, Winters F. Using monetary incentives to reduce attrition in the survey of income and program participation. Paper presented at: Proceedings of the Survey Research Methods Section of the American Statistical Association; 1999.

Asch S, Connor SE, Hamilton EG, Fox SA. Problems in recruiting community-based physicians for health services research. *J. Gen. Intern. Med.* 2000;15(8):591-599.

Department of Health and Human Services, Behavioral Health Coordinating Committee. Addressing prescription drug abuse in the United States: Current activities and future opportunities. 2013; http://www.cdc.gov/HomeandRecreationalSafety/pdf/HHS_Prescription_Drug_Abuse_Report_09.2013.pdf. Accessed 28 May, 2014.

Dykema J, Stevenson J, Day B, Sellers SL, Bonham VL. Effects of incentives and prenotification on response rates and costs in a national web survey of physicians. *Eval. Health Prof.* 2011;34(4):434-447. doi: 10.1177/0163278711406113

Greenbaum TL. *Moderating focus groups: A practical guide for group facilitation.* Thousand Oaks, CA: SAGE Publications; 2000.

Johnston S, Liddy C, Hogg W, Donskov M, Russell G, Gyorfi-Dyke E. Barriers and facilitators to recruitment of physicians and practices for primary care health services research at one centre. *BMC Medical Research Methodology.* 2010;10:109. doi: 10.1186/1471-2288-10-109

Martins Y, Lederman RI, Lowenstein CL, et al. Increasing response rates from physicians in oncology research: a structured literature review and data from a recent physician survey. *Br. J. Cancer.* 2012;106(6):1021-1026. doi: 10.1038/bjc.2012.28

Murgado-Armenteros EM, Torres-Ruiz FJ, Vega-Zamora M. Differences between online and face to face focus groups, viewed through two approaches. *Journal of Theoretical and Applied Electronic Commerce Research.* 2012;7(2):73-86. doi: 10.4067/S0718-18762012000200008

Reid DJ, Reid FJM. Online focus groups: an in-depth comparison of computer-mediated and conventional focus group discussions. *International Journal of Market Research.* 2005;47(2):131-162.

Shettle C, Mooney G. Monetary incentives in U.S. government surveys. *Journal of Official Statistics.* 1999;15:231-250.

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. *The NSDUH report: State estimates of nonmedical use of prescription pain relievers.* Rockville, MD: Substance Abuse and Mental Health Services Administration; January 2013.

Thorpe C, Ryan B, McLean SL, et al. How to obtain excellent response rates when surveying physicians. *Fam. Pract.* 2009;26(1):65-68. doi: 10.1093/fampra/cmn097

U.S. Food and Drug Administration. FDA announces enhanced warnings for immediate-release opioid pain medications related to misuse, abuse, addiction, overdose and death; http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm491739.htm. Accessed 18 April, 2016.

U.S. Food and Drug Administration. Goal of label changes: Better prescribing, safer use of opioids. 2013; http://www.fda.gov/forconsumers/consumerupdates/ucm367660.htm. Accessed 15 April, 2016.

VanGeest J, Johnson TP. Surveying nurses: identifying strategies to improve participation. *Eval. Health Prof.* 2011;34(4):487-511. doi: 10.1177/0163278711399572

VanGeest JB, Johnson TP, Welch VL. Methodologies for improving response rates in surveys of physicians: a systematic review. *Eval. Health Prof.* 2007;30(4):303-321. doi: 10.1177/0163278707307899

Woodyatt CR, Finneran CA, Stephenson R. In-person versus online focus group discussions: a comparative analysis of data quality. *Qual. Health Res.* 2016;26(6):741-749. doi: 10.1177/1049732316631510