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

**TITLE OF INFORMATION COLLECTION:** Formative Research Study to Understand the Impact of Generic Substitutes for Various Patient and Caregiver Populations

## DESCRIPTION OF THIS SPECIFIC COLLECTION

1. **Statement of need:**

The Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), Office of Generic Drugs (OGD) is seeking OMB approval under the generic clearance 0910-0695 to conduct focus groups for the project "Formative Research Study to Understand the Impact of Generic Drug-Device Substitutes for Various Patient and Caregiver Populations'.

Based on the supporting statement for generic clearance 0910-0695,[1] the purpose of information collection under this generic clearance is "to provide tools to assess the need for communications on specific topics and to assist in the development and modification of communication messages to promote public health and compliance with regulations." The specific collection described in this memo aims to: (1) examine behavioral implications of generic drug-device substitutions for three drug-device combination products across four patient groups and one caregiver group; (2) Assess how the design and functionality of generic drug-device combination products (generic combination products) affect perceptions of product quality and efficacy and device usability; and (3) Explore participants' views on how generic combination products compare to branded products.

Congress passed the Generic Drug User Fee Amendments (GDUFA, Title III of the Food and Drug Administration Safety and Innovation Act (Public Law 112-144)) in July 2012. The FDA Reauthorization Act of 2017 (Public Law 115-52) reauthorized GDUFA for Fiscal Years 2018-2022. Under GDUFA, the FDA obtains industry and public input to create regulatory science initiatives regarding research on generic drugs that advance public health.[2] Once marketed, certain generic drugs are often not preferred over brand drugs[3] [4] [5] [6] even though generic drugs generally cost less than brand drugs. Similarly, compared with brand combination products, generic combination products are an emerging market and present a somewhat unique situation. Although the performance, safety, and effectiveness are equivalent, design features including size, shape, color, and packaging may differ between generic and branded devices.[7] Research to examine behavioral implications of generic combination product substitutions for three combination products and assess how the design and functionality of generic combination products affect perceptions of product quality, efficacy and device usability, is needed to inform

[1] http://www.reginfo.gov/public/do/PRAViewICR?ref_nbr=201509-0910-002

[2] http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm370952.htm

[3] Scher, S. (2013) The Branded Advantage. *Ophthamol Mgmt*. July: p18 http://www.ophthalmologymanagement.com/printarticle.aspx?articleID=108618

[4] Alloway, RR, Isaacs R, Lake K, Hoyer P, First R, Helderman H, Bunnapradist S, Leichtman A, Bennett MW, Tejani A, Takemoto SK. (2003) Report of the American Society of Transplantation Conference on Immunosuppressive Drugs and the Use of Generic Immunosuppressants. *A J Transpl* 3: 1211.

[5] Liow K, Barkley GL, Pollard JR, Harden CL, Brazil CW. (2007) Position statement on the coverage of anticonvulsant drugs for the treatment of epilepsy. *Neurology* 68: 1249.

[6] American Thyroid Association, The Endocrine Society, and American Association of Clinical Endocrinologists. (2004) Joint Statement on the U.S. Food and Drug Administration's Decision Regarding Bioequivalence of Levothyroxine Sodium. *Thyroid* 14: 486.

[7] Food and Drug Administration, Center for Drug Evaluation and Research (FDA/CDER), Office of Generic Drugs. (2012). Fact about generic drugs. Retrieved from http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm.

the FDA guidance on the development of generic combination products and effectively review generic combination products. To address this regulatory science need regarding generic combination products, the FDA awarded a contract to RTI International (Contract Number: HHSF223201810113C).

Through this contract with RTI International, patient groups and caregiver groups views on how the design and functionality of generic combination products affect perceptions of product quality, efficacy and device usability will be assessed through feedback received by participants in focus groups.

2. **Intended use of information:**
Data collected from these focus groups will be used to inform future research on generic combination product development.

3. **Description of respondents:**

RTI will conduct 20, 90-minute in-person focus groups at professional research facilities across the U.S. with up to 10 participants in each group for a total of 200 participants. The following cities were selected to represent the Midwest, East, South, and West regions: Minneapolis, MN; Bethesda, MD; Atlanta, GA; and Phoenix, AZ. If we are unable to conduct focus groups in one of the four cities, we will identify an alternate city within the same region.

Focus groups will be conducted with the following groups that use drug devices (i.e., auto-injectors and dry powder inhalers):

**<u>Autoinjector Groups (n=100):</u>**

- Adult Caregivers – EpiPen (n=40)
  - Adults who provide primary care for an individual that currently uses the *EpiPen, EpiPen Jr autoinjector*
- Adult Users – EpiPen (n=20)
  - Adults who currently use the *EpiPen, EpiPen Jr*, autoinjector
- Adult Users – Other Auto Injectors (n=20)
  - Adults who currently use any brand of autoinjector that is *not EpiPen, EpiPen Jr, autoinjector*
- Adolescent Users – EpiPen (n=20)
  - Youth, ages 13-17 who currently use the *EpiPen, EpiPen Jr autoinjector*
  - Youth who use other brands (but not those listed above) will be excluded

**<u>Dry Powder Inhaler (DPI) Groups (n=100):</u>**

- Adult Naïve DPI Users (n=40)
  - Adults who currently use a DPI, but have never used *Advair Diskus*
- Adult Experienced DPI Users (n=40)
  - Adults who: (1) currently use the *Advair Diskus brand* of DPI, and (2) have been using any DPI for more than 6 months
- Adolescent Advair Diskus Users (n=20)
  - Youth ages 13-17, who *currently use the Advair Diskus brand* of DPI

To be eligible to participate, respondents have to be able to read, understand, and speak English. Individuals will be ineligible for participation if they have other characteristics that could potentially bias responses (e.g., connections to the pharmaceutical industry; employment in the public health, advertising, or marketing industry or with the Department of Health and Human

Services) or if they have participated in market research in the past 3 months. For the "Naïve DPI Users" group, participants will be eligible if they use a dry powder inhaler other than the Advair Diskus. For the "Experienced DPI Users" group, participants will be eligible if they currently use an Advair Diskus inhaler and having been using an inhaler for more than 6 months. We will recruit for a mix of gender, race, and ethnicity, and education.

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

We anticipate the focus groups will take place in October-November of 2019, or within six weeks following RTI's IRB and OMB approval.

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

FDA will rely on RTI's IRB through an IRB Authorization Agreement (IAA). RTI's IRB approved the study procedures and all associated documents on May 03, 2019. In addition, the study procedures and all associated documents will be submitted to the Office of Management and Budget (OMB) for review. We will not field the study until we have approval from OMB. After receiving approval, we will work with local market research firms in each of the cities to recruit participants and provide the facilities for hosting the focus group discussions.

To recruit adolescent participants, the recruitment firms will identify parents of children in our age range through their community partners and/or proprietary database and will contact them by telephone. Recruitment firm staff will first present the study to the parent/guardian, confirm that they are the parent/guardian, and request permission for their child participate in a focus group, and audio record the focus group. If they are not the adolescent's parent/guardian or will not permit the focus group or audio recording, the screening process will be terminated. Otherwise, once the parent/guardian grants verbal permission to screen their adolescent, recruitment firm staff will ask to speak with him/her.

After receiving permission from the parent/guardian for screening, the recruiter will administer the screener to the adolescent to determine eligibility (***Appendix A)***. If eligible, the recruiter will invite the adolescent to participate in the study and, if interested, will schedule their participation in a focus group. After scheduling their participation, the recruiter will speak with the parent/guardian once more to inform them of the scheduled appointment time and to note that the parent/guardian must sign a parent permission form before their adolescent can participate in the study ***(Appendix B).*** The recruiter will also collect a phone number and email address from the adolescent and parent/guardian, so they can be reminded of their upcoming focus group 1-2 days beforehand. Individuals who are invited to participate in this study may choose not to respond or may decline to provide consent or assent for the study; or in the case of youth aged 13 to 17, a parent or guardian may refuse permission for their child or ward to participate. Individuals who agree to participate may nevertheless drop out at any time.

It is possible that there will be more than one adolescent aged 13-17 living in the home. If this is the case, recruitment firm staff will ask the parent/guardian if all children in this age range are at home. If the answer is yes, they will ask for permission to speak to the oldest child. If this adolescent is eligible, they will proceed with recruitment and scheduling. If the oldest child is ineligible, they will terminate the call. If the oldest child is not at home when recruitment firm staff contact the parent/guardian, they will ask to speak to the next oldest child in the specified age range and so forth until they can screen at least one of the adolescents in the specified age range (if the parent/guardian gives them permission to do so and the child wants to). If no children in the specified age range are at home when the recruitment firm contacts the parent/guardian, they will ask the parent/guardian when they should call back to screen the oldest child. For adults, the recruiter will administer the screen to the adults to determine eligibility ***(Appendix C).*** If eligible, the recruiter will invite the adolescent to participate in the study and, if

interested, will schedule their participation in a focus group. If a person refuses to participate, the recruiter will thank them for their time.

After a person agrees to participate, they will be sent a confirmation email ***(Appendix D)*** that lists the date, time, and location of the focus group session. The market research firm will call the participant the day before the focus group session to remind them of the session and confirm that they plan to attend.

The firms will overrecruit two individuals for each group to ensure sufficient participation in case of no-shows or last-minute cancellations. RTI will work with the market research firms to closely monitor the progress of recruiting. The firms will provide frequent updates throughout the recruitment process, providing RTI with data from the screener on these eligible participants and basic demographic information. Before each focus group, the market research firms will provide RTI and FDA with participants' screening responses, which RTI will review to confirm eligibility.

The focus groups will be convened at professional market research facilities. FDA and RTI team members will be able to observe the focus groups remotely in real time through a secure, password-protected online streaming system (e.g., BlueJeans) or possibly from behind a one-way mirror. Observers will be able to use a chat feature to send the moderator questions to be asked at the end of the group. The firms will audio-record the focus groups and RTI will provide FDA with transcripts of each focus group.

Upon arrival at the market research facility, participants in any of the adult groups will read and sign an informed consent form (approved by RTI's IRB) ***(Appendix E)***.

For the adult focus groups, a trained RTI staff member will administer the informed consent prior to the beginning of the focus group, including providing a hard copy of the informed consent to the participant and answering any questions the participant may have. Participants will be advised that participation is voluntary, and they can choose to skip any question they do not wish to answer. The consent form (***Appendix E***) will also indicate that they will receive $125 for their participation. Participants will be required to provide their written consent before proceeding with the focus groups by signing their first name and dating a copy of the informed consent form. While in the field, the signed hard copies will be kept in a folder in a private study room at the market research facilities accessible only by the project staff. While in transit, the signed hard copies will be kept in a personal bag that project staff will keep on hand at all times. The signed hard copies will be locked in a cabinet which can be accessed only by project staff. Participants will receive a duplicate blank (not signed) copy of the consent form for their records.

For the adolescent focus groups, adolescent participants must provide written assent to participate in the study. In addition, focus group facility staff will email or mail the parent or guardian a permission form prior to the study date. For emailed permission forms, parents or guardians can print a signed copy to bring (or have their child bring) to the facility on the day of the focus group, For mailed permission forms, two copies will be sent: one for the parent or guardian to sign and return to the facility, and the other for the parent or guardian to keep for their records. Permission forms will also be available at the facility for parents or guardians to sign on the day of the focus group if needed. All adolescent participants must have a permission form signed by a parent or guardian before they can participate in the focus group. After receiving the signed parent permission form, a trained RTI staff member will give adolescent participants the assent form (***Appendix F***) prior to the beginning of the focus group and answer any questions the participant may have. Participants will be advised that participation is voluntary, and they can choose to skip any question they do not wish to answer. The assent form will also indicate that they will receive $125 for their participation. Participants will be required to provide their written

assent (including *only* their first names) before proceeding with the focus groups. Youth participants will be given a copy of the assent form to keep for their records. While in the field, the signed hard copies will be kept in a folder in a private study room at the market research facilities accessible only by the project staff. While in transit, the signed hard copies will be kept in a personal bag that project staff will keep on hand at all times. The signed hard copies will be locked in a cabinet which can be accessed only by project staff.

Participants will also complete a brief worksheet ***(Appendix G)*** approved by RTI's IRB and FDA after consenting to the study and prior to the focus group. The worksheet will ask participants questions about their device use, such as their (or their family member's, if in the Caregiver group) diagnosis, the length of their device use (e.g., three months), how often they use their device, their level of satisfaction with the device, if they received training on how to use their device, and their level of satisfaction with that training.

An experienced moderator will conduct the focus group discussions, and a trained staff member will provide notetaking and logistical assistance. The moderator will use a semi-structured guide ***(Appendix H)*** developed by RTI and FDA to facilitate the discussions and ensure that all major topics of interest are addressed. The moderator will start each group by introducing themselves, explaining the ground rules, and reviewing key points from the informed consent. After addressing these items, the moderator will move on to the discussion questions. During certain activities, a second moderator will enter the room and assist the primary moderator.

FDA will provide RTI with brand and generic auto-injectors and dry powder inhalers that will be given to the participants. For the auto-injector focus groups, the moderator will provide each participant with trainer versions of the generic and branded epinephrine auto-injectors for participants to handle and review. As stated in the epinephrine auto-injectors' prescribing information the trainer version of the generic and branded epinephrine auto-injectors, have no actual medicine or needles will be inside the devices so there will be no risk of accidental dosing or injury.[8] [9] The moderator will have an actual EpiPen device that does contain medicine and a needle, but no participants will handle the actual device. The moderator will handle the actual EpiPen to show to participants for viewing purposes only. The actual and trainer devices can be distinguished by color and labeling (i.e., yellow for the actual EpiPen device, and gray for the trainer device). The trainer device is also marked as "TRAINER" on the packaging. For the dry powder inhaler focus groups, the moderator will provide each participant with empty Advair Diskus as well as empty generic version of the Advair Diskus inhaler for participants to handle and review. FDA will ensure that all devices have been emptied of any and all medicine prior to delivery to RTI. No device distributed to focus group participants for review will contain any medicine so there will be no risk of accidental dosing or injury. For both the autoinjectors and inhalers, the moderator will give participants the empty box with the instructions of use. Participants will return the branded and generic devices at the end of the focus group.

After each focus group is completed and the participants have left the facility, the moderator will review and add to the focus groups notes as needed. The notetaker and moderator will discuss any issues that arise related to logistics, the discussion guide, and/or participant interactions. RTI and FDA will discuss what is learned during these informal debriefings; RTI will not make any process changes unless FDA requests them.

[8] NDA019430 Epipen and Epipen Jr. Prescribing Information; approved 08/23/2018; available on Drug@FDA. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019430s074lbl.pdf

[9] ANDA 090589 Epinephrine and Epinephrine Jr. Prescribing Information; approved 08/16/2018; available on DAILYMED. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=04f07f15-55e2-411b-abb8-07eab37f5664

Data collection will take approximately eight days (two days in each city). Each focus group will last no more than 90 minutes. Following their participation in the focus groups, individuals will have completed their participation in the study.

After the data collection is complete at all locations, the study team will create a summary report of the observations and insights from the focus groups and submit the report and transcripts to FDA. RTI and the recruitment firms will be the only ones who will possess the audio files; FDA will never be given the audio files from the focus groups.

6. **Confidentiality of Respondents:**

All data collection activities will be conducted in full compliance with FDA regulations to maintain the privacy of data obtained from respondents and to protect the rights and welfare of human research subjects as contained in their regulations. All those who handle or analyze data will be required to adhere to the standard data security policies of RTI.

Data from the screening instrument and consent form will be collected. The focus groups will be audio recorded and transcribed. We will audio record the interviews to verify the interview notes, but the audio recordings will not include full names and will be stored on password-protected computers that only the project staff can access. The focus group facilities will retain their copies of the audio recordings for 30 days, and then destroy the recordings. Some project staff may observe the discussion behind a one-way mirror. They will not record participants' names and all participants' comments will be kept secure to the extent provided by law.

The focus group facilities will destroy the focus group screeners containing the identifying information after the focus groups are completed. No personally identifiable information will be connected to participants' responses. However, we will have participants' first names and/or signatures on the signed informed consent forms; this information will be stored in locked file cabinets on RTI's campus and will be separated from participants' de-identified responses, which will be stored on password protected computers.

This research will have a certificate of confidentiality ***(Appendix I)***. The focus group facilities will be informed of the certificate of confidentiality and its protection.

All data collection activities will be conducted in full compliance with applicable FDA regulations to maintain the privacy of data obtained from respondents and to protect the rights and welfare of human research subjects as contained in their regulations. Respondents will receive information about privacy protections as part of the informed consent process.

The local market research facilities already have personal identifiable information (PII) such as names and contact information from people in its research database from which participants will be recruited. This information will be included on the focus group screener documents for recruitment purposes to aid in contacting potential participants prior to the focus groups. The recruitment firms will not share the PII with RTI or FDA. Also, the recruitment firms will destroy the focus group screeners containing the PII after the focus groups are completed. There will be

no link between the data collected and the participants' identities. FDA and RTI will not have the full names or any contact information for any of the participants.

The focus groups will be conducted in person at the four market research firm locations. The focus groups will take place in a private focus group room so that only the RTI moderator and project staff can hear the participants' responses. Some project staff may observe the discussion behind a one-way mirror or via live-streaming. They will not record participants' names. Livestreaming connections will be secure, using industry-standard firewalls and security practices. All data will be encrypted in transit using secure hypertext transfer protocol (HTTPS). The following protections are in place to ensure privacy when administering the telephone screener. After receiving permission from the parent/guardian for screening, the recruiter will administer the screener to the adolescent to determine eligibility. Adolescents will be asked if they have privacy for the discussion before being beginning the screening questionnaire. If not, or if the parent or guardian is still on the phone, the recruiter administering the screener will suggest that he/she moves to a private area (a separate room with a door, if possible) or ask the parent/guardian to hang up the phone.

Other procedures to protect participants' confidentiality include:

- All screener and focus group data will be analyzed and reported in aggregate.
- At both FDA and RTI, access to project data and materials will be limited to only research staff working on the project who have been granted access by the FDA Project Officer or RTI Project Director.
- Focus group participants will be asked not to share anything that is discussed during the focus group with anyone outside of the group.

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' ADP Systems Security Policy as described in the DHHS 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:**

Consumers who participate in the 90-minute in-person focus groups will receive a token of appreciation of $125 will be given to the participants. This token of appreciation of $125.00/participant is intended to provide enough incentive to participate in the study rather than another activity, improve coverage of these hard to reach populations, improve data quality of the study, reduce the chance of cancellations or insufficient recruitment numbers, recognize the travel burden and cost (e.g., sometimes patients with Chronic Obstructive Pulmonary Disease (COPD) can be quite ill, and travel is more burdensome), childcare costs, and to convey appreciation for contributing to this important activity. [10] Numerous focus groups must be scheduled to accommodate the needs of a diverse group of eight to 10 participants. Incentives must be high enough to equalize the burden placed on respondents in respect to their time and cost of participation.

[10] Russell, ML., Moralejo, DG., Burgess, ED. (2000). Paying research subjects: Participants' perspectives. *Journal of Medical Ethics, 26*(2), 126–130.

The proposed incentive rate is also in accordance with standard practice and based on RTI's experience with specific hard-to-reach populations, the amount of time the participant spends in the study, what is required of them, recent consultation with market research firms, and OMB-approved incentives on recent FDA projects.

In reviewing OMB's guidance on the factors that may justify provision of incentives to research participants, we have determined that the following principles apply:

*a)* ***Improved coverage of specialized hard-to-reach respondents.***

Hard-to-reach populations are subgroups that may be difficult to involve in research due to various determinants, such as their physical or geographic location, or their social or economic conditions. OMB offers a justification which supports the use of incentives "to improve coverage of specialized respondents, rare groups, or minority populations".[11] Our study involves hard-to-reach (rare) populations with a number of specific eligibility requirements (i.e., adolescents, adults, and caregivers affected by asthma/COPD and use specific branded drug devices) in addition to being demographically and geographically diverse. Further, there is not an existing research panel from where potential participants could be recruited which further complicates the recruitment. Therefore, our study requires unique incentives to ensure participation. The $125 incentive will help to facilitate sample diversity and sufficient show rates.

There are only a finite number of consumers that meet the eligibility requirements for this study. For example, a study found that the prevalence of anaphylaxis in the general population is at least 1.6%.[12] Within that small population, we would need to find people that are prescribed an epinephrine autoinjector *and* have that autoinjector be the branded Epipen, *and* the person would need to be a part of the focus group facility's panel or in an area that could be exposed to their ads to participate in the study. The same situation applies to the COPD population. In other words, the population will be extremely hard to reach making it critical that incentives are able to entice people that *do* meet the criteria to participate. The pool of potential consumers is further restricted when considering the geographic parameters for the study and the availability of contact information accessible by the recruitment facilities and the requirement to have at least a somewhat diverse mix of participants. Therefore, it is critical to maximize the number who respond to ensure that we have a good mix of gender, race, and education within each hard to reach population. Lower amounts would result in higher recruiting costs and burden to the public due to the need for additional recruitment.[13]

**b)** ***Similar incentives were previously approved under recent OMB packages.***

According to item 76 in the Memorandum for the President's Management Council, past experience can be utilized to justify a more elevated honorarium: "Agencies may be able to justify the use of incentives by relating past survey experience, results from pretests or pilot tests, or findings from similar studies. This is especially true where there is evidence of attrition and/or poor prior response rates".[11]

Below are higher incentives that have also been approved for in-person studies of 90 minutes or less that involve hard-to-reach populations (in these examples, the populations focus on specialists and although we are not recruiting healthcare providers, our population is equally hard

[11] Office of Management and Budget. (2006). Questions and Answers When Designing Surveys for Information Collections.

[12] Wood, R. A., Camargo Jr, C. A., Lieberman, P., Sampson, H. A., Schwartz, L. B., Zitt, M., ... & Simons, F. E. R. (2014). Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. *Journal of Allergy and Clinical Immunology*, *133*(2), 461-467.

[13] Krueger, R.A., & Casey, M.A. (2009). *Focus groups: A practical guide for applied research*. (4th Ed.). Thousand Oaks, CA: Sage Publications, Inc.

to reach and recruit as specialists).

- $300 for specialists for a 90-minute in-person focus group for the FDA (OMB No. 0910-0687).
- $250 for specialists to participate in a 60-minute focus group for the FDA (OMB No. 0910-0677)

There are also a number of examples of 60-minute in-person studies that had an incentive of $75 or $100. Although the payment for these studies are less than the amount we are requesting, the in-person studies were only 60 minutes and they did not recruit hard-to-reach populations. Increasing the participation time to *90 minutes* paired with the niche audiences that this study needs to recruit, warrants the somewhat higher incentive rates. These studies include:

- *Eye Tracking Study of Direct-to-Consumer Prescription Drug Advertisement Viewing* (OMB Control number 0910-0772; 2014)
  - $100 for 60 minutes with obese consumers
- *Hearing, Aging, and Direct-to-Consumer Television Advertisements* (OMB Control number 0910-0818; 2016)
  - $75 for 60 minutes with general population consumers
- *Focus Groups on FDA's Accelerated Approval Process (under generic OMB Control Number 0910-049; 2018)*
  - $75 for 60 minutes with general population consumers

***c) An incentive will improve data quality by improving validity and reliability.***

OMB's guidance states that a "justification for requesting use of an incentive is improvement in data quality. For example, agencies may be able to provide evidence that, because of an increase in response rates, an incentive will significantly improve validity and reliability to an extent beyond that possible through other means".[11]

Several studies have demonstrated that the use of gifts of gratitude are an effective method for increasing response rates, particularly among hard-to-reach populations. [14] Numerous empirical studies have established that providing incentives can significantly increase participation rates, and that larger incentives (e.g., $100, $150) perform significantly better than smaller incentives. [15,16,17,18] If the incentive is not adequate, participants may agree to participate and then not show up or drop out early. Low participation may result in inadequate data collection or, in the worst cases, loss of government funds associated with recruitment, facility fees, and moderator and observer time.[19]

As well as preventing a low show rate, incentives are necessary to ensure adequate representation among harder-to-recruit populations and can help attract a reasonable cross-section of participants, reflecting diversity in age, income, and education.[20,21] Numerous studies have shown that incentives can reduce nonresponse bias for key subgroups. Griffin et al.[22] and Lesser et al.[23]

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[14] Shaghagi A, Bhopal RS, Sheikh A. Approaches to recruiting 'hard-to-reach' populations into research: A review of the literature. *Health Promot Perspect.* 2011;1(2):86-94.

[15] Shettle, C., & Mooney, G. (1999). Monetary incentives in US government surveys. *Journal of Official Statistics*, *15*(2), 231.

[16] Martinez-Ebers V. Using Monetary Incentives with Hard-To-Reach Populations in Panel Surveys. *Int J Public Opin Res*. 1997;99(1):77-86.

[17] Hsu, J. W., Schmeiser, M. D., Haggerty, C., & Nelson, S. (2017). The effect of large monetary incentives on survey completion: Evidence from a randomized experiment with the survey of consumer finances. Public Opinion Quarterly, 81(3), 736-747.

[18] Church (1993): Estimating the effect of incentives on mail survey response rates. Public Opinion Quarterly, 57(1), 62-79.

[19] Morgan, DL., Scannell, AU. (1998). Planning Focus Groups. Thousand Oaks, CA: Sage.

[20] Groth, SW. (2010). Honorarium or coercion: use of incentives for participants in clinical research. Journal of the New York State Nurses Association.

[21] Willis, G. (2005). *Cognitive interviewing: A tool for improving questionnaire design.* Thousand Oaks, CA: Sage.

found that incentives reduced nonresponse bias for gender. Incentives have also been effective in increasing participation from minority respondents.[24]

Leverage-salience theory argues that monetary incentives can help to recruit people who otherwise might not be motivated to respond (e.g., people who do not care about the topic,[25] lack altruistic motives for responding, have competing obligations)[26] or are typically less likely to participate in research.[27] Using incentives to bring in a cross section of consumers can reduce nonresponse bias if these participants (those less interested in the topic, men, minorities, high income) have different responses and feedback than those who would participate without incentives.[28]

Further, the decision was made to use a cash incentive because research has consistently shown that cash incentives result in greater response rates than lottery tickets or other non-monetary incentives and can lead to improved data quality[16,29,30]

***d) This incentive is consistent with those used in focus group studies between the contractor (RTI) and the vendor.***

Agencies may justify the use of incentives by "relating past survey experience".[11] RTI has consulted with several research firms with experience recruiting and hosting qualitative research across multiple markets (Schlesinger Group, L&E Research, Focus Pointe Global, Plaza Research, Fieldwork), including those indicated for the current study (Atlanta, GA; Phoenix, AZ; Minneapolis, MN and the Washington, DC area). All of the contacted research firms have extensive experience working with government-funded studies and understand the processes for working within the parameters of these studies, including incentive parameters. All research firms confirmed that the incentive amount of $125 is the minimum amount they can offer and still expect to recruit a demographically and geographically diverse group of respondents. That amount also helps to compensate them for an estimated two-and-a-half hours of time (one-and-half hours in the focus group, plus an average of an hour in travel to and from the group). If, for instance, the focus group facility for the Washington D.C. area is actually located in Bethesda, Maryland, a cross-section of inner-city and suburban participants would need to travel a considerable distance to reach the facilities.

Offering an incentive below these rates may result in increased costs exceeding the amount saved with a lower incentive. Consequences of insufficient incentives include increased time and cost of recruitment, increased "no-show" rates, and increased probability of cancelled or postponed interviews.

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[22] Griffin, J. M., Simon, A. B., Hulbert, E., Stevenson, J., Grill, J. P., Noorbaloochi, S., & Partin, M. R. (2011). A comparison of small monetary incentives to convert survey non-respondents: a randomized control trial. *BMC medical research methodology*, *11*(1), 81.

[23] Lesser, V.M., Dillman, D.A., Carlson, J., Lorenz, F., Mason, R., and Willits, F. (2001) Quantifying the Influence of Incentives on Mail Survey Response Rates and Nonresponse Bias. Paper presented at the annual meeting of the American Statistical Association, Atlanta, GA.

[24] Singer, E. & Kula, R. A. (2002). Paying Respondents for Survey Participation. In M. Ver Ploeg, R. A. Moffitt, & C. F. Citro (Eds.), Studies of Welfare Populations: Data Collection and Research Issues, Washington, D.C.: National Academy Press.

[25] Groves, R. M., Presser, S., & Dipko, S. (2004). The role of topic interest in survey participation decisions. *Public Opinion Quarterly*, *68*(1), 2-31.

[26] Singer, E., & Ye, C. (2013). The use and effects of incentives in surveys. The ANNALS of the American Academy of Political and Social Science, 645(1), 112-141.

[27] Guyll, M., Spoth, R., & Redmond, C. (2003). The effects of incentives and research requirements on participation rates for a community-based preventive intervention research study. *Journal of Primary Prevention*, *24*(1), 25-41.

[28] Castiglioni L, Pforr K. The effect of incentives in reducing non-response bias in a multi-actor survey. *Presented at the 2nd annual European Survey Research Association Conference*, Prague, Czech Republic, June, 2007

[29] Singer, E., Van Hoewyk, J., Gebler, N., & McGonagle, K. (1999). The effect of incentives on response rates in interviewer-mediated surveys. *Journal of Official Statistics*, *15*(2), 217.

[30] Edwards, P., Roberts, I., Clarke, M., DiGuiseppi, C., Pratap, S., Wentz, R. and Kwan, I. (2002) Increasing response rates to postal questionnaires: Systematic review. *British Medical Journal* 324, 1183.

Cash incentives will be distributed by the market research facilities upon completion of each focus group.

8. **Questions of a Sensitive Nature:**

There will be no questions of a sensitive nature asked of participants during the focus groups.

9. **Description of Statistical Methods:**

Using the transcripts, RTI will conduct thematic analysis of the open-ended data to identify trends in patient and caregiver responses. RTI will provide create a summary report of the data, including trends and cross-cutting insights that are found.

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

Approximately 300 hours in total based on 90-minute focus groups with a maximum of 10 participants across 20 focus groups. A total of 200 respondents will participate in the study.

This will be a one-time (rather than annual) collection of information. FDA estimates the burden of this collection of information as follows:

| **Type/Category of Respondent** | **No. of Respondents** | **Participation Time** (minutes) | **Burden** (hours) |
|---|---|---|---|
| Number to complete the study | | | |
| Adults, EpiPen | 20 | 90 | 30 |
| Adults, Other AIs | 20 | 90 | 30 |
| Caregivers, EpiPen | 40 | 90 | 60 |
| Adolescents, EpiPen | 20 | 90 | 30 |
| Adolescents, DPI | 20 | 90 | 30 |
| Experienced Users, DPI | 40 | 90 | 60 |
| Naïve Users, DPI | 40 | 90 | 60 |
| Total Reporting Burden Hours | 200 | -- | 300 |

**REQUESTED APPROVAL DATE:** July, 2019

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