

United States Food and Drug Administration
Generic Clearance: Testing Communications on Drug Products
OMB Control Number 0910-0695
Gen IC Request for Approval

Title of Gen IC: 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.”

The supporting statement for the generic information collection approved under OMB control number 0910-0695 states that 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.” This information collection aims to: (1) examine behavioral implications of generic drug-device substitutions for autoinjectors and dry powder inhalers; (2) assess how the design and functionality of generic drug delivery devices affect perceptions of product quality and efficacy and device usability; and (3) explore participants’ views on how generic drug-device 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 under which FDA obtains industry and public input to create regulatory science initiatives that support research on generic drugs to advance public health.¹ The FDA Reauthorization Act of 2017 (Public Law 115-52) reauthorized GDUFA for fiscal years 2018-2022. Once marketed, certain generic drugs often are not preferred over brand drugs^{2, 3, 4, 5} even though generic drugs generally cost less. Increased approvals for brand drug-device combination products have resulted in a rapidly expanding market for generic drug-device combination products. These complex products present unique regulatory and product use environments and challenges. Although the performance, safety, and effectiveness of a generic drug-device combination product must be equivalent to that of its brand drug (reference listed drug), there may be certain design feature differences (including size, shape, color, and packaging) between generic and branded devices.⁶ To inform FDA on developing generic drug-device combination products and effectively reviewing applications for generic combination products, we need research examining behavioral implications of generic combination product substitution for two commonly

¹ <http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm370952.htm>

² Scher, S. (2013) The Branded Advantage. *Ophthalmol Mgmt.* July: p18 <http://www.ophtalmologymanagement.com/printarticle.aspx?articleID=108618>

³ 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.

⁴ 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.

⁵ 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.

⁶ 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>.

prescribed combination brand products. This research will assess how the design and functionality of generic combination products affect patient and caregiver perceptions of product quality, efficacy and device usability. To address the need for regulatory science about generic drug-device combination products, FDA awarded a contract to RTI International (Contract Number: HHSF223201810113C). Through this contract with RTI International, OGD/CDER/FDA will enhance its understanding of how the design and functionality of generic drug-device combination products affect patient and caregiver perceptions of product quality, efficacy and device usability. This information will be collected through professionally conducted caregiver focus groups and/or patient focus groups that include users of the Advair Diskus dry powder inhaler (DPI) or the EpiPen auto-injector (AI) and used to inform policy and further research about developing generic DPIs and AIs.

To date, RTI has conducted ten in-person focus groups with adults, adult caregivers, and adolescents who have experience using certain drug-device combination products (e.g., dry powder inhalers like the Advair Diskus and autoinjectors like the EpiPen). Due to the COVID-19 pandemic, we have modified our data collection approach to virtually conduct the remaining four focus groups and focus on the use of autoinjectors like the EpiPen.

2. Intended Use of the Information:

Data collected from these focus groups will be used to inform future research on generic drug-device combination product development.

3. Description of Respondents:

RTI will conduct four 90-minute, virtual focus groups each with up to six participants. RTI has already conducted ten 90-minute, in-person focus groups each with up to 10 participants. In total, we will have up to 100 adults, adult caregivers, and adolescents with experience using drug-device combination products (e.g., autoinjectors like the EpiPen and dry powder inhalers like the Advair Diskus) participate in these focus groups and will identify their knowledge, perceptions, and attitudes about generic drug-device quality and effectiveness. The following cities were selected to represent the Midwest, East, South, and West regions: Minneapolis, MN; Bethesda, MD; Atlanta, GA; and Los Angeles, CA.

To date, RTI has completed ten in-person focus groups focusing on DPIs (N=40) and AIs (N=27) and plans to virtually conduct the remaining four focus groups.

RTI has collected data on the following segments:

In-Person Autoinjector Groups (n=27):

- o Adult Caregivers – EpiPen (n=15)
 - Adults who provide primary care for an individual that currently uses the *EpiPen*, *EpiPen Jr*, or *Epinephrine Injection USP* brand of autoinjector
- o Adult Users – EpiPen (n=6)
 - Adults who currently use the *EpiPen*, *EpiPen Jr*, or *Epinephrine Injection USP* brand of autoinjector
- o Adolescent Users – EpiPen (n=5)
 - Youth, ages 12-17 who currently use the *EpiPen*, *EpiPen Jr*, or *Epinephrine Injection USP* brand of autoinjector
 - Youth who use other brands (but not those listed above) will be excluded
- o Adult Users –Other auto-injectors (n=1)
 - Adults who currently use any brand of autoinjector other than *EpiPen*, *EpiPen Jr*, or *Epinephrine Injection USP* brand of autoinjector

In-Person Dry Powder Inhaler Groups (n=40):

- o Adult Naïve DPI Users (n=18)
 - Adults who currently use a DPI, but have never used *Advair Diskus*
- o Adult Experienced DPI Users (n=18)
 - Adults who: (1) currently use the *Advair Diskus brand* of DPI
- o Adolescent Advair Diskus Users (n=4)
 - Youth ages 12-17, who *currently use the Advair Diskus brand* of DPI
 - The population above is prioritized; it is possible that recruiting could be expanded to include youth who use other DPI brands.

As a result of the COVID-19 pandemic, we have modified our data collection approach to conduct the remaining four focus groups virtually. This shift to a virtual focus group environment will reduce the risks of COVID exposure to study participants and staff and the ability for participants with medical conditions or limited mobility to access a research facility. In addition, the virtual focus groups will allow for more geographic diversity in our participant sample.

Our participant segments for the virtual focus groups follow (the number in parentheses reflects the participant number we will recruit to account for no shows):

Virtual Autoinjector Groups (n=32):

- o Adult Caregivers – EpiPen (1 group; n=8)
 - Adults who provide primary care for an individual that currently uses the *EpiPen, EpiPen Jr, or Epinephrine Injection USP brand* of autoinjector
- o Adult Users – EpiPen (2 groups; n=16)
 - Adults who currently use the *EpiPen, EpiPen Jr, or Epinephrine Injection USP brand* of autoinjector
- o *Epinephrine* Adolescent Users – EpiPen (1 group; n=8)
 - Youth, ages 12-17 who currently use the *EpiPen, EpiPen Jr, or Epinephrine Injection USP brand* of autoinjector
 - Youth who use other brands (but not those listed above) will be excluded

Eligible participants for the four virtual focus groups will be adults, adult caregivers, and adolescents who have experience using autoinjectors and can speak and read English fluently. No virtual groups will be conducted with DPI users. For the virtual focus groups, eligible participants must have a high-speed internet connection, have a laptop/computer with a webcam and audio, and be able to receive a package of focus group materials in the mail. Each adolescent must have permission to participate from one parent or guardian. No data will be collected from parents, and parents are not included in the sample population of adolescent users. 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.

4. How is the Information Collected:

FDA will rely on RTI’s institutional review board (IRB) through an IRB Authorization Agreement (IAA). RTI’s IRB approved the study procedures and all associated documents on December 7, 2021. FDA is submitting the study procedures and all associated documents for Office of Management and Budget (OMB) review and will not field the study until we have OMB approval. After receiving approval, RTI will work with local market research firms in each of the cities to recruit participants and send participants the necessary materials for the focus groups.

Completed in-person focus groups: To recruit adolescent participants, the recruitment firms identified parents of children in our age range through described strategies (proprietary database, community partners, media advertisements) and contacted the parents of potential participants by telephone (**Appendices A and B**). Recruitment firm staff first presented the study to the parent/guardian, confirmed that they were the parent/guardian, and requested permission for their child to participate in an audio-recorded focus group. If they were not the adolescent's parent/guardian or did not permit the focus group or audio (or video if necessary) recording, the screening process was terminated. Otherwise, once the parent/guardian granted permission to screen their adolescent, recruitment firm staff asked to be redirected to the potential adolescent participant.

After receiving permission from the parent/guardian for screening, the adolescent completed the screener to determine eligibility. If eligible, the adolescent was invited to participate in the study. If the adolescent agreed to participate, they were scheduled for a focus group at a pre-selected time. After scheduling their participation, the recruiter contacted the parent/guardian and the adolescent to confirm the scheduled appointment time. Information related to parent permission (**Appendix G**) requirements was also shared with the adolescent (i.e., permission must be granted before adolescent can participate in the study). The recruiter collected a phone number and email address from the adolescent and parent/guardian so they could be reminded of their upcoming focus group 1-2 days beforehand (**Appendix J**).

Individuals invited to participate in this study could choose not to respond or decline to provide consent or assent for the study; or in the case of youth aged 12 to 17, a parent or guardian could refuse permission for their child or ward to participate. Individuals who agreed to participate could drop out at any time.

It is possible that there was more than one adolescent aged 12-17 living in the home. If this was the case, recruitment firm staff asked the parent/guardian if all children in this age range were at home. If the answer was yes, they asked for permission to gauge eligibility with the oldest child. If this adolescent was eligible, they proceeded with recruitment and scheduling. If the oldest child was ineligible, they terminated the call. If the oldest child was not at home when recruitment firm staff contacted the parent/guardian, they asked to speak to the next oldest child in the specified age range and so forth until they could screen at least one of the adolescents in the specified age range (if the parent/guardian granted permission to do so and the child wanted to). If no children in the specified age range were at home when the recruitment firm contacted the parent/guardian, they asked the parent/guardian when they should call back to screen the oldest child. (**Appendices A and B**)

For the adult in-person focus groups, a trained RTI staff member administered the informed consent prior to the beginning of the focus group. This process included providing a hard copy of the informed consent to the participant and answering any questions from the participant. Participants were advised that participation is voluntary, and they could choose to skip any question they do not wish to answer. The consent form (**Appendix E**) also indicated that they would receive \$125 for their participation. Participants were 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 of the consent forms were 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 were kept in a personal bag that project staff kept on hand at all times. The signed hard copies were scanned for storage on a secure server and locked in a cabinet that can be accessed only by project staff. Participants received a duplicate unsigned copy of the consent form for their records. RTI staff ensured that for all adult participants, a signed consent was secured prior to data collection.

For the adolescent in-person focus groups, adolescent participants were required to provide written assent to participate in the study. In addition, focus group facility staff emailed or mailed the parent or guardian a permission form prior to the study date. For emailed permission forms, parents or guardians could print and sign a copy to bring (or have their child bring) to the facility on the day of

the focus group. For mailed permission forms, two copies were 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 were also available at the facility for parents or guardians to sign on the day of the focus group if needed. All adolescent participants had to have a permission form signed by a parent or guardian before they could participate in the focus group. After receiving the signed parent permission form, a trained RTI staff member gave adolescent participants the assent form (**Appendix F**) prior to the beginning of the focus group and answered any questions from the participant. Participants were advised that participation was voluntary, and they could choose to skip any question they did not wish to answer. The assent form indicated that they would receive \$125 for their participation. Participants were required to provide their written assent (including only their first names) before proceeding with the focus groups. Youth participants were given a copy of the assent form to keep for their records. While in the field, the signed hard copies of the assent forms were 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 were kept in a personal bag that project staff kept on hand at all times. The signed hard copies were locked in a cabinet that could be accessed only by project staff. RTI staff ensured that for all youth participants, both a signed assent and corresponding signed parental permission form were secured prior to data collection.

The in-person focus groups were convened at professional recruitment facilities. FDA and RTI team members observed the focus groups remotely in real time through a secure, password-protected online streaming system (e.g., Zoom) or from behind a one-way mirror. Observers were able to use a chat feature to send the moderator questions that were asked at the end of the focus group. The market research firms audio-recorded the focus groups, and RTI provided FDA with transcripts of each focus group. We did not video record the in-person focus groups.

Upon arrival at the recruitment facilities, in-person participants in the adult focus groups read and signed their first name on an informed consent form (approved by OMB and RTI's IRB). If a participant was in an adolescent group, their guardian read and signed a parent permission form, and the adolescent participant signed their first name on an assent form. Guardians were given a copy of the permission form, and adolescents were given a copy of the assent form for their records. (see 10.0 for consent procedures).

For the in-person focus groups, participants completed a brief worksheet (**Appendix H**) approved by FDA after consenting to the study and prior to the focus group. The worksheet asked participants questions related to their device use such as: their (or their family member's) diagnosis; the length of their device use (e.g., three months); how often they use the 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 conducted the focus group discussions, and a trained staff member provided notetaking and logistical assistance. The moderator used a semi-structured guide (**Appendix I**) developed by FDA and RTI to facilitate the discussions and ensure that all major topics of interest were addressed. The moderator started each group by introducing themselves, explaining the ground rules, and reviewing key points from the informed consent. After addressing these items, the moderator moved on to the discussion questions. During certain activities, a second moderator assisted the primary moderator to facilitate the discussion.

For the AI focus groups, FDA provided each participant with trainer versions of the generic and branded epinephrine pen for participants to handle and review. For in-person groups, the moderator passed around the devices for manipulation and observation. Because FDA provided the trainer version of the generic and branded epinephrine pens, no actual medicine or needle was inside the device, so there was no risk of accidental dosing or injury.

For the DPI focus groups, FDA provided each participant with an Advair Diskus as well as the generic version of the Advair Diskus inhaler for participants to handle and review. FDA ensured that all medicine was removed from the devices prior to delivery to RTI. The moderator passed around the devices for participants to observe and manipulate.

For both the autoinjectors and inhalers, the participants also had an empty box with the instructions for use to review. In-person participants returned the branded and generic devices at the end of the focus group.

After each focus group was completed and the participants left the facility, the moderator reviewed and added to the focus groups notes as needed. The notetaker and moderator discussed any issues that arose related to logistics, the discussion guide, and/or participant interactions. RTI and FDA discussed what was learned during these informal debriefings. RTI made no process changes unless FDA requested them, and the changes were submitted and approved by RTI's IRB. In-person data collection took approximately four days (two days in each city). Each focus group lasted no more than 90 minutes. Following participation in the focus groups, enrolled individuals completed their participation in the study.

After data collection was complete at all locations, the study team created a summary report of the observations and insights from the focus groups and submitted the report and transcripts to FDA. RTI and the recruitment firms were the only parties in possession of the audio files from the in-person focus groups; FDA was not given the audio files from the in-person focus groups.

Transcripts were redacted so that no identifying information (including participant name) was included prior to submission to FDA.

Virtual focus groups: The recruitment process for the virtual focus groups will be identical to the in-person focus group recruitment process with few exceptions. For virtual focus groups, we will ask for permission to video record the group and to mail materials to the adolescent participant prior to the group. In addition, for virtual groups, the recruiter will collect a mailing address so they can send material to be used during the focus group. Permission/consent/assent will be secured electronically when scheduling the participant for the focus group. Information about how to join the virtual group will be emailed to participants/parents in advance (**Appendix V**).

For the virtual focus groups (adult and adolescent), after a participant is determined to be eligible and confirms interest in study participation (i.e., is scheduled for the focus group), the professional recruitment firm will send them an e-mail with the informed consent form (adult) or parental permission and assent forms (youth). The consent/permission/assent (**Appendices Q, R, and S**) forms will identify the investigators, briefly explain the procedures, and explain the purpose of the study. The forms will explain that: participation is completely voluntary, participants can refuse to answer any questions they prefer not to answer; and they can withdraw from the study for any reason at any time without penalty. The forms will explain that the focus group will be video and audio-recorded, and livestreamed. The consent/permission/assent forms will also provide: the project's toll-free number; the toll-free phone number for the RTI IRB; information about the relevant laws associated with informed consent; the OMB number; and the study expiration date. Participants (and guardians for the adolescent groups) will be asked to formally indicate whether they consent or decline to participate (or give or refuse to give their permission for adolescent groups) via an electronic system (e.g., selecting "yes, I agree to participate" or "no, I do not agree to participate" in the focus group). The recruitment facility will provide a record of each participants' consent (or permission and assent) when they send the final recruitment grid.

After receiving approval from the Office of Management and Budget and approval from RTI's Institutional Review Board (IRB), we will work with a recruitment partner to recruit participants and schedule the focus group discussions at pre-selected times. The virtual focus groups will use Zoom, a

web conferencing platform. Staff members and FDA team members may observe the virtual focus groups by joining the discussion without audio (microphone) or video.

The RTI team will audio and video record the virtual focus groups. Recordings will only include first names of participants. The session recordings will be accessible using a password-protected link for a limited time (e.g., one week) after the meeting to allow FDA team members to review the recording if they were unable to observe the focus group in real time. At the end of that period, the video recordings will no longer be accessible and will be destroyed. RTI will provide FDA with transcripts of each of the virtual focus groups.

All consent documentation will be reviewed prior to the date of the focus group. Prior to the meeting date, participants will be mailed a packet of materials, including the autoinjector trainer device and instructions for joining the virtual focus group (**Appendix W**). The recruitment facility will also confirm each participant is able to access the Zoom platform by conducting a test run of the login process. Upon joining the Zoom “room” for the virtual focus groups, participants will be placed into a waiting room. Moderators will track attendance based on a participant grid provided by the recruiters. Study staff will admit participants one-by-one into the Zoom room to “check-in.” This 1:1 interaction will allow study staff to change the displayed name to first name only, answer participant questions, and check to ensure that the participant’s mailed materials are available and accessible for the discussion. The participant will then return to the waiting room. After all participant “checks” are complete, the group will be re-admitted to the Zoom room together for the discussion.

During the virtual focus groups, participants will use the poll and chat functions in Zoom to participate in certain portions of the discussion. An experienced moderator will facilitate the focus group discussions, and a trained staff member will provide notetaking and logistical assistance. The moderator will use a semi-structured guide (**Appendix T**) developed by FDA and RTI 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 may assist the primary moderator to facilitate the discussion.

For the virtual AI focus groups, FDA will provide each participant with trainer versions of the generic and branded epinephrine pen for participants to handle and manipulate during the focus group. Participants will receive the trainer auto-injectors within a separate sealed envelope as part of their focus group package in the mail. Because FDA is providing the trainer version of the generic and branded epinephrine pens, the devices will contain no medicine or needle, so there will be no risk of accidental dosing or injury. Virtual participants will be asked to properly dispose of the devices at the end of the focus group.

After the participants leave the Zoom platform after each focus group, 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 make no process changes unless FDA requests them, and the changes have been submitted and approved by RTI’s IRB. Virtual data collection will take approximately four days. Each focus group will last no more than 90 minutes. Following participation in the focus groups, enrolled individuals will have completed their participation in the study.

After data collection is complete for the four virtual focus groups, 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. Study team members, including FDA, who were unable to watch the live streaming of the virtual focus groups, will have access to the focus group recording for a short period (e.g., 1 week) after the discussion. Before sending the password-protected link to the recordings, any

identifying information that may have been inadvertently provided will be bleeped out.

Prior to submission to FDA, transcripts will be redacted to remove all identifying information. RTI will not begin recording the online focus groups until every participant's identity has been protected (i.e., first names only).

4. Confidentiality of Respondents:

In-person focus groups: All data collection activities were 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 required by FDA regulations. Respondents received information about privacy protections as part of the informed consent process.

The local market research facilities used personal identifiable information (PII) (such as names and contact information) from people in its research database to recruit participants. Participants who joined the panel during the study or who reached the screener via promotion through community partners or media advertisements provided names and contact information for use by the local market research facilities only. This information was included on the focus group screener documents for recruitment purposes to aid in contacting potential participants prior to the focus groups. The recruitment firms did not share the PII with RTI or FDA. Also, the recruitment firms destroyed the focus group screeners containing the PII after the focus groups were completed. There was no link between the data collected and the participants' identities. FDA and RTI did not have the full names or any contact information for any of the participants.

The in-person focus groups were conducted at the two market research firm locations. The focus groups took place in a private focus group room so that only the RTI moderator and project staff could hear the participants' responses. Some project staff observed the discussion behind a one-way mirror or via live-streaming. They did not record participants' names. Livestreaming connections were secure, using industry-standard firewalls and security practices. All data was encrypted in transit using secure hypertext transfer protocol (HTTPS).

The following protections were in place to ensure privacy when administering the telephone screener to youth/adolescents. After receiving permission from the parent/guardian for screening, the recruiter administered the screener to the adolescent to determine eligibility. Adolescents were asked if they had privacy for the discussion before beginning the screening questionnaire. If not, or if the parent or guardian was still on the phone, the recruiter administering the screener suggested that he/she move 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 each participant's confidentiality included:

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

These confidentiality methods were approved by RTI's IRB before collecting any information.

Virtual focus groups: All steps to protect the privacy of participants will mirror those used for the in-person focus groups (outlined above). We discuss unique aspects of the virtual groups below.

The virtual focus groups will be conducted via the Zoom web conferencing platform. We will ask participants to ensure they are in a private space or to use the blurring background filter on Zoom, so that only the RTI moderator, project staff, and other participants in the focus group can hear the participant's responses. Project staff other than the moderator and notetaker may observe the virtual groups, but they will not have audio (microphone) or video enabled, and they will not interact with the participants in any way. Observers who do not take these precautions will be removed from the Zoom room.

5. Amount and Justification for Proposed Incentive:

For in-person focus groups, we provided participants with a cash incentive of \$125. For virtual focus groups, once the focus group is complete, we will provide online participants with \$125.

This \$125.00/participant token of appreciation is intended to provide enough incentive for the person to participate in the study rather than another activity. This token of appreciation is intended to: improve coverage of these hard to reach populations; improve study data quality; reduce the chance of cancellations or insufficient recruitment numbers; childcare costs; and to convey appreciation for contributing to this important activity.⁷ 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 with respect to their time and cost of participation.

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 for 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 that supports the use of incentives "to improve coverage of specialized respondents, rare groups, or minority populations".⁸ Our study involves hard-to-reach (rare) populations with a number of specific eligibility requirements (i.e., adolescents, adults, and caregivers affected by serious, life-threatening allergic reactions and use specific branded drug devices) in addition to being demographically and geographically diverse. Further, there is no existing research panel from which to recruit potential participants, which further complicates recruitment for this study. 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 who 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%.⁹ Within that small population, we would need to find people who are prescribed an

⁷ Russell, ML., Moralejo, DG., Burgess, ED. (2000). Paying research subjects: Participants' perspectives. *Journal of Medical Ethics*, 26(2), 126-130.

⁸ Office of Management and Budget. (2006). Questions and Answers When Designing Surveys for Information Collections.

⁹ 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.

epinephrine autoinjector *and* have the autoinjector is 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 applied 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 who *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 of potentially eligible participants who respond to ensure that the focus groups have a good mix of gender, race, and education within this hard to reach population. Lower incentive amounts would result in higher recruiting costs and burden to the public due to the need for additional recruitment.¹⁰

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 The \$125 was previously approved for the first phase of this study and it would be judicious to keep the same incentive amount for the virtual phase of the study.

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 as hard 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 provided an incentive of \$75 or \$100. Although the payment for these studies are lower 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)
 - o \$100 for 60 minutes with obese consumers
- *Hearing, Aging, and Direct-to-Consumer Television Advertisements* (OMB Control number 0910-0818; 2016)
 - o \$75 for 60 minutes with general population consumers
- *Focus Groups on FDA’s Accelerated Approval Process (under generic OMB Control Number 0910-049; 2018)*
 - o \$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

¹⁰ Krueger, R.A., & Casey, M.A. (2009). *Focus groups: A practical guide for applied research*. (4th Ed.). Thousand Oaks, CA: Sage Publications, Inc.

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.¹¹ 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.^{12,13,14,15} 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.¹⁶

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 that reflects diversity in age, income, and education.^{17,18} Numerous studies have shown that incentives can reduce nonresponse bias for key subgroups. Griffin et al.¹⁹ and Lesser et al.²⁰ found that incentives reduced nonresponse bias for gender. Incentives have also been effective in increasing participation from minority respondents.²¹

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,²² lack altruistic motives for responding, have competing obligations)²³ or are typically less likely to participate in research.²⁴ 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.²⁵

¹¹ 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.

¹² Shettle, C., & Mooney, G. (1999). Monetary incentives in US government surveys. *Journal of Official Statistics*, 15(2), 231.

¹³ Martinez-Ebers V. Using Monetary Incentives with Hard-To-Reach Populations in Panel Surveys. *Int J Public Opin Res*. 1997;99(1):77-86.

¹⁴ 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.

¹⁵ Church (1993): Estimating the effect of incentives on mail survey response rates. *Public Opinion Quarterly*, 57(1), 62-79.

¹⁶ Morgan, DL., Scannell, AU. (1998). *Planning Focus Groups*. Thousand Oaks, CA: Sage.

¹⁷ Groth, SW. (2010). Honorarium or coercion: use of incentives for participants in clinical research. *Journal of the New York State Nurses Association*.

¹⁸ Willis, G. (2005). *Cognitive interviewing: A tool for improving questionnaire design*. Thousand Oaks, CA: Sage.

¹⁹ 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.

²⁰ 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.

²¹ 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.

²² Groves, R. M., Presser, S., & Dipko, S. (2004). The role of topic interest in survey participation decisions. *Public Opinion Quarterly*, 68(1), 2-31.

²³ 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.

²⁴ 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.

²⁵ 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

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^{16,26,27}

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 used for the current study (Atlanta, GA; Los Angeles, CA; 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, or in the case of virtual interviews, the additional time needed to conduct the test-runs with the recruitment facility and then sign in early for the main focus 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. The conduct of the remaining four AI focus groups in the virtual environment eliminates the cost and time of travel but does not eliminate the need for childcare for participants with children in the home. In addition, the virtual environment requires participants to expend time and effort to secure the time and privacy to effectively participate in the focus group without interruptions, to receive and store focus group materials until the day of the focus group, and to ensure that their computer and internet resources will function properly with the Zoom platform.

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 having to cancel the focus group (note: a minimum of 4 people are needed to conduct the focus group). Importantly, if we have to cancel a focus group the day the group is scheduled to take place due to no shows, we will still have to pay the participants that were scheduled to attend and pay to reschedule the participants and find new participants—thus, incurring additional costs. Using the \$125 incentive rate that has proved sufficient in the past, we anticipate reducing no shows and not having to cancel and reschedule focus groups.

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

6. Questions of a Sensitive Nature:

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

7. Description of Statistical Methods:

²⁶ 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.

²⁷ Edwards, P., Roberts, I., Clarke, M., DiGiuseppi, C., Prata, S., Wentz, R. and Kwan, I. (2002) Increasing response rates to postal questionnaires: Systematic review. *British Medical Journal* 324, 1183.

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

9. Burden Hour Computation: *(Number of responses (X) estimated response or participation time in minutes (/60) = annual burden hours):*

RTI has completed ten in-person focus groups focusing on DPIs (N=40) and AIs (N=27). The burden hours for **in-person focus groups** (already collected) are calculated as follows:

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
Number to complete the study			
Adults, EpiPen	6	90	9
Adults, Other AIs	1	90	1.5
Caregivers, EpiPen	15	90	22.5
Adolescents, EpiPen	5	90	7.5
Adolescents, DPI	4	90	6
Experienced Users, DPI	18	90	27
Naïve Users, DPI	18	90	27
Total Reporting Burden Hours	67	--	100.5

For **virtual focus groups**, Approximate hours, in total, based on 90-minute focus groups with a maximum of eight participants for each of four focus groups. A total of 32 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	16	90	24
Caregivers, EpiPen	8	90	12
Adolescents, EpiPen	8	90	12
Total Reporting Burden Hours	32	--	48

10. Date(s) to be Conducted:

OMB approval was obtained for **in-person focus groups** prior to commencing research. The in-person focus groups took place in October and November of 2019 and January through March of 2020.

We anticipate the **virtual focus groups** will take place in Spring of 2022.

11. Requested Approval Date: April 2022

12. FDA Contacts:

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