TITLE PAGE

Protocol Title: Qualitative Research to Support Ellipta Ease-of-Use Questions in Pediatric Patients With Asthma

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CONFIDENTIAL

GlaxoSmithKline

HEALTH OUTCOMES STUDY PROTOCOL - QUALITATIVE RESEARCH

UNIQUE IDENTIFIER	*trackHO / eTrack ID* HO-17-18594 / 208129
FULL TITLE	*Qualitative Research to Support Ellipta Ease-of-Use Questions in Pediatric Patients with Asthma*
ABBREVIATED TITLE	*Pediatric Ease of Use Items*
FINAL PROTOCOL APPROVED	*DD-MMM-YYYY* *(Enter date of Senior Line Manager approval signature)*
SPONSORSHIP	*Sponsored*
DIVISION	Pharma
BUSINESS UNIT	Research & Development
DEPARTMENT	*USHO*
STUDY ACCOUNTABLE PERSON	PPD *PharmD, MS - GSK*
CONTRIBUTING AUTHORS	PPD *MSPH* *Executive Director, Patient-Centered Outcomes Assessment* *RTI Health Solutions (RTI-HS)*

ASSET ID	*Enter the asset ID of the GSK product being assessed or the class in which GSK has a product if applicable*
GSK ASSET	*Fluticasone furoate (ARNUITY ELLIPTA)*
INDICATION	*Asthma*

REVISION CHRONOLOGY:

Version Date	Document Type	Change(s) since last version
Enter original protocol FPA	Original	n/a
Enter protocol amendment FPA	*Amendment 01*	*e.g. Addition of exclusion criteria*

Description: *Pediatric Ease of Use Items*
Unique Identifier: *trackHO / eTrack ID*

SPONSOR SIGNATORY

PPD

21 Sept 2017

Richard H Stanford, PharmD — *DD-MMM-YYYY*

Senior Director — Date

PPD

Sept 21, 2017

Martin D. Marciniak
Vice President
Customer Engagement, Value
Evidence & Outcomes

PROTOCOL SYNOPSIS

Unique Identifier	*HO-17-18594/ 208129*
Abbreviated Title	Pediatric Ease of Use Questions
GSK Product	ELLIPTA
Rationale	To develop items to assess ease of inhaler use by pediatric patients with asthma and their caregivers for implementation in clinical trials
Objectives (Primary, Secondary)	A range of devices has been developed to administer inhaled therapy for asthma, including dry powder inhaler (DPI) devices that are produced in many formats. GlaxoSmithKline (GSK) has developed and is currently marketing ELLIPTA, a DPI that is preloaded with a drug therapy to treat patients with asthma. GSK and RTI-HS have previously collaborated to develop items to assess ease of inhaler use for implementation in clinical trials of adults. In the current project, GSK would like to incorporate the previously developed questions into a clinical trial with pediatric patients (aged 5 to 11 years). A secondary objective will be to evaluate the ability of children aged 5 to 11 years to produce an audible sound using the ELLIPTA whistle.
Study Design	A cross-sectional, qualitative study including two iterative sets of cognitive interviews with 16 subjects (pediatric patients with asthma who are currently using an asthma maintenance inhaler and their caregivers).
Study Population and Sampling Methods	Eligible subjects for the cognitive interviews must: *Child inclusion criteria* • Be 5 to 11 years of age • Have asthma • Currently use maintenance inhalers to treat their asthma • Be willing and able to provide assent • Be willing and able to participate in a 45-minute interview conducted in English *Caregiver inclusion criteria* • Be 18 + years of age • Be a caregiver (parent or legal guardian) of a child with asthma that meets the criteria above • Be willing and able to provide signed and dated informed consent and parental permission in English • Be willing and able to participate in a 45-minute interview

Data Source	All data will be provided by the participants at the individual patient interviews and during patient recruitment.
Data Analysis Methods	The descriptive analyses will include the computation of frequencies and percentages for categorical variables (e.g., gender, education level) and the computation of means, standard deviations, and ranges for continuous variables (e.g., current age, age at diagnosis). Analysis will follow standard qualitative data-collection and analysis methods that include two main guiding principles: researcher neutrality and systematic process. Data will be systematically collected via field notes and audio recording. The analysis goal of the first set of interviews is to evaluate the proposed mode of administration by age group and to identify any initial problems with item wording or response options. The analysis goal of the second set of interviews is to test the adequacy of modifications based on the first set of interviews and to inform any further revisions, inform the mode of administration by age group, and gather additional qualitative data about the final item set prior to implementation in the clinical trial. Each interview also offers an opportunity to identify any additional concepts that patients and their caregivers think should be addressed regarding ease of use (if any), contributing to the content validity of the final instrument. A final report will summarize the entire questionnaire development process, including analysis methods and results.
Sample Size and Power	Target population of 16 child/caregiver dyads (32 total participants) participating in 2 sets of interviews (approximately 8 dyads per interview set). We anticipate this to be a sufficient sample size to evaluate the developed ease of use items.
Limitations	The study design limitation rests in its qualitative nature. While data obtained from participants are considered reliable, their external validity cannot be confirmed as generalizable to the entire population of individuals with asthma who may participate in a clinical study. Response bias is another potential limitation associated with the proposed design in that individuals willing to participate in a clinical trial of a new treatment may be different than those willing to participate in a qualitative study. Despite these limitations, a qualitative approach is the only study design that will meet the study objective of obtaining this data directly from individuals using inhalers to treat their asthma.

TABLE OF CONTENTS

ABBREVIATIONS

AE	adverse event
CE	concept elicitation
CFR	Code of Federal Regulations
DPI	dry powder inhaler
ePRO	electronic patient reported outcome
FDA	Food and Drug Administration
GSK	GlaxoSmithKline
ICF	informed consent form
IRA	inter-rater agreement
IRB	institutional review board
NRS	numerical rating scale
PRO	patient-reported outcome
RTI-HS	RTI Health Solutions

1 INTRODUCTION/BACKGROUND

Asthma is a chronic inflammatory disorder of the airways defined by airflow obstruction. The obstruction may or may not be completely reversed with specific therapy. Airway inflammation is the result of interactions between various cells, cellular elements, and cytokines. Airway inflammation may cause recurrent or persistent bronchospasm, which causes symptoms that include wheezing, breathlessness, chest tightness, and cough, primarily at night or after exertion (Kelly et al., 2017).

Asthma affects an estimated 300 million individuals worldwide (Global Initiative for Asthma [GINA], 2017). The World Health Organization (WHO) has estimated that 13.8 million disability-adjusted life-years are lost and 346,000 asthma deaths are reported per year worldwide (GINA, 2017).

A range of devices has been developed to administer inhaled therapy for asthma, including dry powder inhaler (DPI) devices that are produced in many formats. GlaxoSmithKline (GSK) has developed and is currently marketing ELLIPTA, a DPI that is preloaded with a drug therapy to treat patients with asthma.

2 OBJECTIVES

2.1 Primary

The objective of the study is to revise ease of use items developed for adults (Appendix A) to be appropriate for completion by pediatric patients in future clinical trials and to evaluate the newly developed items in patients with asthma aged 5 to 11 years and their caregivers.

2.2 Secondary

The secondary objective of the study is to evaluate the ability of children aged 5 to 11 years to produce an audible sound using the ELLIPTA whistle prior to use of the whistle in future clinical trials.

3 RESEARCH METHODOLOGY

3.1 Study Design

This cross-sectional, qualitative study will involve up to 16 child and caregiver dyads (total of 32 participants). Specifically, two iterative rounds of cognitive debriefing (targeting 8 dyads per round) will be conducted at two different qualitative research facilities that specialize in recruitment and the conduct of qualitative studies. Given the pediatric population, the proposed methods and procedures have been developed based on the recommendations provided by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force for Good Practices for the Assessment of Children and Adolescents (Matza et al., 2013). Specifically, the adult ease of use items will be modified to incorporate language appropriate for children. In addition, varying modes of administration will be assessed, including interview administration for children aged 5 to 7 years and for those who are reported by the caregiver to not be able to or to have difficulty reading. Draft pediatric and caregiver items are provided in Appendix B.

Given the age of the pediatric participants, caregivers will also be included in the interview room; however, the caregiver will be asked to sit behind the child and remain silent during the interview in order to avoid influencing the child's responses.

The interviews will be conducted by two experienced interviewers from RTI-HS. One interviewer will take primary responsibility for leading the interview while the second records detailed field notes. Field notes will incorporate both the verbal exchange between the participant and interviewer and the nonverbal cues that may influence interpretation of the data, particularly important in interviews with children. A standardized, semistructured discussion guide (Appendix C) will be used to ensure consistency of data collection across interviews. Each interview will last approximately 45 minutes. All interviews will be audio recorded and transcribed by a medical transcriptionist for use in preparing a written summary report.

Each interview will be conducted at a research facility in Raleigh, NC, or Detroit, MI; both facilities specialize in the recruitment of participants and facilitation of qualitative studies (e.g., hosting, recording).

The qualitative research facilities will identify and screen potential study subjects using a screener developed by RTI-HS in collaboration with GSK (Appendix D). Specifically, the facility staff will identify possible subjects and contact them via telephone to determine whether they are interested in participating in the study, relying on the database of individuals who expressed interest in participating in qualitative research or who have participated in prior qualitative research. If an individual is interested, he or she will be evaluated using the screener developed for this study and, if qualified, will be scheduled for an interview. Patient and caregiver demographic information (e.g., age, ethnicity) will also be collected during screening. These variables will be used to ensure a study sample that is reasonably representative of the anticipated clinical trial population. Additional variables for the purposes of stratification are not recommended given that these would limit the generalizability of the sample. Throughout the recruitment process, the qualitative research facility will provide progress updates to RTI-HS (i.e., the number and demographic characteristics of participants recruited). However, no identifying information about individual participants will be exchanged between the facility and RTI-HS.

3.2 Study Population

3.2.1 Eligibility Criteria

Eligible subjects for the cognitive interviews must:

Child inclusion criteria

- Be 5 to 11 years of age
- Have asthma
- Currently use a maintenance inhaler to treat their asthma
- Be willing and able to provide assent
- Be willing and able to participate in a 45-minute interview in English

Caregiver inclusion criteria

- Be 18 + years of age
- Be a caregiver (parent or legal guardian) of a child with asthma that meets the criteria above
- Be willing and able to provide signed and dated informed consent and parental permission in English
- Be willing and able to participate in a 45-minute interview

3.2.2 Sampling

The patient population will consist of a convenience sample of child and caregiver dyads. Participants will be screened and recruited for the study based on the above listed inclusion criteria which were developed with the aim of recruiting a population similar to that included in the planned clinical trial.

3.3 Data Source / Data Collection

All data will be provided by interview participants either during recruitment or during the interview. The qualitative research facilities will enter demographic and asthma-specific data provided by participants into a Microsoft Excel spreadsheet and provide it to RTI-HS. The qualitative data from the interviews will be systematically collected by RTI-HS via field notes and audio recordings. Following the conclusion of the interviews, all audio files will be transcribed and prepared for analysis.

3.3.1 Endpoints

3.3.1.1 Primary Endpoint

The evaluation of items to assess ease of inhaler use for implementation in clinical trials with pediatric patients aged 5 to 11 years and their caregivers.

3.3.1.2 Secondary Endpoint

The determination of the number of participants aged 5 to 11 years able to produce an audible sound using the ELLIPTA whistle.

3.4 Sample Size / Power Calculations

Target population of 16 of child/caregiver dyads consisting of 1 child (aged 5 to 11 years) with asthma currently using a maintenance inhaler and his or her caregiver (for a total sample of 32 participants). The interviews will be conducted in two iterative sets (approximately 8 dyads or 16 participants per set) to allow for refinement of the items between sets.

Formal sample size calculations based on hypothesis testing were not performed due to the qualitative nature of this study. However, conducting two sets of interviews with a targeted total of 32 individuals is

expected to provide an adequate sample for systematic qualitative analysis and assessment of the research objective.

Specifically, it is anticipated that the comprehension and appropriateness of the instructions and items will be fully demonstrated across the evaluated age range by the completion of the second set of interviews. However, if participants provide feedback or the interviewers observe that the instructions or items are not clear or that the measure does not fully assess key ease of use inhaler attributes, an increased sample size would be recommended (e.g., revision of the items and the conduct of additional set[s] of interviews).

3.5 Hypotheses

Not applicable

4 DATA ANALYSIS CONSIDERATIONS

RTI-HS will perform descriptive analyses to summarize the demographic and clinical data provided by participants at screening and qualitative analysis of interview data. The descriptive analyses will include the computation of frequencies and percentages for categorical variables (e.g., gender, education level) and the computation of means, standard deviations, and ranges for continuous variables (e.g., current age, age at diagnosis). The number of participants aged 5 to 11 years who are able to produce an audible sound using the ELLIPTA whistle will also be reported, as will the number of attempts required (up to 3 attempts per participant).

Analysis will follow standard qualitative data-collection and analysis methods that include two main guiding principles: researcher neutrality and systematic process. Data will be systematically collected via field notes and audio recordings.

Following the conclusion of the patient interviews, all audio files will be transcribed and prepared for analysis.

Analysis of the resulting data (captured in both field notes and transcripts) will ensure that an accurate reflection of the combined results (across interview sets) has been captured.

The analysis goal of the first set of interviews is to evaluate the proposed mode of administration by age group and identify any initial problems with item wording or response options. The analysis goal of the second and final set of interviews is to test the adequacy of modifications based on the first set of interviews, inform any further revisions required to optimize the items, and gather additional qualitative data about the final item set before implementation in the clinical trial. Each interview also offers an opportunity to identify any additional concepts patients and/or their caregivers think should be addressed regarding ease of use (if any) in order to contribute to the content validity of the final instrument.

A final report will summarize the entire questionnaire development process, including analysis methods and results. The summary report will describe the implications of the cognitive debriefing interviews,

including rationale for item development, modification(s), and mode of administration by age. In addition, the report will include representative quotes from participants.

5 LIMITATIONS

One limitation of this study design rests in its qualitative nature. While data obtained from participants are considered reliable, their external validity cannot be confirmed as generalizable to the entire population of individuals with asthma who may participate in a clinical study.

Response bias is another potential limitation associated with the proposed design in that individuals willing to participate in a clinical trial of a new treatment may be different than those willing to participate in a qualitative study. For instance, those who agree to participate in a clinical trial may experience a greater severity of asthma. Both of these limitations have been addressed by designing the selection criteria for the cognitive debriefing interviews to be similar to the clinical trial criteria.

6 STUDY CONDUCT, MANAGEMENT & ETHICS

6.1 Ethics Committee/IRB Approval

RTI International's (RTI's) institutional review board (IRB) will review and approve the study protocol, screening materials, all data-collection materials, and the informed consent documents.

RTI, of which RTI-HS is a part, holds a Federal-Wide Assurance (FWA #PPD effective until June 16, 2020) from the US Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) that allows for the review and approval of human subjects protocols through the IRB committees. These committees are also registered with OHRP for research regulated by both the US DHHS and the Food and Drug Administration (FDA) (registration expires February 2, 2020). The RTI FWA requires IRB review for all studies conducted by RTI that involve human subjects, regardless of the funding source. Depending on the level of risk and nature of the research, a study may be ruled as exempt from IRB review by an IRB chair or designated IRB member. Studies that are not exempt must be approved either by an IRB chair or designated IRB member (if the study qualifies for expedited review) or by a full IRB committee.

RTI currently has three IRB committees available to review research protocols. Each committee meets monthly. One of the IRBs is constituted with appropriate medical expertise among its members to review biomedical clinical trials. These IRBs have been audited by the FDA and are fully compliant with applicable regulatory requirements. The committees review research studies to ensure adherence to appropriate regulations that govern human subjects research, including the Code of Federal Regulations 45, CFR 46, and 21 CFR 50 and 56, and with all applicable provisions of the International Conference on Harmonisation. All studies involving human subjects undergo an annual IRB review.

RTI-HS will obtain prospective approval of the study protocol, protocol amendments, informed consent forms, and any other relevant documents from one of the three RTI IRB committees.

Compliance with GSK and regulatory standards provides assurance that the rights, safety, and well-being of patients participating in non-interventional studies are protected (consistent with the principles that have their origin in the Declaration of Helsinki) and that the study data are credible and responsibly reported.

This study was designed and shall be implemented and reported in accordance with the Guidelines for Good Pharmacoepidemiology Practices of the International Society for Pharmacoepidemiology (2007), the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (von Elm et al., 2008), and with the ethical principles laid out in the Declaration of Helsinki.

6.2 Informed Consent

Prior to each interview, RTI-HS staff will conduct the informed consent discussion, comprised of the informed consent discussion with parents/guardians, and the parental consent and child assent discussion with the parents/guardians and the child/interview participant.

This discussion will include (but will not be limited to) an overview of the study procedures, the voluntary and confidential nature of the research, and audio recording details. Children and parents/guardians will be encouraged to ask any questions about the study at this time. If the parent/guardian agrees to participate in the interview, he/she will sign and date the parental informed consent form. If the child agrees to participate in the interview, the child will be asked to acknowledge assent (if appropriate) on the child assent form. Signed consent, permission, and assent forms will be maintained by RTI-HS in a controlled documents room accessible only to the RTI-HS project team and separate from other study documentation. Each parent and participant will be given an unsigned copy of both the parental consent and assent forms.

6.3 Data Protection

The qualitative research facilities will enter demographic and asthma-specific data provided by participants into a Microsoft Excel spreadsheet provide it to RTI-HS.

The qualitative data from the interviews will be systematically collected by RTI HS via field notes and audio recordings. All information provided during the interview will be kept highly confidential. Patient interviews will only use first names for participants. These first names will not be included in the study report. While the interviews will be audio recorded and transcripts will be made from the audio recording of the interviews, participants' names will never be associated with the responses given. Any names (even first names) mentioned during the course of the discussions will be omitted from the transcripts. Upon completion of the transcripts and final written report, all audio recordings will be destroyed.

All signed and dated informed consent (the only form with identifying information will be maintained at RTI-HS in a secure location (a controlled documents room) separate from other study documentation to further ensure participant confidentiality.

If the results of this study are presented at scientific meetings or published in scientific journals, no information will be included that could identify you or your answers personally. Publications will comply with internal GSK standards and the International Committee of Medical Journal Editors guidelines.

6.4 Personally Identifiable Information (PII)

All patient information collected during the patient interviews will be de-identified as described above. No patient information will be associated or linked to any particular participant.

6.5 Adverse Event (AE), Pregnancy Exposure, and Incident Reporting

No solicited safety data capture is required for prospective studies using primary data collection without a GSK drug of interest. However, if during the course of the study participation an adverse event suspected to be associated with the use of a GSK product is identified in a patient, it must be reported to the local health authority in accordance with national regulatory requirements for individual case safety reporting, and a spontaneous report must be sent to GSK. Adverse reactions identified for non-GSK products should be reported to the local health authority in accordance with national regulatory requirements for individual case safety reporting or the marketing authorization holder.

7 EXTERNAL INVOLVEMENT

7.1 Third Party Supplier

L&E Research
5505 Creedmoor Road, Suite 200
Raleigh, NC 27612
Phone: PPD

Shifrin-Hayworth, Inc.
26400 Lahser Rd, Suite 430
Southfield, MI 48033
Phone: PPD
Fax: PPD

7.2 External Expert/Health Care Professionals (Consultants & Research PIs)

Qualitative Research Partner:
RTI-Health Solutions
3005 Boardwalk Street, Suite 105
Ann Arbor, MI 48108 USA

8 REFERENCES

Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Online appendix. 2017. Available at: http: http://ginasthma.org/2017-online-appendix-global-strategy-for-asthma-management-and-prevention/. Accessed September 12, 2017.

International Society for Pharmaceutical Engineering (ISPE). Guidelines for good pharmacoepidemiology practices (GPP). Pharmacoepidemiol Drug Saf. 2008 Feb;17(2):200-8.

Kelly WF III, Cohee BM, Oppenheimer JJ, Argyros GJ. Allergic and Environmental Asthma Overview of Asthma. April 13, 2017. Available at: http://emedicine.medscape.com/article/137501-overview. Accessed June 14, 2017.

Matza LS, Patrick D, Riley AW, Alexander JJ, Rajmil L, Pleil AM, et al. Pediatric patient-reported outcome instruments for research to support medical product labeling: report of the ISPOR PRO Good Research Practices for the Assessment of Children and Adolescents Task Force Value Health 2013;16(4):461-79.

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008 Apr;61(4):344-9.

APPENDIX A: ADULT EASE OF USE ITEMS

ELLIPTA Inhaler Ease of Use Questionnaire

Paper copies of the Ease of Use questions will be used by the administrator (Investigator or designee) to record subjects' answers to the questions. The site will enter the answers into the electronic case report form (eCRF).

INSTRUCTIONS: The administrator (Investigator or designee) will complete the following questions related to the ELLIPTA inhalers used during this study. **Check only one** response for the question asked.

Survey questions VERSION "A" **OR** "B" to be completed at visit 2 per randomization at visit 2.

ELLIPTA Inhaler Questionnaire (VERSION A)

Instructions: Please complete the following questions related to the ELLIPTA inhaler that you used during this study. Choose only **one** response for each question.

1. How easy or difficult is it to use the ELLIPTA inhaler?
   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

2. How easy or difficult is it to tell how many doses are left in the ELLIPTA inhaler?
   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

3. If your **current daily inhaled COPD medication** was available in the ELLIPTA inhaler, how likely or unlikely would you be to request the medication in the ELLIPTA inhaler from your doctor?
   - □ Very likely
   - □ Likely
   - □ Unlikely
   - □ Very unlikely

APPENDIX B: PEDIATRIC AND CAREGIVER EASE OF USE ITEMS

Interviewer-administered version (recommended for ages 5-7 and any participants that appear to have difficulty reading the self-administered version for ages 8-11). To be administered by trained clinic-staff (not the parent or caregiver).

Instructions: "*I am going to ask you some questions about using this inhaler [interviewer has demonstrator ELLIPTA]. The name of the inhaler is ELLIPTA. I will read the question and answers to you. Then I will ask you to choose the answer that matches what you thought about using the ELLIPTA at home. Do you have any questions for me?*"

[Pause and answer any questions from participant. After answering any questions, read the first question and the responses as written below. Repeat the question and responses as needed for the participant. Once the participant has selected a response, read the second question and responses. If the child needs help in understanding the questions or responses, you can explain or define individual words but please take care not to influence his or her answer].

1a. How easy is it to use the ELLIPTA inhaler?

- □ Very easy
- □ Easy
- □ Hard
- □ Very hard

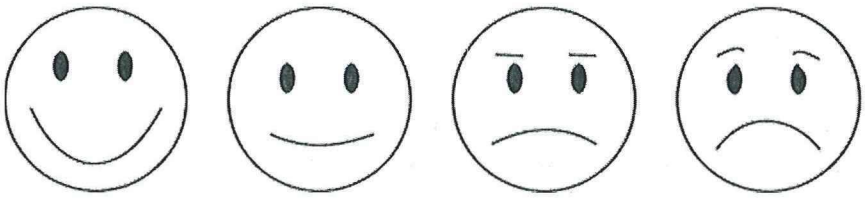
Or

1b. Is it easy to use the ELLIPTA inhaler?

- □ Yes
- □ No

Or

1c. How easy is it to use the ELLIPTA inhaler?



Very easy Easy Hard Very hard

2a. How easy is it to tell how many puffs are left in the ELLIPTA inhaler?

□ Very easy
□ Easy
□ Hard
□ Very hard

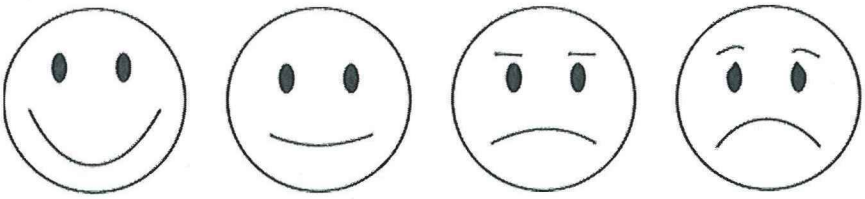
Or

2b. Is it easy to tell how many puffs are left in the ELLIPTA inhaler?

□ Yes
□ No

Or

2c. How easy is it to it to tell how many puffs are left in the ELLIPTA inhaler?



Very easy Easy Hard Very hard

Self-completed version (recommended for ages 8-11). For any participants that have difficulty completing self-administered version, the interview-administered version for ages 5-7 can be used.

Proposed verbal instructions to be read by trained clinic staff: "I am going to give you a paper with two questions about the inhaler you used during the study *[interviewer has demonstrator ELLIPTA]. The name of the inhaler is ELLIPTA. Read the questions and choose the answer that best matches what you thought about using the ELLIPTA at home. Do you have any questions?*" [Pause and answer any questions from participant. If participant needs help in understanding the questions or responses, you can explain or define individual words but please take care not to influence his or her answer].

Please choose one answer.

1a. How easy is it to use the ELLIPTA inhaler?

□ Very easy
□ Easy
□ Hard
□ Very hard

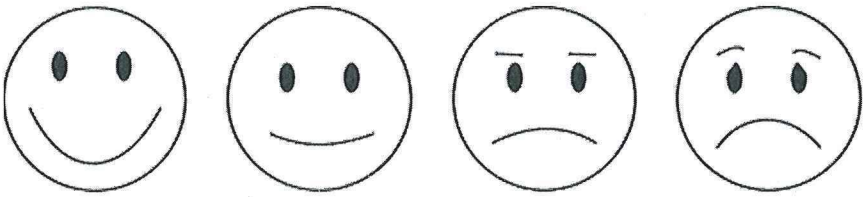
Or

1b. Is it easy to use the ELLIPTA inhaler?

□ Yes
□ No

Or

1c. How easy is it to use the ELLIPTA inhaler?



Very easy Easy Hard Very hard

2a. How easy is it to tell how many puffs are left in the ELLIPTA inhaler?

□ Very easy
□ Easy
□ Hard
□ Very hard

Or

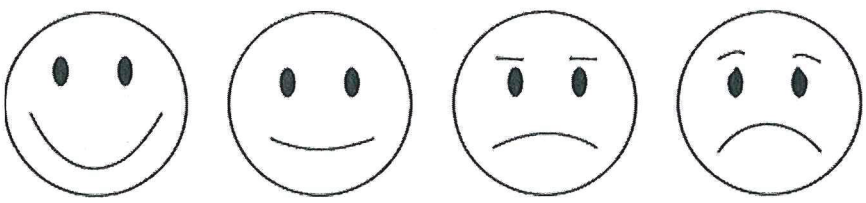
P
P
D

2b. Is it easy to tell how many puffs are left in the ELLIPTA inhaler?

□ Yes
□ No

Or

2c. How easy is it to it to tell how many puffs are left in the ELLIPTA inhaler?



Very easy Easy Hard Very hard

Caregiver Version

[The following two items are being evaluated as observer-reported outcome (ObsRO) items for children that are not able to report on ease of use or remaining doses].

Please answer the following question based on what you observed when your child used the study inhaler (called the ELLIPTA) at home. Choose only **one** response for each question.

1. How easy was it for your child to use the ELLIPTA inhaler?
   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

2. How easy was it for your child to tell how many doses were left in the ELLIPTA inhaler?

   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

[The below items are being evaluated as PRO items based on the experience of the caregiver].

Please answer the following questions based on your experiences while your child was using the study inhaler (called the ELLIPTA) at home. Choose only **one** response for each question.

1. How easy was it for you to tell how many doses were left in the ELLIPTA inhaler?

   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

2. If your child's **current daily inhaled asthma medication** was available in the ELLIPTA inhaler, how likely would you be to request the ELLIPTA inhaler from your child's doctor?

   - □ Very likely
   - □ Likely
   - □ Unlikely
   - □ Very unlikely

APPENDIX C: INTERVIEW GUIDE

Interview Discussion Guide:
Pediatric Inhaler Ease of Use

NOTE: This guide is to be utilized as a topic guide, to encourage spontaneity of responses and foster a relaxed tone throughout the discussion. The guide is not intended to be followed in a verbatim question format. Discussion starts only after informed consents, parental permission forms and assents are completed.

I. Introduction

A. Introductions

"Hi, my name is _____and I work for a company called RTI Health Solutions. What is your first name?"

B. Explain the purpose of the interview

"We are doing a study to learn about what kids think of the inhalers they use for asthma. We want to figure out the best way to ask kids about using an inhaler. We will be talking to other kids like you and their parents to make questions that will be easy to answer.

First, I am going to ask you some questions about the inhaler that you use for your asthma and what you think about it. Then I'm going ask you to listen to [or read for children 8-11] some questions and let me know what you think about them. There are no right or wrong answers to these questions. I just want you tell me what you really think! When we are done, I am going to ask your [mom, dad, other caregiver] some questions about your inhaler and have them answer some questions to tell me how we can make those questions better. [Caregiver/parent will be asked to sit behind the child to avoid influencing the child's responses during the child interview portion. For the caregiver portion, there will be quiet activities such as paper and crayons available for the child while the interviewers are speaking with the caregiver].

Do you have any questions for me before we get started?

OK, let's begin..."

II. Discussion with Child: Warm-up (Same questions for all children)

- Can you tell me about the inhaler that you use every day? Not the inhaler that might be called a "rescue" inhaler (for when you are having trouble breathing), but the one that you use all the time.
- What do you call this inhaler?
- What do you think about using [child's name for inhaler]? Is it hard to use? Why? Do you like to use it? Why (or why not)?
- Do you remember who taught you how to use [child's name for inhaler]? Was it hard to learn how to use it?
- Does anyone help you when you use it?
- How do you remember to use it every [night, morning or night and morning]?
- Do you know when the [child's name for inhaler] is almost out of medicine? How?

- Can you tell me how you take your medicine? Can you pretend you have your [child's name for inhaler] with you now and show me how you use it? How do you get the inhaler ready? After it is ready, what do you do to use it? What else do you have to do when you use your inhaler?
- Thank you for telling me about your [child's name for inhaler]. Now I want to ask you some questions about using an inhaler. When you are answering the questions, I want you to think about the inhaler that you just told me about we just talked about [**Note: for the purposes of cognitive debriefing, replace ELLIPTA with the child's name of his/her maintenance inhaler, do this verbally for the children in the 5-7 age range, for the children that are 8-11 can update "ELLIPTA" on the questionnaire to the name that the child calls their inhaler (if just "inhaler" can put one line through ELLIPTA)**].

Debrief (Children 5-7):

Instructions: I will read the question and answers to you. Then I will ask you to choose the answer that matches what you thought about using the [child's name for inhaler] at home. Do you have any questions for me?"

1a. How easy is it to use the [ELLIPTA] inhaler?
- □ Very easy
- □ Easy
- □ Hard
- □ Very hard

[Interviewer notes the response selected by the child].

- Could you please tell me what it is about [child's name for inhaler] that makes you say it's [child's answer] to use? What did you have to think about to answer?
- Was it hard to understand my question? Why? Was it hard to choose an answer? Why?
- What would it be like if it was [opposite of what child chose – hard or easy]?
- Is easy and very easy the same for you or are they different? What things are easy for you? What things are very easy for you?
- Is hard and very hard the same for you or are they different? What things are hard for you? What things are very hard for you?

Thank you, now I have another question to ask you.

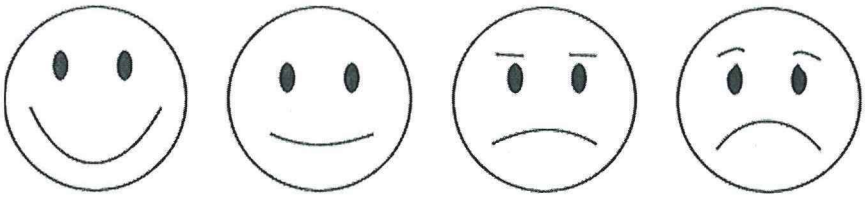
1b. Is it easy to use the [ELLIPTA] inhaler?

□ Yes
□ No

- What makes you answer [child's response] to this question? What did you have to think about?
- Is this question the same or different than the one we just talked about?
- Was this question easier or harder for you to answer? Why?

Thank you, now I am going to ask another question, but this time I have a different way for you to tell me your answer [*interviewer provides child with sheet that has the item and responses, interviewer reads the question and the response under each face, when pointing to the face and asks the child to circle the face that matches their answer*].

1c. How easy is it to use the [ELLIPTA] inhaler?



Very easy Easy Hard Very hard

- Do you think the faces make is easier to answer the question? Why?
- [Only ask if a different response from 1a was chosen] You circled [child's response]. Why did you choose that answer?
- If you had to tell me about [select a face], what words would you use? What feeling does the face make you think of? Why?
- Which of the three questions that I asked you was the easiest to answer? Why?

Thank you, now we have three more questions for you before we talk to your [mom, dad, other caregiver].

2a. How easy is it to tell how many puffs are left in the [ELLIPTA] inhaler?

□ Very easy
□ Easy
□ Hard
□ Very hard

[Interviewer notes the response selected by the child].

- Could you please tell me what it is about [child's name for inhaler] that makes you say it's [child's answer] to tell how many puffs are left?
- What does a puff mean?
- What did you have to think about to answer?
- Was it hard to understand my question? Why? Was it hard to choose an answer? Why?
- What would it be like if it was [opposite of what child chose – hard or easy] to tell how many puffs were left?
- Is easy and very easy the same for you or are they different? What things are easy for you? What things are very easy for you?
- Is hard and very hard the same for you or are they different? What things are hard for you? What things are very hard for you?

Thank you, now I have another question to ask you.

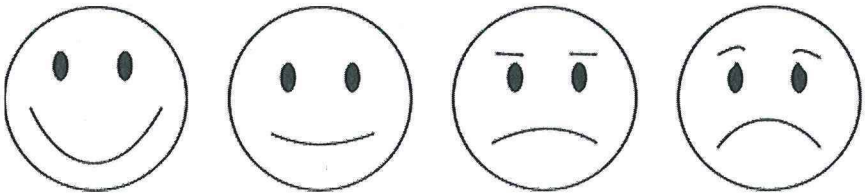
2b. Is it easy is it to tell how many puffs are left in the [ELLIPTA] inhaler?

□ Yes
□ No

- What makes you answer [child's response] to this question? What did you have to think about?
- Is this question the same or different than the one we just talked about?
- Was this question easier or harder for you to answer? Why?

Thank you, now I am going to ask another question where you circle your answer [*interviewer provides child with sheet that has the item and responses, interviewer reads the question and the response under each face, when pointing to the face and asks the child to circle the face that matches their answer*].

2c. How easy is it to it to tell how many puffs are left in the [ELLIPTA] inhaler?



Very easy Easy Hard Very hard

- Do you think the faces make is easier to answer the question? Why?
- [Only ask if a different response from 1a was chosen] You circled [child's response]. Why did you choose that answer?
- If you had to tell me about [select a face], what words would you use? What feeling does the face make you think of? Why?
- Which of the three questions that I asked you was the easiest to answer? Why?

Thank you, is there anything else about how easy or hard it is to use your inhaler that you think I should know? Okay, now we will ask your (mom, dad, other caregiver) a few questions.

Debrief (children 8-11):

I would like you to read and answer a few questions for me. When you read them, I would like you to read them out loud. I would also like to you tell me what you are thinking about when you decide on an answer. There are no right or wrong answers, I just want to understand how you think about the question.

[Provide the child the child with the first question]

Let's start with the first sentence:

Please choose <u>one</u> answer.

- What does that sentence mean to you? Was it hard to understand?

Let's go on to the question, can you read the question out loud?

1a. How easy is it to use the [ELLIPTA] inhaler?

Can you read each of the answers below the question out loud and choose a response?

□ Very easy
□ Easy
□ Hard
□ Very hard

- Could you please tell me what it is about [child's name for inhaler] that makes you say it's [child's answer] to use? What did you have to think about to answer?
- Was it hard to understand my question? Why? Was it hard to choose an answer? Why?
- What would it be like if it was [opposite of what child chose – hard or easy]?
- Is easy and very easy the same for you or are they different? What things are easy for you? What things are very easy for you?
- Is hard and very hard the same for you or are they different? What things are hard for you? What things are very hard for you?

Thank you, now I have another question for us to look at.

Can you read this question out loud?

1b. Is it easy to use the [ELLIPTA] inhaler?

Can you read each of the answers below the question out loud and choose a response?

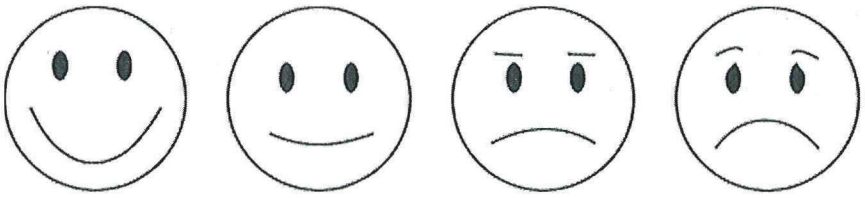
□ Yes
□ No

- What makes you answer [child's response] to this question? What did you have to think about?
- Is this question the same or different than the one we just talked about?
- Was this question easier or harder for you to answer? Why?

Thank you, now I am going to show you another question. Can you read this question out loud?

1c. How easy is it to use the [ELLIPTA] inhaler?

Can you read each of the words below the pictures of faces out loud and choose a response?



Very easy Easy Hard Very hard

- Do you think the faces make is easier to answer the question? Why?
- [Only ask if a different response from 1a was chosen] You circled [child's response]. Why did you choose that answer?
- If you had to tell me about [select a face], what words would you use? What feeling does the face make you think of? Why?

Let's look back at all 3 of these questions. Which one was the easiest to answer? Why? Which question did you like the best? Why?

Thank you, now we have three more questions for you before we talk to your [mom, dad, other caregiver].

Can you read this question aloud?

2a. How easy is it to tell how many puffs are left in the [ELLIPTA] inhaler?

Can you read the answers under the question aloud and choose an answer?

□ Very easy
□ Easy
□ Hard
□ Very hard

- Could you please tell me what it is about [child's name for inhaler] that makes you say it's [child's answer] to tell how many puffs are left?
- What does a puff mean?
- What did you have to think about to answer?
- Was it hard to understand my question? Why? Was it hard to choose an answer? Why?
- What would it be like if it was [opposite of what child chose – hard or easy] to tell how many puffs were left?
- Is easy and very easy the same for you or are they different? What things are easy for you? What things are very easy for you?
- Is hard and very hard the same for you or are they different? What things are hard for you? What things are very hard for you?

Thank you, now I have another question to ask you.

2b. Is it easy is it to tell how many puffs are left in the [ELLIPTA] inhaler?

Can you read the answers under the question aloud and choose an answer?

□ Yes
□ No

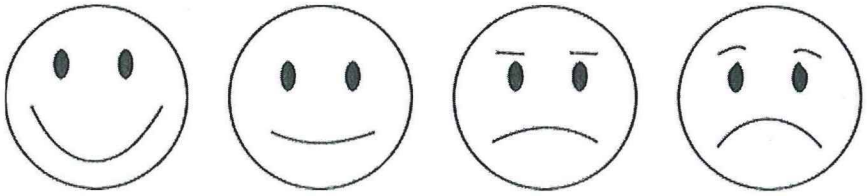
- What makes you answer [child's response] to this question? What did you have to think about?
- Is this question the same or different than the one we just talked about?
- Was this question easier or harder for you to answer? Why?

Thank you, now we have one more question for you.

Can you read the question out loud?

2c. How easy is it to it to tell how many puffs are left in the [ELLIPTA] inhaler?

Can you read each of the words under the pictures of the faces out loud and choose an answer?



Very easy Easy Hard Very hard

- Do you think the faces make is easier to answer the question? Why?
- [Only ask if a different response from 1a was chosen] You circled [child's response]. Why did you choose that answer?
- If you had to tell me about [select a face], what words would you use? What feeling does the face make you think of? Why?

Let's look back at all 3 of these questions. Which one was the easiest to answer? Why? Which question did you like the best? Why?

Thank you, is there anything else about how easy or hard it is to use your inhaler that you think I should know? Okay, now we will ask your (mom, dad, other caregiver) a few questions.

III. Discussion with Parent

- Can you tell me about the inhaler that your child uses every day? Not the inhaler that might be called a "rescue" inhaler, but the one that is sometimes called a maintenance inhaler?
- Based on your observations, do you think that your child finds it easy or hard to use? Why?
- Do you help your child use his or her inhaler? Why or why not?
- How do you know when the inhaler is almost out of medicine? Does your child let you know? Do you check how much is left yourself? Why or why not? How often do you check?
- What else do you think is important to know about how easy or difficult it is for your child to use his or her inhaler?

Thank you for your sharing your experiences, now we would like to discuss some questions that have been developed for a research study. As part of the research study, children with asthma would be using ELLIPTA every day for a month. The children and their parents will be asked to answer questions at the end of the study about their experiences with the ELLIPTA inhaler. We would like you get your thoughts on the questions and will be asking you to read the questions out loud and tell us what you're thinking about as you answer it.

Before we begin the questions, let's start with the **instructions**.

Please answer the following question based on what you observed when your child used the study inhaler (called the ELLIPTA) at home. Choose only **one** response for each question.

- In your own words, what are the instructions asking you to do?
- What changes could be made to the instructions to make them clearer?

Thank you, let's go to the first question.

1. How easy was it for your child to use the ELLIPTA inhaler?
   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

- In your own words, what is this question asking? How did you select your answer?
- Who, in your opinion, is the best person to answer this question, you or your child? Why?
- What do you think about this set of response options?
- How could this question or the response options be improved?

Let's continue to the second question.

2. How easy was it for your child to tell how many doses were left in the ELLIPTA inhaler?

   - □ Very easy
   - □ Easy
   - □ Difficult
   - □ Very difficult

- In your own words, what is this question asking? How did you select your answer?
- Who, in your opinion, is the best person to answer this question, you or your child? Why? [If not covered above or discussed in response, probe to understand if child or parent keeps track of remaining maintenance inhaler doses].
- What do you think about this set of response options?
- How could this question or the response options be improved?

Thank you, now we would like to ask some questions based on your experiences. Let's start with the instructions:

Please answer the following questions based on your experiences while your child was using the study inhaler (called the ELLIPTA) at home. Choose only **one** response for each question.

- In your own words, what are the instructions asking you to do?
- What changes could be made to the instructions to make them clearer?

Thank you, let's go to the first question.

1. How easy was it for you to tell how many doses were left in the ELLIPTA inhaler?

   □ Very easy
   □ Easy
   □ Difficult
   □ Very difficult

- In your own words, what is this question asking? How did you select your answer?
- Who, in your opinion, is the best person to answer this question, you or your child? Why?
- What do you think about this set of response options?
- How could this question or the response options be improved?

Thank you, we have one final question to review.

2. If your child's **current daily inhaled asthma medication** was available in the ELLIPTA inhaler, how likely would you be to request the ELLIPTA inhaler from your child's doctor?

□ Very likely
□ Likely
□ Unlikely
□ Very unlikely

- In your own words, what is this question asking? How did you select your answer?
- Who, in your opinion, is the best person to answer this question, you or your child? Why?
- What do you think about this set of response options?
- How could this question or the response options be improved?

After each question completed.

- What did you think about these questions? What is missing from these questions about how easy or difficult it is for your child to use an inhaler?

IV. Evaluate ELLIPTA Whistle [Pediatric Participants]

Now we would like show you a special whistle that makes a noise when you breathe in (instead of breathing out like other whistles). This whistle helps kids figure out how to use a new type of inhaler. I will show you how the whistle works and then I will give you a brand-new whistle to try and make the same noise. There is no medicine in the whistle, it is empty.

Do you have any questions for me before we start?

[*Interviewer provides the instructions for how to use the whistle and demonstrates use*].

Now, can you try and make a sound using the whistle? [*As soon as the child makes an audible noise – no further attempts are required. If an audible noise is not made on the first or second attempt, the interviewer will encourage the child, such as "no problem, can you give it another try for me?" Child is given up to 3 times to make an audible noise.*]

Thank you for trying out this whistle!

V. Wrap-up

Thank you again for your and your (son's, daughter's, other) time today, your input has been very helpful!

APPENDIX D: SCREENER

Facility Screener

Qualitative Research to Support ELLIPTA Ease-of-Use Questions in Pediatric Patients with Asthma

[Note to recruiter, the screening can only be conducted with a parent or legal guardian]

Thank you for your interest in this interview study about asthma inhaler devices.

To be eligible to participate in this interview study, all child participants will need to have a diagnosis of asthma and currently using an asthma maintenance inhaler. If you are interested, we will ask you some questions to see if your child is eligible to participate. Would you like to continue with the questions to see if you and your child are eligible for an interview?

YES	→	**Go to recruitment script and screening questions**
NO	→	**Stop call and thank the individual for his or her time.**

Recruitment Script

On behalf of RTI International (RTI) and a pharmaceutical company, we're recruiting children (aged 5 and 11) who use a maintenance inhaler due to their asthma. The goal of this interview study is to gain a better understanding of how children interpret and understand questions related to comparing asthma inhalers. The questions will be used in future studies evaluating inhalers.

Eligible participants and a parent/guardian will be asked to come to [FG FACILTY LOCATION], on [DATE] to participate in an interview. RTI interviewers will describe the study to both child participants as well as their parents/guardians and answer any questions. During the interview, we will ask you to remain seated behind your child (so as not to influence their responses) as the RTI interviewers speak with them. After they speak with your child, the RTI interviewers will also interview you to understand your experiences with your child's use of inhalers and ask you to review some questions developed for future studies. We will also show your child a whistle developed to teach children how to use an inhaler and ask them to try and use the whistle.

The interviews are expected to last approximately 30 minutes for each interview (up to 60 minutes total). In appreciation for your family's time, you will receive a total of $150 ($50 for the child participant, $100 for the parent/guardian's time).

The interviews will be audio recorded and transcribed (without any names) to ensure the interviewers don't miss anything participants say and to help write a report summarizing the results of the interviews. The recordings will not be linked to participants' names and will be destroyed upon completion of the project. These transcripts will be given to the client, but no names or identifying information will be included.

If you still think that you and your [son/daughter] would be interested in participating in one of these interviews, I just need to ask you just a couple of questions to make sure [he or she] qualifies. Would you like to continue?

[If "Yes," please continue screening]

1 **[ASK if unknown to screener] Is your child male or female?**

- ☐ Male
- ☐ Female

2 **What is your [your son/daughter's] current age? _____**

- ☐ Aged 5 through 11 → **CONTINUE**
- ☐ If younger than 5 or older than 11 → **STOP, does not qualify**

Note: participant must be aged of 5 or 11 to participate. Please try to recruit the following (these are targets only; please do not turn away eligible participants):

- **No more than 2 participants aged 10 or 11 (total)**

3 **What is your relationship to the child? _____**

Must be parent or legal guardian of child to continue

4 **Has your child been diagnosed by a physician or other health care provider with asthma?**

- ☐ YES
- ☐ NO→ **STOP, does not qualify**

5 **When was your child diagnosed with asthma? _____**

6 **Does your child currently use a daily maintenance (preventative) inhaler for their asthma? (NOTE: make sure the inhalers used are not rescue inhalers, i.e. inhalers that are only used during an asthma attack)**

- ☐ YES → **Go to next question**
- ☐ NO → **STOP, does not qualify**

7 What maintenance inhaler does your child use?

Check all that are reported:

- ☐ **Spiriva Handihaler**
- ☐ **Symbicort MDI (metered dose inhaler)**
- ☐ **Combivent Respimat**
- ☐ **Advair Diskus**
- ☐ **Flovent**
- ☐ **Ellipta Breo**
- ☐ **Atrovent MDI**
- ☐ **Arcapta Neohaler**
- ☐ **Other _____ (please check with RTI to confirm this is an acceptable maintenance inhaler)**

8 What would you say is your child's reading level?

- ☐ Unable to read
- ☐ Just starting to learn to read
- ☐ Kindergarten reading level
- ☐ 1st grade reading level
- ☐ 2nd grade reading level
- ☐ 3rd grade reading level
- ☐ 4th grade reading level
- ☐ 5th grade reading level
- ☐ 6th grade reading level
- ☐ 7th grade reading level
- ☐ 8th grade reading level
- ☐ 9th grade reading level or higher

[ALL RESPONSES CONTINUE]

9 How would you describe your child's race? (Check all that apply.)

- ☐ White/Caucasian
- ☐ Black/African-American
- ☐ American Indian
- ☐ Asian
- ☐ Hispanic
- ☐ Other

[ALL RESPONSES CONTINUE]

Parent/Guardian Demographics

10 How would you describe your race? (Check all that apply.)

- ☐ White/Caucasian
- ☐ Black/African-American
- ☐ American Indian
- ☐ Asian
- ☐ Hispanic
- ☐ Other

11 What is your current age? _____

12 (If unclear) Are you male or female?

- ☐ Male
- ☐ Female

13 What is your current employment status?

- ☐ Employed full-time
- ☐ Employed part-time
- ☐ Not employed or retired
- ☐ Student (part-time or full-time)

14 What is the highest grade or level of education you have completed?

- ☐ Less than high school
- ☐ High school diploma or equivalent (GED)
- ☐ Some college
- ☐ College degree
- ☐ Professional or advanced degree

[If you have any questions about patient eligibility please contact PPD **at** PPD PPD

If NOT qualified: Please be sure to thank the caller for his/her time and interest in this project. Let caller know, however, that it does not appear that their child qualifies for this particular project.

If Qualified:

Thank you for answering those questions. It looks like you and your child are eligible to participate in an interview.

Let's go ahead and schedule your interview. [Note: parents or legal guardians MUST accompany the child to the interview. Older siblings are not allowed to sign consent forms on behalf of parent/guardian]

[Record the parent's/guardian's name, child's name, contact information and schedule the interview]:

Parent's/guardian's first name: _____

Child's first name: _____

Interview Date/Time: _____

Thank you for speaking with me today and please do not hesitate to contact me [name; number] if you have any questions!