Title:
Screening for Autism Spectrum Disorders Using Auditory Brainstem Responses

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Grant Title:
Screening Device for Autism Spectrum Disorders using High Stimulation Rate ABR with Continuous Loop Averaging Deconvolution

1) Protocol Title

High stimulation rate ABR in ASD and non-ASD children

2) Objectives*

The purpose of this proposal is to develop and assess the feasibility of an automated auditory brainstem response (ABR) based neurological screening device and software module that will provide early detection of increased risk for autism spectrum disorder (ASD) and other neurological conditions (e.g., speech impairment or sudden infant death syndrome (SIDS)). Recordings will be obtained at a range of stimulation rates from 19 to 250/second to determine the optimal rate to be used for newborn screening.

3) Background*

ASD is characterized by persistent deficits in communication and social interaction across multiple contexts and restricted, repetitive patterns of behavior, interests, or activities. Symptoms cause clinically significant impairments in social, occupational, or other important areas of current functioning. The term "spectrum" refers to the wide range of symptoms, skills, and levels of impairment or disability that children with ASD can have. Some children are mildly impaired by their symptoms, while others are severely disabled.

The incidence rate of ASD is 1:59. Based on 3.94 million births in the United States in 2016, 66,780 new cases of ASD will be diagnosed from that birth cohort alone. Although the incidence rate of hearing loss is 3:1000, over 5 times smaller than ASD, universal hearing screening has been instituted in most states for more than 20 years. Approximately 2 million babies per year are currently screened with ABR technology, one million with Intelligent Hearing Systems (IHS) equipment alone. Current screening protocols use moderate auditory stimulation levels, 35 dB nHL, to focus on hearing sensitivity. The typical testing time is approximately 7 minutes plus electrode and insert earphone placement time. The new system tested in this study will add a supra-threshold testing level required for neurological evaluation, and will introduce only an additional minute to the screening process. These additions will capitalize on the initial prep-time and cost of disposables used for hearing screening, while providing important information on the newborn's neurological status at almost no additional cost. Not screening for neurological conditions at this stage represents an enormous loss of opportunity to provide early diagnosis and intervention to these infants. Substantially improved outcomes can be achieved through early diagnosis and intervention.

The practice of early screening and identification of ASD is encouraged by the nation's Healthy People 2020 objectives and the American Academy of Pediatrics. Although ASD symptoms are present in the early developmental period and can be recognized in the first two years of life, the median age of ASD diagnosis still remains older than 4 years and has not decreased in recent years

(Brett et al., 2016). Recommendations from the Autism and Developmental Disabilities Monitoring Network (ADDM) include enhancing strategies to address the need for decreasing the age when children receive their first evaluation for and a diagnosis of ASD and are enrolled in community-based support systems (Baio, 2014). Given that about 46% of children with ASD have average to above average intellectual ability (Baio, 2014), early intervention provides a significant opportunity to improve the outcomes of these individuals in particular, as well as those with more severe intellectual disabilities.

The system developed will serve to provide an objective measure of neurological function that can be used for screening purposes at any age to determine the transmission rate and synchrony of neurological pathways. Of particular interest is the reported link between ABR peak latency delays and ASD (Dabbous, 2012; Fujikawa-Brooks et al., 2010; Kwon et al., 2007; Maziade et al., 2000; Miron et al., 2015; Rosenhall et al., 2003; Roth et al., 2012; Russo et al., 2010; Tas et al., 2007; Thivierge et al., 1990; Wong et al., 1991). Although evoked potentials can be acquired using visual and somatosensory stimulation; auditory stimulation provides an ideal method as it requires no patient participation and is painless. Tests using ABR can be conducted in a minimally invasive procedure by only applying three surface scalp electrodes and sound stimulation while an infant is in natural sleep. Newborn hearing screening is currently routinely conducted universally across the United States and in many developed countries around the world using the same ABR technology. Expanding hearing screening to neurological screening could be accomplished with minimal cost and test time using the proposed techniques.

Significant latency differences in the peak components of ABRs have been identified in children with ASD compared to aged matched normal children (Dabbous, 2012; Fujikawa-Brooks et al., 2010; Kwon et al., 2007; Maziade et al., 2000; Rosenhall et al., 2003; Roth et al., 2012; Russo et al., 2010; Tas et al., 2007; Thivierge et al., 1990; Wong et al., 1991). Studies have also shown that prolonged ABRs occurred in infants who later had social engagement problems (Geva et al., 2011) and repetitive behaviors (Cohen et al., 2013). More recently, Miron et al. (2015) showed that prolonged ABR occurred in young infants later diagnosed with ASD and that this prolongation, especially in wave V, was capable of accurately classifying ASD. Although the sensitivity (84% & 80%) and specificity (56% & 70%) measures for Cohen et al. (2013) and Miron et al. (2015), respectively, are encouraging, the resulting high false positive rate would be of concern for any screening tool. It is important to point out that these values were derived primarily from testing at-risk infants and that a broader study including a large number of well-babies is required to fully develop latency norms and new specificity and sensitivity measures.

There are several options to improve test sensitivity and specificity. Choosing the proper cut-off value for absolute and interpeak latency difference between normal and ASD infants are critical for optimizing any

screening tool. In addition to abnormalities in ABR latencies, studies have shown that ABR amplitudes are also abnormal in some children with ASD (Coutinho et al., 2002; N. Russo et al., 2009). Miron et al. (2015), hypothesize that predicting ASD based on both ABR amplitude and latency may be even more accurate than predicting based solely on ABR latency. Furthermore, the use of higher stimulation rates may provide an additional way to differentiate normal versus ASD infants.

4) Inclusion and Exclusion Criteria*

Subjects will be children between the ages of 1.5 and 5.5 years. Our target age group is 3.5 to 4.5 years of age but younger or older children may be included as well. Parents must be able to communicate effectively in English to participate in the study.

A formal ASD diagnosis (i.e., community diagnosis or educational eligibility diagnosis) is required for children to be part of the ASD group. Children in the control group will not have a diagnosis of ASD or any other developmental disability. Control children will be age and gender matched with the ASD subjects. All children will be screened to insure that they do not have hearing problems, a history of middle ear infections, or a current ear infection. All children will be given an Otoacoustic Emissions (OAE) hearing screening test prior to ABR testing to confirm that their peripheral auditory system is normal.

Exclusion criteria for all subjects include: hearing problems, history of middle ear infections or current ear infection, and other abnormalities or impairments that could impact neurological functioning such as seizures, comorbid syndromes or diseases, sensory disorders, craniofacial abnormalities, other developmental or physical disabilities, or having a sibling with ASD or another developmental disability.

5) Procedures Involved*

Data collection is anticipated to occur from September 2019 through May 2021.

Phone Screen:
Parents/guardians who call to inquire about the study will be screened over the phone to determine if they meet the inclusion criteria. Subjects who meet inclusion criteria will be invited to come to the lab. The Phone Intake Form is attached.

Lab Session:
All assessments will be completed during one lab visit. A second visit may be needed if testing cannot be completed during the initial visit. The lab session will include some or all of the following assessments:

Informed Consent:
The study will be described to the parent/guardian and informed consent will be obtained. The Informed Consent document is attached.

Head Circumference:
The circumference of the child's head will be measured using a measuring tape.

OAE:
In order to make sure that the subject has normal hearing, an Otoacoustic Emissions (OAE) measurement will be conducted. OAEs are a routine audiometric test conducted to measure cochlear function. OAEs will be recorded using the SmartDPOAE system on the Duet Platform (Intelligent Hearing Systems Corp). The OAE procedure involves placing a small probe in the ear, similar to an insert earphone, presenting soft sounds to the ear at 65 and 55 dB SPL and measuring the acoustical output from the ear. The OAE system provides a pass or refer output based on the measurements. Children with passing OAE results will be retained for the ABR portion of the study.

ABR:
Neurological function will be assessed using ABR. ABRs will be recorded using the SmartEP system on the Duet Platform (Intelligent Hearing Systems Corp). Various stimulation rates (19-250/sec) using a 75 dB nHL100 μsec click will be used to compare ABR peak latency and amplitude differences between children with ASD and control children. The ABR procedure involves placing 4 small electrodes (Ambu Neuroline 720) on the subject's head (right and left mastoids, high and low forehead) and inserting earphones in both ears. Prior to placing the electrodes, a disposable electrode prep pad (70% isopropyl alcohol, purified water, and pumice) will be used to gently clean the skin at the electrode site. Click sound stimuli of a moderate level (75 dB nHL) are presented at various stimulation rates. This intensity level is routinely used for hearing assessment and is considered safe for short duration stimuli. ABR data will be recorded and peaks identified and measured. A flyer describing the SmartDPOAE and SmartEP systems is attached.

ASRS
All children, including controls, will be evaluated using the Autism Spectrum Rating Scale (ASRS) questionnaire to verify ASD symptomology in the ASD children and lack of symptomology in the control children. The ASRS will be completed by the child's parent or guardian. A sample of the ASRS questionnaire is attached.

ASQ-3:
The Ages and Stages Questionnaire, Third Edition (ASQ-3) will be used to evaluate the child's development in the areas of communication, gross motor, fine motor, problem solving, and personal-social. The ASQ-3 will be completed by the child's parent or guardian. A sample of the ASQ questionnaire is attached.

Family Information Form:
The Family Information Form contains questions regarding birth indicators (e.g., birth weight, gestational age, birth complications), demographic information (e.g., race, ethnicity, parent education, parent occupation, family income), and siblings. The Family Information Form will be completed by the child's parent or guardian. The Family Information Form is attached.

6) Data and Specimen Banking*

At the close of the study period, when all final data have been entered, a final read-only data set will be generated to document the data used for publication as well as for potential use in future research.

7) Data Management*

Paper forms will be used to collect consent and demographic/family history information as well as for the ASRS and ASQ assessments. Paper forms will be scanned and stored on a secure, encrypted cloud-based system (i.e., Box) and the forms will be physically stored in a locked file cabinet.

A unique subject identifier will be assigned and used for all OAE and ABR data acquisition. OAE and ABR data will be recorded on the data acquisition system, stored electronically identified by subject number only, and backed up daily to a secure computer at the University of Miami. A deidentified database (records will be identified by subject numbers only, names will not be included) containing all study data will be created and will be accessible only to authorized study personnel. Identifying information will not be included in the analyses nor released to non-study personnel. Deidentified raw OAE and ABR data will be transferred using a secured Box account to Dr. Savio at Intelligent Hearing Systems for review to assure that the data meet the required quality for the study.

<u>Data analysis plan:</u>
The following statistical analyses will be performed:
1) Analysis of variance and t-tests will be conducted to determine if there are significant differences between the ASD and control groups, sex and ear on ABR peak latency and amplitude.
2) Sensitivity and specificity measures will also be conducted using Receiver Operating Characteristic (ROC) curves and d-prime measures. The optimal stimulation rate for ASD detection will be determined using these measures.

Factor: Click stimulation rate (five levels): 19, 39, 61, 120, and 250 per second. The three lower rate levels were selected to replicate previous research. The upper levels were selected to obtain ABRs with discernible peaks while challenging the neural transmission of the auditory system.

Dependent Variables: Absolute peak latencies and amplitudes.

Data and Safety Monitoring (DSM) Plan:

This study was designated as a clinical trial by NIH. It is registered on clinicaltrials.gov and a data and safety monitoring plan was developed. This is a case-control study involving the recording of data routinely used for hearing assessment using non-invasive techniques; therefore, it is considered low risk. As such, it does not warrant a formal DSM board. However, an independent monitor, Dr. Jorge Bohoquez, was assigned and will review all study activities. Dr. Bohoquez is a professor of Biomedical Engineering at the University of Miami and has no conflict of interest with the PI, Intelligent Hearing Systems or the primary investigators at the Department of Psychology of the University of Miami. Dr. Bohoquez has extensive experience with ABR acquisition at high stimulation rates and has conducted independent research validating the data acquisition methods used in this study. As such, he is qualified to independently review the study overall and specifically the validity and quality of the ABR data being acquired. Dr. Bohoquez will have full access to the study records and data for review as needed. Dr. Bohoquez will review all data capture, storage, verification, and disposition activities quarterly. A quarterly DSM report will be generated and will contain the following information: (a) study recruitment progress; (b) study retention and reasons for drop-out; (c) protocol and data completeness; (d) data analysis; and (e) data quality. The Data and Safety Monitoring Plan that was submitted to and approved by NIH is attached.

8) Risks to Subjects*

The potential risks to the subjects are minimal. The OAE and ABR equipment and procedures to be used have been used in previous studies with human subjects, with no adverse effects. The equipment is specifically designed to protect subjects from possible electric shock originating from the test equipment to the subjects and from exposure to high sound intensity levels. The device to be used has been approved by the US FDA and has passed all required IEC60601 safety tests from independent, accredited testing laboratories. The proposed testing methods have also been previously used in human clinical and research studies. There are no known side effects, risks or complications associated with the OAE and ABR assessments. Possible adverse events (AEs) may include a skin rash associated with the recording electrodes. These can be identified by skin redness or rash at the time that the electrode is removed. No serious adverse events (SAEs) are anticipated as the ABR and OAE procedures are routinely used for hearing evaluation throughout the world.

Any AE or SAE during data acquisition at the University of Miami will be reported by the University of Miami Site Director (IRB PI), Dr. Christine Delgado, immediately to 1) the PI at Intelligent Hearing Systems, 2) the IRB board, 3) the study team, and 4) Independent Data Safety Monitor. The PI at Intelligent Hearing Systems will report the event within 48 hours to 5) NIH-NIDCD Staff and 6) Office of Human Research Protection.

Any adverse event associated with the data recording equipment will be handled as a device complaint by the manufacturer (Intelligent Hearing Systems) through their complaint and reporting procedure QOP-85-02-WI2 (attached). Personnel using the equipment will contact IHS immediately at 1-800-447-9783 to report any concerns, issues or problems during the data recording process. The timeline for reporting any SAEs is outlined in the reporting procedure as mandated by the FDA.

All AEs will be reported to the Office for Human Research Protections (OHRP) in a report containing the following information:
Name of the institution: University of Miami
Title of the research project: Screening Device for Autism Spectrum Disorders using High Stimulation Rate ABR with Continuous Loop Averaging Deconvolution
Grant proposal: 1R43DC018430-01
Grant Principal Investigator: Rafael E. Delgado
Principal Investigator on IRB Protocol: Christine Delgado
Number of the research project assigned by the IRB: _____ [TBD]
Explain in detail the problem that occurred
Actions the institution is taking or plans to take to address the problem: (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).

A PDF file containing the report will be emailed to: **IRPT.OS@hhs.gov**

9) Potential Benefits to Subjects*

A benefit to subjects will be obtaining information as to their current hearing status. Subjects will be provided with information pertaining to the OAE test results based on automated interpretation from the recording system. Subjects not passing the initial OAE screening will be informed of the test result and advised to consult their pediatrician and/or the Florida Diagnostic and Learning Resources System (FDLRS) for potential follow up. Additionally, control subjects with deviant scores on the ASRS or ASQ may be advised to consult their pediatrician and/or the Florida Diagnostic and Learning Resources System (FDLRS) for potential follow up. No other specific information will be provided to subjects. A final study report with summary data will be made available to participants upon requests and the results will also be posted at clinicaltrials.gov.

10) Vulnerable Populations*

The primary aim of the study is to develop an improved method to screen children for ASD. As such, the use of children as subjects is critical in the assessment of the feasibility of the proposed techniques. Parents will be given the alternative to not participate in the study.

11) Setting

Data collection will be conducted on the second and third floors of the Department of Psychology, Flipse Building at the University of Miami. Address: 5665 Ponce de Leon Blvd., Coral Gables, FL 33146.

12) Resources Available

Dr. Christine Delgado (Research Assistant Professor, Department of Psychology) is the Director of the Children's Registry and Information System (CHRIS) project. Her research focuses on the identification of early risk factors for children with disabilities and the tracking of outcomes of preschool children with disabilities.

Dr. Elizabeth Simpson (Assistant Professor, Department of Psychology) conducts research on understanding infant social cognitive development, including the ultimate and proximate mechanisms that shape individual differences in social perception. She longitudinally studies human and nonhuman primate infant development, including studies of imitation and face perception.

Dr. Anibal Gutierrez (Research Associate Professor, Department of Psychology) is an Associate Director of the Center for Autism and Related Disabilities (CARD). He is also a Board Certified Behavior Analyst with experience in the assessment and treatment of problem behavior and in the development of adaptive skills for individuals with autism. His research focuses on early intervention, variables related to treatment effectiveness for individuals with autism, and the use of technology to bring about behavior change.

Dr. Guillermo Savio (Research Scientist, Intelligent Hearing Systems Corporation) has published extensively in the field of auditory evoked potentials and has extensive experience recording data from pediatric populations. He will train the research assistant in recording techniques and will be available for assistance as needed. He will also review and analyze all raw OAE and ABR data to assure quality.

Oren Miron (Research Associate, Biomedical Informatics, Harvard University) has conducted several studies on the prediction of autism risk in newborns using ABR.

Dr. Jorge Bohorquez (Associate Professor in Practice, Biomedical Engineering Department) has experience with the development of methods and equipment for neurophysiology and neuro-monitoring and objective hearing assessment. Dr. Bohorquez will serve as the independent monitor for this study.

The research assistant (TBD) will be trained by study personnel to conduct the sessions.

Each research team member will complete the required CITI training courses.

13) Prior Approvals

A Data and Safety Monitoring Plan was submitted to and approved by NIH.

14) Recruitment Methods

Recruitment will take place through the Center for Autism and Related Disabilities (CARD) and through other means such as by posting or distributing flyers at various child-friendly establishments in our community (e.g., preschools, museums, pediatrician's offices, retail businesses). The recruitment flyers are attached. Parents may contact the study investigators at their convenience, at which point the study will be described in detail and information regarding potential participants will be obtained. This prescreening will allow the researchers to determine whether the family is eligible to participate. Only children who meet the inclusion criteria for the study will be invited to schedule a lab session.

Participants will be compensated $50 at the completion of the study. Partial compensation will be made for participants who begin but do not complete the study. Participants will be paid through ClinCard (a reloadable debit card for research studies) or through check. The ClinCard is the preferred method of paying research participants for their participation, and is managed by the Office of Research Administration (ORA). Participants will complete and sign a payment form, with their full name, date of birth, and address, in order to receive payment for participation. This information will not be linked to any of the study data and will only be used for payment purposes.

15) Local Number of Subjects

100 children 1.5-5.5 years of age will be recruited to participate in the study, including 50 children with ASD and 50 age and gender-matched controls. Additional subjects will be recruited as needed to achieve a complete age and gender matched control group and to accommodate for subjects who did not fully complete the session.

16) Confidentiality

Paper forms used to collect consent and demographic/family history information as well as for the ASRS and ASQ assessments will be scanned and stored on a secure, encrypted cloud-based system (i.e., Box) and the forms will be physically stored in a locked file cabinet. OAE and ABR data will be recorded on the data acquisition system, stored electronically identified by subject number only, and backed up daily to a secure computer at the University of Miami. Deidentified raw OAE and ABR data will be transferred using a secured Box account to Dr.

Savio at Intelligent Hearing Systems for review to assure that the data meet the required quality for the study. A deidentified database (records will be identified by subject numbers only, names will not be included) containing all study data will be created and will be accessible only to authorized study personnel. Identifying information will not be included in the analyses nor released to non-study personnel. All local computers or cloud-based storage systems (e.g., Box) used will require a password to gain access. If requested, data will be provided to NIH and authorized University of Miami employees or other agents for the purposes of official audits or reviews.

17) Provisions to Protect the Privacy Interests of Subjects

The confidentiality practices described above will be conducted to protect the privacy interest of subjects. Any persons collecting or assessing participant data will have completed CITI certifications and will be included on the IRB protocol.

18) Consent Process

When the family arrives for the session, a trained member of the research team will give the parents an overview of the entire study, as well as detailed descriptions of what the visit will entail, and will answer any questions. Parents will provide consent in order for their children to participate.

INFORMED CONSENT FORM

STUDY INFORMATION:
Title: How Children With and Without Autism Process Sounds
Principal Investigator: Christine Delgado, Ph.D.
Department: Psychology
Phone Number: 305-284-3371
Email Address: cdelgado@umiami.edu
Study Contact Email: UMChildDevelopment@miami.edu
Sponsor: This research study is supported by a grant (1R43DC018430-01) from the National Institutes of Health (NIH), National Institute on Deafness and Other Communication Disorders (NIDCD) to Intelligent Hearing Systems.

PURPOSE: The goal of this study is to measure brain responses in children while they listen to click sounds. The ways in which children's brains respond to these sounds may be linked to developmental disorders, such as autism.

ELIGIBILITY: We will study children with autism and children without autism. Your child must be healthy and between the ages of 1.5 and 5.5 years old.

PROCEDURE: During your visit, you will be asked to provide us with information about your child and your family. You will also be asked questions about your child's development. We will measure the size of your child's head using a measuring tape. We will also conduct two tests on your child that are very similar to the hearing test your child most likely received in the hospital shortly after he/she was born. First, we will give your child a routine hearing test that involves placing earphones in his/her ears. If your child's hearing is normal, we will conduct another test. This second test involves placing earphones in your child's ears and small stickers called "electrodes" on your child's head. Sounds will be played through the earphones and the electrodes will measure brain activity in response to those sounds. Both tests are painless and require that the child be quiet and lie still. If you choose, your child can watch a silent video or participate in some other quiet/calm activity during this time. You will be with your child for the entire duration of your visit. The study is designed to be completed in one session, but if this is not possible you may be asked to return for a second session. The two tests should take no more than 30 minutes and the total session should take about 90 minutes.

RISKS: The risks of being in this study are minimal. The equipment and procedures have been used in previous studies with human children and adults with no negative effects. The devices that will be used on your child have been tested for safety and are approved by the U.S. Food and Drug Administration (FDA). There are no known side effects, risks, or complications associated with these tests. Rarely a skin rash or irritation may occur where the stickers were placed on the skin.

BENEFITS: Test results pertaining to the hearing status of your child will be provided to you. The overall findings of the study will provide information about brain activity in children with autism that may be used to develop and improve screening tests for

newborns. If we can find out that a child is at risk for autism or another developmental disability when they are first born, then this may lead to better support for these children. If you would like, after the study is finished, we will share with you our findings.

COSTS: You may have transportation costs for being in this study. You will not receive compensation for transportation in this study.

PAYMENT TO PARTICIPANT: If you agree to be in this research study, we will pay you $50.00 at the completion of the study for your time and effort. We will give you a partial payment for an incomplete visit if you do not return to complete the study.

CONFIDENTIALITY: Data collected for this study will be accessed and analyzed by collaborators at the University of Miami, Harvard University, and Intelligent Hearing Systems. The NIH is funding this study and may, therefore, request to review and obtain copies of your records. Your records may also be reviewed for audit purposes by authorized University of Miami employees or other agents who will be bound by the same provisions of confidentiality. Any data from the study provided to other entities or presented/published will be in aggregate/summary form and will not include any identifying information. Paper forms will be stored in a locked file cabinet and electronic information and data will be stored in a secure, encrypted data storage platform that is password protected. Data analyses will be conducted using a de-identified database (i.e., all names and identifying information will be removed).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you or your child. At most, the web site will include a summary of the results. You can search this web site at any time.

SHARING INFORMATION: Families who participate in our study may be interested in participating in other research projects at the University of Miami. Please indicate below if you would like for us to provide your contact information to researchers conducting other studies that you and/or your child may be eligible to participate in.

[ ] Yes, I give permission to share my contact information.

[ ] No, I do not wish to share my contact information.

RIGHT TO WITHDRAW: Your participation is voluntary. That means you can decide that you do not want you or your child to be in the study. Once you begin, you can request to stop any procedure at any time. You can decline to answer or skip any question you do not wish to answer. No consequences will result from either declining or discontinuing participation. Upon request, we will give you a copy of this consent form.
QUESTIONS: Ask us questions now or at any time during your visit(s). Talk to the research team if you have questions, problems, concerns, or complaints, want more information, want to offer a suggestion, think you or your child has been injured, or

would like a copy of the results. You can contact Dr. Christine Delgado at 305-284-3371 or by email at cdelgado@umiami.edu.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). The Human Subject Research Office (HSRO) provides administrative support to the University of Miami's IRBs. Please call the HSRO at 305-243-3195 if you are a participant in any research being conducted at UM and:

- Your questions, concerns, or complaints are not being answered by the research team
- You cannot reach the research team
- You want to talk to someone besides the research team
- You have questions about your rights as a research participant
- You want to get information or provide input about this research

PARTICIPANT'S (PARENT'S) STATEMENT/SIGNATURE:

- I have read this form and the research study has been explained to me.
- I have been given the chance to ask questions, and my questions have been answered. If I have more questions, I have been told who to call.
- I agree to my child being in the research study described above.
- I will receive a copy of this consent form after I sign it, upon request.

_____
Printed Name of Child

_____
Printed Name of Parent/Legally Authorized Representative

_____ _____
Signature of Parent/Legally Authorized Representative Date

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date