## Research Plan

**Title of Research Project:** NCS Formative Research Project #8 – Development and Validation of Autism Case Confirmation Approaches for Use in the National Children's Study

**PI:** _____Name_____

### Overview

This project will be carried out as a formative research study in support of the National Children's Study. The _____Institution_Name_____ houses a National Children's Study (NCS) Center (PI: __NCS_PI_Name_____).

The _____Institution_Name_____ NCS Center is working with a group of nine other NCS Centers on this formative research project to examine the criterion validity of three autism case-confirmation instruments that could potentially be incorporated into the final NCS protocol. This project will not involve subjects from other NCS activities but will involve recruitment of a new, purposive sample from the ten participating NCS Centers. The lead NCS Center for this project is the Johns Hopkins Study Center (PI Laura Caulfield). The investigator leading this formative project is Craig Newschaffer of Drexel University who collaborates with the Johns Hopkins Center team.

### Research Questions Addressed by this Project

As mentioned, the goal of this project is to assess the criterion validity of new autism spectrum disorder (ASD) case confirmation instruments. The three instruments being considered are designed to be administered by staff without special training and experience related to neurodevelopmental disabilities, and to be less time-consuming to administer than current gold-standard tools. Project goals are as follows:

- To assess criterion validity by estimating sensitivity and specificity for three new ASD case confirmation tools (individually and in combinations) against gold standard classification based on the current accepted gold-standard tools - the Autism Diagnosis Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R).
- To provide qualitative information on the implementation of ASD case confirmation assessment using streamlined tools and staff without special training and experience in neurodevelopmental assessment.

### Rationale for Research

Most ASDs can be reliably identified by age three, but the average age of diagnosis is considerably later. Recent CDC data indicate that community diagnoses still underestimate ASD prevalence by >20%. Passive surveillance of community diagnosis is therefore problematic as an NCS case identification strategy. NCS Research Plans have endorsed an active approach to autism case-identification, including administration of a parent self-report autism

screener (the Modified Checklist for Autism in Toddlers) during the participants' second year of life. Latest data on the M-CHAT suggest sensitivity and specificity as high as 95% and 99%, respectively. However, with population ASD prevalence estimated at 0.9%, M-CHAT screening in the NCS study population (a community sample of 100,000 births) will still yield more false positives (990) than true positives (865)--therefore, some follow-up case-confirmation in NCS will clearly be necessary. In recent NIH RFAs, the ADOS and ADI-R have been required as case-confirmation tools – and these tools are considered the gold standard for ASD confirmation. However, administration time for these instruments can exceed three hours, the administration setting should ideally be a specialized research clinic, and assessors not only typically have existing clinical experience but also must undergo extensive instrument-specific training and reliability establishment. Our goal is to determine if alternate case confirmation approaches that would not be overly burdensome to NCS in terms of participant time or study resources, can confirm ASD cases with satisfactory validity when administered by NCS field staff with no previous ASD expertise.

## Methods

### *a. Study Population*

To be eligible for the MAIN study sample, children need be scheduled for an autism evaluation where they will receive, at minimum, an ADOS from an assessor who has met standards for clinical or research reliability and a DSM-based diagnostic assessment. Children must be 33 to 39 months old at the time of the scheduled evaluation. These children will be recruited from the following sources:

- Subjects participating in the NAME OF ONGOING AUTISM STUDY(IES) THAT WILL BE A RECRUITMENT SOURCE AT YOUR SITE WITH IRB PROTOCOL APPROVAL NUMBERS. ADD NEEDED ADDITIONAL DESCRIPTIVE INFORMATION ON THESE STUDIES. Only subjects who have given permission to be contacted for additional research will be recruited.
- Subjects scheduled for clinical assessment at the NAME OF CLINIC. ADD ANY NEEDED DETAIL (E.G., ADDITIONAL ELIBIBILITY/EXCLUSION CRITERIA YOU MAY NEED TO IMPLEMENT) FOR CLINICALLY RECRUITED SUBJECTS.

We will also recruit children into a SUPPLEMENTAL sample. These children need to be scheduled for an evaluation for a developmental delay without prior autism suspicion and be 33 to 39 months old at the time of the scheduled evaluation. These children will be recruited from the following sources:

- Subjects participating in the NAME OF ONGOING AUTISM STUDY(IES) THAT WILL BE A RECRUITMENT SOURCE AT YOUR SITE WITH IRB PROTOCOL APPROVAL NUMBERS. ADD NEEDED ADDITIONAL DESCRIPTIVE INFORMATION ON THESE STUDIES. Only subjects who have given permission to be contacted for additional research will be recruited.
- Subjects scheduled for clinical assessment at the NAME OF CLINIC. ADD ANY NEEDED DETAIL (E.G., ADDITIONAL ELIBIBILITY/EXCLUSION CRITERIA YOU MAY NEED TO IMPLEMENT) FOR CLINICALLY RECRUITED SUBJECTS.

Children will be enrolled from March 1, 2011 through December 31, 2011. We expect to enroll a total of XX children – XX in the main sample and XX in the supplemental sample.

***b. Consent Process***

Consent will be obtained by INDICATE WHICH STUDY STAFF WILL DO THIS / UNDER WHAT CONDITIONS ETC. Informed consent of the parents will be obtained before the commencement of any study procedures.

***c. Data Collection***

Once consented, subjects will be scheduled for a study visit where they will complete the ***parent self-report, direct observation,*** and ***parent interview*** instruments. The order in which the instruments are completed will be randomized. Study visits must occur at least one week prior to the date of the already-scheduled autism or developmental delay assessments. Each of the instruments is described in more detail below.

***Parent Self-Report***. Parent self-report data will be collected through a web-based, video-guided survey tool. The tool includes video clips that will be presented in pairs, with the first clip showing a child with typical development (TD) in order to provide a point of comparison for the behaviors exhibited in the second clip by a child with an ASD. Voiceovers describing and contrasting the behaviors are incorporated and parents will answer questions after viewing the video clips. The 20 questions involve rating relevant behaviors as absent, possibly present, or definitely present. Questions are constructed at a 6th grade comprehension level with options to either read or listen. Average time to complete is 20 minutes.

***Parent Interview.*** The parent interview will employ the Autism Diagnostic Interview-Screener (ADI-S) – a measure was developed based on questions from the ADI-R. The Preschool version of the ADI-S is for children under the age of five and includes approximately 30 to 40 questions, depending on the language level of the child (i.e., parents of children who have not yet acquired phrase speech are not administered the verbal items). The ADI-S items inquire about social and communication behaviors, and restricted and repetitive behaviors and interests that have been observed during the past 3 months. The measure also includes a small set of questions regarding early history. The interview takes approximately 25 minutes to administer and is designed to be administered by interviewers with minimal levels of training.

***Direct Observation***. The direct observation will use the STAT-NCS, an interactive, play-based assessment adapted from the Screening Tool for Autism in Two-year-olds (STAT). The STAT-NCS takes 20 minutes to administer and consists of 12 items assessing social-communicative behavior in the areas of play (2 items), imitation (4 items), and communication (6 items). The examiner presents each item in a prescribed manner and then observes and scores the child's response live. Each item is scored on two separate dimensions: Response to Press and Social Engagement. STAT-NCS has been designed to be administered by assessors with no previous autism or child development expertise who receive a web-based training tutorial modified from an existing training tutorial previously developed for the STAT.

Study assessors will be staff with backgrounds similar to future NCS field workers. They will ***not*** have substantive prior experience in child development and/or autism/developmental delay assessment. Prior to beginning data collection they will complete web-based training modules and pass online tests of competency in instrument administration procedures. Study assessors will be blinded to whether a particular subject is part of the MAIN or SUPPLEMENTAL sample.

In addition to the data items from the above instruments, study staff will also record the following data: subject month and year of birth; study visit date; parent gender; and subject gender.

***Direct observation*** To ensure correct use of the direct observation measure, the first 3 assessments administered by each NCS staff person at each site will be videotaped and reviewed by the instrument developers at University of Washington. Feedback regarding administration and scoring will be provided. If there is staff turnover, this process will be repeated. If performance following the third assessment is unacceptable, additional videotapes may be requested. We anticipate that approximately 30-120 videotapes will be reviewed across all sites, depending on the number of staff at each site and their training needs, as described above.

Once the previously scheduled assessment is completed, study staff will record the following data from the subject's record: child's month and year of birth; assessment date; assessment type (research/clinical); reported major comorbidities; summary results from any ASD screeners (M-CHAT, SRS, etc) if available; type of IQ test administered, if applicable; IQ test results if available; summary ADOS scores; reliability level of assessor (clinical vs research); ADI summary scores, and indication of whether the clinician felt the child met DSM-IV-TM criteria for an ASD diagnosis (autistic disorder, Aspergers disorder, or PDDNOS). Also, the clinician who performs the gold standard assessment will give subjective ratings of: 1) the level of ASD suspicion based on existing information prior to assessment and 2) certainty of DSM diagnosis (if applicable) after assessment.

## Benefits and Risks

Participants gain no direct benefit from participation. Indirect benefits include contributing to formative research that will help assure autism is investigated most effectively in the National Children's Study. There are no medical risks to participation. There is a risk of loss of confidentiality, although efforts (described below) will be made to maintain subject confidentiality.

## Compensation

Parents will be provided $50 for their time and travel costs.

## Confidentiality Assurances

A SECTION CAN BE INSERTED HERE ADDRESSING ISSUES RELATED TO CONFIDENTIALITY PROTECTION IN THE RECRUITMENT STAGE OF THE STUDY IF THIS IS SOMETHING YOU TYPICALLY DO. YOU CAN INCLUDE ISSUES LIKE: HOW STAFF ACCESSES POTENTIAL ELIGIBLES; CONFIDENTIALITY PROTECTION TRAINING OF STAFF; HIPAA ISSUES IF APPROACHING CLINICAL POPULATIONS; ETC.

At the time of the consent, an anonymous study ID will be assigned. The link between the study ID and identifying information will be maintained locally by _XXXGROUP MAINTAINING ID-IDENTIFIER LINKXXXX_. INSERT APPROPRIATE LANGUAGE FOR YOUR IRB CONSISTENT WITH THE LANGUAGE IN YOUR SITE NCS DATA SECURITY PLAN AROUND MAINTAINING PHYSICAL SECURITY OF HARDCOPY DATA WITH IDENTIFIERS AND/OR

COMPUTER FILES (LIKE A LOCALLY-CREATED SPREADSHEET) THAT WILL STORE THESE LINKAGES.

Data from all participating study sites will be entered into a web-based data base. The only identifier entered into this database will be the anonymous study ID. Local study staff will log the parent completing the parent self-report tool in to a web-based system (separate from the data entry system) with their anonymous study ID, so that self-report data is properly associated with other subject information but no parent identifiers are entered.

All electronic data collected through these web-based tools will be stored only in one database on a Battelle server located in the NCS VLAN within the Battelle Information Security Center (BISC) environment. This environment is designed to meet NIST SP800-53, Rev. 3 security controls to the Moderate level.

Digital video files will be encrypted and uploaded to a secure server at the University of Washington for quality assurance review. After the submission of the project final report, video files will be destroyed except for those files selected for use in future training materials chosen from only those families giving consent.

## Collaborative Agreements

As mentioned, this is an NCS Formative Research Project, carried out by the NCS Center at _Institution Name__ coordinated by NCS Investigator Craig Newschaffer of Drexel University in collaboration with the Johns Hopkins Study Center (Center PI Laura Caulfield). There is no formal collaborative agreement with Johns Hopkins or Drexel University. The _Institution Name_ NCS Center has been approved to do this formative study directly by the NCS Program Office.

## Other IRB Approvals

The coordinated project is being reviewed by the IRB at Drexel University where Dr. Craig Newschaffer has responsibility for overseeing project activity.

Each of the nine other NCS Centers participating will also be receiving independent IRB approval from their home institutions and Battelle Memorial Institute, who will serve as the data coordinating center, will also submit for IRB approval.

Because the project is being completed as part of a federal contract, like all other NCS activities, and involves the collection of data on more than nine individuals, OMB approval is also required.