Test to Stay in School: COVID-19 Testing Following Exposure in School Communities

Phase: N/A – prospective, interventional, cohort study

Funding Sponsor:

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)

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STATEMENT OF COMPLIANCE

This study will be conducted in compliance with the protocol, International Council for Harmonisation (ICH) E6 (R2) guideline for Good Clinical Practice (GCP), and the applicable regulatory requirements from the United States Code of Federal Regulations (CFR), including 45 CFR 46 (Human Subjects Protection); 21 CFR 50 (Informed Consent), 21 CFR Part 54 (Financial Disclosure), and 21 CFR 56 (Institutional Review Board [IRB]); as well as international regulatory requirements, if applicable.

All individuals who are responsible for the conduct, management, or oversight of this study have completed Human Subjects Protection and ICH GCP Training.

STUDY PRINCIPAL INVESTIGATOR

The signature below documents the review and approval of this protocol and the attachments (e.g., package inserts), and provides the necessary assurances that this clinical study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality and according to local legal and regulatory requirements and to the principles outlined in applicable United States (U.S.) and international regulations and ICH guidelines.

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Principal Investigator Name (Print or Type)

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Study PI Signature Date

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CoC	Certificate of Confidentiality
COVID-19	Coronavirus Disease 2019
DCC	Data Coordinating Center
DCRI	Duke Clinical Research Institute
DUHS	Duke University Health Systems
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
FERPA	Family Education Rights and Privacy Act
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council for Harmonisation
IRB	Institutional Review Board
NC	North Carolina
NCDHHS	North Carolina Department of Health and Human Services
NIH	National Institutes of Health
PHI	Protected Health Information
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus -2
UNC	University of North Carolina
U.S.	United States

PROTOCOL HISTORY OF CHANGES

Version	Date	Summary of Changes
v1.0	17 SEP 2021	N/A - Original protocol
v2.0	1 OCT 2021	Two screening questions have been added to the protocol. These screening questions will be administered via the existing REDCap link and will allow the study team to determine which consent/assent packet to send to potential participants.
v3.0	27 OCT 2021	Data management platform was changed to AirTable to increase security and ease of use. Option for study team to obtain verbal consent was added.
v4.0	30 NOV 2021	Broadened language to allow flexibility in testing frequency and time points based on evaluation of safety data (e.g. tertiary transmission) and feedback from the study safety committee and NCDHHS. Updated consent forms to reflect the protocol modifications.

PROTOCOL SYNOPSIS

Protocol Title:	Test to Stay in School: COVID-19 Testing Following Exposure in K-12 School Communities
NCT #	NCT05052580
Phase:	N/A, a prospective, interventional study
Objectives:	Primary: 1. Evaluate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission following exposure in Kindergarten through 12th grade schools. Secondary: 1. Characterize the effect of individual-level mitigation practice (e.g., masking) on SARS-CoV-2 spread. 2. Characterize the effect of exposure setting on SARS-CoV-2 spread. 3. Describe COVID-19-related school absences for up to 14 days following within-school SARS-CoV-2 exposure.
Study Design:	Participants in school communities who have been exposed to SARS-CoV-2 will be tested for COVID-19 on the day after exposure (day 1) and at days 3, 5, and 7 following initial known exposure. Data will be reviewed weekly by a study safety committee and NCDHHS, and updates to the testing protocol (test frequency and test time points) will be made based on analysis of data. Mitigation practices including masking, the context of exposure (classroom, school bus, after school sporting event, lunch, etc.), and results of COVID-19 test will be documented.
Study Population:	School communities
Number of Participants:	Up to 1,000,000
Number of Sites:	Single coordinating site
Duration of Study:	2 years

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Background Information

1.1.1 COVID-19 and Kindergaten-12th grade school closures

Widespread Kindergarten through 12th grade school closures are the most important COVID-19-related threats to child health. Since February 2020, children have accounted for one-tenth of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases; up to 2.2% and 0.04% of pediatric cases have resulted in hospitalization or death, respectively, and as many as 50% of cases are asymptomatic.[1,2] However, children have been far from spared of the downstream effects of this pandemic. In March 2020, most Kindergarten through 12th grade schools preemptively closed to in-person education in an attempt to limit viral spread. Most publically-funded Kindergarten through 12th grade schools across the nation, responsible for educating >55 million of the nation's children, remained closed in the early 2020, citing concerns about viral transmission and risks to students and staff. Because public schools play such a vital role in the educational, social, and emotional development of young children as well as the delivery of vital services such as food and healthcare, it is not surprising that early data show food insecurity has doubled; 65% of children 9-13 years are less physically active; 1/6th of children have worsened behavioral health; suicidality may be increasing, and physical abuse is more severe.[3-7] The potential consequences of these findings are deep and far-reaching; children with food insecurity are twice as likely to be in fair or poor health, more likely to be hospitalized, and more likely as adults to have poor job readiness. Chronic absenteeism in early primary school decreases the likelihood of reading at grade level by the third grade and increases the risk of drop out by 4 times compared to proficient readers.[8] Adults with less than a high school education are 2.4 times as likely as high school graduates to rate their health as poor and live 10 years fewer than those with graduate education. Considering these profound impacts, access to in-person education is imperative.

In North Carolina (NC), schools have been able to show low secondary transmission of SARS-CoV-2 within school buildings.[9] Data in school communities confirms that mitigation strategies such as proper masking have been imperative in reducing spread in schools.[9-11]

Yet, current policies and procedures requiring quarantine after close contact exposures to limit further spread have led to hundreds of thousands of missed school days and have threated the school workforce, greatly impeding school operations and the ability of children to appropriately learn. In the fourth quarter of 2021 in NC alone, more than 40,000 students and staff were required to quarantine as a result of being a close contact of a COVID-19 case (unpublished). Fortunately, recent CDC and local guidance have eliminated quarantines for most exposed, unvaccinated, asymptomatic children who are wearing a mask and who are in close contact with another masked, infected child within the classroom setting. However, many quarantines continue to result in unvaccinated adults, children exposed to infected adults, and masked exposures occurring outside of the classroom (e.g., athletics or busing). Moreover, schools and local governments are steadily lifting mask mandates, even as local community cases rise, contributing to exponential increases in quarantines that not only keep children and staff out of schools and parents out of work, but have often overwhelmed school resources and the public health system.

To address the issue of quarantines while ensuring that the school and surrounding community remain safe from SARS-CoV-2 spread, some locales have begun implementing a "test to stay strategy", whereby a close contact undergoes serial testing over a specified duration of time.

The close contact must wear a mask during this time period but is not required to undergo quarantine as long as the screening tests remain negative and the contact remains asymptomatic. While this strategy is supported by strong scientific premise and initial data are promising, the impact of this strategy on quarantine, and secondary and tertiary within-school transmission has not been systematically evaluated.

This study will partner with schools to allow students and staff to remain in school following exposure if they continue to test negative for COVID-19 over pre-determined intervals. This study aims to collect data to assess the spread of SARS-CoV-2 in school communities with varying mitigation strategies to provide data-backed guidelines for mitigation strategies in schools. The study team will work with NCDHHS and a safety monitoring team on a weekly basis to interpret data, evaluate safety, and design next steps (e.g. testing frequency and timing).

1.2 Scientific Rationale

This study will evaluate spread of SARS-CoV-2 following known exposure in schools. This information will be critical for determining future policies surrounding COVID-19 testing, quarantine, and mitigation practices in the Kindergarten through 12th grade school environment. Staff and students who participate in this study will provide consent for testing and collection of data on demographic factors, symptoms, quarantine, test results, and tertiary spread. The existing partnerships with schools established through the ABC Science Collaborative, a partnership between Duke and University of North Carolina (UNC) faculty and Kindergarten through 12th grade schools in NC, which was formed in the summer of 2020 will be leveraged.

This study will be conducted across multiple age groups of school-age children and staff, multiple educational settings, and multiple different educational cultures to increase the potential generalizability of study results. Additionally, this study aims to prospectively collect real-world data, which otherwise would be unavailable, to guide evidence-based decision- and policymaking surrounding transmission and quarantine.

1.3 Potential Benefits

Participants may benefit from COVID-19 testing, symptom screening, masking and early identification of COVID-19. Additionally, individuals may benefit from a broader understanding of appropriate mitigation strategies to reduce spread of SARS-CoV-2, reduced need for quarantine, and increased school attendance. For the school community, this study will permit students and staff to stay in school provided they test negative, minimizing disruption to school and home operations. The broader impact that data collection has on advancing the scientific understanding of COVID-19 and associated outcomes may benefit others in the future. Additionally, this study aims to prospectively collect real-world data, which otherwise would be unavailable, to guide evidence-based decision- and policymaking surrounding transmission and quarantine.

1.4 Known Potential Risks

Community-level risk(s): For school communities to participate in this protocol, there is a potential risk for increased exposure to SARS-CoV-2 from elimination of quarantine; however,

frequent testing, symptom screening and requirements for masking in a controlled environment are designed to minimize this risk to the community.

Individual-level risk(s): Risks associated with this study include risks associated with the COVID-19 testing procedure, specifically risks associated with lower nasal swab and the potential loss of confidentiality.

- **Potential Risks of Nasal Swabs:** Risks include mild irritation, insignificant local pain, and minor bleeding.
- **Potential Risk of Loss of Confidentiality:** There is a potential risk of loss of confidentiality. Every effort will be made to protect the participant's protected health information (PHI) as well as other identifying information, but this cannot be guaranteed.

2 OBJECTIVES AND OUTCOME MEASURES

	Objective	Endpoints
Primary:	Evaluate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission following exposure in Kindergarten through 12th grade schools.	• Proportion and number of students with positive COVID-19 test following known exposure. • Proportion and number of staff with positive COVID-19 tests following known exposure. • Proportion and number of exposures undergoing the test-to-stay protocol that result in additional transmission. • Time to test positivity among those exposed to SARS-CoV-2 and undergoing the test-to-stay protocol.
Secondary #1:	Characterize the effect of individual-level mitigation measures (e.g., masking) on SARS-CoV-2 spread.	• Proportion and number of masked students with positive COVID-19 test who were exposed to SARS-CoV-2 from masked versus unmasked individuals. • Proportion and number of masked staff with positive COVID-19 test who were exposed to SARS-CoV-2 from masked compared to unmasked individuals • Proportion and number of unmasked students with positive COVID-19 tests who were exposed to SARS-CoV-2 from masked compared to unmasked individuals • Proportion and number of unmasked staff with positive COVID-19 tests who were exposed to SARS-CoV-2 from masked compared to unmasked individuals
Secondary #2	Characterize the effect of exposure setting on SARS-CoV-2 spread.	• Proportion and number of students with positive COVID-19 test after indoor vs. outdoor exposure. • Proportion and number of students with positive COVID-19 test after athletic vs. classroom exposure. • Proportion and number of students with positive COVID-19 test after bus vs. classroom exposure.
Secondary #3:	Describe COVID-19-related school absences for up to	• Total number of school days missed due to symptoms after exposure.

	14 days following SARS-CoV-2 exposure.	• Total number of school days missed due to isolation after positive COVID-19 test. • Total number of school days missed due to quarantine after SARS-CoV-2 exposure.

3 STUDY DESIGN

3.1 Overall Design

Study design: This is a prospective, interventional study with a primary objective of evaluating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission following exposure in Kindergarten through 12th grade school students and staff. Participants will be tested with a COVID-19 testing kit that is Food and Drug Administration (FDA)-authorized under an emergency use authorization (EUA) for non-prescription use for both symptomatic and asymptomatic evaluation in children and adults. During the initial phase of this study, participants who consent to participate in this study will be tested at days 1, 3, 5, and 7 following a known COVID-19 exposure on day 0. If a participant does not know of the exposure until more than one day following the exposure, they will be tested on the day they become aware of the exposure and then resume the aforementioned testing schedule (e.g. participant identifies exposure 3 days after the exposure, test on day 3, day 5, and day 7). After the initial phase, the number of tests may be reduced and the test time points may change based on analysis of current data. All modifications will be made only if deemed safe by the safety monitoring committee and NCDHHS.

If the COVID-19 tests are negative, the participant will remain in the school environment. A positive COVID-19 test or the development of symptoms on any day after exposure would require isolation according to school, local and state guidelines. Demographic information, daily presence or absence of symptoms, whether the infected person or close contact was masked, setting of the exposure, test results, and school absences will be collected following consent. Data regarding school level mitigation practices will also be collected. Data collected from this study may be combined with school-provided data and publicly available community data.

3.2 Study Definition of Enrollment

Study enrollment is defined as the participant has provided informed consent (or assent) and completed at least one day of testing in an effort to avoid quarantine.

3.3 Study Definition of Completion

An individual will complete the study after completing all testing days and symptom monitoring (up to 14 days), or data entry that explains why all testing was not completed (e.g., positive test, symptoms, quarantine).

4 STUDY POPULATION

4.1 Selection of the Study Population

4.1.1 Inclusion Criteria

1. Consent completed
2. Child or adult that is part of a school community
3. Known exposure to SARS-CoV-2

4.1.2 Exclusion Criteria

There are no exclusion criteria for this study, all inclusion criteria must be met for participation. Some restrictions to inclusion may apply based on school-specific policies (e.g., optional masking).

4.2 Participant Discontinuation/Withdrawal

A participant or his/her parent (or legal guardian) may voluntarily withdraw consent to participate in the study at any time. Participants are not obligated to state the reason for withdrawal. No additional study data will be collected after consent has been withdrawn, however, all data collected prior to consent withdrawal will be maintained in the database.

4.3 End of Study

Participants will be considered off study at the end of the school semester in which they enrolled onto the study.

5 STUDY PROCEDURES

5.1 Summary of Evaluations

	Enrollment/Baseline	**Testing Period**	**Follow-Up**
PROCEDURE	**Day 0**	**Day 1, 3, 5, 7**	**Up to Day 14**
Screening	X		
Informed consent/assent	X		
Confirm eligibility criteria	X		
Demographics	X		
Mitigation data collection	X		
Exposure information	X		

COVID-19 testing and results collection		X	
Symptom data		X	X
Safety Assessment		X	

5.2 Screening Questions

Several screening questions will be asked via REDCap prior to consent to assure the correct consent is assigned to the person completing the form (e.g. parent/adult consent, or consent/assent combination). These screening questions ask about language preference (e.g. English or Spanish), and the age of the person who had a within-school COVID-19 exposure (e.g. less than 7 years of age, between 7 and 17 years of age, and 18 years of age or older). No identifiable information will be collected until after informed consent has been obtained. These questions will be used for screening purposes only.

5.3 Enrollment/Baseline

Participants or their parent/legal guardian will provide informed consent (or assent). Applicable informed consent from the participant or parent/legal guardian (and assent if applicable) for all participants will be documented. After consent, the participant will be assigned a unique ID by the school nurse or administrator. The school nurse or administrator will collect study-related variables via a spreadsheet using one of two different methods. The school nurse may use AirTable, a system designed by Technology and Data Solutions, or standard excel spreadsheets, which will be sent to the research team. The research team will have access to individual-level data but will not have access to names or other identifiers. While the study team will have access to the consents completed via REDCap, the team will not know which unique ID belongs to which individual.

The following information will be collected from the student at the time of enrollment. Information may be collected directly from the participant, their parent/legal guardian, or via a school nurse. The information will include the following:

- Participant demographics (age, sex, English proficiency, and vaccination status)
- Mitigation data collection including whether the participant was masked or unmasked, and vaccination status (if known)
- Exposure details include when exposure occurred, where it occurred, and if the individual who caused the exposure was masked or unmasked

5.4 Testing Period

Eligible participants will undergo COVID-19 testing on days 1, 3, 5, and 7 following known SARS-CoV-2 exposure. If a participant is not aware of the exposure until after the day of exposure, testing will begin immediately on the day of exposure awareness and then resume according to the study schedule (see **Table 1** below for examples). Testing will occur at home or at school according to the Instructions for Use. Participants will be asked to report symptoms for during the testing period. Safety and testing results will also be collected. Pending approval from NCDHHS, the number of tests and the test time points may be changed if deemed safe based on analysis of prior data. For example, if these stakeholders agree that the Test to Stay protocol is safe with two tests rather than four, this change in test frequency may be made. When designing this protocol, the study team used a very conservative approach to prevent undue harm to participants. Over the next several weeks and months, the study team will work closely with stakeholders to modify the test time points and total tests performed to identify the optimal testing protocol which is sustainable for schools (time, resources) but also deemed to be safe.

Table 1. Testing Schedule based on knowledge of exposure

Exposure day	Knowledge of exposure day	Testing days
0	0	1, 3, 5, 7
0	1	1, 3, 5, 7
0	2	2, 3, 5, 7
0	3	3, 5, 7
0	4	4, 5, 7
0	5	5, 7

5.5 Follow-Up

Participants will be asked to report symptoms for up to 14 days following SARS-CoV-2 exposure. Schools will be asked to report tertiary spread and number of close contacts for individuals who tested positive.

6 ASSESSMENT OF SAFETY

Participants will be asked to self-report safety events related to testing and after each testing event on pre-specified testing days. Because these tests have undergone rigorous safety assessments, this study will only collect safety events related to known testing procedures risks, which include nose irritation, local pain around nose, and nose bleeding. Serious and unanticipated safety events are not expected to occur in this study and therefore no expedited safety reporting will occur. Participants will be provided with contact information if they experience any concerning safety events and wish to report them outside of the study safety assessment survey. The study principal investigator will review aggregate safety information and determine if any of the safety information requires Institutional Review Board (IRB) submission and review according to Duke University Health System (DUHS) IRB reporting policies.

7 Study Termination

This study may be terminated at any time by the funding agency or the study principal investigators. Reasons for termination may include but are not limited to, if in their judgment, there are no further benefits to be achieved from the study. If the study is terminated, notifications will be made to the IRB of record and study participants, in accordance with all applicable regulations governing the study and site/investigator.

8 STATISTICAL CONSIDERATIONS

8.1 Study Endpoints

8.1.1 Primary Endpoints

Primary Objective: Evaluate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission following exposure in Kindergarten through 12th grade schools.

Primary Endpoints:

- Proportion and number of students with positive COVID-19 test following known within-school exposure.
- Proportion and number of staff with positive COVID-19 tests following known within-school exposure.
- Proportion and number of exposures undergoing the test-to-stay protocol that result in additional (tertiary) transmission.
- Time to test positivity among those exposed to SARS-CoV-2 and undergoing the test-to-stay protocol.

8.1.2 Secondary Endpoints

Secondary Objective #1: Characterize the effect of individual-level masking on SARS-CoV-2 spread.

Secondary #1 Endpoints:

- Proportion and number of masked students with positive COVID-19 test who were exposed to SARS-CoV-2 from masked versus unmasked individuals.
- Proportion and number of masked staff with positive COVID-19 test who were exposed to SARS-CoV-2 from masked compared to unmasked individuals
- Proportion and number of unmasked students with positive COVID-19 tests who were exposed to SARS-CoV-2 from masked compared to unmasked individuals
- Proportion and number of unmasked staff with positive COVID-19 tests who were exposed to SARS-CoV-2 from masked compared to unmasked individuals

Secondary Objective #2: Characterize the effect of exposure setting on SARS-CoV-2 spread.

Secondary #2 Endpoints:

- Proportion and number of students with positive COVID-19 test after indoor vs. outdoor exposure.
- Proportion and number of students with positive COVID-19 test after athletic vs. classroom exposure.
- Proportion and number of students with positive COVID-19 test after bus vs. classroom exposure.

Secondary Objective #3: Describe COVID-19-related school absences for up to 14 days following within-school SARS-CoV-2 exposure.

Secondary #3 Endpoints:

- Total number of school days missed due to symptoms after exposure.
- Total number of school days missed due to isolation after positive COVID-19 test.
- Total number of school days missed due to quarantine after SARS-CoV-2 exposure.

8.2 Analysis Plan

Summary statistics of the schools and the students/staff will be presented using data collected during study enrollment. Means/medians with standard deviations (and interquartile ranges) will be tabulated.

8.2.1 Primary Analysis

For the primary endpoint the proportion of students/staff with positive COVID-19 test will be reported and the trend by week will be presented in graphical form. To account for the within-school correlation of outcomes, 95% confidence intervals will be estimated for the proportion using a generalized estimating equations approach using a working independence correlation structure.[12]

8.2.2 Secondary Analysis

The proportion and number of students/staff who reported masking and unmasking will be reported and presented in graphical form. The primary analysis will be repeated for masked and unmasked participants (students and staff) separately. The primary analysis will be repeated for masked and unmasked source of exposure separately.

School absences will be analyzed by absences due to symptoms, positive COVID-19 test, or due to quarantine for exposure to SARS-CoV-2. To account for the within-school correlation of outcomes, analyses will be conducted using a generalized estimating equations approach using a loglink suitable for count outcomes, with a working independence correlation structure.

To account for within-school correlation, a risk between the schools using a generalized estimating equation approach with an identity link and a working independence correlation structure will be estimated. The risk difference will be estimated for each semester during the study period, as well as overall. Students will be censored by end of data or study withdrawal. Censoring will be addressed by incorporating inverse-probability censoring weights into the regression model, with censoring risk estimated with a Kaplan-Meier estimator.

8.2.3 Subgroup Analysis

Exploratory subgroup analysis may occur from the information collected as part of this study.

8.3 Sample Size Considerations

No formal sample size calculation was completed for this study. This study will enroll up to 1,000,000 participants.

9 Future Use of Study Records

The research data collected in this study, and provided to the sponsor, will be kept indefinitely.

Information about this study, including study results, will be published without further permission from the participant as detailed in the informed consent form. Participants will not be identified in any publications or presentations made about the study.

After the study is completed, information about the study, including study data, may be provided to the National Institutes of Health (NIH). Identifiable data will be kept at the DCRI and the DCRI will not share these data with the NIH. With NIH approval, the data submitted may be used by other researchers for future research. The study data submitted will be de-identified, meaning it will not include any information that can identify the participant. The study team may also share the de-identified study data with other researchers. When the participant's de-identified study data are provided to other researchers for the purposes of future research, it will be done without obtaining additional permission.

10 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Data collected for this study will include data provided from schools, data collected by school nurses and administrators, data entered by the participant and/or their parent/guardian directly into the Data Coordinating Center (DCC)-held database or into REDCap, and data entered into the DCC-held database or REDCap by the study team. All data received from schools will be de-identified, aggregate data and be provided in accordance with the Family Education Rights and Privacy Act (FERPA) regulations.

While the study team currently receives data spreadsheets from school nurses and administrators via Duke Box, the team will slowly transition to AirTable, which will increase security while decreasing school-level burden. Each approved school nurse or administrator will be issued their own username. Only authorized users will have access. An AirTable instance

will be built for each district such that only individuals from the specific district will have access. Data will be entered in real-time, reducing the potential for errors and burden of downloading and uploading spreadsheets to Duke Box. Unique IDs will be used rather than participant names.

11 QUALITY CONTROL AND QUALITY ASSURANCE

The principal investigator will ensure that all study personnel are appropriately trained and applicable documentation is maintained. The DCC will implement quality control procedures beginning with the data entry system and generate data quality control checks that will be run on the database.

12 ETHICS/PROTECTION OF HUMAN PARTICIPANTS

12.1 Informed Consent Process

Informed consent and assent procedures are initiated prior to the individual agreeing to participate in the study and continuing throughout the individual's study participation. For this study, participants will be consented once per semester, following their initial SARS-CoV-2 exposure for that semester. Risks and possible benefits of participation in this study will be provided to the participants and their parents/guardians, as appropriate, prior to consenting via REDCap. The school nurse or administrator will be responsible for providing the REDCap link to parents and staff for consent; however, the school nurse will not be involved in the consent process. The Duke study team will be available to discuss the study and answer questions.

In situations where access to internet is limited, and eConsent is a barrier, the study team will administer verbal consent. In accordance with the Duke Learning Management System (LMS) training titled, "Informed Consent Process and Procedures for Clinical Research" and the "Requirements of Study Personnel Conducting the Consent Process" document (last updated: 9/28/2021), the person obtaining verbal consent will meet the following requirements:

- Has completed all training required for individuals conducting research with humans (e.g. CITI, HIPAA, and RCR training)
- Has completed all consent-specific training involving the consent process at Duke (e.g. the training referenced above)
- Possesses sufficient knowledge of study, as determined by PI, to be able to adequately address questions from a potential participant
- Is listed as Key Personnel for the study and identified on Delegation of Authority log by PI as having authority to consent participants
- Has prior experience or plans to be observed for at least the first two consents

Per the LMS training and the document cited above, "The most appropriate individuals for this role on the study include the PI, co-PI, clinical research coordinator, clinical research nurse coordinator, and regulatory coordinator; however, this does not preclude others on the study team from assuming this role provided the criteria are met." Ultimately, the PI will make the determination on who is eligible to obtain informed consent. For individuals who do not possess prior experience, the PI will implement a plan by which the individual is observed conducting

consent at least the first two times by an individual experienced in the process (“Observer”), and the Observer will provide immediate feedback, including corrective actions. Documentation of successful completion of informed consent observation will be maintained in accordance with individual CRU policies, e.g., personnel files, study regulatory binder, etc.

This study enrolls children. Per 21 CFR 50.3 (o) and 45CFR 46.402 (a) “children” is defined as persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations (or the research), under the applicable law of the jurisdiction in which the clinical investigation (or the research) will be conducted and so the legal age for consent may be different in different jurisdictions.

Consent forms with detailed descriptions of the study procedures, risks, and potential benefits will be approved by the IRB. Consent forms (and assent forms, if appropriate) will be provided to the participant or the participant’s parent/guardian electronically to read and note any questions. The consent must be completed prior to performing any study-specific procedures.

If information about new potential risks related to participating in this study emerges or procedures are modified, the consent/assent forms will be updated to reflect those potential risks, and the participants currently active in the study will be re-consented with the updated consents. If the consent forms are changed for any other reason and the local IRB requires re-consenting of active participants, the participant will be asked to review and complete the new consent forms electronically.

A copy of the executed informed consent/assent documents will be provided to the participant and/or the participant’s parent/legal guardian (as appropriate) for their records.

The assent process for the study will occur as appropriate, as described, per protocol.

12.1.1 Pediatric Assent

The participant should be informed about the study to the extent compatible with the participant’s understanding. As required by local regulatory authorities, the participant should assent to participate in the study. A separate IRB--approved assent form, describing (in simplified terms) the details of the study, study procedures, and risks, may be used. Assent forms do not substitute for the consent form signed by the participant’s parent or legal guardian.

Under 21 CFR 50.52, and 50.55, and 45 CFR Part 46.405, the IRB of record is responsible for determining that adequate provisions are made for soliciting the assent of children.

12.2 Assent Process

This study includes minor participants who may be enrolled in the study only with the consent of their parent/legal guardian. The minor participant will be informed about this study to the extent compatible with his/her neurodevelopmental abilities. Participants who are nonverbal or minimally verbal, have significant intellectual disability, are younger than seven years old, or have marked thought disorganization or positive psychotic symptoms are very unlikely to be considered developmentally able to provide assent. If the participant is developmentally able to understand the concepts of voluntary participation in research, the participant will be given a simplified, developmentally appropriate assent form to review and will be asked to sign and personally date the assent form. Electronic consent will be obtained via REDCap.

Assent does not substitute for the permission form signed by the participant's parent/legal guardian.

12.3 Documentation of Permission, Assent, and Consent

Permission, assent, and consent must be documented using forms and processes determined by the DUHS IRB.

Prior to enrollment of participants into this study, the protocol, the applicable informed consent/assent template, and any materials or advertisements presented to participants will be reviewed and approved by the DUHS IRB.

Should amendments to the protocol and consent/assent documents be required, the amendments will be written by the sponsor and approved by the DUHS IRB.

For non-English speakers, a fully translated consent may be used to obtain informed consent. The fully translated consent must be approved by the DUHS IRB and executed according to local requirements.

The informed consent process will be conducted and the form fully executed, before the participant undergoes any study-specific procedures.

12.4 Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor. Participants will provide information in the nurse's office or in a private space, adhering to school policies. This will vary from school to school but will follow each school's regular policies and procedures. This will occur during the school either before, during or after the day, when the participant learns that they have had an exposure. The information provided by participants will strictly relate to their COVID-19 exposure and testing.

The principal investigator will ensure that the use and disclosure of PHI obtained during a research study complies with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. The rule provides U.S. federal protection for the privacy of PHI by implementing standards to protect and guard against the misuse of individually identifiable health information of participants participating in clinical trials. Authorization is required from each research participant (i.e., specific permission granted by an individual to a covered entity for the use or disclosure of an individual's protected health information). A valid authorization must meet the implementation specifications under the HIPAA Privacy Rule. Authorization may be combined in the informed consent document (if approved by the IRB).

The study participant's contact information will be securely stored for use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the DCC. All study data systems used by the DCC research staff will be secured and password protected.

To further protect the privacy of study participants, this study is covered by a Certificate of Confidentiality (CoC) from the NIH. The CoC limits the ability of courts and other agencies from forcing the study team to share participant information or body fluids during a legal or legislative action without the participant's permission. The CoC does not restrict the parents from sharing information voluntarily.

13 DATA HANDLING AND RECORD KEEPING

The investigator is obligated to conduct this study in accordance with U.S. Federal Regulation 21 CFR 312.60-68 as specified by applicable state and federal laws, and the International Council for Harmonisation: Good Clinical Practice: Consolidation Guideline.

13.1 Data Handling

Data will be captured using multiple systems and approaches. All data collected in the context of this study will be stored and evaluated per applicable regulatory requirements and guidance for electronic records.

Data will be stored and evaluated in a manner that protects participant confidentiality in accordance with the legal stipulations applying to confidentiality of data.

13.2 Data Management Responsibilities

The DCC for this study will be responsible for data management, quality review, analysis, and reporting of the study data.

13.3 Data Capture Methods

School personnel will collect a subset of the study-required data. This data will be provided to the DCC via spreadsheets with patient identification numbers or through AirTable. The school will hold the key to connect the participant identification numbers to the participant names and this key will not be shared with the PI or any of the DCC study team.
Participant/parent/guardian-reported data will be entered directly into the DCC-held database or the Duke REDCap system.

13.4 Types of Data

Data for this study will include participant reported information including demographics, mitigation practices, exposure information, safety, and COVID-19 test results. Additional de-identified data may be provided by schools, including demographics and school attendance; these data will be provided in aggregate or at the individual level.

13.5 Study Records Retention

All records will be retained for at least 6 years after study completion, per Duke Policy.

13.6 Protocol Deviations

A protocol deviation is any noncompliance/unplanned excursion from approved investigational plan (e.g., protocol), or ICH GCP guidelines. The noncompliance may be on the part of the

participant, investigator, or staff. No protocol deviations will be reported for this study, but indirectly tracked via missing data in the database.

14 PUBLICATION POLICY

The study will adhere to authorship standards described in the International Committee of Medical Journal Editors' Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals. Authorship credit should be based on:

- Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data
- Drafting the article or revising it critically for important intellectual content
- Final approval of the version to be published
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Additional authorship requirements imposed by individual journals will also be met. Authorship credit will be assigned in an equitable fashion and will be commensurate with participation and effort on the individual manuscript. Committee members will appear as authors on manuscripts based solely on actual contributions to the writing of the manuscript.

All investigators funded by the NIH must submit or have submitted for them to the National Library of Medicine's PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. The NIH Public Access Policy ensures the public has access to the published results of NIH-funded research. It requires investigators to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication. Further, the policy stipulates that these papers must be accessible to the public on PubMed Central no later than 12 months after publication.

Refer to:

http://publicaccess.nih.gov/

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html

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