2021H0080: SARS-CoV-2 study of viral evolution (COVE)

Final Rule (For office use only)

Study 2021H0080 - Identification

Title of Study*	SARS-CoV-2 study of viral evolution (COVE)
Principal Investigator*	Richard Robinson (robinson.2346)
Study Department*	Medicine | School Biomedical Sciences Microbial Infection and Immunity (CC12837)
Department Signer	Eugene Oltz (Signed: 01/13/2021)

Principal Investigator - Richard Robinson

Contact Information

Email: robinson.2346@osu.edu
Phone: (614) 2934164

Conflict of Interest (COI)

✓ Completed (Expires: 06/30/2021)

Academic Information

Associate Professor (2320)
Medicine | School Biomedical Sciences
Microbial Infection and Immunity (cc12837)
Medicine (Medicine_CCH6)
100% FTE

PI Eligibility

✓ Eligible

Type of Research

Select the appropriate option below based on the type of review required for the research.

Exempt research: This option should be selected for research that involves human subjects that is not subject to regulations requiring IRB review and approval. Final determination is made by ORRP staff.

Expedited or full IRB-reviewed research: This option should be selected for review by the Biomedical Sciences, Behavioral and Social Sciences, or Cancer IRBs at Ohio State including research reviewed through either expedited or full board processes. This option should also be selected for any research which will be ceded to another non-Ohio State IRB, such as WIRB, NCI CIRB, or another external institution.

Don't know: This option should be selected if the investigator is uncertain whether the research is exempt or should be reviewed by an IRB.

What type of review is required for your project?*

- □ Exempt research
- ■ IRB-reviewed research (includes WIRB, NCI, CIRB, and other external IRB review)
- □ Don't know (screening questions to determine if exempt research)

Review Board

Research at Ohio State involving human subjects that requires Institutional Review Board (IRB) review is reviewed by one of three university IRBs or one of multiple external IRBs, including Western IRB (WIRB), National Cancer Institute Central IRB (CIRB), and Nationwide Children's Hospital (NCH) IRB. Board assignments are made to ensure that proposed research receives appropriate scientific or scholarly review by individuals with the qualifications to determine that the rights and welfare of research participants are protected. Final board assignment is determined by ORRP.

Selection of one of the three Ohio State IRBs below will connect to the initial review of human subjects research.

Selection of one of the external (non-Ohio State) IRBs will connect to an external review application which provides the necessary information for ORRP staff to perform pre-screening of the application to determine that institutional requirements have been met (e.g., COI disclosure, education) and that the research meets the conditions necessary to be forwarded for external IRB review.

Select the board to review this research.*

- □ Ohio State Behavioral and Social Sciences IRB
- ■ Ohio State Biomedical Sciences IRB
- □ Ohio State Cancer IRB
- □ National Cancer Institute Central IRB (CIRB)
- □ Nationwide Children's Hospital IRB
- □ Western IRB (WIRB)
- □ Other external IRB

Multi-site Study

Multisite research includes projects or studies that involve collaboration with sites or individuals external to Ohio State. The IRB must determine whether external sites or personnel need IRB approval in order to participate in study activities.

EXAMPLES OF MULTI-SITE RESEARCH:

- Ohio State is the lead institution of a group of sites participating in the same research project, where all sites are recruiting subjects and administering research interventions.
- An Ohio State investigator is participating in a research project, where another institution is the lead institution.
- Ohio State is the IRB of record for one or more other sites participating in a research project.

EXAMPLES OF NON-MULTI-SITE RESEARCH:

- An Ohio State investigator is conducting research at a local elementary school that involves recruiting participants and performing study interventions, where no school employees are engaged in the research.
- An Ohio State investigator and research staff interact with clients at a local pharmacy, and a letter of support from the pharmacy is in place.

Is this a multi-site study?*	□ Yes ■ No

Location of Research

Research to be conducted at locations other than approved performance sites may require a letter of support or another institution's approval if personnel are engaged. See OHRP Engagement Guidance or contact ORRP at irbagreements@osu.edu or 614-688-8457 for more information.

Ohio State Approved Research Sites

Ohio State Columbus Campus

Address	Applied Microbiology Services Lab (AMSL) Biological Sciences Building, 484 W 12th Avenue

Columbus, OH

Domestic Research Sites – Non-Ohio State Locations

You have listed no alternate domestic research sites.

International Research Sites

You have listed no international research sites.

Study Personnel

Enter all Ohio State study team members below. External collaborators will be entered on a different page. Study team members should only be listed in one category (i.e., PI, co-investigator, or key personnel).

Co-investigators and key personnel are defined as individuals who participate in the design, conduct, or reporting of human subjects research. At a minimum, include individuals who recruit participants, obtain consent, or who collect study data.

Additional contacts can also serve in another role on the project.

All individuals listed as Ohio State study team members will have access to all submitted information, including completion status of team members' administrative and training requirements (CITI, RCR, COI disclosure), and may edit submissions on behalf of the principal investigator.

Electronic signatures are required of all Ohio State investigators named on the submission.

Study Team

Additional Contact - Michael Oglesbee

Contact Information

Email: oglesbee.1@osu.edu
Phone: (614) 2929672

Co-Investigator - Mikkel Quam

Contact Information

Email: quam.7@osu.edu
Phone:

Academic Information

Assistant Professor - Practice (9M) (3160-9M)

Conflict of Interest (COI)

✓ Completed (Expires: 06/30/2021)
Umea University

Public Health | Division of Epidemiology (cc10495)
Public Health (Public_Health_CCH6)
100% FTE

Activities Performed

Protocol development/study design; Data analysis/interpretation; Manuscript preparation; Access participant Protected Health Information (PHI);

Co-Investigator - Daniel Jones

Contact Information

Email: jones.5658@osu.edu
Phone:

Conflict of Interest (COI)

✓ Completed (Expires: 06/30/2021)
Association of Molecular Pathology

Academic Information

Professor (6640)
Medicine | Pathology (cc12857)
Medicine (Medicine_CCH6)
50% FTE

Physician (6380)
Health Sciences | FGP Pathology (cc12911)
Health Sciences (Health_Sciences_CCH6)
50% FTE

Activities Performed

Protocol development/study design; Data analysis/interpretation;

Co-Investigator - Abigail Norris Turner

Contact Information

Email: ant@osumc.edu
Phone: (614) 3663510

Conflict of Interest (COI)

✓ Completed (Expires: 06/30/2021)
American STD Association

Academic Information

Associate Professor (2320)
Medicine | IM Infectious Diseases (cc11289)
Medicine (Medicine_CCH6)
100% FTE

Activities Performed

Protocol development/study design; Data analysis/interpretation; Manuscript preparation;

Co-Investigator - Seth Faith

Contact Information

Email: faith.3@osu.edu
Phone:

Conflict of Interest (COI)

✓ Completed (Expires: 06/30/2021)
Federal Bureau of Investigation; Pennsylvania State University; American Academy of Forensic Sciences; Ohio Bureau of Criminal Investigation

Academic Information

Director-00 (4034)
Research | Infectious Disease Institute (cc10995)
Academic Affairs (Academic_Affairs_CCH6)
100% FTE

Activities Performed

Protocol development/study design; Recruitment; Access participant Protected Health Information (PHI);

External Co-Investigators & Key Personnel

Enter the names of external collaborators who are engaged in the research. Only external personnel whose activities will be covered by an Ohio State IRB should be included.

"Engaged" individuals are those who intervene or interact with participants in the context of the research or who will obtain individually identifiable private information for research funded, supervised, or coordinated by Ohio State University. See OHRP Engagement Guidance or contact ORRP at irbagreements@osu.edu or 614-688-8457 for more information.

External Collaborators

You have listed no external collaborators.

Funding and Financial Conflicts

If the research is federally funded and involves a subcontract to or from another entity, an IRB Authorization Agreement may be required. Contact ORRP for more information.

Is the research funded or has	□ Yes ■ No □ Pending

funding been requested?*

Is any support other than monetary (e.g., drugs, equipment, etc.) being provided for the study?*

□ Yes
■ No
□ Pending

Provide a copy of the grant application or funding proposal.

Uploaded Files

No files have been uploaded.

Financial Conflict of Interest

All Ohio State investigators and key personnel must have a current COI disclosure (updated as necessary for the proposed research) before IRB review. Examples of financial interests that must be disclosed include (but are not limited to) consulting fees or honoraria; stocks, stock options or other ownership interests; and patents, copyrights and royalties from such rights. For more information, see Office of Research Compliance COI Overview and eCOI.

Please indicate if any Ohio State University investigator (including principal or co-investigator), key personnel, or their immediate family members has a financial conflict (including salary or other payments for services, equity interests, or intellectual property rights) that would reasonably appear to be affected by the research, or a financial interest in any entity whose financial interest would reasonably appear to be affected by the research. Select 'none' if no financial conflicts exist.*

■ None
□ Richard Robinson
□ Seth Faith
□ Mikkel Quam
□ Daniel Jones
□ Abigail Norris Turner

Conditions required for expedited IRB review

The Federal Regulations establish two main criteria for an expedited review:

a. The research may not involve more than "minimal risk." "Minimal risk" means that “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” (45 CFR 46.102(i) and 21 CFR 56.102(i)).
b. The entire research project must be consistent with one or more of the federally defined categories.

The expedited review procedure may not be used where identification of the participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the participant's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The expedited review procedure may not be used for classified research involving human subjects.

Investigators are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (i.e., expedited or convened) utilized by the IRB.

Protocols involving the collection, storage, and/or distribution of data and/or specimens for future research uses do not qualify for expedited IRB review. Convened review is required.

For more information regarding the expedited review procedures, see the Expedited Review Procedures policy.

Are you requesting **Expedited Review**?*

■ Yes □ No

Expedited Review Categories

Select the appropriate category(ies) for expedited review that describe the proposed research. Check all that apply. If the research meets the conditions for expedited review, the review of the protocol will be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. See 45 CFR 46 and 21 CFR 56 for more information.

The categories in this list apply regardless of the age of the participants, except as noted.

Category #1

Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

a. Research on drugs for which an investigational new drug application (21 CFR 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
b. Research on medical devices for which (i) an investigational device exemption application (21 CFR 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

□ Apply for category #1

Category #2

Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these participants, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week.
b. From other adults and children (defined as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.45 CFR 46.402(a)), considering the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these participants, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

□ Apply for category #2

Category #3

Prospective collection of biological specimens for research purposes by non-invasive means.

a. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

□ Apply for category #3

Category #4

Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

a. Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

□ Apply for category #4

Category #5

Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or

diagnosis).

■ Apply for category #5

Category #6

Collection of data from voice, video, digital or image recordings made for research purposes.

□ Apply for category #6

Category #7

Research made on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

□ Apply for category #7

Institutional Approvals

Check all that apply and provide applicable documentation.

□ No institutional approval

Comprehensive Cancer Center (CCC) Clinical Scientific Review Committee (CSRC)

Approval or exemption required prior to IRB review for all cancer-related research.

□ Comprehensive Cancer Center (CCC) Clinical Scientific Review Committee (CSRC)

Institutional Biosafety Committee (IBC)

Approval required prior to IRB review for research involving biohazards (recombinant DNA, infectious or select agents, viruses, toxins), gene transfer, or xenotransplantation.
Note: Laboratories processing clinical research samples (e.g., blood, serum, tissue, urine,

feces, saliva, bile), must be registered with the IBC. As applicable, contact IBCinfo@osu.edu to confirm laboratory registration.

■ Institutional Biosafety Committee (IBC)

Human Gene Transfer (HGT) Institutional Review

IBC approval required before IRB approval can be granted. HGT institutional review occurs after IRB approval.

□ Human Gene Transfer (HGT) Institutional Review

Upload approval letters for all applicable committees above.*

Uploaded Files

IBC Approval 2020R00000046.pdf

Uploaded by Richard Robinson on 01/13/2021

Summary, Background, and Objectives

Summarize the proposed research using **non-technical** language that can be readily understood by someone outside the discipline. **Use complete sentences (limit 300 words).***

To monitor the spread of SARS-CoV-2 and inform campus policies, The Ohio State University (OSU) established a COVID testing program for surveilling the prevalence of SARS-CoV-2 positive students and employees (https://safeandhealthy.osu.edu/testing). For this program, participants provide a saliva sample to the CLIA-certified OSU Applied Microbiology Services Lab (AMSL), which is located on campus and tests each saliva sample for the presence of SARS-CoV-2 using an FDA-approved PCR assay. After the PCR assay is completed, the excess volume of saliva is discarded. We propose to save these otherwise discarded samples for viral gene sequencing (to identify whether the virus present is a variant of concern, or VOC) and antibody measurements to determine if a VOC survives despite the presence of virus-specific antibody. Samples will be stored for a finite period (5 years) and will be coded prior to storage and use. An AMSL staff member (Co-I Seth Faith) will serve as an honest broker to ensure samples are coded prior to storage and use; no other study team members will have access to the codex linking a code to PHI. The creation of a COVE will enable us to identify relationships of public health importance, such as the relationship between COVID PCR positivity, VOCs and virus-specific antibody.

Summarize existing knowledge and previous work that support the expectation of obtaining useful results without undue risk to human subjects. **Use complete sentences (limit 300 words).***

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological agent of Coronavirus Disease 2019 (COVID19), a recently emerged infectious disease with no cure. Since its initial evolution in bats and emergence in 2019, SARS-CoV-2 has continued to evolve in humans and an increasing number of variants have been discovered worldwide, including the United States. These variants are concerning, as they may be more infectious than previous isolates, elicit different pathologies and immune responses, or-in the worst case scenario-evade current vaccines. Despite these worldwide concerns, the United States lags behind other countries in sequencing efforts to identify and track SARS-CoV-2 variants (43rd worldwide per The Washington Post; https://www-washingtonpost-com.cdn.ampproject.org/c/s/www.washingtonpost.com/world/2020/12/23/us-leads-world-coronavirus-cases-ranks-43rd-sequencing-check-variants/?outputType=amp) , placing Americans at a serious and potentially grave disadvantage. Our objective is to study excess saliva specimens that are currently being collected as part of the OSU COVID testing program and would otherwise be discarded in the absence of such a study. These samples would then be used for viral sequencing and antibody measurements to identify patterns that associate with SARS-CoV-2 transmission in the OSU Community.

List the objectives and/or specific scientific or scholarly aims of the research study.*

We will use remnant/excess saliva samples from Ohio State University (OSU) students and employees to track prevalence and transmission of SARS-CoV-2 variants, as well as identify relationships between SARS-CoV-2 variants and antibodies in coded saliva specimens. These specimens are currently being collected as part of the OSU COVID testing program (https://safeandhealthy.osu.edu/testing) and would otherwise be discarded.

Upload research protocol*

Uploaded Files

Clean Version 3 COVE IRB protocol.docx

Uploaded by Richard Robinson on 02/15/2021

Track Changes Version 3 COVE IRB protocol.docx

Uploaded by Richard Robinson on 02/15/2021

Research Methods & Activities

Use the boxes provided below to provide information on all interventions and activities that are to be performed in the research. Based on the selections chosen in the list of activities and components, completion of additional form pages may be necessary to provide required information for IRB review.

Identify and describe all interventions and interactions that are to be performed solely for the research study.*

Saliva (approximately 6 teaspoons per collection) is currently being collected by the CLIA-certified Applied Microbiology Services Lab, as part of the OSU COVID testing program. For this study, we will store excess volumes of saliva that are no longer needed for COVID testing (i.e. otherwise discarded) for the following specific research related to COVID: (1) Identify Variants of Concern (VOC) and their prevalence on campus over time. (2) Determine if the presence of a given VOC corresponds to lower levels of infection- or vaccine-elicited antibody levels in the same saliva sample.

Check all research activities and/or components that apply.*

- □ Anesthesia (general or local) or sedation
- □ Audio, video, digital, or image recordings
- □ Biohazards (e.g., rDNA, infectious agents, select agents, toxins)
- □ Biological sampling (other than blood)
- □ Blood drawing
- □ Coordinating center
- □ Data repositories (future unspecified use, including research databases)
- ■ Data, not publicly available
- □ Data, publicly available (e.g., census data, unrestricted data sets)
- □ Deception
- □ Devices
- □ Diet, exercise, or sleep modifications
- □ Drugs or biologics (including dietary supplements/ingredients)
- □ Emergency research
- □ Focus groups
- □ Food supplements
- □ Gene transfer
- □ Genetic testing
- □ Internet or e-mail data collection
- □ Magnetic resonance imaging (MRI)
- □ Materials that may be considered sensitive, offensive, threatening, or degrading
- □ Non-invasive medical procedures (e.g., EKG, Doppler)
- □ Observation of participants (including field notes)

□ Oral history (does not include dental or medical history)
□ Placebo
□ Pregnancy testing
□ Program Protocol (Umbrella Protocol)
□ Radiation (e.g., CT or DEXA scans, X-rays, nuclear medicine procedures)
□ Randomization
■ Record review (which may include PHI)
■ Specimen research
□ Stem cell research
□ Storage of biological materials (future unspecified use, including repositories)
□ Surgical procedures (including biopsies)
□ Surveys, questionnaires, or interviews (group)
□ Surveys, questionnaires, or interviews (one-on-one)
□ Other (Specify)

Provide data collection forms, subject material, subject diaries, and/or other instruments, if applicable. Do not include case report forms for multi-site industry-initiated or cooperative group studies.

Uploaded Files

COVE Data Collection Form.xlsx

Uploaded by Richard Robinson on 02/18/2021

Provide surveys, questionnaires, interview guides, and/or focus group guides, if applicable.

Uploaded Files

No files have been uploaded.

Provide subject information, such as newsletters, instruction sheets, appointment reminder cards, drug/device

Uploaded Files

No files have been uploaded.

information, if applicable.

Duration

Estimate the time required from each participant, including individual interactions, total time commitment, and long-term follow-up, if any. For studies with no subject time involvement, such as record review studies with a waiver of consent or observational studies, enter 'not applicable.'*

No time is required from each participant, as the specimens for this study will comprise excess volumes of saliva samples no longer needed for COVID testing, as provided by the Applied Microbiology Services Lab.

Number of Participants

The number of participants is defined as the number of individuals who agree to participate (i.e., those who provide consent or whose records are accessed, etc.) even if all do not prove to be eligible or complete the study. The total number of research participants may be increased only with prior IRB approval.

Provide the total number of participants (or number of participant records, specimens, etc.) for whom you are seeking Ohio State University approval.*

36,000

□ Unlimited participant numbers

Total number of participants* 36000

Explain how this number was derived (e.g., statistical rationale, attrition rate, etc.).*

We cannot predict the total number of saliva samples that will be stored and analyzed for this study because the COVID pandemic is ongoing and there are no projections of when it will end, even after the majority of OSU students and employees are vaccinated. We can, however, estimate the number of samples we anticipate collecting within the first month of our study at current positivity rates. The AMSL is currently processing 7,000 saliva samples per working day. Assuming an average 2% PCR positivity rate, which has been the case for the past month, this means ~140 samples per working day will be COVID PCR positive and

subsequently stored. Assuming an average of 21 working days per month, we estimate storing 3,000 saliva samples per month or 36,000 saliva samples per year. This is the basis for our requesting 36,000 participants. Should we near this capacity or if it turns out that more samples are needed, an amendment will be submitted to increase the number at that time.

Participant Population

Specify the age(s) of the individuals who may be included in the research:*

Adults 18 years and older

Specify the participant population(s). Check all participant groups that apply.*

■ Adults
□ Adults with impaired decision-making ability
□ Children
□ Neonates (uncertain viability/nonviable)
□ Non-English speaking
□ Pregnant women/fetuses – only if pregnant women will be intentionally recruited and/or studied.
□ Prisoners
□ Student research pools (e.g., psychology, linguistics)
□ Unknown (e.g., research using secondary data/specimens, non-targeted surveys, program protocols)

Describe the characteristics of the proposed participants, and explain how the nature of the research requires/justifies their inclusion.*

Participants will comprise OSU students and employees who are enrolled in the OSU COVID testing program.

Will any participants be excluded based on age, gender, race/ethnicity, pregnancy status, language, education, or financial status?*

□ Yes ■ No

Are any of the participants likely to be vulnerable to coercion or undue influence?*

□ Yes ■ No

Participant Identification, Recruitment and Selection

Participant Identification

Provide evidence that you will be able to recruit the necessary number of participants to complete the study.*

No recruitment activities are associated with this study.

Describe how potential participants will be identified (e.g., advertising, individuals known to the investigators, record review). Explain how the investigator(s) will gain access to this population, as applicable.*

Participants are enrolled in the OSU COVID testing program. Their saliva arrives to the AMSL, where it is tested for the presence of SARS-CoV-2 by PCR. It is at this location that the PI and their study team will access the sample and use the samples for the following viral gene sequencing and antibody measurements. Viral gene sequencing and antibody measurements will be performed in-house (i.e. within the AMSL) using a recently purchased sequencing instrument and ELISA plate reader, respectively.

Participant Recruitment and Selection

Select investigator(s) and/or key personnel who will recruit participants or identify records and/or specimens.*

□ Richard Robinson
■ Seth Faith
□ Mikkel Quam
□ Daniel Jones
□ Abigail Norris Turner

Describe the process that will be used to determine participant eligibility.*

Co-I Faith will review saliva records on a weekly basis to identify samples which were positive for SARS-CoV-2; he or a designee will then pull these samples from their temporary holding fridge, remove identifiers and replace with a code. Samples will then be transferred into a freezer for subsequent virus sequencing and antibody measurements.

Describe the recruitment process, including the setting in which recruitment will take place. Enter 'not applicable' if the research involves only record review and no participant

interaction.*

Not applicable

Explain how the recruitment process respects potential participants' privacy.*

Not applicable

Provide copies of proposed recruitment materials (e.g., ads, fliers, website postings, and recruitment letters).

Uploaded Files

No files have been uploaded.

Provide copies of consent materials used during the recruitment process (e.g., oral/written scripts).

Uploaded Files

No files have been uploaded.

Incentives to Participate

For more information regarding incentives for participation, see the ORRP policy, Recruiting Methods, Recruiting Materials, and Participant Compensation.

Will participants receive compensation or other incentives (e.g., free services, cash payments, gift certificates, classroom credit) to participate in the research study?*

□ Yes ■ No

Alternatives to Study Participation

Other than choosing not to participate, are there any alternatives to participating in the research?*

□ Yes ■ No

Informed Consent Process

Indicate the consent process(es) to be used in the study. Check all that apply.*

□ Informed Consent - Form
□ Informed Consent - Verbal Script/Online
□ Informed Consent – Addendum
□ Alteration of Consent Process
□ Alteration of Parental Permission
□ Assent - Form
□ Debriefing Script
□ Assent - Verbal Script/Online
□ Parental Permission - Form
□ Parental Permission - Verbal Script/Online
□ Translated Consent/Assent - Form(s)
□ Waiver of Assent
■ Waiver of Consent Process
□ Waiver of Consent Documentation
□ Waiver of Parental Permission
□ Waiver of Parental Permission Documentation

Select the investigator(s) and/or key personnel who will obtain consent from participants or their legally authorized representatives.*

■ None
□ Richard Robinson
□ Seth Faith
□ Mikkel Quam
□ Daniel Jones
□ Abigail Norris Turner

Who will provide consent or permission (i.e., participant, legally authorized representative, parent and/or guardian)?*

■ Not Applicable

Describe the consent process. Explain when and where consent will be obtained and how subjects and/or their legally authorized representatives will be provided sufficient opportunity (e.g., waiting period, if any) to consider participation.*

■ Not Applicable

Explain how the possibility of coercion or undue influence will be minimized in the consent process.*

■ Not Applicable

Will any other tools (e.g., quizzes, visual aids, information sheets) be used during the consent process to assist participant comprehension?*

□ Yes ■ No

Will any other consent forms be used (e.g., for clinical procedures such as MRI, surgery, etc.)?*

□ Yes ■ No

Waiver of Consent Process

Complete the questions below to request a waiver of the consent process. NOTE: Waivers of consent do not apply to greater than minimal risk research.

For additional guidance, see HRPP policy Informed Consent Process and the Elements of Informed Consent and the IRB Reviewer Reference Sheets - Appendix 1.

Is the research (or demonstration project) subject to the approval of state or local government officials and designed to study public benefit or service programs or procedures for obtaining benefits under those programs, changes in or alternatives to those programs or procedures, or changes in methods or levels of payment for benefits or services under those programs?*

□ Yes ■ No

Explain how the research (or research activities to which the waiver of consent applies) involves no more than minimal risk.*

This study will use otherwise-discarded, excess saliva samples that have been provided to the Applied Microbiology Services Lab (AMSL) for COVID-testing. There is no additional risk to keeping samples from these participants compared to when they first consented to having their saliva sample used for surveillance testing related to COVID19 community spread. The only risk is loss of confidentiality, which is minimal.

Explain why the waiver will not adversely affect the rights and welfare of the participants.*

As part of the OSU COVID screening program, each participant will have already consented to the following HIPAA AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION statement: “I voluntarily authorize OSUWMC to use and/or disclose my COVID-19 test results to The Ohio State University as part of the ongoing surveillance testing related to COVID-19 community spread. I understand that my COVID-19 test results are considered Protected Health Information (PHI) and no payment will be exchanged for disclosure of my test results. I further understand that I have the right to revoke this authorization, in writing, by sending written notification to: Office of Compliance and Integrity-Privacy, 650 Ackerman Road, Columbus, Ohio 43202. I understand that PHI used or disclosed pursuant to this authorization may be redisclosed by the recipient and its confidentiality may no longer be protected by federal or state law. I consent to the use of electronic signature and understand that my documenting consent below, I have affirmatively executed this authorization.” Additional consent beyond that which subjects have already agreed (i.e. the above HIPAA AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION statement) is not being sought for this study and we are requesting a waiver of consent for the following reasons: (1) our study will use leftover human specimens that are not individually identifiable; (2) the use of these samples poses no additional risk to the original donor than that to which they are already aware (i.e. the potential loss of privacy). The intent of our study is also related to surveillance of COVID19 community spread, to which donors have already consented per the statement above.

Explain why the research could not 'practicably' be carried out without the requested waiver.*

The AMSL processes ~7000 saliva samples per day for COVID PCR testing. It is not practical to contact this number of individuals per day to request their permission to store their otherwise-discarded, excess saliva samples. Furthermore and related to the nature of our project, which is surveillance, only testing the saliva samples of people who consented would skew the data and thus introduce errors in our data interpretation.

Explain why (for research involving identifiable private information/biospecimens) the research could not 'practicably' be carried out without using such information or

biospecimens in an identifiable format.*

Biospecimens will not have identifiable information on them; rather, they will be coded such that no study team members will be able to access PHI.

Will the participants be provided with additional pertinent information after participation (e.g., debriefing)?*

□ Yes ■ No

Explain why or why not.*

No actionable data will be obtained from this study (i.e. the participants will have already been notified of their SARS-CoV-2 status prior to our studying their saliva samples), so no pertinent information will come directly from this project.

Privacy of Participants

Describe the provisions to protect the privacy interests of the participants.*

Our study will protect the privacy and security of participant data according to OSU policy and applicable law, including HIPAA and Ohio State law. Data for this project will be obtained only on participants who have signed the HIPAA AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION statement detailed above. All reports and publications generated by our study will not reveal identifiable participant data. The COVE project will limit access to participant data by "roles" in compliance with minimum necessary standards. An honest broker (Co-I Seth Faith) will limit access to the codes that link participant PHI to the sources of the specimens through physical or cyber procedures; by using this honest broker approach, the risk for improper release of PHI is reduced. Appropriate measures will be taken to implement administrative, technical, and physical safeguards to protect participant data. Individuals associated with this protocol are trained in the protection of participant privacy; such training will be modified as necessary to address privacy and security issues arising from new systems and processes created by the AMSL and COVE study.

Does the research require access to personally identifiable, private information?*

■ Yes □ No

Describe the personally identifiable private information involved in the research. List the information source(s) (e.g., educational records, medical records, etc.).*

Medical record number (MRN). The medical records needed for this study include the saliva donor's history of COVID and their COVID vaccination status.

Confidentiality of Data

Explain how information is handled, including storage, security measures (as necessary), and who will have access to the information. Include both electronic and hard copy records.*

The COVE project will limit access to participant data by "roles" in compliance with minimum necessary standards. An honest broker (Co-I Seth Faith) will limit access to the codes that link participant PHI to the sources of the specimens through physical or cyber procedures; by using this honest broker approach, the risk for improper release of PHI is reduced. Appropriate measures will be taken to implement administrative, technical, and physical safeguards to protect participant data. Individuals associated with this protocol are trained in the protection of participant privacy; such training will be modified as necessary to address privacy and security issues arising from new systems and processes created by the AMSL and COVE study.

Explain if any personal or sensitive information that could be potentially damaging to participants (e.g., relating to illegal behaviors, alcohol or drug use, sexual attitudes, mental health, etc.) will be collected.*

■ Not Applicable

Explain any circumstances (ethical or legal) where it would be necessary to break confidentiality.*

■ Not Applicable

Indicate what will happen to identifiable data at the end of the study*

□ Identifiable data will not be collected

□ Identifiers will be permanently removed from the data and destroyed (resulting in de-identified data)
■ Identifiable/coded(linked) data will be retained and stored confidentially (as appropriate)
□ Identifiable data will be retained and may be made public with participant consent (e.g., ethnographic research)

Certificate of Confidentiality

If your study is not NIH-funded, will you be requesting a Certificate of Confidentiality from the NIH?

□ Yes ■ No

HIPAA Research Authorization

PHI is health information that is individually identifiable and created or held by a covered entity. Health information is considered individually identifiable when it contains one or more of the 18 HIPAA identifiers or when there is a reasonable basis to believe the information can be used to identify an individual.

For more information, see 45 CFR Parts 160 and 164 or Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule.

Authorization: although similar to informed consent, an authorization focuses on privacy risks and permission to specifically use or disclose PHI.

Partial waiver of HIPAA authorization: permits access to and use of PHI for recruitment purposes, prior to obtaining authorization. Specifically, it allows for the identification and, as appropriate, contact of potential participants to determine their interest in study participation. Note: A partial waiver does not permit retention or other use of the information beyond its original purpose.

Full waiver of HIPAA authorization: waives the requirement to obtain an individual's authorization for the use of PHI for a particular research project (such as a retrospective chart review), or for a specific portion/population of the research (such as a waiver that applies only to review of health records of patients previously treated that are used as controls).

Alteration of HIPAA authorization: allows a change in certain authorization requirements, while still requiring authorization for the use of PHI. Examples include making an exception to the required language in an authorization form or eliminating the requirement to obtain a signed authorization (e.g., authorization provided over the phone).

This information below is un-editable and can only be revised with the submission of an amendment after approval or withdrawal of the continuing review submission.

For more information, please see http://orrp.osu.edu/irb/irbforms/hipaa/.

Is individually identifiable Protected Health Information (PHI) subject to the HIPAA Privacy Rule requirements to be accessed, used, or disclosed in the research study?*

■ Yes □ No

Indicate how authorization requirements will be met (check all that apply).*

□ Written Authorization
□ Partial Waiver (for identification and recruitment purposes only)
■ Full Waiver (authorization will not be obtained)

□ Alteration (written authorization will not be obtained or all required elements will not be included)

Full Waiver of HIPAA Research Authorization

Complete this page to request a full waiver of HIPAA authorization to access, use, or disclose Protected Health Information (PHI) for the proposed research. A Full waiver of HIPAA authorization waives the requirement to obtain an individual's authorization for the use of PHI for a particular research project (such as a retrospective chart review), or for a specific portion/population of the research (such as a waiver that applies only to review of health records of patients previously treated that are used as controls).

List the source(s) of PHI applicable to the waiver (e.g., OSUWMC Information Warehouse, eResults, physician's office records, clinical database, etc.). Be as specific as possible.*

OSUMC IHIS and Ohio State University Reporting and Analytics Environment (RAE). These two PHI sources will be accessible to Co-I Seth Faith (in his role as AMSL Director) and Co-I Mikkel Quam (in his role as member of the Ohio State's Comprehensive Monitoring Team, CMT).

Describe the PHI that will be accessed (viewed) for the research under the waiver (e.g., medical record number, health history, diagnosis, test results, etc.).*

Lab test results/microbiology and medical record number (MRN). The MRN will be restricted to two Co-Is, Seth Faith and Mikkel Quam, and is needed to determine subjects previous COVID infection history and vaccination history. This information is needed to properly interpret presence of antiviral antibody in saliva (was it due to vaccination or prior infection?), or the possibility that the virus we are looking at represents re-infection.

Describe information that will be recorded. Be as specific as possible, including date ranges, when applicable. Spell out all abbreviations.*

Lab test result/microbiology #1: The COVID PCR "Ct value", which a numerical indication of how much virus is in a given saliva sample. The Ct value ranges between 0-40, and is inversely proportional to the concentration of virus in a sample. Lab test result/microbiology #2: The date which a COVID PCR was performed. MRN/COVID infection history #1: Whether the subject was previously diagnosed with COVID MRN/COVID infection history #2: If the subject was previously diagnosed with COVID, the date that the individual was diagnosed. MRN/Vaccination history #1: Whether the subject was previously vaccinated against COVID MRN/Vaccination history #2: If the subject was previously vaccinated

against COVID, the date that the individual was vaccinated. MRN/Vaccination history #3: If the subject was previously vaccinated against COVID, which vaccine was received (e.g. Pfizer, Moderna).

Select all study team members who will access medical information:*

□ Richard Robinson
■ Seth Faith
■ Mikkel Quam
□ Daniel Jones
□ Abigail Norris Turner

Provide a copy of the data collection form(s) used (e.g., Excel spreadsheet, etc.) to record the information above.*

Uploaded Files

COVE Data Collection Form.xlsx

Uploaded by Richard Robinson on 02/18/2021

Explain why access to and/or use of the PHI is essential to conduct the research.*

To address our research objectives, we need to know if a given saliva sample is positive for COVID19, when the test was performed, whether the donating individual has a prior history of COVID19 and when this was diagnosed, as well as their COVID19 vaccination history (i.e. date of vaccination and which vaccine). To obtain this information, it is necessary to access a sample's accompanying MRN. Only Co-I Seth Faith and Co-I Mikkel Quam will have access to this PHI.

Explain how the PHI described above represents the minimum necessary information to accomplish the objectives of the research.*

Our research objectives are to determine if an association exists between a VOC and (1) its concentration in saliva (a measure of virus infectivity), as well as (2) its persistence in saliva despite the presence of anti-viral antibodies (a measure of antibody resistance). To address these objectives, at a minimum we need the PCR lab results of given sample (the "Ct value", which is inversely proportional to the concentration of virus in a saliva sample), and the date that the sample was provided (this will tell us whether the sample was collected before the rollout of COVID vaccines). We also need to know each subjects' previous COVID infection history and vaccination history, as this information is needed to properly

interpret presence of antiviral antibody in saliva (was it due to vaccination or prior infection?), or the possibility that the virus we are looking at represents re-infection.

Explain how the access, use, or disclosure of PHI presents no more than a minimal risk to the privacy of the individual.*

The risks of our storing and using coded saliva samples does not exceed the risk of COVID testing that was already performed on the same samples, to determine their infectivity as part of the OSU COVID surveillance program. The proposed samples for testing are remnant samples that would otherwise be disposed of after PCR testing is completed. The risk of a confidentiality breach will be minimal. Residual saliva samples are stored in containers labeled with a code that can only be linked to patient information through a restricted access database (see below). Furthermore, the potential gains in the understanding of prevalence of VOCs in the OSU Community, as well as their association with virus-specific antibody responses, will aid in the real-time public health responses.

Describe your plan to protect identifiers and associated PHI (or links to identifiable data) from improper use or disclosure, including where PHI will be stored (include both the building/room number and/or specific server information), what security measures will be applied, and who will have access to the information. Describe the safeguards used for electronic records, hard copy records, or both, as applicable.*

Saliva specimens arrive to AMSL with identifiers provided through MyChart (e.g., MRN, MPI, DOB, Name). These identifiers and the associated COVID PCR assay results are collected and stored in OSUMC IHIS and on the OSUMC secured servers (L:drive) in order to maintain security and confidentiality. For physical specimens and electronic records, Identifiers will be removed and replaced with a code prior to use for this study. Samples will be coded in a manner such that nobody other than Co-I Seth Faith (our honest broker) can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems. The key to this coding system will be kept by Co-I Seth Faith. Access to data associated with each sample will be limited to the research study team and kept on OSU secured servers. Any paper copies will be kept in the locked research offices of research study team members.

Will identifiers (or links to identifiable data) be destroyed?*

□ Yes
■ No
□ N/A - Will not record identifiers or create links or codes to connect data

Provide the legal, health, or research justification for retaining the identifiers. Legal justification should include a brief description/citation of the legal requirement.*

We have two justifications for requesting use of coded samples, as opposed to de-identified samples: Justification #1 (a research justification): After obtaining viral sequence results for a given sample, we occasionally may need to ask Co-I Seth Faith (our honest broker) to re-review a sample's associated lab results in the event of any unexpected discrepancies. The following scenarios illustrate when such a request of Co-I Faith would be needed: (1) Our sequencing methodology does not detect virus in saliva samples that were previously identified as COVID+. (2) We plan to sequence all COVID+ saliva samples; however, a potential limitation of our sequencing platform (i.e. the Illumina platform) is that those samples with a very low virus concentration will not have a sufficient amount of starting material for sequencing. If this is the case--and there are no published studies to tell us otherwise--we may ask Co-I Faith to return to a given sample's associated lab results in order to troubleshoot why our sequencing assay is not working, and to guide future assay conditions. This is not a trivial concern for us, as an important question we hope to address is whether a given SARS-CoV-2 variant of concern (VOC) associates with higher virus concentration in the saliva specimen. Justification #2 (a health and legal justification): although the AMSL is not currently required by federal or state law to report VOC to the CDC or Ohio Dept of Health (ODH), respectively, this may change in the near future as public understanding of VOC concerns grow (see https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance.html). By using coded samples, as opposed to deidentified samples, the AMSL can more nimbly respond to changes in federal or state VOC reporting policies, as the use of codes would enable contact/communication with the original saliva donor should this be required in the future by the CDC or ODH.

Explain why a waiver (instead of written authorization) is needed to conduct the research (e.g., no longer in regular contact with individuals, scientific validity, etc.).*

We are requesting a waiver for three reasons: (Reason 1) Our study will use leftover/remnant human saliva specimens that are not individually identifiable. (Reason 2) Our use of these samples poses no additional risk to the original donor than that to which they are already aware (i.e. the potential loss of privacy). (Reason 3) A critical component of the OSU COVID surveillance program is student provision of saliva for COVID testing, which is performed by the AMSL. Students can opt out of COVID testing (albeit under very specific circumstances); however, once a student has provided saliva sample to the AMSL and received test results, they cannot withdraw their saliva submission, and the AMSL is no longer in regular contact with the individuals.

Reasonably Anticipated Benefits

List the potential benefits that participants may expect as a result of this research study. State if there are no direct benefits to individual participants.*

There are no direct benefits to individual participants.

List the potential benefits that society and/or others may expect as a result of this research study.*

This study will benefit society insomuch that it will identify viral sequence variants and immunological factors that associate with COVID transmission.

Risks, Harms & Discomforts

Describe all reasonably expected risks, harms, and/or discomforts that may apply to the research. Discuss severity and likelihood of occurrence. As applicable, include potential risks to an embryo or fetus if a woman is or may become pregnant.*

The specimens that we will be storing are excess saliva samples that were already provided to the AMSL. There is a small risk of loss of confidentiality, as participant identifiers are present on the saliva samples when they are first received by the AMSL; however and as detailed above, these identifiers are removed and replaced with a code that no one on the study team other than Co-I Faith will be able to link a code to an individual.

Describe how risks, harms, and/or discomforts will be minimized.*

To limit risk of loss of confidentiality, any and all identifying information on each saliva sample will be removed and replaced with a code.

Assessment of Risks & Benefits

Discuss how risks to participants are reasonable when compared to the anticipated benefits to participants (if any) and the importance of the knowledge that may reasonably be

expected to result.*

We believe the risks to participants are reasonable when compared to the importance of the knowledge that may reasonably be expected to result from our establishing this biorepository. Currently, excess saliva samples from participants in the OSU COVID testing program are being discarded. These samples represent an enormous resource that could be used in studies to discover and understand virus sequences and antibody patterns that affect SARS-CoV-2 transmission. Such a virus sequence was recently discovered at OSU by Co-I Dan Jones (https://www.dispatch.com/story/news/2021/01/13/ohio-state-discovers-new-strain-covid-19-columbus/6652807002/) and our study would enable tracking the incidence of such variants on campus over time and their relationship to vaccine rollouts.

Monitoring

Does the research involve greater than minimal risk (i.e., are the harms or discomforts described for the study beyond what is ordinarily encountered in daily life or during the performance of routine physical or psychological tests)?*

□ Yes ■ No

Participant Costs/Reimbursements

Are there any additional costs that may result from study participation (e.g., parking, study drugs, diagnostic tests, etc.)?*

□ Yes ■ No

Uploaded Files Review

To access or upload a file, click on a page below.

Domestic Site Documentation

No documents have been added for review.

International Site Documentation

No documents have been added for review.

Grant Applications

No documents have been added for review.

Institutional Approval Letters

IBC Approval 2020R00000046.pdf	01/13/2021

Research Protocol

Clean Version 3 COVE IRB protocol.docx	02/15/2021
Track Changes Version 3 COVE IRB protocol.docx	02/15/2021

Data collection forms and/or other instruments

COVE Data Collection Form.xlsx	02/18/2021

Subject Information

No documents have been added for review.

Surveys and/or questionnaires

No documents have been added for review.

Recruitment materials (e.g., ads, fliers, website postings, and letters)

No documents have been added for review.

Other Files

REDCAP COVE APPROVAL.pdf	02/18/2021

Other Files/Comments

This page should be used to provide ORRP or the IRB with additional information related to the current submission.

The general comments text area can be used to provide clarification to ORRP staff or the IRB members.

The general upload box below should be used to upload any additional documents necessary for this submission that were not already captured previously in the form. Examples of documents which may be uploaded include the detailed cover letter response for modifications or deferrals, IRB approvals for external sites at the time of continuing review, or a memo to IRB reviewers from the investigator.

Uploaded Files

REDCAP COVE APPROVAL.pdf

Uploaded by Richard Robinson on 02/18/2021

Additional comments for this submission.

02.24.21 Comments Thank you for the pre-review of our study, which indicated the following concern (our response is detailed below). CONCERN #1. Please note that exemption requests can only be applied to records already in existence as of the data of protocol submission. As the study is requesting specimens not yet in existence please revise to request IRB review. RESPONSE. We have revised the study to request IRB review. 02.18.21 Comments Thank you for the pre-review of our study. In response to the pre-review, we have made several significant changes to our study which are described in our responses to the pre-review concerns below: CONCERN #1. Please upload documentation confirming that this project has been submitted to and approved through the Ohio State COVID-19 Impact and Planning Assessment: https://redcap.bmi.osumc.edu/redcap/surveys/?s=KMPPTEHPDW. RESPONSE. We have uploaded this documentation as requested. CONCERN #2. Per Ohio State policy, informed consent is required for collection and storage of materials for future use. Please incorporate a plan to obtain verbal or written consent from participants. RESPONSE. The most significant change to our protocol is that we will no longer be banking materials for future use, and modified the study so that it fulfills the requirements for exemption Category #4. For this reason, waiver of consent is requested and a justification is provided. CONCERN #3. The funding proposal uploaded with the submission appears to be for a specific research project that will be conducted using samples acquired by the repository. Please confirm whether any external funds will be used to support operations of the repository itself. If not, revise the Funding and Financial Conflicts page of the Buck-IRB application to check “No” and remove the funding proposal. RESPONSE. The funding proposal has been removed, and there are currently no external funding requests pending. Financial support for this project instead is being provided by OSU President Kristina Johnson, directly to the OSU Infectious Disease Institute and Applied Microbiology Services Lab. CONCERN #4. Clarify whether samples stored in the repository will be coded (identifiers replaced with a code that can be traced back to the individual) or de-identified (identifiers removed and no code exists that would link back to identifiable information). Throughout the submission, both terms are used. Revise for clarification. RESPONSE. We have clarified throughout the document that the samples used in this study will be coded.

Saliva sample code [1]	Sample assay date [2]	COVID PCR Result (Ct value) [3]	Variant of Concern (VOC) present [4]	SARS-CoV-2 N-specific antibody level [5]	SARS-CoV-2 Spike-specific antibody level [6]	History/Date of COVID infection [7]	History/Date of COVID vaccination [7]	COVID vaccine type (Pfizer or Moderna) [8]
0001								
0002								
…								

[1] The sample code roughly correlates with its order of receipt by the AMSL. For example, sample 0001 arrived to the lab before sample 0100

[2] This is the date on which the sample was first tested in AMSL (a CLIA certified lab) using the SalivaDirect assay

[3] The "Ct" value is a PCR machine readout which is inversely proportional to the virus concentration in the saliva

[4] The presence of a VOC will be determined via the Illumina Sequencing Platform, which is run in house at the AMSL (i.e. samples will not be shipped off site for sequencing)

[5] To be determined by ELISA or analagous method, N-specific antibody responses are elicited by a SARS-CoV-2 infection

[6] To be determined by ELISA or analagous method, Spike-specific antibody responses are elicited by either a SARS-CoV-2 infection or vaccination with either the Pfizer or Moderna COVID vaccine

[7] This information is accessible via the MRN, and is needed to interpret the origin of any N- or SPIKE-specific antibodies present in the saliva

[8] As new vaccines other than Pfizer and Moderna begin to roll out, these new vaccines will be added to this column.

Version 3

Research protocol title:

SARS-CoV-2 study of viral evolution (COVE)

Principal investigator:

Richard T. Robinson, PhD

Co-Investigators:

Michael Oglesbee, DVM, PhD, DACVP

Leona Ayers, MD

Seth Faith, PhD

Mikkel Quam, PhD

Dan Jones, MD PhD

Sponsor:

The Ohio State University (OSU)

Version: 3

Date: 02.12.2021

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Section **Page Number**

I OBJECTIVES:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological agent of Coronavirus Disease 2019 (COVID19), a recently emerged infectious disease with no cure. Since its initial evolution in bats and emergence in 2019, SARS-CoV-2 has continued to evolve in humans and an increasing number of variants have been discovered worldwide, including the United States. These variants are concerning, as they may be more infectious than previous isolates, elicit different pathologies and immune responses, or—in the worst case scenario—evade vaccine-elicited antibody responses. Despite these worldwide concerns, the United States lags behind other countries (i.e. 43rd worldwide) in sequencing efforts to identify and track SARS-CoV-2 variants, placing Americans at a serious and potentially grave disadvantage. **This study will use residual, leftover saliva specimens collected as part of the OSU COVID surveillance program (https://safeandhealthy.osu.edu/testing) to surveille the diversity of SARS-CoV-2 variants in the OSU Community, and to determine if an association exists these variants and levels of SARS-CoV-2 specific antibody. These saliva specimens would otherwise be discarded in the absence of our study.** These samples will not be used to establish a bank or distribute to other researchers for unspecified research; rather, they will be used to identify sequence variants and antibody patterns that are important for public health monitoring. We refer to this project as the "SARS-CoV-2 study of viral evolution", or "COVE."

II BACKGROUND AND RATIONALE:

SARS-CoV-2 is an infectious virus which spreads via liquid droplets and/or aerosols. Infection with SARS-CoV-2 can be asymptomatic or lead to a variable disease course affecting multiple organ systems (respiratory, cardiovascular, nervous and gastrointestinal) – referred to collectively as coronavirus disease 2019 (COVID19); for this reason, the symptoms of COVID19 are variable and include fever, cough, dyspnea, malaise, nausea, ageusia/anosmia, delirium and death. A number of antiviral and host-directed therapies have been or are being explored as COVID19 treatments, including nucleoside analogs (e.g. remdesivir), interferons, convalescent plasma, monoclonal antibodies, and anti-inflammatories (e.g. dexamethasone). Prophylactic vaccines against the SARS-CoV-2 Spike protein have also recently become available. These treatments and vaccines are causes for optimism during the current COVID19 pandemic; however, even after vaccines become widely available, an improved understanding of the viral sequences and antibody responses which impact viral transmission will continue to be needed in the foreseeable future.

The discovery of factors which influence SARS-CoV-2 transmission are most effectively studied in well-tracked cohorts of individuals at risk of SARS-CoV-2 exposure. Such a cohort exists at OSU, which established a campus-wide surveillance program that uses a saliva-based nucleic acid amplification test to identify SARS-CoV-2 infected OSU students and employees. As part of the OSU COVID testing program, asymptomatic students and employees are asked to provide a small volume of saliva, a portion of which is subsequently tested for the presence of SARS-CoV-2 genetic material via a polymerase chain reaction (PCR) assay; excess saliva not needed for PCR testing is otherwise discarded. The OSU COVID testing program is administered on site by the CLIA-certified, OSU Applied Microbiology Services Laboratory (AMSL) that is part of the Infectious Diseases Institute. Individual PCR results are provided to the student or employee via MyChart; cumulative, deidentified PCR results are published on the OSU COVID dashboard (https://safeandhealthy.osu.edu/dashboard).

We are establishing COVE to study excess saliva not needed for PCR testing, for the specific purpose of identifying local variants of concern (VOC) and antibody responses that associate with SARS-CoV-2 transmission within the OSU Community.

III. STUDY OVERVIEW

A. Design: Our study will use residual biological specimens (i.e. excess saliva) and associated data (i.e. COVID PCR results) from individuals participating in the OSU COVID surveillance program (https://safeandhealthy.osu.edu/testing). Samples from OSU COVID surveillance participants are collected daily, and analyzed for the presence of virus in a CLIA-certified laboratory (AMSL). Currently, these samples are discarded after a 7-day holding period. We propose to save these otherwise discarded samples, for viral gene sequencing (to identify whether the virus present is a VOC) and antibody measurements (enabling us to determine if a VOC survives despite the presence of virus-specific antibody). Samples will be stored for a finite period (5 years), and will be coded prior to storage and use. An AMSL staff member (Co-I Seth Faith) will serve as an honest broker to ensure samples are coded prior to storage and use; no study team members will have access to the codex linking a code to PHI. The creation of a COVE will enable us to identify relationships of public health importance, such as the relationship between COVID PCR positivity, VOCs and virus-specific antibody.

B. Study Sites: Our study subjects are OSU students and employees who, as part of the campus COVID screening testing program (https://safeandhealthy.osu.edu/testing), provide approximately three milliliters (~3 mL) of saliva to the OSU Applied Microbiology Services Laboratory (AMSL) for CLIA-certified PCR testing. Only fifty microliters (50 μL, or ~1/60th of the original saliva volume) is required for the AMSL's testing purposes; we propose to store the remaining, excess volume which would otherwise be discarded. The saliva collection site, PCR testing site (AMSL), and storage site are each located on the OSU Columbus campus and are listed below:

- **Saliva collection site: Jesse Owens North (JON) Recreation Center** (2151 Neil Avenue, Columbus, OH 43210). JON is a site where OSU students and employees provide a ~3 mL saliva sample into a sterile conical centrifuge tube. At regular intervals, these saliva samples are transported to the AMSL.
- **CLIA-certified PCR testing site: Applied Microbiology Services Laboratory (AMSL)** (Rooms 809/815/822/828/832, Biological Sciences Building, 484 W 12th Avenue, Columbus, OH 43210). The AMSL is operated by the Department of Microbiology, College of Arts and Sciences, and the Infectious Diseases Institute, Office of Research. The AMSL provides CLIA-certified COVID19 testing services using saliva samples, and is ramping up to test 9,000 saliva samples per day by mid-January 2021 (personal communication, Dr. Seth Faith, AMSL Director); since mid-August 2020, the percent positive rate has fluctuated between 0.76% to 5.90% (**FIG 1**). Currently, the excess volume of saliva that is not needed

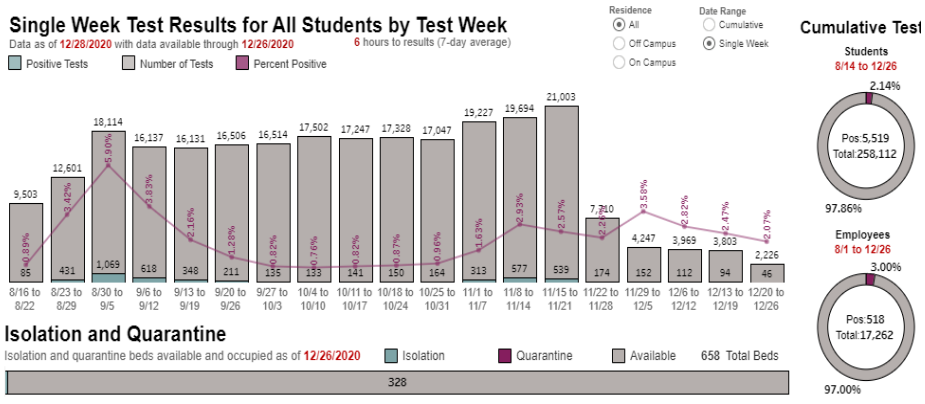

FIG 1. COVID positivity rates among OSU students & employees since the OSU COVID testing program began. Shown are weekly data from the OSU COVID19 dashboard, from 08/16/20-12/26/20. Currently, after saliva samples are tested for virus and results are shared, the samples themselves are discarded. We propose to use these excess saliva samples for viral sequencing and antibody level measurements.

for PCR testing (~2.950 mL) is discarded; we propose to retain this excess volume for research purposes in the storage site below.

- **Saliva storage site: Applied Microbiology Services Laboratory (AMSL).** In addition to being the site of PCR testing, the AMSL will also serve as the storage site of excess saliva volumes that are no longer needed for PCR testing and would otherwise be discarded. Samples will be stored at -80°C.

IV. PARTICIPANTS

A. Study population

Our study subjects will comprise OSU undergraduate students, graduate students, professional students and employees who provided a saliva sample to the AMSL for PCR testing, as part of the OSU COVID screening program.

B. Subject Recruitment

Subjects will not be recruited for this study. Rather, this study will use leftover human specimens that are not individually identifiable. These specimens comprise excess saliva that was previously collected for COVID surveillance at OSU. Prior to their storage and use for research purposes, all identifying information will be removed from each specimen, and replaced with a code. AMSL Director and Co-I Seth Faith will serve as an honest broker to ensure samples are coded prior to storage and use.

C. Informed Consent

At the time someone provides saliva to the AMSL for the OSU COVID surveillance program, they provide electronic consent to the following *HIPAA AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION* statement:

> "I voluntarily authorize OSUWMC to use and/or disclose my COVID-19 test results to The Ohio State University as part of the ongoing surveillance testing related to COVID-19 community spread. I understand that my COVID-19 test results are considered Protected Health Information (PHI) and no payment will be exchanged for disclosure of my test results. I further understand that I have the right to revoke this authorization, in writing, by sending written notification to: Office of Compliance and Integrity-Privacy, 650 Ackerman Road, Columbus, Ohio 43202. I understand that PHI used or disclosed pursuant to this authorization may be redisclosed by the recipient and its confidentiality may no longer be protected by federal or state law. I consent to the use of electronic signature and understand that my documenting consent below, I have affirmatively executed this authorization."

We are not seeking additional consent beyond that which subjects have already agreed (i.e. the above *HIPAA AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION* statement) and are requesting a waiver of consent for the following reasons: (1) our study will use leftover human specimens that are not individually identifiable; (2) the use of these samples poses no additional risk to the original donor than that to which they are already aware (i.e. the potential loss of privacy). The intent of our study is also related to surveillance of COVID19 community spread, to which donors have already consented per the statement above.

D. Benefit to participants.

The information gained will not directly benefit the participants, but will lead to a better understanding of COVID19 evolution, spread and immunity within the OSU Community. We hope this information will aid in lessening the morbidity and mortality related to SARS-CoV-2 infection in the future. Furthermore, our study readouts (virus sequences and antibody levels) are also not actionable at the individual level, insomuch that the information we gather from a given saliva sample will not pertain to patient management (e.g. we are not sequencing human genes linked to cancer risk).

E. Risk to participant.

The risks to the subjects are reasonable, as the saliva storage and use does not exceed the risk of standard testing that was already performed on these sample to determine infectivity. The risk of confidentiality breach is minor as secure processes will be in place to ensure the highest level of security. Overall, the potential gains in the understanding of prevalence of VOCs in the OSU Community, as well their association with virus-specific antibody responses, will aid in the real-time responses of Public Health.

F. Compensation for participation.

Participants will not be compensated for participating.

G. Withdrawal.

Given the importance of COVID surveillance, OSU students can only opt out of AMSL testing under very specific circumstances (see “Can I opt-out of testing?” at https://safeandhealthy.osu.edu/information/faculty-and-staff/testing/student-testing-program). Once a saliva sample has been provided to AMSL, however, students are unable to withdraw their saliva submission. For this reason, subjects technically cannot choose to have their residual saliva withheld from our study.

H. Participant Confidentiality

Our study will protect the privacy and security of participant data according to OSU policy and applicable law, including HIPAA and Ohio State law. Data for this project will be obtained only on participants who have signed the *HIPAA AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION* statement detailed above. All reports and publications generated by our study will not reveal identifiable participant data.

The COVE project will limit access to participant data by "roles" in compliance with minimum necessary standards. An honest broker (Co-I Seth Faith) will limit access to the codes that link participant PHI to the sources of the specimens through physical or cyber procedures; by using this honest broker approach, the risk for improper release of PHI is reduced. Appropriate measures will be taken to implement administrative, technical, and physical safeguards to protect participant data. Individuals associated with this protocol are trained in the protection of participant privacy; such training will be modified as necessary to address privacy and security issues arising from new systems and processes created by the AMSL and COVE study.

V. DATA/SPECIMEN COLLECTION AND STORAGE PROCEDURES

A. Data Collection: Our data collection process is an extension of current processes that are already in place at AMSL. The current process is as follows: saliva samples are collected at the JON Recreation Center by trained staff and transported to the AMSL, where COVID PCR testing is performed and excess saliva volume is discarded. Our protocol will extend this process, such that at the time when excess saliva would otherwise be discarded they would instead be stored and used for viral sequencing and antibody level measurements. Prior to storage and use, samples will be stripped of any identifiers and coded in a manner such that only Co-I Seth Faith (our honest broker) can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems.

B. Acquiring, handling and testing of samples: As part of the OSU COVID screening program (https://safeandhealthy.osu.edu/testing), participants provide a saliva sample at the JON Recreation Center. Samples are collected by trained study staff and delivered to the OSU AMSL for processing and testing. Study staff have IATA training for the safe handling and transport of biospecimen. Results from the assays (i.e. the presence or absence of SARS-CoV-2 genetic material) are relayed to the subjects via OSU MyChart. Test results are simultaneously reported to the Ohio Department of Health and the university Case Investigation and Contact Tracing Team (CICTT), operating under the auspices of Columbus Public Health. The CICTT contacts test positive individuals by telephone and e-mail within 24 hours of the test. For our study, excess residual saliva samples will be used for viral sequencing and antibody level measurements only after COVID test results are reported to the individual and ODH. Viral sequencing will be performed using the Illumina Sequencing Platform, which is owned and operated within the AMSL. Antibody level measurements will likewise be performed in the AMSL using commercially available kits and reagents.

C. Data Protection: Saliva samples arrive to AMSL with personal identifiers. These identifiers and the associated COVID PCR assay results are collected and stored by AMSL in RedCap on OSU secured servers in order to maintain security and confidentiality. Identifiers will be removed and replaced with a code prior to storage and use for this study. Samples will be coded in a manner such that anyone other than Co-I Seth Faith (our honest broker) cannot link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems. The key to this coding system will be kept by Co-I Seth Faith. Access to data associated with each sample will be limited to the research study team and kept on OSU secured servers. Any paper copies will be kept in the locked research offices of research study team members.

D. Data Analysis: The results of our SARS-CoV-2 sequencing and antibody level measurements will be analyzed in a manner that is consistent with current standards of peer-reviewed, biomedical sciences literature. The PI all study team members will take all possible measures to ensure that the study and results obtained are done using standardized protocols, using appropriate controls and eliminating any biased approach to the study. All efforts would be taken to set up experiments and present data in such a way that informs OSU policies on risk reduction and optimal vaccination surveillance.

E. Power and sample size: We cannot predict the total number of saliva samples that will be stored and analyzed for this study, as the COVID pandemic is ongoing and there are no projections of when it will end, even after the majority of OSU students and employees are vaccinated. We can, however, estimate the number of samples we anticipate collecting within

the first month of our study at current positivity rates. The AMSL is currently processing 7,000 saliva samples per working day. Assuming an average 2% PCR positivity rate, which has been the case for the past month (**FIG 1**), this means ~140 samples per working day will be COVID PCR positive and subsequently stored. Assuming an average of 21 working days per month, we estimate storing ~3000 saliva samples per month.

VI. RELEASE OF SPECIMENS OR DATA

Specimens will be used for to identify and surveille VOCs in the OSU Community, and relate the presence of these VOC to levels of SARS-CoV-2 antibody levels in the same specimens. Specimens and data are not being banked for future unspecified research, nor will they be released to other researchers without the explicit permission of the IRB.

VII. STUDY OVERSIGHT

Oversight for our study will be provided by Co-I Dr. Michael Oglesbee and Co-I Dr. Leona Ayers. Co-I Oglesbee is the Director of the OSU Infectious Disease Institute (IDI) and a member of the OSU Comprehensive Monitoring Team (CMT) which makes policy recommendations to OSU President Kristina Johnson. Co-I Ayers is an OSU Academy Professor, Medical Director of the AMSL, and former member of the OSU Cancer Institutional Review Board (IRB). The oversight of Co-I Oglesbee and Co-Ayers will help ensure that the study activities are aligned with questions of importance to the CMT and OSU Leadership, and well as the maintenance of AMSL CLIA-certification.

VIII. REFERENCES

1. Centers for Disease Control and Prevention: HIV/AIDS Surveillance Report 2002;14.

2. OSHA Rules and Regulations, "Occupational Exposure to Bloodborne Pathogens"; Final Rule: 29 CFR Part 1910-1030, Federal Register, vol. 56, No. 235, December, 1991.

3. Collaborative IRB Training Initiative (CITI) Basic Course in Biomedical Research. www.citiprogram.org.

4. National Biospecimen Network Blueprint. Costella Group Inc. Durham, NC, Bethesda, MD. Science Management and Research Administration. www.ndoc.org.

5. Eiseman E, Hager SB. Handbook of Human Tissue Sources: A National Resource of Human Tissue Samples. Santa Monica, CA: RAND. 1999.

6. US Department of Transportation, Code of Federal Regulations, 49 CFR Part 172, Subpart H. www.shipsafeshipsmart.com.

7. NCI Best Practices for Biospecimen Resources, June 2007. (http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf)

8. Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under the Health Information Technology for Economic and Clinical Health Act and the Genetic

Information Nondiscrimination Act; Department of Health and Human Services, 45 CFR Parts 160 and 164: Part II, Office of the Secretary, Federal Register, Vol. 78 Friday, No. 17 January 25, 2013. http://www.gpo.gov/fdsys/pkg/FR-2013-01-25/pdf/2013-01073.pdf

Institutional Biosafety Committee

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2020R00000046

Immunological mechanisms of COVID-19 associated cytokine storm
Richard Robinson
Microbial Infection and Immunity

May 4, 2020

Dear Dr. Robinson :

The Institutional Biosafety Committee (IBC) has **APPROVED** the above referenced IBC Protocol. The IBC specified that your experiments be conducted under BSL-3 and ABSL-3 containment.

Date of Approval: 05/04/2020
Date of Expiration: 05/04/2025

During this five year approval period, annual reviews are required. The protocol is due for Annual Reviews no later than the first through fourth anniversary of the approval date.

The eProtocol online system will send the Principal Investigator annual reminders. However, the Principal Investigator is responsible for submitting an Annual Review in advance of the annual review due dates to ensure continuing IBC approval. It is very important that these deadlines are not missed. Failure to submit an Annual Review on time may potentially result in the termination of the protocol.

To continue this research beyond the five year approval period, a new protocol submission will be required. To avoid a lapse in IBC approval, it is essential that the completed renewal protocol be submitted and approved by the IBC prior to its expiration date.

If a renewal protocol has not been processed and approved by the IBC prior to 05/04/2025, IBC approval for the work under the above referenced protocol will expire. Should IBC approval expire, all activities involving biohazardous materials must cease immediately. Any activities conducted under the protocol after expiration will be in direct violation of federal regulations and institutional and IBC policies.

It is the responsibility of the Principal Investigator to notify the IBC of any proposed changes regarding the work described within this protocol.

Please forward a copy of this document to your sponsored program officer. The sponsored program officer will certify this review for external sponsors.

Sincerely,

Marshall V. Williams, JR. Ph.D.

Marshall V. Williams, Ph.D.
Institutional Biosafety Chair
Institutional Biosafety Committee

Subject: Application Approved
Date: Tuesday, February 16, 2021 at 3:33:53 PM Eastern Standard Time
From: amy.drake@osumc.edu
To: Robinson, Richard

Hi Richard Robinson,

You are approved to proceed with the necessary regulatory/IRB submissions that is required for SARS-CoV-2 study of viral evolution (COVE). This approval will not provide financial support for your project but we do have vouchers for COVID-19 research that are available through the CCTS. For additional information please go to CCTS COVID-19 Vouchers.

I have attached all of your documents that you have submitted with your application and a chart of all the data that was submitted.

COVID-19 Basic and Translational Research

Name	Richard Robinson
Email	richard.robinson@osumc.edu
College	College of Medicine
Department	Microbial Infection and Immunity
Study Title	SARS-CoV-2 study of viral evolution (COVE)
Class	/Other
Does the study propose to collect Biospecimens?	No
What type of specimens?	
Leftover / Anonymized Samples?	
Where will this research be conducted?	Other
Type of Study	Observational
Patient Identification	Coded Limited Data

Describe potential negative impacts on research participants.	None. Our proposed research meets the criteria of IRB Exemption Category 4. Namely, our study represents secondary research use of otherwise discarded biospecimens (excess student saliva samples no longer needed by the OSU Applied Microbiology Services Lab for COVID19 testing). Information about these biospecimens will be recorded by the investigator in such a way that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, and the investigator will not contact the subjects or try to re-identify subjects.
Describe how this protocol may impact the safety and workload of the clinical care team?/td>	No impact, as clinical care teams are not involved in this study.
Describe efforts ensure the safety of the research team from undue risk of exposure.	Members of the research team will not be obtaining consent or otherwise interacting for potentially infectious individuals. Rather, they will instead be handling potentially infectious biospecimens (saliva). Saliva samples will be handling inside a Biosafety Cabinet using BSL2 practices, per Applied Microbiology Services Lab (AMSL) protocols. The AMSL is a CLIA-certified lab located on the 8th floor of the Biological Sciences Building.
Will member of the research team be directly handling COVID-19 bio-specimens?	No
What risks (non-resource oriented) may the study pose to our clinical mission?	None. This is not a clinical study, nor does it require additional effort or exposure burden on research staff members (no clinical workforce is involved).
What impact with this study have on your existing research?	This study will enhance my existing research program on SARS-CoV-2. Furthermore, this study has public health importance as it will identify SARS-CoV-2 variants of concern (VOC) in the OSU Community and their relationship to saliva infectivity and virus-specific antibody responses.
What additional effort or exposure burden does this impose on clinicians?	None, as no clinicians are involved in this study.

What additional effort or exposure burden does this impose on research workforce?	None, as the activities of this project fall under the responsibilities and roles of the involved researchers. Funds for this work are internal and provided by the OSU Infectious Disease Institute (budget attached).
What impact will the protocol have on the supply of Personal Protective Equipment (PPE)?	None. All PPE is provided by the Applied Microbiology Services Lab (AMSL).
Do you currently have the clinical supplies required to conduct this research?	Yes
What other information should be considered in this COVID Impact and Planning Assessment?	Our study will use residual biological specimens (i.e. excess saliva) and associated data (i.e. COVID PCR results) from individuals participating in the OSU COVID surveillance program (https://safeandhealthy.osu.edu/testing). Samples from OSU COVID surveillance participants are collected daily, and analyzed for the presence of virus in a CLIA-certified laboratory (AMSL). Currently, these samples are discarded after a 7-day holding period. We propose to save these otherwise discarded samples, for viral gene sequencing (to identify whether the virus present is a VOC) and antibody measurements (enabling us to determine if a VOC survives despite the presence of virus-specific antibody). Samples will be stored for a finite period (5 years), and will be coded prior to storage and use. An AMSL staff member (Co-I Seth Faith) will serve as an honest broker to ensure samples are coded prior to storage and use; no study team members will have access to the codex linking a code to PHI. The creation of a COVE will enable us to identify relationships of public health importance, such as the relationship between COVID PCR positivity, VOCs and virus-specific antibody. Funds for this study have been allocated by the OSU President to the Infectious Disease Institute (budget attached). IRB approval of this study is pending.