PRINCIPAL INVESTIGATOR: Emily E. Ricotta, PhD, MSc

STUDY TITLE: Analysis of the immune response to COVID-19 vaccination and outcomes in individuals with and without immune deficiencies and dysregulations

STUDY SITE: NIH Clinical Center (CC)

Cohort: Affected patients and healthy volunteers

Consent Version: August 11, 2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal investigator: Emily E. Ricotta, PhD, MSc, 301-761-7784, emily.ricotta@nih.gov

Study coordinator: Anita Ginigeme, MS, 301-761-7099, anita.ginigeme@nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

This study is about how people with immune deficiencies respond to COVID-19 vaccines.

The immune system defends the body against disease and infection. Immune deficiencies are health conditions that decrease the strength of this response. Vaccines work by stimulating the immune system to create a defense against a specific type of germ, like the SARS-CoV-2 virus that causes COVID-19. People with immune deficiencies have weakened immune systems, so we do not know if they respond as well to vaccines as people without immune deficiencies. In this study, we will compare immune system responses to COVID-19 vaccines in people with and without immune deficiencies to look for differences.

Although we are studying participants who are receiving COVID-19 vaccines, it is important to know that you will not receive any vaccinations as part of this study.

We would like to collect samples from you for this study.

We are asking you to join the study because you either have an immune deficiency or you do not, and you are planning to receive the COVID-19 vaccine as part of your medical care. If you join the study, we will collect 1 blood sample from you before your first COVID-19 vaccination. We will collect another blood sample about 2-4 weeks after each of your COVID-19 vaccination(s), including any booster doses you may receive while you are still in the study, through the 5th dose of COVID-19 vaccine you may receive. You can have the blood samples taken at the NIH or locally at a doctor's office or laboratory. If you are unable to come to the NIH or have your blood drawn locally, you can collect a few drops of blood at home by

fingerstick. We will send you supplies and instructions for collecting the sample and sending it in to us. Each time you provide a blood sample, you will also complete at least 2 online questionnaires about your health, COVID-19 history, and/or any side effects you may have from the vaccinations.

These are the minimum requirements of this study, and will require you to be on the study until about 1 month after your last vaccination at a minimum.

If you have already received a COVID-19 vaccine, you can still join this study. You will start the study at the point that corresponds to where you are in your vaccination schedule. If you join after you have completed a full vaccination schedule but before receiving additional booster vaccinations, you will start from the beginning, including collection of a blood sample before your booster vaccination.

You may also choose to participate in optional procedures.

- You may come to the NIH to give blood samples 1 and 3 days after each COVID-19 vaccination.
- You may choose to give blood samples at the NIH or local facilities or provide fingerstick samples from home 6, 12, and 24 months after your last COVID-19 vaccination, including any booster doses, through the 5th COVID-19 vaccine dose you receive. We would also ask you to complete 1 online questionnaire about your health each time you give a blood sample.
- You may choose to collect saliva samples at home after you received all doses of a COVID-19 vaccine, or after any booster doses through the 5th COVID-19 vaccine dose you receive and we ask that you send them to us every 2 weeks for 6 months while you are in this study. We will provide you supplies and instructions for doing this.
- You may choose to answer additional questionnaires about COVID-19 symptoms or your beliefs and behaviors around COVID-19 vaccination.
- If you decide to participate in the optional procedures you will remain on study for up to 2 years after the booster vaccination, through the 5th COVID-19 vaccine dose you receive.

We will use your samples for clinical and research tests.

We will do clinical and research tests that tell us about your immune system and how it responded to the COVID-19 vaccine. In general, we will give you the results of the clinical tests, but not the research tests. If you provide saliva samples, we will test them for SARS-CoV-2, and give you the results. If you have a SARS-CoV-2 infection, we will ask you to complete an online symptom questionnaire and refer you for care as needed.

Participating in the study has some risks and discomforts.

Drawing blood can cause pain, bruising, fainting, and, rarely, infection where the blood was drawn

The fingerstick may cause brief pain.

Being in this study will not help you, but you will help us.

If you participate, you will help us learn about how people with immune deficiencies respond to COVID-19 vaccines. This information may be useful in designing more effective vaccines to help prevent the spread of SARS-CoV-2 in the future.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being enrolled is a minor then the term "you" refers to "you and/or your child" throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to learn about how people with immune deficiencies respond to COVID-19 vaccines. These vaccines are an important public health tool to help fight the COVID-19 pandemic, by reducing people's risk of developing severe COVID-19 illness and possibly helping prevent the SARS-CoV-2 virus from spreading. However, because these vaccines are new, we do not know if the vaccines are as effective when given to people with immune deficiencies as they are in healthy people. Therefore, we are doing this study to help answer that question.

We are asking you to join this research study because you have an immune deficiency or you are a healthy person without an immune deficiency, and you plan on getting a COVID-19 vaccine. We will compare the information we collect from each of these groups to help us understand if there are differences in the ways people with and people without immune deficiencies respond to COVID-19 vaccines.

WHAT WILL HAPPEN DURING THE STUDY?

If you are interested in taking part in this study, we will first ask you some questions about your current and past health and may review your medical records to make sure you can participate.

Required procedures: If you are able to participate in this study and decide to join, you will provide a blood sample before you receive your COVID-19 vaccination. You will have about 2 tablespoons of blood drawn from a vein in your arm using a needle. Your blood sample can be drawn at the NIH or at a local doctor's office, clinic, or Quest Diagnostics laboratory. If your blood is drawn by a local office, clinic, or Quest, your sample will be labeled with a coded identifier, your date of birth, and gender. It is necessary to have your date of birth on your sample as a safety check. If you are unable to come to the NIH or have your blood drawn locally,

you can collect a few drops of blood that will total less than 1 teaspoon at home by fingerstick. We will review the proper collection procedure with you and provide the necessary materials to collect, package, and ship the samples with all costs covered by the study team. You will also complete 2 online questionnaires about your current and past health and COVID-19 history. It will take about 5 to 10 minutes to complete these.

We will ask you to let us know when you have received your COVID-19 vaccination. Between 2 and 4 weeks after your vaccination, we will ask for another blood sample. Like the first sample, you will have about 2 tablespoons drawn at the NIH or a local doctor's office or Quest laboratory. If you cannot do this, you can take a few drops of blood (less than 1 teaspoon) at home by fingerstick. We will send you the kit, instructions, and mailing supplies for collecting it and sending it in to us. You will also complete 2 online questionnaires about any changes in your health and side effects you may have from the vaccine.

If you receive a second (booster) vaccination, we will ask you to repeat the blood draw or fingerstick and questionnaires about 3 to 4 weeks later. If you get additional booster vaccination(s) while you are still in this study, these procedures will be repeated. We will collect samples through the 5th COVID-19 vaccine dose you receive. If you receive a 6th shot, we will no longer ask for samples from you.

If you have already received a COVID-19 vaccine, you can still join this study. You will start the study at the point that corresponds to where you are in your vaccination schedule. If you join after you have completed a full vaccination schedule but before receiving additional booster vaccinations, you will start from the beginning, including collection of a blood sample before your booster vaccination through the 5th COVID-19 vaccine dose you receive.

Optional NIH visits: In addition to the required procedures above, you have the option of having about 2 tablespoons of blood drawn at the NIH 1 and 3 days after each vaccination you receive. (Some people will only receive 1 vaccination.) These visits are optional, so you can still be in the study if you cannot or do not want to participate in them.

Optional long-term follow-up procedures: You also have the option of giving extra blood samples about 6 months, 12 months, and 24 months after the last COVID-19 vaccination you receive, including additional booster doses through the 5th COVID-19 vaccine dose you receive. If you agree to provide these samples, you will have about 2 tablespoons of blood drawn at the NIH or a local doctor's office or Quest laboratory. If you cannot do this, you can take a few drops (less than 1 teaspoon) of blood at home by fingerstick. We will send you the kit, instructions, and mailing supplies for collecting it and sending it in to us. You will also complete 1 online questionnaire about any changes in your health each time you give a blood sample. It will take about 3 to 5 minutes to complete this.

Optional saliva collection: You also have the option of sending in saliva samples about every 2 weeks for 6 months while you are in this study. This involves spitting into a cup or sample tube and sending it in to us. We will send you supplies and instructions for doing this and mailing the samples back to us. We will test your saliva samples for the SARS-CoV-2 virus. We will share the results of these tests with you. If a test shows that you have a SARS-CoV-2 infection, we will ask you to complete an online questionnaire about your symptoms. We will refer you for care as needed. If you get additional booster vaccinations, you will have the option to participate in the

saliva collections for another 6 months while you remain in the study, through your 5th COVID-19 vaccine dose.

Research and clinical tests: We will also use your blood for research tests of your immune system to see how your body responds to the COVID-19 vaccine. In addition, we will test your blood for SARS-CoV-2 antibodies.

If you have blood drawn at the NIH, we may use some of your samples for clinical laboratory tests that count the different types of cells in your blood and test for your HLA type. HLA type is a marker for the immune system, similar to a blood type. Doctors sometimes use it to match bone marrow or organ transplants. We might study whether your HLA type affects your immune response to the COVID-19 vaccine.

If one of your saliva tests shows that you have a SARS-CoV-2 infection, we will collect samples of the virus from your saliva. We will do genetic tests on the virus and put the results in a public research database so they can be shared with other researchers. This genetic testing will be for the virus only, and it will not give us any genetic information about you. When we put the viral genetic information in the database, we will include general information about you, including your age range (eg, 20-30, 40-50, etc.), sex, and whether you have an immune deficiency. It will not include any information that could be used to identify you.

If you are co-enrolled in another NIH protocol, data that is collected in that study may be shared with and used for research in this study, so that you do not have to repeat these procedures/tests.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for at least 1 month after the last COVID-19 vaccination you receive, including additional booster doses, through the 5th COVID-19 vaccine dose you receive. If you agree to the long-term follow-up procedures, your participation will last for up to 2 years after the last COVID-19 vaccination you receive.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 500 people participate in this study.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

Blood draw: Drawing blood can cause pain, bruising, fainting, and, rarely, infection where the blood was drawn.

Fingerstick: The fingerstick may cause brief pain.

Saliva collection: There are no risks associated with this procedure.

Questionnaire completion: There is a minimal risk of loss of confidentiality of information collected in the questionnaires.

What are the risks related to pregnancy?

There are no risks related to pregnancy.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You will not benefit from being in this study.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because it will help us learn more about how people with immune deficiencies respond to COVID-19 vaccination. What we learn on this study may also be useful in designing more effective vaccines to prevent the spread of SARS-CoV-2.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could look for other studies to join.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

We will share the results of the clinical laboratory tests done with your blood samples. We will also tell you the results of the SARS-CoV-2 tests done on your saliva samples.

The rest of the tests done on this study are for research only, including the SARS-CoV-2 antibody tests. The results of research tests should not be used to make any decisions about your health, and we will not share them with you. Still, it is possible that we might happen to find something important to your health. For example, a study evaluation could show that you might have a health condition that needs treatment. If this happens, the result will need to be confirmed in a clinical laboratory. In this case, we may ask for an additional sample for this testing or can recommend other places you can get tested. We will then share these results with you when they are available. We can counsel you and your healthcare provider about the results. If you have any questions about study results, please contact us.

EARLY WITHDRAWAL FROM THE STUDY

You may be removed from the study by the investigator for any of the following reasons:

- You do not or cannot follow study requirements.
- You lose the ability to provide consent for study procedures.
- You change your mind about letting us store your samples and data.
- You get another type of vaccine (other than a COVID-19 vaccine) or develop a medical condition that may interfere with the research tests being done on this study.

If your participation in this study ends early for any reason, we will still store and use your samples and data unless you ask us not to.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding immune responses to COVID-19 vaccination, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be

used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

PAYMENT

Will you receive any type of payment for taking part in this study?

You will be compensated for the time and inconvenience of participating in this study. How much you receive will be based on the number of procedures you complete and in-person study visits you have, as follows:

- $10 for each fingerstick sample
- $20 for each blood sample collected outside of NIH (e.g., Quest)
- $50 for each blood sample collected at NIH (total per visit)
- $5 for each saliva sample

In addition, you will receive a $10 bonus each time you complete the required blood collection or fingerstick sample after each vaccination within the indicated time period (up to $20 total).

You will also get a $10 bonus if you complete all required and optional sample collections being done for this study.

The maximum total compensation you can receive is $595 if you receive both doses of a 2-dose vaccine while on study and complete all possible on-site sample collections and visits. If you receive additional booster vaccination(s) and agree to remain on study for additional visits, you will be compensated for each additional visit/sample collection according to the amounts listed above.

You will be paid after each study visit or sample collection that you complete, but no more than once per week. The method of payment will be check, debit card, direct deposit, or ACH (Automated Clearing House) payment.

If you are unable to finish the study, you will receive payment for the parts you completed. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year.

REIMBURSEMENT

Will you receive reimbursement or direct payment by NIH as part of your participation?

This study does not offer reimbursement for parents and participants, or payment of, hotel, travel, or meals.

COSTS

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center. Similarly, you will not have any costs for blood drawn at Quest laboratories, as we will pay Quest directly for these. However, you may be billed for blood draws performed outside of NIH at sites other than Quest (eg, local doctors' offices or clinics). In this case, we will reimburse you up to $85 for each blood draw.

To receive compensation and/or reimbursement for this study, you will be asked to provide your Social Security Number. If you do not provide one, you can still participate in the study, but you may not be able to receive compensation and/or reimbursement.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor (NIAID) or their agent(s)

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy

Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Emily Ricotta, 301-761-7784, emily.ricotta@nih.gov. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Parent/Guardian of a Minor Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I give permission for my child to take part in this study.

Signature of Parent/Guardian	Print Name of Parent/Guardian	Date

Signature of Parent/Guardian	Print Name of Parent/Guardian	Date

Assent: I have had this study explained to me in a way that I understand, I have been given the opportunity to discuss it, and I have had the chance to ask questions. I agree to take part in this study.

Assent of Minor:

Signature of Minor	Print Name of Minor	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date