IDCRP-120: PAIVED Influenza Vaccine Efficacy Research Study Informed Consent Document (Main)

Research Study Title: A Pragmatic Assessment of Influenza Vaccine Effectiveness in the DoD (PAIVED)
Principal Investigator: CAPT Timothy Burgess, MC, USN
Participating Site Principal Investigator:

You are being asked to participate in a research study. Your participation is entirely voluntary, and you may decide not to take part or to withdraw at any time without losing the benefits of your routine medical care. Your decision to participate will not affect your future medical care or career in any way. Any new significant findings developed during the course of the research which may affect your willingness to participate further will be explained to you.

Before you agree to participate, the investigator must tell you about (i) the purposes, procedures, and duration of the research; (ii) any procedures which are research; (iii) any reasonably foreseeable risks, discomforts, and benefits of the research; (iv) any potentially beneficial alternative procedures or treatments; (v) how confidentiality will be maintained; (vi) any available compensation or medical treatment if injury occurs; and (vii) the possibility of unforeseeable risks. If you are a participant stationed in California, please read the California Bill of Rights.

i) Purpose, procedures, and duration of the research:
The purpose of the study is to compare the effectiveness of the standard flu vaccine (or flu shot). There are three common types of flu shots given to the public: egg-based, cell-cultured, and recombinant (combined dead flu cells). We are trying to determine whether one type of flu shot is better than another flu shot for preventing flu. You are being asked to take part in this research study because you are receiving a flu shot. We will enroll up to 18,000 people at up to 9 participating sites over 4 flu seasons. If you participate in this study, the effectiveness of the flu shot you received will be compared to the effectiveness of the other two types of flu shots received by other participants. The FDA has approved all of these vaccines. We will follow everyone who participates in this study to see if they develop the flu or flu-like symptoms after receiving the flu vaccine. In addition to assisting with the selection the optimal flu vaccine for the DoD, this study provides enhanced surveillance of respiratory infections including COVID-19 in the hopes of improving our understanding of disease causes and burden, and will shed light on any association between flu, flu vaccination and COVID-19 infection.

If you agree to participate, you will receive a flu shot during the regularly scheduled immunization event. We will use a process called randomization (like rolling dice) to determine which type of flu vaccine you will receive. There is a 33%, or 1 in 3, chance of you receiving any one specific type of flu vaccine. If you would like to know which vaccine type you have been assigned, you may ask for that information; however, since the process is randomized, you will not be able to choose which flu shot you receive.

We will ask you to fill out a small questionnaire about your medical history, flu history, and vaccine history.

We will also be collecting your cell phone number and email address, and you will receive an email or text message **once a week during the flu season** to ask if you have had any flu symptoms in the past 7 days. If you report that you have flu symptoms, you will be asked to complete a larger electronic symptom diary, which will take you approximately 10 minutes to complete each day for 7 days. A study staff member will also call you to schedule either a virtual phone visit or an in-person visit.

If you participate in virtual visits, we will ask you to self-collect a nasal swab and a blood sample consisting of a few drops of blood from your fingertip. We will also ask about your flu symptoms. We will collect the same information and another self-collected blood sample approximately 28 days after you report your flu-like symptoms so that we can see how well the shot works to help your body fight off the flu.

If you are scheduled for an in-person visit, we will ask you to collect a self-collected nasal swab and bring it with you to your study visit. At your study visit, you will be asked about your flu symptoms, have an in-clinic nasal swab taken, and either have an intravenous blood draw or a self-collected blood kit completed. You will have the option of what type of blood draw you prefer. Approximately 28 days after your report your flu-like symptoms, you will have your second in-

person visit. At this visit, you will answer questions about your illness, and have either a self-collected blood sample or an intravenous blood draw taken so that we can see how well the shot works to help your body fight off the flu.

OPTIONAL STUDY ACTIVITIES:

We will ask if you want to provide a cheek cell swab before your vaccination. This sample is optional. The cheek swab is a simple non-invasive procedure in which a small brush is used to rub the inside of your cheek to collect cells for genetic testing to examine how genetics and biology (your immune response) affect vaccine effectiveness. Please let us know your decision by providing your **initials** below:

_____Yes, I do give permission to collect a cheek swab . **_____No, I do not give permission** to collect a cheek swab.

We will ask if you want to provide some additional optional blood samples. These will be collected using a simple kit that collects a few drops of blood from your fingertip. The kits can be completed at home and sent back to us in a pre-paid mailer. If you opt-in, we will collect one sample on the day of your vaccination, and a second sample 14-30 days after receiving your vaccination. At the end of the flu season, you may be asked to provide an additional blood sample if you reported feeling sick during the flu season. Due to availability of study resources, not all participants who agree to provide these blood samples will be selected to participate in this part of the study. Please let us know your decision by providing your **initials** below:

_____Yes, I do give permission to provide additional research blood samples.

_____No, I do not give permission to provide additional research blood samples.

ii) Procedures which are research:

The randomization to determine which standard flu shot you will receive is research. Research means it is part of the research process and not standard of care. The flu shots are FDA approved and are not research. The optional cheek cell swab, weekly emails, questionnaires, and the potential follow up virtual phone visits where you provide a self-collected nasal swab and self-collected blood samples which will only happen if you develop the flu-like symptoms are research.

iii) Any reasonably foreseeable risks, discomforts, and benefits of the research:

There is no additional risk to you in receiving your FDA approved flu shot. There are common side effects and research staff are trained to assess and address the problem in accordance with clinical care guidelines. There are small risks associated with the at home self-collected nasal swab and the self-collected blood draw that would occur when you have your virtual phone research visit (if you get sick).

The potential risks of the nasal swab include: discomfort, pain, and nose bleeding. The potential risks of the self-collected finger stick blood draw may involve feeling uncomfortable with puncturing your own finger with a lancet and pain at the puncture site. There are small risks associated with the cheek swab, which include: discomfort, slight pain, and sore or raw feeling inside your cheek. There is also a small risk of a breach of confidentiality; we will cover what steps will be taken to keep your information secure in section v (5).

There are no direct benefits to you for taking part in the study. Your participation will allow clinicians and scientists to better understand the conditions that are consequences of the flu shot, including which flu shots work better. This can help health care providers in the future to provide better care to prevent severe illness from the flu.

iv) Compensation:

You will be compensated for completion of certain study activities in accordance with DoDI 3216.02. During your study participation, you will be compensated $10 for each self-collected blood draw, $10 for each nasal swab, $50 for each intravenous blood draw, and $10 for completing the flu symptom diary.

Under 24 USC 30, payment to Federal Employees and Active Duty military personnel for participation in research while on duty is limited to blood donation and may not exceed $50 per blood draw. They may not receive any other payment or non-monetary compensation for participation in a research study unless they are off duty or on leave during the time they are participating in the protocol. However, if you are a recruit in training, you cannot be compensated, due to DoD policy, while during training. There are no restrictions on payment while off-duty. In order to receive payment for your participation in this study, you may be asked to provide your social security number and home address on a Payment Verification Form. The form will be stored in a locked cabinet at the study site and the Henry M. Jackson Foundation offices. You will be asked to complete this paperwork if you have more than one flu illness in this season and/or if you participate in the sub-study or other optional blood draws. Compensation is allowed for research participation as approved by the IRB. Payment may not come directly from a federal source. Payment from a federal contractor or non-federal source is permissible.

v) Any potentially beneficial alternative procedures or treatments:
Your alternative is not to participate in this research study. You will still receive your annual flu shot per military requirements. You may withdraw at any time from the study. In order to withdraw from the study, you must contact the Principal Investigator at flushotstudy@idcrp.org. If you decide not to participate or withdraw from this study, you will continue to receive medical care without losing any rights to medical care that you are already receiving. Participating in this study will not affect your care or if you receive a flu vaccine. Your participation in this study may be stopped without your consent if participating in the study may be harmful or dangerous to you, or if you lose the right to have medical care at the military treatment facility where the study is conducted.

vi) How confidentiality will be maintained:
All study documents with personal information (including name, medical record information, date of birth, DoD ID number) will be maintained in secure files and on password-protected computers. This information will only be available to study staff who are authorized to use it. However, there is always the possibility that records are mishandled, and that someone without proper authorization could get access to the personal information in your medical records or other information researchers have stored about you. These events are rare, but should they occur, are promptly reported to the Institutional Review Board (IRB) and Privacy Office, which supervises our study. All available precautions are taken to prevent such occurrences. If you become ill, your blood samples and nasal swab will be stored with an assigned study number to identify the sample and will not include personal identifiers (name, DoD ID etc.).

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of "Military Health System Notice of Privacy Practices," can be found online.

Procedures to protect the confidentiality of the data in this study include but are not limited to the following: 1) Data will be stored on password-protected computers that can only be accessed by the research team. 2) Any documents that link the participant information and assigned identification numbers will be kept in a secure location separate from data files. 3) Data will be entered into a nationally recognized secure database, REDCap.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss. If you have any questions or concerns about your rights as a research subject or have any additional concerns that cannot be addressed by the PI, you can contact the Director of Human Subject Protections Program at the Institutional Review Board that oversees this study, 301-295-9534.

vii) Any available compensation or medical treatment if injury occurs:
If you are in need of medical treatment because you have contracted the flu, please see your regular medical provider, as treatment is not provided in this study.

viii) Possibility of unforeseeable risks:
There is always the possibility of unforeseeable risks, however, the flu shot that you will receive is FDA approved and commonly used. All flu shots used in this study are FDA approved.

ix) Authorization to Use and/or Disclose Protected Health Information For Research (HIPAA):
Purpose of this Authorization.
You are asked for permission to use or disclose your protected health information for this research study. The Health Insurance Portability & Accountability Act of 1996, Public Law 104-109 (HIPAA), establishes privacy standards to protect your health information. This law requires the researchers to obtain your authorization before they use or disclose your protected health information for research purposes in the study discussed in this form.
Authorization:
The disclosure of your protected health information is necessary in order to be able to conduct the research project described. The demographic information will help us understand if flu shot effectiveness varies between groups of people. The information on your prescription medicines, history of medical conditions, flu and vaccination will help us to understand how current and past medical treatments impact the effectiveness of the flu shot.

Records of your participation in this study may only be disclosed in accordance with state and federal law, including the Privacy Act (5 U.S.C. 552a) and the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (45 CFR 160 & 164). You have the right to revoke your authorization at any time, please notify the study Principal Investigator in writing if your wish to revoke your authorization. Note: Protected health information of military service members may be used or disclosed for activities deemed necessary by appropriate military command authorities to ensure the proper execution of the military mission.

(a) What health information will be used or disclosed (released) about you?
Name, address, date of birth, age, phone numbers, email addresses, DoD identification number, health information including prescription medications, vaccinations, as well as history of past flu and treatment you were prescribed by your care provider when you had flu-like symptoms. This protected health information will be gathered from any military health system, military treatment facility, Defense Health Agency, or Veteran Affairs treatment centers, in which you received treatment in the past 5 years.

(b) Who will be authorized to use or disclose (release) your health information?
This protected health information will be gathered from any military health system, military treatment facility, and Defense Health Agency treatment centers. Military Treatment Facilities who have treated you over the past 10 years, and the Defense Health Agency, are permitted to make the requested use/disclose of your PHI.

(c) Who may receive your health information?
The Military Health System (MHS) will use or disclose your health information. The Study Doctor(s) may access, use, disclose, and share your health information with:
- Uniformed Services University of the Health Sciences Institutional Review Board (USUHS IRB)
- Infectious Disease Clinical Research Program (IDCRP)
- Naval Medical Center San Diego (NMCSD), Naval Medical Center Portsmouth (NMCP), Walter Reed National Military Medical Center (WRNMMC), Walter Reed Army Institute of Research (WRAIR), San Antonio Military Medical Center (SAMMC), part of Brooke Army Medical Center (BAMC), Madigan Army Medical Center (MAMC), Womack Army Medical Center (WAMC), Wilford Hall Medical Center (Lackland AFB), or Department of Defense (DoD) representatives.
- Henry M. Jackson Foundation
- State and Federal government representatives, when required by law
- Defense Health Agency (DHA)
- Food and Drug Administration (FDA)
- Centers for Disease Control and Prevention (CDC)

- National Institute of Allergy and Infectious Disease (NIAID) and their representatives
- World Health Organization Influenza Reference Laboratory

The researchers and those listed above agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and federal law.

(d) What if you decide not to sign this authorization?

You do not have to sign this Authorization, but if you do not, you will not get to participate. The MHS **will not** condition (withhold or refuse) treatment that is not part of this study, payment, enrollment, or eligibility for benefits on whether you sign this Authorization.

(e) Is your health information requested from future research studies?

Yes, your health information *is* requested for use or disclosure (release) in future studies. You are in a study where blood, cheek cells and nasal samples (biospecimens) are being collected as part of the research study. After all the required tests are finished, the investigator wants to save the remaining specimens indefinitely for possible use in future research, which may have public health benefit. The stored samples from this research study will not be labeled with any part of your name or social security number and may be shared with researchers and investigators within the Department of Defense and with researchers outside of the military for future research. The specifics of these future studies are unknown at this time, but these studies will frequently be in the area of acute respiratory illnesses. Results of these future studies will not be returned to you or your doctor and will not influence your clinical care. You must revoke your permission by initialing your choice below. Please **initial** the applicable boxes below:

_____**Yes, I do give permission** to use my health information (from my health records) for future research studies.

_____**No, I do not give permission** to use my health information (from my health records) for future research studies.

_____**Yes, I do give permission** to use my bio specimens **(blood, cheek swab and nasal swabs**) in future research studies with benefits to the public health.

_____**No, I do not give permission** to use my bio specimens (**blood, check swab and nasal swabs**) in future research studies with benefits to the public health.

(f) Can you access your health information during the study?

You may have access to your health information at any time unless your identifiers are permanently removed from the data.

(g) Can you revoke this authorization?

You may change your mind and revoke (take back) your Authorization at any time except to the extent that the MHS has already acted in reliance on your Authorization. Even if you revoke this Authorization, any person listed above who received your Authorization for purposes of the research study may still use or disclose (release) any already obtained health information as necessary to maintain the integrity or reliability of this research.

If you revoke this Authorization, you may no longer be allowed to participate in this research study. If you want to revoke your Authorization, you must write to the Principal Investigator at flushotstudy@idcrp.org.

(h) Does this authorization expire?

No, it does not expire.

(i) What else may you want to consider?

No publication or public presentation about the research described above will reveal your identity without another signed Authorization from you.

If all information that does or can identify you is removed from your health information, the remaining deidentified information will no longer be subject to this Authorization and may be used or disclosed (released) for other purposes. Once your health information is shared or disclosed (released) outside of the MHS, the privacy of your health information cannot be guaranteed, and it may no longer be protected by the Federal privacy laws (such as the HIPAA Privacy Rule).

Complete confidentiality cannot be promised, particularly for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities.

If you agree to participate in this study, you will be offered a copy of this consent form and HIPAA authorization for your records. The following Principal Investigators or a member of the research staff will be available to answer any questions concerning procedures throughout the study:

Principal Investigator
OR CAPT Timothy Burgess, MC, USN
flushotstudy@idcrp.org

SIGNATURE OF PARTICIPANT

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop. Please complete the section below **to document your agreement to participate in this study.**

Participant's Signature	**Today's Date**	**Printed Name of Participant**

SIGNATURE OF RESEARCH STAFF

I have carefully explained the nature and purpose of the research to the subject. I answered all questions that the subject had regarding the research.

Signature of Research Staff	**Today's Date**	**Printed Name of Research Staff**