UNIVERSITY OF MICHIGAN
IN COOPERATION WITH CENTRAL, EASTERN AND WESTERN MICHIGAN UNIVERSITIES
CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. *Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.*

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title:

Comparative Study of Influenza Vaccines in Adults – **FLU-VACS**

1.2 Company or agency sponsoring the study:

National Institute of Allergy and Infectious Disease

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Arnold S. Monto MD, Professor
Department of Epidemiology, School of Public Health
University of Michigan

Suzanne E. Ohmit DrPH, Assistant Research Scientist
Department of Epidemiology, School of Public Health
University of Michigan

Duane Newton, PhD, Assistant Clinical Professor
Pathology, Clinical Virology
University of Michigan Hospital

Matthew Boulton, MD MPH, Associate Professor
Department of Epidemiology, School of Public Health
University of Michigan

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

We are conducting year 2 of a 3 year research study to compare two licensed influenza vaccines to each other and to placebo (a preparation similar to vaccine but with no active ingredients). Influenza is a serious respiratory illness caused by a group of viruses. Influenza outbreaks occur every year usually in the winter months. Vaccination is the first line of defense against influenza. People who are vaccinated are usually protected because their bodies respond to the material included in the vaccine by making antibodies that fight infection – this is known as the immune response. Two vaccines are licensed for use in the prevention of influenza – one is the inactivated (killed) influenza vaccine (product names Fluzone or Fluvirin) that is given as an injection ("flu shot"), and the other is the newer live-attenuated (weakened) influenza vaccine (product name FluMist) that is given by nasal spray. Both are licensed for use in healthy adults under age 50 years. We do not know whether these vaccines will work equally well, or whether one will work better than the other, for example in terms of how long protection lasts. In order to test the vaccines, we will need to perform laboratory tests on blood specimens from you to measure your immune response to vaccination. We will also need to perform laboratory tests on throat swab specimens from you if you have a respiratory illness. Our research study will help to determine how the vaccines will be used to control influenza outbreaks, and will contribute to future studies when the FluMist vaccine is tested in the elderly and those with chronic health conditions.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

It is important that you provide complete and accurate information in order to ensure that you are eligible for participation. Eligibility for continued participation will be reviewed each year.

- Persons must be adult men and women aged 18-48 years (have not yet reached their 49th birthday).
- Persons must expect to live in the study area during the remaining 2-year study period (through Spring 2007) and be interested in participating both years.
- Persons must be willing to receive the licensed live-attenuated influenza vaccine (FluMist) or placebo given as a nasal spray, or the licensed inactivated vaccine (Fluzone or Fluvirin) or placebo given as an intramuscular injection.
- Persons must be willing to provide multiple blood specimens collected by venipuncture each year they are in the study. During each of the first two years of the study, blood specimens will be collected three times – at the enrollment visit, at the follow-up visit 3-5 weeks later, and at the end of the influenza season visit (approximately 4-6 months later); during the third year of the study, blood specimens will be collected twice only, at visits before and after the influenza season.

- Persons must be willing to notify study personnel in the event of respiratory illness meeting the influenza-like illness case definition, to provide information on illness symptoms and permit collection of a throat culture (swab) specimen for laboratory studies.
- Persons must be willing to not receive any influenza vaccine while participating - other than that (influenza vaccine or placebo) received as study medication.

Who Should Not Participate?

- Persons with any health condition for which the inactivated influenza vaccine is recommended including chronic health conditions of the heart or lungs, including asthma; chronic metabolic diseases including diabetes; loss of kidney function; Thalassemia or sickle cell anemia; or immunosuppression due to HIV infection or current treatment for cancer, leukemia or lymphoma.
- Persons who are currently pregnant, nursing mothers or are planning a pregnancy within one month of study enrollment.
- Persons who are allergic to egg, egg protein or the antibiotic Gentamicin (also known as Garamycin), or the preservative Thimerosal.
- Persons who have had a prior serious reaction to influenza vaccine, or ever had Guillian Barre' syndrome.
- Persons who are living in a household with or have direct occupational contact with immunosuppressed individuals (including health care workers with direct patient contact).
- Persons who have received an influenza vaccine for this influenza season (2005-06) or those who plan to receive an influenza vaccine during their participation in the study - other than that (influenza vaccine or placebo) received as study medication.
- Persons who have received any other vaccine within one week prior to enrollment (may delay enrollment).
- Persons who have had a respiratory illness or illness with fever within 3 days of enrollment (may delay enrollment).
- Persons who are participating in another research study involving any study medication.

3.2 How many people (subjects) are expected to take part in this study?

1,980 persons are expected to participate; 83% (approximately 1,650) of participants will receive one of the two licensed influenza vaccines and 17% (approximately 330) will receive placebo. Participants will be enrolled at 6 study sites in Michigan.

4. INFORMATION ABOUT STUDY PROCEDURES

4.1 What exactly will be done to me in this study? What kinds of research procedures will I receive if I agree to take part in this study?

We are currently conducting year 2 of a 3 year study. The study will be conducted among healthy adult participants aged 18-49 years.

In year 1, participants were assigned by chance to receive one of the two, licensed influenza vaccines (83% chance) or placebo (17% chance), given either as nasal spray (live-attenuated vaccine or placebo) or injection (inactivated vaccine or placebo). In year 2, receipt of vaccine or placebo will continue as assigned in year 1 for returning participants. Participants new to the study in year 2 will be

assigned by chance to receive one of the two, licensed influenza vaccines (83% chance) or placebo (17% chance), given either as nasal spray (live-attenuated vaccine or placebo) or injection (inactivated vaccine or placebo). Participants and staff will not be able to select or change the medication assignment, nor will they know whether vaccine or placebo is given. In study year 3, all participants will continue to be followed but no vaccine or placebo will be given.

Each year of the study blood specimens will be collected at each scheduled visit in order to measure how your body responds to vaccination and/or how well you were protected from influenza infection. Your blood specimens may, if you permit, become part of an anonymous databank for use in future studies of respiratory viruses. During the influenza season, participants with influenza-like illness will provide information on symptoms and come in for collection of a throat culture (swab) specimen for virus identification.

Specifically, during this year (year 2) of the study:

- At the enrollment visit (September-December) participants will have a pre-vaccination blood specimen (single tube – 8.5ml, 2 teaspoons) collected for laboratory studies, and receive a single dose of one of the two influenza vaccines or placebo, given as a nasal spray (0.5 ml FluMist or placebo) or intramuscular injection (0.5 ml Fluzone/Fluvirin or placebo).

- Participants will return to the study site 3-5 weeks later (October-January) to have a post-vaccination blood specimen (single tube – 8.5ml, 2 teaspoons) collected for laboratory studies.

- During the influenza season (November-April), participants will be sent a brief biweekly voice (phone) or email message with reminders to contact the study staff in the event of influenza-like illness (defined as two or more of the following symptoms: fever [or feverish], cough, chills, nasal congestion, headache, body aches or sore throat). Participants with illness will be asked to return to the study site within 72 hours of illness onset, provide information on illness symptoms and duration, and permit collection of a throat culture (swab) specimen for virus identification. Ill participants will be contacted by phone to collect illness follow-up information.

- At the end of the influenza season (April-May), participants will return to the study site for collection of the post-season blood specimen (single tube – 8.5ml, 2 teaspoons) for laboratory studies.

During the third year of the study when duration of protection due to vaccination is evaluated, no vaccine (or placebo) will be given to participants. However, participants will remain enrolled, and will have blood specimens collected on two occasions (pre-season [October-November] and post-season [April-May]) and will continue to be followed for influenza-like illness with specimens collected for virus identification.

4.2 How much of my time will be needed to take part in this study? When will my participation in the study be over?

This is a 3-year research study and study subjects who enrolled in Fall 2004 are invited to participate all three years; those first enrolled during study year 2 (Fall 2005) are invited to participate two years. The enrollment visit (September-December) where blood is collected and vaccine (or placebo) administered will take 45-60 minutes; the follow-up visit (approximately 3-5 weeks later) and end of season visit (April-May) where the second and third blood specimens are collected will take approximately 15-20 minutes each. If influenza-like illness occurs during the influenza season (November-April), the illness

visit with collection of symptom information and throat culture (swab) specimen will take approximately 15-20 minutes. Total annual study involvement is approximately 1.5 – 2 hours over 7 – 9 months.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

In previous studies some participants receiving the FluMist vaccine experienced mild flu-like symptoms including cough, runny nose, sore throat, chills, tiredness, headache and low-grade fever. Some recipients of the inactivated vaccine (Fluzone or Fluvirin) may experience local reactions (soreness, redness, swelling) at the injection site, and other mild symptoms such as fever, chills, fatigue, headache and muscle aches. These data suggest far lower risk of harm associated with vaccination than with influenza illness.

Allergic reactions to vaccine components while rare are possible. Participants will be asked to stay at the study center for at least 15 minutes following vaccination for observation.

Collection of blood specimens by venipuncture can cause minor discomfort, fainting or bruising. Collection of throat swab specimens may be accompanied by brief discomfort consistent with other minor diagnostic procedures. These risks will be minimized by having the procedures performed by trained staff.

The FluMist influenza vaccine is not recommended for women who are pregnant, nursing mothers or women who plan a pregnancy within one month following vaccination. It is important that if you are sexually active, you use contraception (e.g. oral, injection, IUD, condoms, diaphragm).

Participating in this research study will not necessarily protect you from getting influenza.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even when the researchers are careful to avoid them. If you believe that you have been harmed, notify the researchers listed in Section 10 of this form. If first aid or emergency care is required, the cost of this care may be billed to your insurance company, but if it is not covered by your insurance, the University of Michigan will pay for it. Additional medical care will be provided if the University determines that it is responsible to provide such treatment. If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Please note: It is important that you tell the researchers about any injuries, side effects, or other problems that you experience during this study. You may also need to tell your regular doctors.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time may increase the risks to you. Receiving any other study medications, especially vaccines, could interfere with evaluation of your immune response

to the influenza vaccine you receive and affect study results of both studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You may not receive any personal benefits from being in this study. However, 5 out of every 6 study participants will receive one of the licensed influenza vaccines (FluMist, Fluzone or Fluvirin) – these vaccines are likely to lower your risk of influenza illness. Your participation may provide valuable information on how the vaccines should be used in responding to influenza outbreaks, and will contribute to future studies when the FluMist vaccine is tested in the elderly and those with chronic health conditions.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

You are under no obligation to participate in this study, and are free to withdraw from the study at any time. If you do not wish to participate in this study but would like to receive the live-attenuated (FluMist) or inactivated (Fluzone or Fluvirin) influenza vaccines to lower your risk of influenza infection, these vaccines are licensed and available from local health care providers or health departments.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please notify one of the persons listed in Section 10 “Contact Information” (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

It is not likely that you would suffer any harm by leaving the study prior to its completion.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.

- ✓ You become ineligible to participate; eligibility for continued participation will be reviewed every year prior to re-enrollment.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Will taking part in this study cost me anything? Will I or my insurance company be billed for any costs of the study? If so, which costs? What happens if my insurance does not cover these costs?

Participation in this study is free. No medical insurance information will be requested by study personnel.

8.2 Will I be paid or given anything for taking part in this study?

Yes, 5 out of every 6 participants will receive a licensed influenza vaccine at no charge (1 out of every 6 participants will receive placebo and it will not protect them from getting influenza). In addition, study participants who complete the three scheduled study visits - enrollment/vaccination visit, one month follow-up visit and end of season visit – will receive at least $100 ($30 for each of the first two visits and $40 for the third visit); additional compensation ($25 per visit) will be received in the event of influenza-like illness with specimen collection (throat culture) for virus identification. Compensation for the first two study visits (enrollment and follow-up) will be distributed at the time of the follow-up visit. Compensation for any illness visits and the end of season visit will be distributed at the time of the end of season visit. Participants with influenza-like illness, who attend an illness visit will be given a $10 coupon at the time of the illness visit, to purchase relief medications of their choice. Compensation in study year 3 will be $100 for 2 scheduled visits; additional compensation ($25 per visit) in the event of influenza-like illness with specimen collection remains the same.

8.3 Who could profit or financially benefit from the study results?

The companies whose products are being studied including Medimmune Vaccines (FluMist), Aventis Pasteur (Fluzone) and Evans/Chiron Vaccines (Fluvirin); the researchers conducting the study; and The University of Michigan. The University of Michigan receives royalties from FluMist (Medimmune Vaccines).

9. CONFIDENTIALITY OF SUBJECT RECORDS

University of Michigan policies require that private information about you be protected. This is especially true for your personal health information.

On the other hand, sometimes the law allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

Study participants will be asked to provide demographic (name, sex, birthdate, age) and contact information (address, phone number, email) and health status information in order to determine study eligibility and permit follow-up. This information will be recorded on study data collection forms and entered into study databases, so we cannot guarantee complete confidentiality. To reduce this risk, all participants will be assigned a study identification number that will be used to identify the subject and link an individual to their data. Access to study documents will be controlled and limited to study staff. Data will be stored in password-protected computers and in locked file cabinets in locked rooms. Blood specimens, stored in the freezer specimen repository, will be identified by study identification number and specimen collection date only. Information obtained through this research may be used for education, study related reports and publications; however, your identity will not be disclosed for these purposes.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

There are many reasons why information about you may be used or seen by the researchers or others during this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- University and government officials may need the information to make sure that the study is done properly.
- Organizations that are funding the study may need the information to make sure that the study is done properly.
- The researchers may need to use the information to create an anonymous databank of information about your condition or its treatment.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I leave the study before it is finished?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Data you provide to us including your name and your personal health information will be destroyed once the proposed laboratory studies are completed (approximately two years after closure of the three year study). Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have left the study or the study is over. Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly.

9.4 What happens to my blood specimens after the study is over?

If you choose to participate in this study, we ask that you permit use of your blood specimens for future research after the current study has been completed. Future studies would involve determining study participants' immune status to other influenza viruses or other acute respiratory infections (for example: rhinovirus, SARS). Blood specimens will become part of an anonymous specimen databank; specimens will be identified with study identification numbers and specimen collection dates only – no names or other personal identifiers will be included.
By agreeing to participate in this study you have also agreed to permit use of your blood specimens for future research studies after the current study is completed. If you do NOT wish to permit your blood specimens to become part of the anonymous specimen databank, please indicate that by signing here: _____

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Dr. Arnold S. Monto
Mailing Address: University of Michigan
School of Public Health I
109 Observatory, Ann Arbor, MI 48109-2029
Telephone: (734)647-1492
Email Address: asmonto@umich.edu

Co-Investigator: Suzanne Ohmit, DrPH
Email: sohmit@umich.edu
Telephone: (734)763-6422

Study Site Coordinators:	Judy Rotthoff, RN	Esther Teich, MA
Email:	jrotthof@umich.edu	eteich@umich.edu
Telephone:	(734)763-5162	(734)615-8331

Study Site Coordinators:	Jeanine Ahearn, BS	Fran Morrow, MSW
Email:	ahear1jr@cmich.edu	fran.morrow@wmich.edu
Telephone:	(989) 774-4446	269-387-4623

You may also express a concern about a study by contacting the Institutional Review Board listed below, or by calling the University of Michigan Compliance Help Line at 1-888-296-2481.

University of Michigan Medical School Institutional Review Board (IRBMED)

Argus I, 517 W. William, Ann Arbor, MI 48103-4943
Telephone: 734-763-4768 Fax: 734-763-9603 E-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy, contact the University of Michigan Health System Privacy Officer at 1-888-296-2481.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file.)*
- The FluMist (live-attenuated) Vaccine Fact Sheet or the Inactivated (Fluzone or Fluvirin) Vaccine Fact Sheet developed by the Centers for Disease Control and Prevention (CDC).

SIGNATURES

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____

Date of Birth: _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____