FOR CCI USE ONLY
Approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations:

Consent Approval Date: _____

Protocol Number: **2013P-000026**

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Statin Therapy in Acute Influenza
PRINCIPAL INVESTIGATOR: Maureen Chase MD, MPH
PROTOCOL NUMBER: 2013P-000026

INTRODUCTION:

You are invited to take part in a research study about a new use for statins to help treat influenza.

You are being asked to take part in this study because you have confirmed influenza infection. Research studies include only people who choose to take part. Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study.

- Your participation is voluntary;
- You may or may not benefit from participating in the study. However, your participation may help others in the future as a result of knowledge gained from the research;
- You may leave the study at any time;
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with your doctor, nurse or with Beth Israel Deaconess Medical Center.

Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

This study is being conducted by Dr. Maureen Chase and is funded through a federal grant sponsored by the National Institutes of Health (NIH), General Medical Sciences Division (NIGMS). The funding agency in this study, NIGMS, is paying Beth Israel Deaconess Medical Center and Dr. Chase to perform this research. BIDMC or Dr. Chase have no additional interests in this research project.

WHY THIS STUDY IS BEING DONE

Infection with the influenza virus can cause a mild, moderate or severe infection and, occasionally death. There is a class of drugs called "statins," which are used rather frequently to

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treat high cholesterol levels. Recently, some research studies indicate that there is an association between statin use and better outcomes ("better" meaning shorter hospital stays, lessened severity of illness) in both people and in animals with infection. However, there have been no studies that have compared the deliberate administration of statins when influenza is present. This study is trying to determine if statins, do in fact, lessen the severity of illness in influenza infection by checking how your body responds to the infection (by looking at markers of inflammation in your blood). The statin medication we will use for this study is called atorvastatin. You will be treated for your infection regardless of your participation in this study as your doctor sees fit.

The statin medication is not FDA-approved for the treatment of influenza and thus is experimental.

WHO WILL PARTICIPATE IN THE STUDY

Approximately 174 people will take part in this study at Beth Israel Deaconess Medical Center, which is the only medical facility in which this study is taking place.

WHAT WILL HAPPEN DURING THE STUDY

If you agree to be in this study, you will be asked to read and sign this consent form. After you sign the consent form, the following things will happen:

1. Screening Procedures: Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. For this research study, the screening procedures will be as follows:
    - A member of the research team will review your medical chart and speak with you and your physician to determine if you are eligible to participate in the study.
    - You will be asked questions about your medical history and the medicines you have taken in the past and are currently taking.
    - If you are a female and are of an age where you can have a child, a urine or blood pregnancy test will be performed to confirm you are not pregnant. If you are pregnant or breast-feeding, you will not be able to participate in this study.

2. Randomization Procedures:
   You will be randomly assigned (like the flip of a coin) to receive either atorvastatin or placebo. You have a 1 in 2 chance of receiving either one.

   Depending upon the group to which you are assigned, you may receive a placebo instead of the study drug. A placebo is an inactive pill that looks like the study drug, but a placebo contains no active medication. Placebos are used to help determine if the results of the study are truly from the study drug.

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Neither you nor your care team will know which one (either atorvastatin or placebo) you are receiving. However this information can be learned in case of an emergency.

3. Research Procedures: If you qualify to take part in this research study, you will undergo these research procedures:

All participants in this study (those receiving the **study treatment** and those receiving **placebo** will receive the following:

a) A blood draw of 2 tablespoons (30 mL) right after you sign the consent to examine markers of inflammation in your blood which tell us something about how your body is responding to an infection, and also to determine how your liver is functioning (which is important because statins do part of their job in the liver).

b) You will take a pill. It may be atorvastatin or it may be placebo. You will take one of these pills once a day for 5 days (or for 7 days if you need to stay in the hospital for 7 days).

c) You will be asked to fill out a diary of your flu symptoms for the next 10 days. You will be sent an electronic or email reminder to complete the survey each day. If you do not have computer or internet access, a member of the research team will call you each day to complete the survey over the phone.

d) We will also perform a more thorough review of your chart, vital signs, lab results, and radiological testing and record this information.

4. Monitoring/Follow-Up Procedures. Procedures performed to evaluate the effectiveness and safety of the research procedures are called “monitoring” or “follow-up” procedures. For this research study, the monitoring/follow-up procedures include:

a) If you stay in the hospital, we will draw 2 tablespoons (30 mL) of your blood once a day while you are taking the study medication (up to 7 days). If you stay in the hospital longer, and continue to have symptoms related to your influenza infection, we will draw blood every other day up to day 14 of your hospital stay.

b) If you are discharged from the hospital today, we will ask that you return to our Research Clinic (GCRC, located across the street on the East Campus) in 3 days to have your blood tested.

c) If you are admitted today, but go home before 3 days in the hospital, we will ask that you

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return to the Research Clinic (GCRC). The purpose of this visit is to draw blood to check labs in order to make sure that the study drug is not affecting you in a negative way and to retest markers of inflammation.

d) We ask that you provide us with a working email address so that we can send you a daily diary survey to see how you are feeling each day for 10 days after you start the study.

e) If you do not have email access, we will ask that you provide us with a working telephone number so that we can call you daily (for 10 days) to complete the survey over the phone.

f) We will also call you in 2 weeks (14 days) to ask how you are feeling.

POSSIBLE RISKS, SIDE EFFECTS, AND DISCOMFORTS

RISKS OF THE RESEARCH STUDY

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

A risk to taking part in this study is the likelihood of receiving a drug or dose of a drug that may not be effective in helping to treat your disease. This means that you may spend time and experience side effects taking a drug that may not provide you with any health-related benefits.

Blood Draw Risk:

More common: The risks and discomforts of blood drawing from a vein include the possibility of pain or bruising at the site of the blood draw;
Less common: occasional feeling of lightheadedness; and
Rarely: infection at the site of the blood draw

Atorvastatin Risk:

Some patients who have taken atorvastatin have complained of an upset stomach and diarrhea. Some other patients have experienced problems with their liver, which are evident from changes in blood levels of certain liver enzymes. The study doctors will be monitoring you for this, and if this happens, you will be advised to stop taking the drug. In addition, atorvastatin can cause muscle aches and weakness (myopathy) and, in very rare cases, muscle breakdown (rhabomyolysis). The risk for both of these complications in the dose used in this study is less than 1 percent. However, the study staff and your doctors will monitor you for these potential complications.

What are the risks to pregnancy?

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You may not participate in this study if you are pregnant because the study drug, atorvastatin, may have harmful effects to a developing fetus which may include, but are not limited to, birth defects, premature delivery and even death. You will be required to take a pregnancy test to verify that you are not pregnant before receiving your first dose of study medication.

Furthermore, if you are a woman capable of becoming pregnant, you must agree to use adequate birth control for 2 weeks after you finish the study medication. For the purpose of this study, use of adequate birth control includes one of the following:

1. oral hormonal contraceptives
2. implanted hormonal contraceptives
3. diaphragm with spermicide
4. condoms
5. Intra-uterine device
6. abstinence

If you believe you have become pregnant while participating in this study (while you are taking drug and up to 2 weeks after you finish), you must inform your study investigators immediately. They will have you take a pregnancy test. If the results demonstrate that you are pregnant, you will not be given any more study drug, and the study investigators will ask to monitor your pregnancy. To monitor your pregnancy may include (but not limited to) office visits, blood work, and questionnaires.

If you are a man capable of fathering children, you must use adequate contraception while participating in this study. For the purposes of this study, adequate birth control means;

1. use of a condom
2. your partner must use an approved method of birth control as listed above

Other Risks

Your condition may not get better or may get worse during this study.

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

Loss of Confidentiality

There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information. However, if your participation becomes known, it could create a problem or hardship for you depending upon the type of information disclosed.

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POSSIBLE BENEFITS

It is not possible to predict whether you will benefit directly from participation in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you may choose not to participate. You will be treated for your influenza regardless of your participation in this study.

Atorvastatin is experimental for treating influenza. This means that you/your relative can only receive it by enrolling in this study.

This research study is not meant to diagnose or treat medical problems. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor.

We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. However, please be aware that there may be risks to leaving the study before it has been completed. If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with your doctor nurses or with Beth Israel Deaconess Medical Center. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

You will not be charged for the atorvastatin, blood tests, and other procedures that are part of this

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research study. However, you and your insurance company will be charged for other tests, procedures or medications of this study that are considered standard treatment for your medical condition.

CO-PAYMENT/DEDUCTIBLE STATEMENT
You will be responsible for any co-payments or deductibles that are standard for your insurance coverage.

PAYMENTS TO YOU:

- You will be paid $30 on the day you return to the CRC after you complete your visit. The payment will be in the form of cash or voucher.
- You will receive $20 after you complete your diary for 10 days. The payments will be in the form of a check.
- You will receive a parking sticker up to 3 hours.

Any payments made to you may be taxable income to you. This does not include any payments you may receive to reimburse (pay you back) you for certain expenses like parking fees or travel. We are required to obtain your name and social security number for preparation and submission of Internal Revenue Service (IRS) Form 1099-Misc. You may receive an Internal Revenue Service Form 1099 from BIDMC if you receive more than $600 or more in one calendar year for taking part in one or more research studies at BIDMC. Questions about your own tax status should be referred to your personal tax advisor.

COST OF RESEARCH RELATED INJURY:
If you are injured as a direct result of your participation in this study you should contact the Investigator at the number provided under the section "Who to Call if You Have Questions" in this form. You will be offered the necessary care to treat your injury. You or your insurance company will be billed for medical care and/or hospitalization related to this injury. You will be responsible for all co-payments and deductibles required under your insurance. BIDMC will consider reimbursement of injury related expenses not covered by your insurance on a case-by-case basis. At this time there is no plan to reimburse you for items such as lost wages or lost time form work. By signing this consent form you have not given up any legal rights.

CONFIDENTIALITY
Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center with protection of confidentiality so far as permitted by applicable law.

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Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

A description of this clinical trial will be available on 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.

USE OF YOUR TISSUE AND DATA FOR COMMERCIAL DEVELOPMENT

As part of this research program, samples of your tissue and information about your medical history may be provided to other researchers and/or outside collaborators without identifying you by name. They may use your tissue and information in other scientific research, product testing or commercial development. It is unknown whether a product will ultimately be developed from any such work that may be performed. In signing this consent form, you are acknowledging and voluntarily consenting to the possibility that your tissue may be used for commercial purposes. You also understand and agree that tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. Beth Israel Medical Deaconess Medical Center has no program to compensate you in the event product testing or commercial development takes place.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting and sharing information about you with others. Please review this section carefully as it contains information about the federal privacy rules and the use of your information.

PROTECTED HEALTH INFORMATION [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use [internally at BIDMC] and disclose [to people and organizations outside the BIDMC workforce identified in this consent] health information about you. This may include information about you that already exists such as your medical records as well as any new information generated as part of this study through blood tests and the microscopic examinations we may ask you to undergo. This is your Protected Health Information.

PEOPLE/GROUPS AT BIDMC WHO WILL USE YOUR PROTECTED HEALTH INFORMATION

Your Protected Health Information may be shared with investigators listed on this consent form as well as the supporting research team [i.e. research assistants, statisticians, data managers, laboratory personnel, administrative assistants]. Your Protected Health Information may also be shared with the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center as it is responsible for reviewing studies for the protection of the research subjects.

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PEOPLE/GROUPS OUTSIDE OF BIDMC WITH WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE SHARED

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this study:

- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], and the Office for Human Research Protections [OHRP].
- Hospital and Clinical Research Accrediting Agencies
- Data and Safety Monitoring boards that oversee this study

Those who receive your Protected Health Information may make further disclosures to others. If they do, your information may no longer be covered by the federal privacy regulations.

WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION

The main reason for using and sharing your Protected Health Information is to conduct and oversee the research as described in this Informed Consent Document. We also shall use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to:

Maureen Chase, MD, MPH
Beth Israel Deaconess Medical Center
Department of Emergency Medicine
1 Deaconess Rd, WCC2
Boston, MA 02215

Please be aware that the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter.

REFUSAL TO SIGN

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If you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

NOTICE OF PRIVACY PRACTICES

In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

WHOM TO CALL IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns, or complaints about this research or experience any problems, you should contact Dr. Chase at (617)754-2341.

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

ICF REVISION DATES:

Composed 1/9/2013
03/01/2013,, 06/25/2013, 10/11/2013, 11/29/2013, 01/14/2014, 06/10/2014,09/17/2014, 02/06/2015, 07/01/2015, 09/22/2015, 12/30/2015, 02/03/2016

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THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

_____ _____

Signature of Subject or Legally Authorized Representative (Parent if the subject is a minor) — Date

_____

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

_____

SIGNATURE OF INVESTIGATOR/Co-Investigator DATE

_____

PRINT INVESTIGATOR'S/Co-Investigator's NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.

THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE

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UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Signature of Interpreter: _____

Printed name of Interpreter: _____

Date: _____