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JANUARY 24, 2019

INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

NAME OF SPONSOR COMPANY:	Pfizer Inc
NUMBER AND NAME OF STUDY:	B7921028; "A PHASE I, OPEN LABEL, FIXED SEQUENCE STUDY TO EVALUATE THE STEADY STATE PHARMACOKINETIC DRUG-DRUG INTERACTION BETWEEN PF-06650833 AND PF-06651600 IN HEALTHY ADULT PARTICIPANTS"
NAME OF PERSON IN CHARGE OF THE RESEARCH STUDY (STUDY DOCTOR/INVESTIGATOR):	Haq Nawaz, M.D.
TELEPHONE NUMBER 24 HOURS:	203-401-0300

INTRODUCTION

You are here today as a possible subject in a drug research study sponsored by Pfizer Inc. Whether or not you are in this study is strictly up to you. You may refuse to take part in this research study. The study staff will be available to answer questions before, during, and after the study.

The sponsoring company (the company paying for this study), Pfizer Inc, employs the study investigator conducting this study.

If you are not completely honest about your health history, you may be harmed by being in this study.

INFORMATION ABOUT THE STUDY DRUGS

PF-06650833 and PF-06651600 will be referred to as "the study drugs" in the rest of this document.

The study drugs are new investigational drugs. They are being studied to treat people with inflammatory conditions and diseases. This includes:

- Alopecia areata (bald patches)
- Vitiligo (loss of skin pigment)
- Rheumatoid arthritis (RA)
- Inflammatory bowel disease
  - Ulcerative colitis
  - Crohn's disease

"Investigational" means that the drugs have not been approved by the United States (US) Food and Drug Administration (FDA).

The doses of the study drugs to be used to treat diseases in people have not yet been determined.

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PF-06650833

Single doses of this study drug up to 6000 mg were well tolerated in healthy subjects. Multiple dose studies in healthy subjects have also been done. Doses up to 1,000 mg four times a day for up to 14 days in healthy subjects, and 400 mg once daily for up to 12 weeks in patient with rheumatoid arthritis have been given. Doses were generally well tolerated.

PF-06651600

Single doses of up to 800 mg and multiple doses of up to 400 mg a day for 14 days and 200 mg daily for up to 3 months have been given to healthy subjects. This study drug was well tolerated.

THIS STUDY WILL BE THE FIRST TIME THAT BOTH OF THESE STUDY DRUGS WILL BE GIVEN TOGETHER TO HUMANS.

In this document, you may see the terms "medication", "treatment", and "treatment period". These are terms used in research studies. This does not mean that you will be receiving medical treatment for any condition. These terms apply to the investigational study drug and parts of the study where you will be receiving this investigational product.

The current study has 2 periods. One group of up to 15 completed subjects is planned. If you are accepted into the study, you will receive:

- A single oral (by mouth) 400 mg dose of PF-06650833 once a day for 5 days in Period 1
- A single oral 100 mg dose of PF-06651600 once a day for 12 days (Days 1 through 12) in Period 2 In addition, on Days 8 through 12 of this period, you will also receive a single oral 400 mg dose of PF-06650833

The study investigator or sponsor may decide to remove you from the study at any time if it seems you are having a significant reaction to the study drug or you fail to follow the protocol requirements.

PURPOSES OF THE STUDY

There are 5 purposes of this study:

1. To evaluate the effects of multiple oral doses of PF-06651600 on the blood levels of multiple doses of PF-06650833 in healthy adult participants
2. To evaluate the effects of multiple oral doses of PF-06650833 on the blood levels of multiple doses of PF-06651600 in healthy adult participants
3. To see how the two new drugs under study are tolerated, if there are significant side effects, and how healthy adult participants feel after taking multiple oral doses when given alone and together
4. To collect exploratory samples for biobanking
   - Biobanking is the collection and storage of blood samples for possible future testing
5. To explore the blood levels of metabolites of PF-06650833 (PF-06787899 and PF-06787900)
   - Metabolites are byproducts or end products of a drug produced as your body processes it

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HOW LONG THE STUDY WILL LAST AND HOW MANY PEOPLE WILL BE IN THE STUDY

You will be in this study up to about 59 days. This does not include the time between screening and dosing, which can be up to 28 days.

This study involves:

- 2 dosing periods (2 separate admissions)
- 19 overnight stays
  - 6 nights for Period 1
  - 13 nights for Period 2
- 1 follow-up phone call (between 28 and 35 days after the last dose of study drug in period 2)

There will be at least 7 days between the last dose in Period 1 and the first dose in Period 2.

WHEN ARE YOU ELIGIBLE TO PARTICIPATE IN ANOTHER DRUG STUDY?

The decision for when you are eligible to screen for another study is based on information from the previous studies, ongoing studies, and this study. You may be eligible to dose in another study as soon as 30 days after the last dose of study drug. This information is true for most drugs. Some drugs may be present in your body longer and that may mean you may have to wait longer before entering into another study. These results are usually known after your last regularly scheduled blood sample is tested. We will always tell you this as soon as possible. We will let you know if there is a longer than usual period of time that you should not be in another drug study after this one. Our goal is to keep you from doing anything that might potentially harm you. Your safety while in these studies is our main concern.

TO BE IN THE STUDY

You cannot screen for this study if you are currently in another research study. This includes being in the follow-up visit period of another research study.

To be in this study, your medical history and screening test results must be acceptable. Also, you must meet each of the following conditions:

- You must be a healthy male or female between the ages of 18 and 55 at the time of signing this informed consent document
- Females subjects must not be pregnant or breastfeeding
- Males and females (who can have children) must be willing to follow birth control requirements listed later in this document
- You must be willing and able to comply with scheduled visits, the study plan, lab tests, lifestyle requirements and other study procedures
- You must have a Body Mass Index (BMI) between 17.5 and 30.5 and weigh more than 50 kg (110 lbs)
- You must be capable of giving signed informed consent and complying with the requirements and restrictions listed in this consent form
- You must not have evidence or history of blood, kidney, glandular, lung, stomach, intestine, heart, blood vessel, liver, psychiatric, nerve, skin or allergic disorders (including drug allergies)
  - Untreated seasonal allergies without symptoms are allowed

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- You must not have any condition that might affect your body's ability to absorb drugs (for example, gastric bypass surgery or gall bladder removal)
- You must not have a known immune system disorder, including a positive blood test for human immunodeficiency virus (HIV – the virus that causes acquired immune deficiency syndrome [AIDS]) at screening or a first degree relative (immediate family) with an inherited immune system disorder
- You must not have an infection with hepatitis B or C viruses, which will be determined through blood tests at screening
- You must not have had any infection requiring treatment within two weeks of screening
- You must not have had any infection requiring hospitalization or intravenous (IV – through a vein) treatment within 60 days before the first dose of study drug
- You must not have had any infection judged to be an opportunistic infection (an infection that happens because of a weakened immune system) by the study investigator within 6 months before the first dose of study drug
- You must not have a known currently active, or history, of recurrent (happens often or repeatedly) bacterial, viral, fungal, mycobacterial (for example tuberculosis [TB]), or other infections
- You must not have a history of recurrent, localized (restricted to a particular place) herpes zoster (shingles) or history of a single episode of herpes simplex or herpes zoster in more than one place on your body
- You must not have a history of a fever within 5 days of the first dose of study drug (in both periods)
- You must not have a history of any disorders involving a rapid increase in the size of the lymph nodes and/or the number of lymphocytes (a type of white blood cell) such as related to Epstein Barr Virus (EBV), lymphoma (cancer of the lymph nodes), history of leukemia or signs or symptoms suggestive of a current disease of the lymphatic system or lymphoid disease
- You must not have a known present, or history of, a cancer other than a successfully treated or excised (removed) non-metastatic (did not spread) basal or squamous cell skin cancer, or cancer that started and remained in the cervix
- You must not have benign ethnic (cyclic) neutropenia (a low neutrophil [type of white blood cell] count sometimes found in people of African descent)
- You must not have received any live vaccines within 6 weeks before the first dose of study drug
- You must not have any medical or psychiatric condition, including recent (within the past year) or active suicidal thoughts or behavior, or lab abnormality that could increase your risk of being in the study or receiving the study drugs
    - You must not have any condition or lab abnormality that could interfere with the interpretation of the study results and, in the judgment of the study investigator, make you an inappropriate subject for this study
- You may not take any prescription or non-prescription drugs, nutritional (dietary) or herbal supplements for at least 7 days before the first dose or at any time during this study
- Tylenol® (acetaminophen) may be used at doses of less than or equal to 1,000 mg a day
    - Its use must first be approved by the study investigator
    - Other non-prescription medicines that are not thought to affect your safety or the overall study results may be allowed on a case-by-case basis if first approved by the study investigator
- You must not have taken any investigational drugs for at least 30 days before the first dose of this study
    - You must not be in another drug study at any time during this study
- You must not have been in a previous study with either of the study drugs
- You cannot be in this study if you are using/taking any drugs of abuse. A urine test will be done to check for drugs of abuse

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- While on this study please do not eat anything that contains poppy seeds, as they may cause a positive drug test
- Your screening blood pressure while lying down must be less than or equal to 139/89 mm Hg
- Your screening ECG (electrocardiogram that measures the electrical activity of the heart) must be normal
- You must not have any significant laboratory test abnormalities
- You must not have evidence of untreated or inadequately treated active or latent (present but not active) TB infection
  - If you are being treated for a latent TB infection, you may not be in the study
- You must not have a history of excessive alcohol use or binge drinking within 6 months before screening
  - Binge drinking is a pattern of 5 (males) or 4 (females) or more alcoholic drinks in about 2 hours
  - You must not drink more than 14 alcoholic drinks a week
  - A drink is defined as 8 oz. of beer, 3 oz. of wine, or 1 oz. of hard liquor
- Study staff may check your breath for the presence of alcohol. If alcohol is detected, you will not be allowed to be in this study
- You must not use tobacco or products with nicotine in an amount greater than the equivalent of 5 cigarettes per day
- You must not have a history of major organ transplant or stem cell/bone marrow transplant
  - Skin grafts are acceptable
- You must not have taken medications that inhibit or induce (direct) certain enzymes in the body within 28 days of the first dose of study drug
  - The study staff will review a list of these types of medications with you
- You must not have donated (such as at a blood bank) a unit of blood (except plasma donations) for at least 60 days before dosing
- You must not donate any blood or blood products at any time during this study and for at least 4 weeks after your last blood draw
- You must not have a history of sensitivity to heparin (a substance that stops blood from clotting) or of low platelets as a result of heparin
- You must be willing and able to comply with the activity and diet restrictions of the study (detailed later in this document)
- You must not be a staff member of the Clinical Research Unit (CRU) directly involved in the study, a relative of a staff member at the CRU directly involved in the study, a staff member of the CRU supervised by the study investigator, or a Pfizer employee, including family members, directly involved with the study

WHAT WILL HAPPEN DURING THE STUDY

<u>Screening</u>:

Before the study starts, you will be asked to:

- Sign this consent form
- Review the study entry criteria
- Give your drug, alcohol, and tobacco use history
- Give your race, age, gender, and ethnicity
- Give your medical history

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  - If you are not completely honest with your medical history, you may be harmed by being in this study
- Tell the study staff if you have taken, in the past 28 days before the first dose any over-the-counter or prescription drugs, vitamins or dietary or herbal supplements
- Review use of birth control

As part of screening you must complete all of the items listed below:

- Vital signs (blood pressure and heart rate while lying down)
- Body temperature
- Height and weight
- Safety lab tests (blood and urine)
  - Includes blood tests for HIV, hepatitis B, hepatitis C and TB
- Urine to test for drugs of abuse (illegal and prescription)
  - If this test is positive, you will not be allowed in the study
  - Urine collection may be monitored by a staff member of the same sex
  - You have the right to refuse to be monitored, but may be disqualified from the study
- The study investigator may decide to do an alcohol breath test
- ECG
- Complete physical exam. This may be done at screening or when you check-in for Period 1 of the study
- You will be asked "How do you feel?"
- Females able to have children will have a blood pregnancy test
- Females who have not had a period for at least 12 consecutive months will have a blood hormone test that will confirm they cannot have children

HIV, Hepatitis and Tuberculosis Testing

As required by this study and if anyone is exposed to your blood, you will have your blood tested for the hepatitis viruses, tuberculosis (TB) and for HIV. HIV is the virus that causes AIDS. If you have a positive HIV or hepatitis test, you cannot be in/remain in the study.

If the HIV test is positive, a follow-up test will be done. If the follow-up test is also positive, you will be told in private and you will also be told about counseling.

It may take weeks or months after being infected with HIV for the test to be positive. The HIV test is not always right.

Positive results for HIV, TB or hepatitis tests or for other infections, or possibly having certain infections, may have to be reported to the State Department of Health. If you have any questions about what information is required to be reported please ask the study investigator or study staff.

Although this testing is intended to be private, complete confidentiality cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

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During the Study:

During the study you will complete all of the items listed below:

- Before being brought to the second floor of the clinic for each of your in-house stays, your belongings will be thoroughly searched
  - You will be asked to empty your bags and set all of your belongings on the table so the staff can go through them
  - You will be asked to empty your pockets, remove your shoes and hat, if you are wearing one, and you will be patted down
  - You will be scanned with a metal detector wand
- Review the study entry criteria (Period 1 only)
- Updates to your medical history, including drug, alcohol, and tobacco use (Period 1 only)
- Updates in any medications used since screening/previous admission
- Blood and urine samples will be collected at various times throughout the study
  - The blood and urine samples will be used for safety labs
  - Blood samples will also be used to measure the levels of study drugs in your blood and levels of metabolites of PF-06650833
    - As part of understanding how your body absorbs, distributes, and gets rid of the study drugs, the samples may also be used to evaluate safety or efficacy (ability to produce a desired effect) aspects related to any concerns during or after the study, for additional metabolite identification and/or evaluation of the laboratory test(s) used to measure the study drugs, as well as for other internal exploratory purposes
- A sample of your blood will be collected and sent to Pfizer's biobank. Pfizer calls this sample a "Banked Biospecimen"
  - This sample will be used to study biological substances in your sample, including your genes. This will help us learn more about the study drugs
    - This sample may be kept by Pfizer in a facility approved by Pfizer for as long as the sample is useful for scientific research. This may be for many years (no time limit)
- A sample of your blood will be collected before the first dose in Period 1 for viral screening
  - This sample will be stored and may be tested at a later date if certain cases of viral infection are suspected during the study
- Females able to have children will have a blood pregnancy test done at each study check-in and at the end of the study
  - Pregnancy tests may be performed at the discretion of the study investigator in all females
- Urine samples to test for drugs of abuse will be collected at the time of each study check-in and may be done at various times throughout the study
  - If this test is positive, you will not be allowed to continue in the study
  - Urine collection may be monitored by a staff member of the same sex
  - You have the right to refuse to be monitored, but may be disqualified from the study
- The study investigator may decide to do an alcohol breath test at check-in and at any time during the study
- A complete physical exam will be done at study check-in (Period 1 only), if it was not done at screening
  - A brief physical exam may be done at various times throughout the study at the discretion of the study investigator
- The use of proper birth control will be confirmed at each study check-in and discharge from the CRU and during the follow-up phone call

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- Blood pressure and heart rate will be measured while you are lying down at various times throughout the study
- Body temperature will be measured at various times throughout the study
- You will be asked "How do you feel?" each day
- An IV catheter may be placed in a vein in one of your arms for blood collection
- ECGs (single measurements) will be done at various times throughout the study
  - It may be necessary to shave your chest so that the patches for the ECGs will stick to your skin
  - Your chest may be marked with a pen to identify the correct areas for ECG patch placement
- You will receive a follow-up phone call between 28 - 35 days after the last dose of study drugs in period 2

A. **Dosing Schedule**:

Dosing is planned as follows:

NUMBER OF SUBJECTS	**STUDY PERIOD**		
15	**1**	**2**	
	STUDY DAYS	**STUDY DAYS**	
	1 - 5	**1 - 7**	**8 - 12**
	PF-06650833, 400 mg once a day	PF-06651600, 100 mg once a day	PF-06651600, 100 mg + PF-06650833, 400 mg once a day

PF-06650833 will be given as two, 200 mg tablets
PF-06651600 will be given as two, 50 mg tablets

On each dosing day, you will receive the study drug(s) after an overnight fast (nothing to eat or drink except water) of at least 10 hours.

Each dose will be taken with about 8 ounces of water and must be swallowed whole. In Period 2 when you are receiving both study drugs, you may receive additional water (up to a little more than 3 ounces), if needed. We will check your mouth after each dose to make sure the study drug(s) has/have been swallowed.

On the days when you are receiving both study drugs, they will be given at the same time (no more than 5 minutes apart).

There will be at least 7 days between the last dose in Period 1 and the first dose in Period 2.

Both you and the study staff will know which of the above you are receiving.

This is a research study. The study drugs will be given to you only during this study and not after the study is over.

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B. Blood Samples:

During the study, blood samples will be taken by individual needle-sticks or by a catheter put directly into a vein in your arm. The catheter procedure consists of putting a small tube in your arm to take blood when required. Catheters are used at the judgment of the study investigator or when required by the study plan. They are not used at the request of the subject.

There will be about 41 blood draws. The total amount of blood drawn during the study will be about 230 mL. This is equal to about a little more than 7½ ounces or a little less than 1 cup. For comparison, the standard blood donation is about 16 ounces (two cups), once in any 56-day period.

As with all studies with blood draws, adequate rest and good eating habits are recommended.

YOUR RESPONSIBILITIES

Activity Restrictions:

- You will be confined to the CRU for 6 days starting with check-in during Period 1 and for 13 days starting with check-in for Period 2
  - If a prolonged drug effect is noted and your safety is a concern, you may need to remain in the CRU longer
  - The study investigator or study staff will decide when you can leave the CRU
- You must not do any strenuous exercise (for example, heavy lifting, weight training, calisthenics or aerobics) for at least 48 hours before each blood collection for safety labs
  - Walking at a normal pace is allowed
- You must call the CRU at the 24-hour phone number listed on the first page of this consent form for approval before taking any drugs other than the study drug(s)
  - You must report all such drugs taken during the study to the study staff
- You must not use tobacco- or nicotine-containing products for at least 24 hours before the start of dosing and while confined to the CRU
- Lying down is not allowed for 4 hours after dosing on study day 5 in Period 1 and study days 7 and 12 of Period 2 unless needed for any study assessments

Diet Restrictions:

- You must not eat or drink anything, except water, for at least 4 hours before each safety laboratory test
- You must not eat or drink anything, except water, for at least 10 hours before collection of all pre-dose blood samples for study drug(s) and dosing, and for 4 hours after dosing on study day 5 in Period 1 and study days 7 and 12 in Period 2
- You must not eat or drink anything with alcohol 24 hours before each check-in and while confined to the CRU
  - You must not drink red wine from 7 days before the first dose through collection of the last blood sample for study drug
- You must not eat or drink anything with caffeine from 24 hours before the start of dosing and while confined to the CRU
  - Food and beverages with caffeine include, but are not limited to, chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®

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- You must not eat or drink anything containing grapefruit or grapefruit related citrus fruits (for example, Seville oranges, pomelos, fruit juices) from 7 days before the first dose through collection of the last blood sample for study drug
  - Breakfast will not be given on study day 5 in Period 1 and study days 7 and 12 in Period 2
  - Breakfast will be served about 30 minutes after dosing on all other study days
- Lunch will be served about 4 hours after dosing
- Dinner will be served about 9 – 10 hours after dosing
- Evening snacks may be allowed at appropriate times

POSSIBLE SIDE EFFECTS AND RISKS OF THE STUDY DRUGS AND PROCEDURES
STUDY DRUGS

This is the first time these study drugs will be given to people together.

PF-06651600

Frequently Reported Negative Effects

The study drug has been studied in the following:

- Healthy subjects (in single doses up to 800 mg and multiple doses up to 400 mg daily for 14 days)
- Subjects with RA (at a dose of 200 mg daily for 8 weeks)
- Subjects with alopecia areata (at a starting dose of 200 mg daily for 4 weeks, followed by a maintenance dose of 50 mg daily for 20 weeks)

In all those studies, the study drug was generally safe and well tolerated. There are also ongoing studies of the study drug in subjects with:

- Ulcerative colitis (a disease due to colon inflammation)
- Crohn's disease (a disease due to colon inflammation)

The negative effects that were reported in more than 5% (1 in 20) subjects with alopecia areata receiving the study drug for up to 20 weeks were:

- Headache
- Infections of the upper respiratory tract
- Acne
- Diarrhea
- Nausea
- Skin infections

Reactivation of Viruses

Certain viruses can be stored in the body and they may reactivate (wake up) and cause negative effects. In studies with the study drug or other similar medications, reactivation of the chicken pox virus (herpes zoster) has caused shingles (a painful or burning skin condition). Reactivation of the herpes simplex virus has caused cold sores or fever blisters in the mouth or genital ulcers. We don't know if the study drug or other similar medications could lead to the reactivation of hepatitis viruses. You will not be allowed to be

in the study if your blood tests show that you have had hepatitis types B or C viruses, or if you have a history of frequent herpes virus infections (for example cold sores or genital herpes) or frequent widespread episodes of shingles. During the study, call the study investigator right away if you think you may have:

- Shingles
- Ulcers in the genital area
- Cold sores

Serious or Unusual Infections

The study drug is a drug that affects your immune system. It can lower the ability of your body to fight infections. This can lead to more serious infections or infections that usually don't occur in people with a normal immune system. Some people have had serious infections or unusual infections while taking the study drug or other similar medications. You should not start taking the study drug if you have any kind of infection. After starting the study drug, tell the study investigator right away if you have any symptoms of an infection. Symptoms of an infection could include:

- Fever
- Weight loss
- Excessive tiredness
- Other symptoms specific to the site of infection, such as a persistent cough

The study drug can make you more likely to get infections or make any infection that you may already have worse.

Cancer

The study drug may increase the risk of certain cancers by changing the way your immune system defends against cancer. Lymphoma and other cancers, including skin cancers, have been reported in patients taking medications that work in a similar way to the study drug. Most people with a history of cancer will not be eligible for this study, except for those who have had:

- Successfully treated skin cancers that were not the melanoma type
- Successfully treated local cancer of the cervix (the lower part of the uterus)

Tell the study investigator if you have had any type of cancer.

Changes in Certain Laboratory Test Results

Some changes in blood tests that have occurred in earlier studies with the study drug are described below. Your blood will be tested before you start taking the study drug and while you are taking it. You will be discontinued from the study if your blood counts drop to a level which would cause concern for your continued participation in the study.

- Decreases in lymphocyte counts. Lymphocytes are white blood cells that help the body fight off infections. If your lymphocytes are low, you might be more likely to have an infection

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- Changes in neutrophil counts. Neutrophils are white blood cells that help the body fight off infections. If your neutrophils are low, you might be more likely to have an infection
- Decreases in platelet counts. Platelets are blood cells that help blood to clot. If your platelets are low, you might be more likely to bruise or bleed. Although bleeding or bruising related to low platelets has not been seen in previous studies with the study drug, there is still a potential risk that this could happen
- Changes in other laboratory tests, such as your blood cholesterol or hemoglobin (red blood cells) levels may also be seen

Skin Effects

Rash and acne have been seen in studies with the study drug. The majority of events were reported as mild or moderate. It is not known if the study drug causes these skin effects. During the study, you should tell the study investigator if you notice any changes on your skin.

Other Effects:

Studies have been done in animals to identify risks that may occur in people that are given the study drug. In studies with dogs, microscopic changes (changes so small as to be seen only with a microscope) in nerves were seen after 9 months of taking doses more than 7 times higher than the dose that will be used in this study (100 mg daily). After 7 months, at even higher doses (more than 15 times higher than the 100 mg dose), a few dogs had hearing loss. All the microscopic changes and hearing loss got better after stopping the drug. Because the dog findings occurred only at doses much higher than will be used in this study, it is unlikely that there are related human risks from the study drug at the doses used in this study. If you develop any changes related to the nervous system, you should tell the study investigator. You may be referred for additional evaluation by a doctor specializing in diseases of the nervous system.

Animal studies do not always predict the side effects people may experience.

PF-06650833

This study drug is a new class of drug. There are no similar drugs already approved that could provide information about its potential safety.

The safety of this study drug for use in the current study is supported by 4 completed studies done in healthy subjects. A total of 139 subjects have been enrolled in these studies. One or more doses have been received by 122 subjects. These studies were up to 14 days in length.

The use of PF-06650833 in this study is further supported by safety data from

- Studies conducted in animals (up to 3 months in length)
- An ongoing study in Rheumatoid Arthritis patients

Overall, this study drug has been generally safe and well tolerated in the doses given to people. The most common side effects reported in healthy subjects have been:

- Headache
- Abdominal pain

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- Nausea
- Vomiting

These side effects have been reported to be mild or moderate in severity. In most cases, they got better without specific treatment. To date, no maximum tolerated dose of this study drug has been identified.

One subject in one of the highest dose groups in the multiple dose study was discontinued due to a variety of gastrointestinal (involving the stomach and intestines) side effects including:

- Nausea
- Vomiting
- Abdominal pain
- Loss of appetite

None of the other subjects in the highest dose group had similar side effects or other signs of not being able to tolerate this study drug.

One subject in the highest dose group in the multiple dose study was discontinued for low neutrophil counts. Neutrophils are a type of white blood cell that helps the body fight infection. Very low numbers of these cells may increase the risk of infection. This subject had low numbers of neutrophils at the time of entry into the study. The subject did not develop persistently low enough numbers to greatly increase the risk of infection. This subject may have had a condition associated with low levels of neutrophils that is a variant of normal. This would not be associated with any increase in the rate of infection. White blood cell counts, including neutrophils, will be checked in this study.

Increases in blood levels of certain liver enzymes have been seen in a few subjects in the single and multiple dose studies in healthy subjects. Liver enzymes are an indication of how the liver is working. These increases were not associated with any symptoms. Blood levels returned back to normal during or shortly after the completion of dosing without treatment. No subjects showed signs or other laboratory tests suggesting liver injury. Increases in blood levels of liver enzymes may be a sign of liver injury. This is especially true when accompanied with other signs that the liver is not working properly. Liver function will be checked with blood tests in this study.

The study drug may cause an unusual type of crystals (particles like grains of salt) to be found in the urine. This is based on data from studies in humans and animals (rats). In humans, crystals have been seen occasionally in the urine in some subjects, particularly at the highest doses tested in the multiple dose study. The occurrence of these crystals has generally been intermittent (that is, not seen on 2 tests in a row) and unpredictable. In most cases, only a few crystals were seen when the urine is looked at under a microscope. In a few cases, at much higher doses than will be used in this study, higher numbers of crystals have been seen. Subjects have not reported any unfavorable side effects with these crystals. Subjects have generally not been aware that they had crystals in their urine. There have been no signs of harmful effects on kidney function at any dose or amount of crystals. Based on chemical testing, these crystals are likely made up of this study drug and/or byproducts of this study drug. Many types of crystals may normally be found in the urine. Not all the unusual crystals seen in subjects in clinical trials with this study drug have been related to study drug. Some subjects have been on a placebo (contains no active drug). Preliminary (new) data from the study in RA patients showed that crystals in the urine were seen in only a very small number of subjects.

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Crystals have also been seen in safety studies in rats given this study drug. In rats receiving very high doses for 3 months, harmful effects to the kidney, including kidney failure, have been seen. These may be related to deposits of crystals in the kidneys. Together, these findings suggest that:

- At very high exposures (blood levels), this study drug can cause the urine crystals
- Prolonged high blood levels of this study drug may have the potential to cause harmful effects in the kidney

There are several marketed drugs that may produce crystals in the urine, and have been associated with drug-induced kidney injury. Clinical experience with these suggests that the risk of kidney injury may be decreased by avoiding dehydration. This can be done by drinking adequate amounts of water. If caught early, harmful effects on the kidney may get better once off the drug. To reduce the chance of developing kidney injury, doses of the study drug in this study will keep blood levels below the level at which kidney injury was seen in animals. The dose in this study is not likely to cause repeated, successive episodes of high amounts of urine crystals. You will be encouraged to drink plenty of fluids. You will also be checked closely with physical exams, and blood and urine tests for the development of urine crystals and/or kidney injury.

One additional early clinical study in 24 healthy subjects has recently been completed. No new side effects was observed.

The study drug was also given to RA patients in an ongoing study to see if the study drug could be an effective treatment for RA, and to get information on its safety and tolerability in RA patients. A total of 269 patients participated in the study and 187 subjects received study drug up to 3 months. The most common side effects were:

- Infections including respiratory tract infections
- Stomach and intestine-related side effects (e.g. nausea, vomiting, stomach pain, diarrhea, flatulence and mucous stool)
- Oral herpes (cold sores)

Three patients developed shingles (reactivation of chickenpox virus).One subject developed high levels of liver enzymes that may have been due to study drug. The subject recovered quickly after the study drug and other background drugs being taken for RA were stopped. You will have testing for liver function throughout the study and will have study drug stopped if there are signs of liver test abnormality suggestive of liver injury.

Animal studies (lasting up to 3 months) have been done with much higher doses and exposures (blood levels) of this study drug than given or seen in people. In these animal studies, harmful effects (changes) at high blood levels were seen in the following:

- Kidneys (as described above)
- Heart and blood vessels surrounding the heart
- Skeletal muscle
- Liver
- Gastrointestinal (GI) tract

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The dose in this study is projected to produce blood levels of the study drug no higher than the maximum blood levels at which no side effects (harmful) were seen in animals.

Animal studies suggest that the study drug may increase pulse (heart rate) and/or decrease blood pressure at high exposures. This data suggest that these changes may be the first effects to be noticed in people given high doses of the study drug. In a study done in dogs, high doses of the study drug may have caused a small increase in an ECG measurement known as the QTc interval. The QTc interval is a measure of the heart's rate of recovery from a contraction (beat).

Animal studies do not always predict the side effects people may experience.

Based on studies in healthy subjects, study drug is not known to cause side effects on:

- Blood pressure
- Pulse rate
- Respiratory (breathing) rate
- ECGs (including QTc)
- Physical exam

Your blood pressure, pulse, and ECGs will be checked throughout this study.

The study drug is a drug that affects your immune system. It may lower the ability of your body to fight infections. This can lead to more serious infections or infections that usually don't occur in people with a normal immune system. Harmful effects on the immune system or an increased rate of infections were not seen in animal studies. However, any drug that affects your immune system has the potential to cause an increased risk of infection. You will be screened for infections before starting the study and checked during the study. The following will be done throughout the study:

- Physical exams
- Body temperature
- Safety lab testing
- General questions about how you are feeling

When you take more than one drug at a time, the side effects can be worse or different than if you take either drug by itself.

During the study, if you experience any of the above side effects, contact the study investigator and/or seek medical care. If you do not understand what all of these side effects mean, please ask the study investigator or study staff to explain them to you.

The study drugs are investigational. All of their side effects are not known. There may be rare and unknown side effects. This includes reactions that may be life threatening. It is important that you report all side effects that you experience as soon as they occur, regardless of whether or not you believe they are caused by the study drug.

All drugs have a potential risk of an allergic reaction that, if not treated promptly, could become life-threatening. You should get medical help and contact the study investigator right away if you think you have any of the following symptoms of a serious allergic reaction:

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- Trouble breathing
- Wheezing
- Difficulty swallowing
- Swelling of the face, mouth, lips, gums, tongue or neck

Other allergic reactions may include:

- Itchiness
- Rash
- Hives
- Blisters
- Palpitations (racing heart)
- Chest discomfort/tightness
- Muscle pains/stiffness

At times, the following may also be symptoms of an allergic reaction:

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain

Any subject who experiences a significant side effect during the study may have the following additional procedures done:

- A heart monitor may be attached to the chest for a continuous reading of heart rhythm and rate
- Vital signs, including blood pressure, may be measured often
- A monitor may be placed on a finger to sense the amount of oxygen in the blood
- A catheter may be inserted into a vein in your arm so that you may be given IV fluids and/or medications
- Other tests or treatment may be given as necessary for your safety including, but not limited to, additional blood draws, collection of urine, stool or other bodily fluids
    - Depending on the severity of your symptoms, you may be referred to outside medical providers or a hospital for additional evaluation and/or treatment
    - The study investigator may notify your emergency contact as appropriate in the event of an emergency while you are taking part in the study

If you are not honest about any side effects you have during the study, you may be harmed by staying in the study.

ADDITIONAL RISKS OR DISCOMFORTS

<u>Testing of DNA and/or RNA (</u>deoxyribonucleic acid and/or ribonucleic acid)

Genes are pieces of DNA that, through material called RNA, give instructions for building the proteins that make our bodies work. These instructions are stored in the form of a code. This is the code that you

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inherit from your parents and that you pass on to your children. DNA, RNA, and proteins can be studied as part of genetic research.

This study may involve studying your biology and whether a particular biological feature (including genes) is related to the effects or action of the study drug or to a disease. This may include analyzing all of your genetic information. This is called "whole genome sequencing". Sequencing a gene is like reading a book one letter at a time. This is a very thorough way to learn about genes.

The genetic analysis is for research purposes only. It is not a medical test. This means that the medical importance of the results may not be known. They may not be related to any medical condition.

The results of tests on your samples will not be given to:

- You
- The study investigator
- Any insurance company
- Your employer
- Your family
- Any physician who treats you

If you do not want genetic testing to be done on your samples, you should not agree to participate in the research described in this document.

Pfizer and researchers will put measures in place to minimize the chance that results from this research could be linked to you. There is always a chance that information from your taking part in the research may be disclosed.

Genetic Information Nondiscrimination Act (GINA)

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not ask for your genetic information that we get from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

You should know that this Federal law does not protect you from genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Blood Samples and IV catheter (if used):

Possible side effects of having your blood drawn or an IV catheter inserted into a vein in your arm include:

- Bleeding at the site of the needle puncture

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- Bruising
- Feeling faint
- Rarely infection or blood clot
- Redness of the vein and/or pain

If you feel faint, tell one of the study staff immediately.

Electrocardiogram (ECG):

Possible side effects from having an electrocardiogram include:

- Irritation or rash from the adhesive on the patches

A rash may result in a long lasting discoloration of your skin. If it is necessary to shave the area where the patches need to be, irritation from shaving may occur.

BIRTH CONTROL, DANGERS OF PREGNANCY AND BREASTFEEDING

Birth control methods, even when used properly are not perfect. If you or your partner become pregnant during the study, the study drugs or procedures may involve unforeseeable risks to the unborn baby. If you want to stop your required birth control during the study, you should tell the study investigator immediately. You may be withdrawn from the study if you stop using birth control or you become pregnant.

The effects of the study drug on the following are not known:

- Sperm
- Pregnancy
- Unborn child
- Breast feeding child

In animals, PF-06651600 was linked with fetal changes in bones and some internal organs, and lower fetal body weights. Animal studies in pregnant rats suggest that high exposure of PF-06650833 may cause abnormal fetal development. It is not known whether these study drugs can affect male or female fertility or whether the study drugs can get into human milk.

Because of the investigational nature of the study drugs, they should not be given to pregnant women, breastfeeding women, or fertile women (women able to become pregnant) who are unwilling or unable to use birth control.

PF-06651600 is not likely to transfer to a partner through semen at significant levels; however, men in the study are required to use birth control.

If you are currently pregnant, planning to become pregnant, or breastfeeding a child, you should not join this study. If you are a male whose partner is currently pregnant or who plans to father a child, you should not join this study. If you are pregnant or become pregnant during the study, your unborn baby may be exposed to the study drugs.

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If the chosen method of birth control is changed or discontinued, you should inform us immediately.

Highly effective methods of birth control for this study include:

FOR FEMALES

You must not donate eggs for reproductive purposes during the study through 28 days after the last dose of study drugs.

It is very important that women do not become pregnant during this study. The only sure way to prevent pregnancy is to not have sex. If you are a woman able to have children and choose to have sex during this study, you must use a highly effective method of birth control consistently and correctly from the start of dosing through the duration of the study and for at least 28 days after the last dose of study drugs.

Females able to get pregnant:

ONE of the following methods:

- Non-hormonal intrauterine device (IUD)
- Bilateral tubal occlusive procedure (tubes blocked) / tubal ligation (tubes tied)
- Male partner sterilization (vasectomy with confirmation of absence of sperm)

Abstinence (completely and persistently refraining from all heterosexual intercourse) may be used only if this is your preferred and usual lifestyle.

Females not able to get pregnant:

- Uterus removed, documented
- Both fallopian tubes removed, documented
- Both ovaries removed, documented
- Postmenopausal (at least 12 consecutive months without a menstrual period with no other medical cause and a blood test confirming that you are unable to get pregnant)

FOR MALES

Male subjects must not donate sperm during the study and for at least 28 days after the last dose of study drugs.

Males able to father children must agree to the following requirements during the study and for at least 28 days after the last dose of study drugs:

- No donation of sperm

PLUS either:

- Abstain from having sex with a female partner who is able to have children as your preferred lifestyle

OR

- Agree to use a condom during any activity that may result in the transfer of semen to another person

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- In addition to male condom use, consider the benefit of a highly effective method of birth control (detailed earlier in this section) for a female partner able to have children

Pregnancy Follow-up:

If you or your partner become pregnant during the study or within at least 28 days after you have stopped the study drugs, please tell the study investigator immediately. Please also tell the doctor who will be taking care of you/your partner during the pregnancy that you took part in this research study. The study investigator will ask if you/your partner or your pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. If you/your partner agree, this information will be collected for safety monitoring follow-up.

POSSIBLE BENEFITS OF THE STUDY

You will get no medical benefit from being in the study. Information from this study may benefit persons with inflammatory conditions/diseases in the future.

ALTERNATIVES TO PARTICIPATING IN THIS STUDY

Since this study is for research only, the only other choice would be not to be in the study.

RELEASE OF YOUR MEDICAL RECORDS AND PRIVACY (CONFIDENTIALITY)

The clinic staff will record:

- Your medical history
- The dose(s) you receive
- The results of exams and tests done during the study

Your name will not appear in the study data. Instead you will be identified by a subject-identification number. The information from the study data may be shared with others.
Your clinic records may include:

- Health information about you
- Documents that directly identify you

People from the groups listed below may need to look at your clinic records to make sure that the study information is correct and that the study was run as it should have been.

These reviews may take place during the study or after the study is over.
Your study information may be shared with the following people or groups:

- Pfizer Inc or its representatives, including its auditors and companies it hires to provide study-related services
- IntegReview Institutional Review Board (IRB), the IRB that approved this study, and any other committees responsible for overseeing the research
- Researchers who are conducting this study at other study centers
- Government health agencies (such as the Food and Drug Administration) in the US or other countries

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- Accrediting agencies

People from these groups may get information from your study data. Or, they may review your clinic records. Because of the need to share information with these people, it may not be possible to keep your identity a secret.

Pfizer will use and share your information only for research or legal reasons or to write research reports. In addition, Pfizer may:

- Look at the study data at a later date
- Add your information to information from other studies for other research reasons

However, your name will never appear in any reports, or in any future communication by Pfizer.
By signing this consent form, you agree to allow the use of your study information even after you leave the study.

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.

Please note the following information regarding the delivery of push notifications and text messages:

- The Sponsor, or a company working for the Sponsor, occasionally may send push notifications and text messages using an automated system to remind you of upcoming appointments, study drug reminders and missed doses, or other study-related information
- To discontinue receiving text messages, please contact the Pfizer NHCRU at 800-254-6398
- Standard text messaging rates apply to all text messages. Message rates differ from carrier to carrier, so please contact your wireless phone provider to inquire about the details of your plan
- The contact information you have provided will be used for the sole purpose of communicating with you about the research study
- The push notifications or text messages received through this program may appear on your mobile phone screen as soon as they are received, even when the phone is locked. These messages could be seen and read by others who are near your phone when the message is received

PAYMENT FOR INJURY RELATED TO THE STUDY

If you experience a research injury, the clinic will arrange for medical treatment at no cost to you. Pfizer will cover the costs of this treatment. A research injury is any physical injury or illness caused by being in this study. There are no plans to offer you payment for such things as:

- Lost wages
- Expenses other than medical care
- Pain and suffering

To help avoid injury it is very important to follow all study directions. You can get more information about medical treatment for research injuries from the study investigator or study staff.

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Remember that you must call the study investigator listed on the first page of this consent form immediately if you experience a research injury. A 24-hour answering service is available.

If you are treated for a research injury that is paid for by Pfizer, Pfizer or its representative will collect your Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. If you are a Medicare beneficiary, Pfizer will report the payment and information about the study you are in to the Centers for Medicare & Medicaid Services (CMS), in accordance with CMS reporting requirements. Pfizer will not use this information for any other purpose.

LEGAL RIGHTS

You will not lose any of your legal rights by signing this consent form.

WHOM TO CONTACT

For answers to questions about this research or to report a research related injury, contact:

Haq Nawaz, M.D.
Call the 24- hour Clinic Telephone Number
203-401-0300

If you are unable to reach anyone at the number listed above, and you need medical attention please go to the nearest emergency room.

You will receive a card with information about this study. This information includes:

- The name or number of the study
- The clinic 24-hour phone number

You should keep this card with you in case you have a medical emergency. You can give this card to any doctor or healthcare professional, if they need more information about the research study to provide the best treatment for you.

If you do not want to talk to the study investigator or study staff, if you have concerns or complaints about the research, or to ask questions about your rights as a study subject you may contact IntegReview.

IntegReview's policy indicates that all concerns/complaints are to be submitted in writing for review at a convened IRB meeting to:

Mailing Address:	**OR**	**Email Address:**
Chairperson IntegReview IRB 3815 S. Capital of Texas Highway, Suite 320 Austin, Texas 78704		integreview@integreview.com

If you are unable to provide your concerns/complaints in writing or if this is an emergency situation regarding subject safety, contact our office at:

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512-326-3001 or
toll free at 1-877-562-1589
between 8 a.m. and 5 p.m. Central Time

IntegReview has approved the information provided in this informed consent form and has given approval for the study investigator to do this study. This does not mean IntegReview has approved your personal participation in this study. You must consider the information in this consent form for yourself and decide whether or not you want to be in the study.

PAYMENT FOR BEING IN THE STUDY

Valid proof of a Social Security number is required before any payment is released.

The amount of payment is based on a number of things including the length of the study.

Study payments will be paid in US dollars. Compensation may be provided on a loadable debit card or by paper check. Pfizer New Haven CRU reserves the right to determine method of payment.

You will be paid $175.00 for travel expenses to and from screening. You will receive this payment within 2 weeks of screening. If you test positive for drugs of abuse, or if you leave the screening early, you will not be paid the $175.00. Travel pay for this study has been included in the subject payment. Additional travel pay is not available for this study.

Further, if you test positive for drugs of abuse:

- You will not be allowed to be in this study
- You will not be allowed to be in any future studies
- You will be removed permanently from our active database

The payment for completing the entire study will be up to $5,150.00. If you do not follow instructions your payment may be less.

If we ask you to return for additional tests, you will be paid $250.00 for each trip to the clinic. During times that you are confined to the clinic, you will not be paid more for repeat or added tests.

If you discontinue from the study, or if you are taken out of the study early, you will be paid for the time you completed. You will not be given the study completion bonus if you drop out of the study early.

If total payment by Pfizer is $600.00 or more in a calendar year, your payment will be reported to the Internal Revenue Service in accordance with Federal tax law.

Pfizer may use information resulting from the study or samples collected in the study to develop products or processes from which it may make a profit. There are no plans to pay you or provide you with any products developed from this research. Pfizer will own all products or processes that are developed using information or samples from the research study.

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The decision to admit you into the study is based upon results of pre-study requirements. No one is assured a place in the study until the first dose is complete. Sufficient numbers of subjects will be brought in to be sure we fill the study.

Study Subjects

- If you successfully complete this study, the total amount you will be paid will be up to $5,150.00 ($4,010.00 plus $1,140.00 completion bonus)
- If you do not follow instructions (including those listed in the New Haven CRU House Rules), if you are late for blood draws, or if you miss procedures, your payment will be reduced
- If you choose to leave or are withdrawn from the study before finishing all visits, your payment will be based on how much of the study you completed
    - This pay will be based on $190.00 for each overnight stay (19), $250.00 for each follow-up visit to the clinic (none are planned) and $100.00 per week for the time between the last dose and the follow-up phone call (4 weeks)
- Partial payments may be made during this study. Details will be provided at screening
- A final payment will be provided to you about 2 weeks after you finish the study

Back-up Subjects

- If you are a back-up subject who is required to stay in the CRU overnight, you will be paid $250.00 per night that you stay
- If you are not required to stay overnight, you will be paid $190.00

You will be paid a pro-rated amount based on the extent of your participation if:

- You are not able to complete the study
- You choose to leave the study
- You are withdrawn from the study early by the study investigator for non-safety related issues
- The study is stopped early
- You are qualified but not chosen to participate

YOUR DECISION TO BE IN THE STUDY

Whether you are in this study is entirely up to you. You cannot be forced to be in this study. You may not want to be in this study. You may leave the study at any time without penalty or loss of any benefits. Your future medical care will not be affected. The study investigator, Pfizer Inc, IntegReview IRB, or the FDA may take you out of the study without your permission at any time for the following reasons:

- You do not follow the instructions of the study investigator
- We find out you should not be in the study
- The study is stopped
- The study becomes harmful to your health
- You do not follow the CRU house rules

If you leave the study or if you are taken out of the study for any reason, you may be asked to return to the clinic for a final visit. You may have some end of study evaluations or tests at this visit. This is to

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ensure your safe exit from the study. Also, the data collected to the point of your withdrawal remains part of the study database and may not be removed.

If you are withdrawn from the study, or decide to stop the study, you can ask that any unused samples that were collected be destroyed, by contacting the study investigator. However, your samples may not be able to be destroyed because:

- They may no longer be traceable to you
- They may have already been used
- They may have been given to a third party

ADDITIONAL COSTS

There will be no charge to you for taking part in this study. The study drugs, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

NEW FINDINGS

If there is new information about the safety of the study drugs or changes in the study tests, we will tell you. You can then decide if you still want to be in the study.

THE REASON FOR INSTITUTIONAL REVIEW BOARDS AND INFORMED CONSENT

What is a consent form?
The informed consent document contains information required by federal regulations. The informed consent document must be reviewed and approved by an Institutional Review Board (IRB). You can tell the IRB has approved this study by dated information at the top of each page.

What is an Institutional Review Board (IRB)?
An Institutional Review Board (IRB) is a group of people that reviews research studies. The main goal of this review is to protect the rights and well-being of the human subjects participating in research studies.

IntegReview, the IRB for this study
IntegReview is an IRB. Its board members provide services in the United States, Japan and Latin America.

To meet the requirements of the federal regulations, the IntegReview Board currently includes:

- Doctors
- Pharmacists
- Nurses
- Toxicologist (people who study the harmful effects of chemicals)
- Other specialists
- Others who do not have a background in science or medicine

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AGREEMENT TO BE IN THE STUDY **PIMS # _____**

This consent form contains important information to help you decide if you want to be in the study. If you have any questions that are not answered in this consent form, ask one of the study staff.

By checking each of the following, you are agreeing that the statements below are true:

		Please Check
A.	This consent form is written in a language I understand.	
B.	I understand the information in this consent form.	
C.	I have been given enough time to ask questions and talk about the study.	
D.	All of my questions have been answered completely.	
E.	I think I have received enough information about the study.	
F.	I agree that I was not pressured by the study investigator or the study staff to be in this study.	
G.	I know that I can leave the study at any time without giving a reason and without affecting my health care.	
H.	I know that my health records from this study may be reviewed by Pfizer Inc and by government officials.	
I.	I know that I can't be in another study while I am in this study.	
J.	I have received the HIV, Hepatitis A, B, and C pamphlets and reviewed the information in them.	

IF YOU DID NOT CHECK THE BOX NEXT TO ANY OF THE ABOVE QUESTIONS, OR YOU ARE UNABLE TO ANSWER ANY OF THE ABOVE QUESTIONS, YOU SHOULD NOT SIGN THIS CONSENT FORM.

- You will get a copy of this signed and dated Informed Consent Document for your records
- You agree to participate in this study
- It is your responsibility to tell the study investigator about all changes in your physical or mental health during the study

_____
Printed Name of Adult Study Subject

_____
Signature of Adult Study Subject Date

_____
Printed Name or Initials of Person Explaining Informed Consent

_____
Signature or ALPHA NUMERIC CODE of Person Explaining Informed Consent Date

THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE

VERSION CONTROL
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ADDITIONAL CONSENT REQUEST (OPTIONAL)

USE OF BIOLOGICAL SAMPLES FOR ADDITIONAL RESEARCH

Pfizer would like your permission to use some or all of the samples collected in this study for additional research that may or may not be related to the study. This additional use of your samples is called "**Additional Research**".

This Additional Research is optional and you do not have to agree. You may take part in the study and contribute samples for use in the study even if you do not want your samples to be used for Additional Research.

If you decide to take part in this Additional Research, you do not have to provide any new samples. Researchers will use samples that already have been collected during the study.

There is no penalty or change to your regular medical care if you decide not to take part in this Additional Research.

1. What is the purpose of this Additional Research?

The aim of this Additional Research is to use these biological samples and the information obtained from them to understand diseases and to advance science. This includes the development of other medicines or treatments.

- This Additional Research might involve learning more about your biology. It may involve studying biological substances in your sample(s), including your genes.
- The Additional Research might include exploratory research of any disease or condition.

2. What are the possible risks of this Additional Research?

There is always a chance that information from your taking part in the Additional Research may be disclosed. Pfizer and researchers will put measures in place to minimize the chance that results from this Additional Research could be linked to you.

The testing of DNA and/or RNA risks language in the consent document for the study applies to this Additional Research.

3. What are the possible benefits of this Additional Research?

This Additional Research is for research purposes only. There is no direct benefit to you from taking part. Information from the Additional Research may help other people in the future and help in the development of new medicines or treatments.

4. What if I agree to this Additional Research and then change my mind?

You can change your mind at any time about allowing your biological samples to be used for this Additional Research. Your decision will not affect your regular medical care or any benefits to which you are entitled. Tell the study investigator if you would like to end your participation in the Additional Research.

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5. What will I have to pay for if I take part in this Additional Research?

There will be no charge to you for allowing your samples to be used for this Additional Research.

6. Will I be paid if I consent to this Additional Research?

You will not be paid for taking part in this Additional Research. Pfizer may use information from this Additional Research to develop products or processes, from which Pfizer could make a profit. There are no plans to pay you or provide you with any products developed from this Additional Research. Pfizer will own or have rights to all products or processes that are developed using information from your samples.

7. What will happen to my personal information?

All information concerning the confidentiality, use, and disclosure of your information contained in the main consent for the drug study applies to this consent as well.

Biological samples will be handled in a manner that protects your privacy and confidentiality. Biological samples will be assigned your study identification code (ID) at the site. The data generated from these biological samples will also be labeled with this ID. The key between your ID and your direct personally identifying information (for example, name and address) will be held at the study site.

It is possible that results from the Additional Research may be included in:

- Further applications to government agencies to market other medicines or devices
- Ethics committees/IRBs involved in research

Pfizer may share the samples and data from the samples with third parties in order to perform the Additional Research described above. The third parties may include other researchers and collaborators at institutions and companies.

8. Where can I find additional information about this Additional Research or the results of this Additional Research?

It may not be possible to link the results of the Additional Research to individuals, including you. Pfizer does not plan to give any information generated during the Additional Research to:

- You
- The study investigator
- Your personal doctor
- Your family
- Your employer
- Any insurance company

9. Contact Information

The study team will answer your questions or concerns regarding the Additional Research. The consent document for the study provides contact information if you need to reach the study team or wish to speak with someone not involved with the Additional Research.

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10. Decision to Participate in Additional Research

Below please check the box next to your choice regarding whether to take part in the Additional Research. Thank you for considering whether to participate.

□ I agree to allow my samples to be used for Additional Research for those purposes described above.

OR

□ I do NOT agree to allow my samples to be used for Additional Research for those purposes described above.

Signatures

- I have read and understand this Additional Consent Request.
- I have had enough time to ask questions and decide whether or not to participate.
- I understand that taking part in the optional uses described in this Additional Consent Request is voluntary.
- I do not give up any of my legal rights by signing this consent document.
- I have been told that I will receive a signed and dated copy of this document.

_____
Printed Name of Adult Study Subject

_____
Signature of Adult Study Subject Date

_____
Printed Name or Initials of Person Explaining Informed Consent

_____
Signature or ALPHA NUMERIC CODE of Person Explaining Informed Consent Date