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**OCTOBER 11, 2018**

**INFORMED CONSENT DOCUMENT**
**AGREEMENT TO BE IN A RESEARCH STUDY**

| | |
|---|---|
| **NAME OF SPONSOR COMPANY:** | Pfizer Inc |
| **NUMBER AND NAME OF STUDY:** | B3491017**;** "A PHASE 1, RANDOMIZED, OPEN-LABEL, SINGLE ORAL DOSE, THREE-WAY CROSSOVER PHARMACOKINETIC STUDY TO ASSESS THE BIOEQUIVALENCE OF OPTIMIZED SUGAR COATED ADVIL® 200 MG TABLETS VERSUS CURRENTLY MARKETED ADVIL® 200 MG TABLETS IN HEALTHY VOLUNTEERS UNDER FASTED CONDITIONS AND TO ASSESS THE FOOD EFFECT ON OPTIMIZED SUGAR COATED ADVIL® 200 MG TABLETS" |
| **NAME OF PERSON IN CHARGE OF THE RESEARCH STUDY (STUDY INVESTIGATOR):** | Sylvester Pawlak, APRN |
| **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 DRUG**

Advil® will be referred to as "the study drug" in the rest of this document.

The study drug is a marketed over-the-counter drug approved by the United States (US) Food and Drug Administration (FDA). It is used to manage pain and fever. The approved dose for adults is 200 to 400 mg every 4 to 6 hours. The maximum daily dose is 1,200 mg. At these doses, there is a low occurrence of side effects. The dose of study drug in this study will be 200 mg. The study drug will be given as a tablet, which you will swallow.

There will be two forms of the study drug in this study. One form is an Advil® 200 mg tablet the way it is currently manufactured (the reference product). The other is an Advil® 200mg tablet manufactured with a new sugar coating process (the test product). The test product is investigational. "Investigational" means that the drug has not yet been approved by the FDA.

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This study is being done to show that the test product (study drug with the new sugar coating) acts the same way in the body as the reference product (study drug the way it is currently manufactured).

The study has three dosing periods. One group of approximately 42 subjects is planned. There are six treatment sequences. If you are accepted into the study, you will be randomly assigned (like the flip of a coin) to one of the treatment sequences. You will receive two single oral (by mouth) 200 mg doses of the test product study drug. One dose will be given while you are fasting (nothing to eat or drink except water). The other dose will be given with food. You will also receive a single oral dose of 200 mg of the reference study drug under fasted conditions. The order in which you receive each dose will be based on your treatment sequence.

In this document, you may see the terms "medication", "treatment", and "treatment period". These are terms used in research studies as mentioned above. 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 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.

**PURPOSES OF THE STUDY**

There are 4 purposes of this study:

1. To assess the bioequivalence of Optimized Sugar Coated Advil® 200 mg tablets (test product) compared to currently marketed Advil® 200 mg tablets (reference product) under fasted conditions
   - Bioequivalence means that the test product and the reference product have the same effects within and on your body
2. To assess the effect of food on a single oral dose of Optimized Sugar Coated Advil® 200 mg tablet (test product)
3. To measure and compare the amount of study drug in your blood after dosing
4. To see how the test and reference products are tolerated, if there are significant side effects, and how people feel after taking them

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

You will be in this study up to about 23 days. This does not include the time between screening and dosing, which can be up to 28 days.

This study involves:

- 3 dosing periods (during one continuous admission)
- 6 overnight stays
- 1 follow-up phone call (14 to 17 days after the last dose)

There will be at least 2 days between each dose.

Approximately 42 healthy male and female subjects will be in this study.

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**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 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. 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.

The half-life of Advil® is about 2 hours. The half-life of a drug is the time it takes for the amount of the drug in the body to decrease by half. It is expected that very little, if any Advil® will remain in your body after 24 hours.

**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 screening
  - Females may be able or unable to have children
- Females unable to have children must meet one of the following criteria:
  - Postmenopausal (at least 12 consecutive months without a period with no other medical cause and a blood test confirming that you are unable to have children)
  - Uterus and/or both ovaries removed (documented)
  - Medically confirmed ovarian failure
- You must have a Body Mass Index (BMI) between 17.5 kg and 30.5 kg and weigh more than 50 kg (110 lbs)
- You must have signed and dated this consent form
- You must be willing and able to comply with scheduled visits, the study plan, lab tests and other study procedures
- You must not have evidence or history of blood, kidney, glandular (including diabetes), lung, stomach, intestine, heart, blood vessel, liver, psychiatric, nerve, or allergic disorders (including drug allergies)
  - Untreated seasonal allergies without symptoms are allowed
- You must not have any condition that might affect your body's ability to absorb drugs (for example, gastric bypass surgery)
  - This includes a history (within 2 years of screening) of gastrointestinal ulcer or bleeding, paralytic ileus (a blockage in the intestines caused by malfunctioning nerves and/or muscles in the intestines), other gastrointestinal blockage disorders or a bleeding disorder
- 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 drug
  - 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

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- You must not have a history of excessive alcohol use within 6 months before screening
  - Females must not drink more than 7 alcoholic drinks a week
  - Males must not drink more than 14 alcoholic drinks a week
  - A drink is defined as 12 oz. of beer, 5 oz. of wine, or 1.5 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 have taken any investigational drugs for at least 30 days before the first dose in this study
  - You must not be in another drug study at any time during this study
- 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 of the following laboratory test abnormalities:
  - Liver enzymes (indicate how your liver is working) greater than or equal to 3 times the upper limit of normal
  - Total bilirubin greater than or equal to 1.5 times the upper limit of normal, or a direct bilirubin (for subjects with Gilbert's syndrome – a harmless mild liver condition in which the liver does not properly process bilirubin) greater than the upper limit of normal
- 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
- While on this study please do not eat anything that contains poppy seeds, as they may cause a positive drug test
- Female subjects must not be pregnant or breastfeeding
- Male subjects able to father children and female subjects able to have children must be able and willing to use a highly effective method of birth control (detailed later in this document) for the duration of the study through at least 14 days after the last dose of study drug
- You may not take any prescription or non-prescription drugs, nutritional (dietary) supplements, or herbal supplements (including St. John's Wort) for at least 14 days before the first dose or at any time during this study
  - 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
  - Birth control medications (detailed later in this document) are allowed
- 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 (cells that help with blood clotting) as a result of heparin
- You must not have a history or a current positive result for any of the following blood tests: human immunodeficiency virus (HIV), Hepatitis B surface antigen (HepBsAg), Hepatitis B core antibody (HepBcAb), or Hepatitis C antibody (HCVAb)
- 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

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- You must not have smoked or chewed a tobacco-containing product or have used smoking cessation products (including nicotine-containing products) within 6 months of the first dose
  - A urine test will be done to check for cotinine (a by-product of nicotine) at screening and admission to the CRU and must be negative
- You must not have a hypersensitivity to the active ingredient ibuprofen, any other component of the product, aspirin or any other non-steroidal anti-inflammatory drug (NSAID)
- You must not have a history of the syndrome of nasal polyps, angioedema (swelling of the lower layer of the skin and tissue just under the skin or mucous membranes) and bronchospastic (constriction of the air passages of the lung [as in asthma]) reactions to aspirin or any other NSAID
- You must not be using any of the following:
  - Weight loss products, energy products and herbal teas within 14 days before the first dose
  - Caffeine and caffeine/xanthine products (for example, Red Bull®) for 24 hours before dosing
  - Alcohol within 24 hours of admission to the CRU
- You must be willing and able to swallow tablet medications

**WHAT WILL HAPPEN DURING THE STUDY**

**Screening:**

Before the study starts, you will be asked to:

- Sign this consent form
- Give your race, age, gender, and ethnicity
- Review the study entry criteria
- Give your medical history
  - If you are not completely honest with your medical history, you may be harmed by being in this study
- Give your drug, alcohol, and tobacco use history
- Tell the study staff if you have taken, in the 14 days before the first dose of study drug, or are taking any over-the-counter or prescription drugs, vitamins or dietary or herbal supplements
- Review/confirm 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)
- Height and weight
- Safety lab tests (blood and urine)
  - Includes blood tests for HIV, HepBsAg, HepBcAb, HCVAb
- Urine to test for drugs of abuse (illegal and prescription) and cotinine
  - 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?"

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- 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 and Hepatitis Testing**

As required by this study and if anyone is exposed to your blood, you will have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes acquired immune deficiency syndrome. This is known as 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 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.

**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 your in-house stay, 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
- 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 drug in your blood
    - As part of understanding how your body absorbs, distributes, and gets rid of the study drug, the samples may also be used for metabolite identification (by-product(s) or end product(s) of a drug produced as the body processes a drug) and/or evaluation of the laboratory test(s) used to measure the study drug, as well as for other internal exploratory purposes
- All females will have a pregnancy test done at study check-in and at the time of discharge from the CRU
- Urine samples to test for drugs of abuse and cotinine will be collected at the time of check-in and may be collected at various times throughout the study
  - If this test is positive, you will not be allowed to continue in the study

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  - 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 for Period 1, if it was not done at screening
  - A limited physical exam will be done at the time of discharge from the CRU and may be done at various times throughout the study
- The use of proper birth control will be confirmed at study check-in, discharge from the CRU, and during the follow-up phone call
- 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 study check-in
- You will be asked "How do you feel?" each day
- An intravenous (IV) catheter will be placed in a vein in one of your arms for blood collection
- You will receive a follow-up phone call between 14 to 17 days after the last dose

A. Dosing Schedule:

Dosing is planned as follows:

| TREATMENT SEQUENCE | TREATMENT | | |
|---|---|---|---|
| 1 | A | B | C |
| 2 | A | C | B |
| 3 | B | A | C |
| 4 | B | C | A |
| 5 | C | A | B |
| 6 | C | B | A |

Treatment A: Test Product, 200 mg tablet, fasted
Treatment B: Reference Product, 200 mg tablet, fasted
Treatment C: Test Product, 200 mg tablet, fed

You will fast overnight (nothing to eat or drink except water) for at least 10 hours before dosing (fasted doses) or breakfast (fed dose).

Each dose will be taken with about 8 ounces (1 cup) of water and must be swallowed whole. We will check your mouth after each dose to make sure the study drug has been swallowed.

You will be given a high fat breakfast about 30 minutes before dosing in the fed state. The meal must be completely eaten within about 20 minutes. Study drug will be given approximately 10 minutes of completing the meal.

An example of a high fat breakfast includes:

- 2 eggs fried in butter
- 2 strips of pork bacon
- 2 slices of toast with butter

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- 4 ounces of hash brown potatoes
- 8 ounces of whole milk.

By reading and signing this consent form, you are agreeing to eat all the foods like this listed in this breakfast menu.

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

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

B. Blood Samples:

During the study, blood samples will be taken by individual needle-sticks and 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 up to about 56 blood draws. The total amount of blood drawn during the study will be up to about 230 mL. This is equal to about little less than 8 ounces or a little less than 1 cup. For comparison, the standard blood donation is about 16 ounces (two cups), once in any 60-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 7 days starting with check-in
  - 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 drugs
  - You must report all such drugs taken during the study to the study staff
- You must not use tobacco- or nicotine-containing products within 6 months before the start of dosing or while confined to the CRU
- Lying down is not allowed for 4 hours after each dosing unless needed for any study assessments

Diet Restrictions:

- You must not eat or drink anything, except water, for at least 10 hours before each pre-dose blood sample for study drug, and 4 hours after each dose
- You must not eat or drink anything, except water, for at least 4 hours before each safety laboratory test

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- Except for 1 hour before and 1 hour after each dose of study drug, you may drink water freely
  - You may drink water when eating the high fat breakfast
- You must not eat or drink anything with alcohol 24 hours before check-in through the collection of the last blood sample for study drug Period 3
- You must not eat or drink anything with caffeine or xanthine from 24 hours before admission to the CRU through collection of the last blood sample for study drug in Period 3 or until discharged from the CRU
  - Food and beverages with caffeine include, but are not limited to, chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- You must not eat or drink anything containing grapefruit or grapefruit related citrus fruits (for example, Seville oranges, pomelos) including smoothies from 7 days before the first dose through collection of the last blood sample for study drug
- You must be willing to eat all of the food offered on dosing days during the study
- A high-fat breakfast will be given about 30 minutes before dosing when dosing in the fed state
  - Breakfast will not be given on the days you are dosing in the fasted state
- Lunch will be served about 4 hours after dosing
- Dinner will be served about 9 hours after dosing
- Evening snacks may be allowed at appropriate times
- Meals will be provided on the days you are not dosed

**POSSIBLE SIDE EFFECTS AND RISKS OF THE STUDY DRUG AND PROCEDURES**

**STUDY DRUG**
Advil® has been on the market in the United States since 1974.

Advil® should not be taken by patients with any of the following:

- Bleeding disorders
- Cardiovascular (heart and blood vessels) disease
- Peptic ulcer or history of peptic ulcer
- Impaired renal (kidney) function

Side effects include the following:

- Dyspepsia (indigestion)
- Abdominal pain and bloating
- Crohn's Disease (inflammation of the large and small intestines)
- Colitis (inflammation of the lining of the colon)
- Constipation
- Diarrhea
- Flatulence (gas)
- Gastritis (inflammation of the lining of the stomach)
- Gastrointestinal bleeding
- Gastrointestinal perforation (formation of a hole in the stomach, large bowel and/or small intestines)
- Gastrointestinal ulcer
- Vomiting, including vomiting blood
- Bloody stools

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- Mouth ulcers
- Nausea
- Dizziness
- Headache
- Stroke
- Nervousness
- Blood in the urine
- Inflammation of the kidneys or the tubes in the kidneys
- Kidney failure
- Protein in the urine
- Cell death in parts of the kidneys
- Asthma
- Wheezing
- Difficulty breathing
- Tightness in the lungs
- Skin blisters, eruptions and lesions
- Detachment of the skin's outermost layer from the skin layers below
- Swelling of the face
- Rash, including urticaria (rash with round red welts with intense itching and swelling)
- Reddening of the skin with small lumps
- Pruritus (itching)
- Purpura (rash with purple spots from bleeding under the skin)
- Tinnitus (ringing or buzzing in the ears)
- Vertigo (loss of balance)
- Edema (build-up of fluid in the body)
- Meningitis (inflammation of the layers lining the brain, caused by bacteria or without a bacterial cause)
- Decrease in hemoglobin (protein in red blood cells that carries oxygen)and hematocrit (measurement of the number of red blood cells relative to the total volume of blood)
- Blurred vision and other visual defects
- Sensitivity reactions
- Serious allergic reactions
- Liver function test abnormalities
- Hepatitis
- Jaundice (yellowing of the skin and/or whites of the eyes)
- Impairment of renal function
  - Acute (comes on quickly) reversible kidney failure has been reported
- Decrease in granulocytes (a type of white blood cell)
- Leukopenia (decrease in the number of white blood cells)
- Anemia (low red blood cell count)
- Aplastic anemia (decrease in all types of blood cells)
- Decrease in platelets
- Increase in the number of eosinophils (a type of white blood cell that can increase during allergic reactions)
- Stevens-Johnson Syndrome (severe skin reaction)
- Heart failure

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- Heart attack
- Angina (chest pain)

It is expected that the side effects of the test product will be the same/similar to those listed for Advil®.

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.

Because the test product is considered investigational, all of its side effects are not known. There may be rare and unknown side effects, including 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.

This drug can cause drowsiness, blurred vision and vertigo. Until you know how the drug will affect you and/or if you experience these side effects, you should use caution by:

- Avoiding stairs
- Not driving a car
- Not swimming or bathing in a tub
- Not working with machinery or at heights

All drugs have a potential risk of an allergic reaction, which 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:

- 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

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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 administered 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**

Blood Samples and IV catheter:

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
- 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:

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**

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

- Sperm
- Pregnancy

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- Unborn child
- Nursing child

If you are currently pregnant, planning to become pregnant or breastfeeding 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. The effects of the study drugs on an unborn or breastfed baby are unknown and may involve unforeseeable risks.

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 birth control consistently and correctly through the duration of the study and for at least 14 days after the last dose.

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 ABLE TO HAVE CHILDREN**

ONE of the following methods:

- Abstinence (completely and persistently refraining from all heterosexual intercourse) only if this is your preferred lifestyle
- Hormonal method of birth control (must remain the same throughout the study and have been in use long enough to ensure its effectiveness)
  - Birth control pills
  - Inserted hormonal intrauterine device (IUD)
  - Injectable progesterone
  - Subdermal (under the skin) implant
  - Transdermal (applied on the skin) patch
  - Vaginal ring
- Correctly placed copper-containing IUD
- Male condom or female condom used WITH a separate spermicide product (foam, gel, film, cream, or suppository)
- Male partner sterilization (vasectomy with confirmation of absence of sperm)
- Bilateral tubal ligation (tubes tied)
- Bilateral salpingectomy (both fallopian tubes removed)
- Bilateral tubal occlusive procedure (tubes blocked) confirmed by personal doctor

Women in this study not able to get pregnant include:

- Women who have had no period for at least 12 consecutive months with no other medical cause plus a blood hormone level confirming that you cannot get pregnant
- Women who have had their uterus and/or both ovaries removed (documented)
- Women who have ovarian failure, confirmed by your personal doctor

It is very important that men do not make women pregnant during this study. The only sure way to prevent pregnancy is to not have sex. If you are a man able to father children and choose to have sex with

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a woman who is able to have children, you and your partner must use a highly effective method of birth control. This is in addition to using a condom (see below). The method must be used consistently and correctly from the start of dosing (earlier for hormonal birth control) through the duration of the study and for at least 14 days after the last dose of study drug.

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

All sexually active male subjects must agree to prevent potential transfer of and exposure to drug through semen to their partners by using a condom consistently and correctly beginning with the first dose of study drug and continuing for the duration of the study and for at least 14 days after the last dose.

Men must not donate sperm for the duration of the study and for at least 14 days after the last dose.

Highly effective methods of birth control for this study include:

**FOR MALES**

ONE of the following methods:

- Abstinence (completely and persistently refraining from all heterosexual intercourse) only if this is your preferred lifestyle
- Consistent use of a male condom used WITH a separate spermicide product (foam, gel, film, cream, or suppository)
- Male sterilization (vasectomy with confirmation of absence of sperm)
- Female partner with one of the following:
  - Hormonal method of birth control (must remain the same throughout the study and have been in use long enough to ensure its effectiveness)
    - Birth control pills
    - Inserted hormonal intrauterine device (IUD)
    - Injectable progesterone
    - Subdermal (under the skin) implant
    - Transdermal (applied on the skin) patch
    - Vaginal ring
  - Correctly placed copper-containing IUD
  - Bilateral tubal ligation (tubes tied)
  - Bilateral salpingectomy (both fallopian tubes removed)
  - Bilateral tubal occlusive procedure (tubes blocked) confirmed by personal doctor

Birth control methods, even when used properly are not perfect. If you or your partner become pregnant during the study, or 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.

**Pregnancy Follow Up:**

If you or your partner become pregnant during the study or within at least 14 days after you have stopped taking the study drug, 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 pain or fever 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 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
- 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

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- 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.

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, medication 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.

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.

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## WHOM TO CONTACT

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

Sylvester Pawlak, APRN
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<br>IntegReview IRB<br>3815 S. Capital of Texas Highway,<br>Suite 320<br>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:

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.

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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 Clinical Research Unit 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 cotinine, 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 $1,850.00. 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 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.

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.

Compensation may be provided on a loadable debit card or by paper check. Pfizer New Haven Clinical Research Unit reserves the right to determine method of payment

<u>Study Subjects</u>

- If you successfully complete this study, the total amount you will be paid will be up to $1,850.00 ($1,400.00 plus $450.00 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

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be based on how much of the study you completed
  - This pay will be based on $200.00 for each overnight stay (6), $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 (2 weeks)
- Partial payments may be made during the 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 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.

**ADDITIONAL COSTS**

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

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**NEW FINDINGS**

If there is new information about the safety of the study drug 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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