INSTITUTE: National Cancer Institute

STUDY NUMBER: 15-C-0157 PRINCIPAL INVESTIGATOR: Ramaprasad Srinivasan, M.D.

STUDY TITLE: Phase I/II Trial of Vandetanib in Combination with Metformin in Subjects with HLRCC or SDH-Associated Kidney Cancer or Sporadic Papillary Renal Cell Carcinoma

Continuing Review Approved by the IRB on 04/24/17

Amendment Approved by the IRB on 09/30/16 (B) Date posted to web: 05/18/17

Phase II Standard

## INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

**Why is this study being done?**

There are no established treatments for patients with advanced non-hereditary papillary kidney cancers or kidney cancers associated with Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) or Succinate Dehydrogenase Renal Carcinoma (SDH-RCC) and these tumors do not usually respond well to the treatments that are currently available and approved by the FDA for treatment of kidney cancer.

Although several treatments are FDA-approved for treatment of the more common, clear cell form of kidney cancer, these treatments generally work for relatively short periods of time and are not curative. Vandetanib is an FDA approved agent for the treatment of advanced medullary thyroid cancer. It has been shown to have activity against a variety of tumors and has been shown to inhibit some forms of papillary renal cancer cells and to cause tumor shrinkage in mice with human papillary kidney cancer. Metformin, an FDA approved agent for treatment of diabetes, has been shown in laboratory experiments to enhance the effect of vandetanib in some forms of papillary kidney cancer. Neither metformin nor vandetanib are approved for use in papillary kidney cancer.

In this study, we will test the combination of metformin and vandetanib. The dose you will be receiving was determined in the first part of the study, called phase 1.

**Why are you being asked to take part in this study?**

You are being asked to participate in this study because you have been diagnosed with advanced hereditary leiomyomatosis and renal cell cancer (HLRCC), succinate dehydrogenase renal cell carcinoma (SDH-RCC) or advanced papillary renal cell carcinoma not related to a hereditary syndrome.

**How many people will take part in this study?**

Up to 73 subjects will take part in the study. This includes up to 27 subjects in the dose finding phase portion (phase 1) of the study and up to 46 subjects in the phase 2 portion of the study. You will be taking part in the phase 2 portion of the study.

**Description of Research Study**

The highest safe dose level for this phase of the study (phase 2) was found enrolling patients in phase 1 portion of the study. You will be receiving vandetanib in combination with metformin at doses that were determined to be safe for further study in the phase 1 portion. This is an open label study, meaning that you will know the doses of the agents you will receive. You will not receive a 'placebo' on this trial.

**What will happen if you take part in this research study?**

*Before you begin the study*

You will need to have the following exams, tests and procedures if you can be in the study. These exams, tests and procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them done recently, they may not need to be repeated. This will be up to the study team.

- A complete medical history, including your cancer history and prior cancer treatments, all drugs that you may be taking, including over the counter drugs, vitamins and herbal supplements.
- A complete physical examination, including assessing your ability to do physical activities and measuring your blood pressure, heart rate and breathing.
- Standard blood and urine tests to evaluate your organs' functioning (such as liver, kidneys, blood sugar and blood electrolytes).
- Evaluation of your cancer, which will include an MRI and CT and other imaging tests as if clinically indicated.
- ECG (electrocardiogram) to assess your heart.
- A pregnancy test will be performed in women who are able to have children. Women who are pregnant or breast-feeding will not be allowed to participate, as the effects of vaccine on a developing fetus or infant are not known.
- Confirmation of diagnosis by NCI Laboratory of Pathology (a review of the slides showing your tumor will be sent to NIH and looked at here by our pathologist).

*During the study*

If you are determined to be eligible for this study and agree to take part, you take vandetanib and metformin at the dose level determined in the phase 1 portion of the study. Your time in this study will be divided into cycles, with each cycle lasting 28 days. You will take vandetanib once per day and metformin twice every day.

With the exception of the first day you are on the trial, you will be taking both medications every day. Take the medications together with a full glass of water after eating a light breakfast. Record the date and time you take the medications on your diary. If you are taking the metformin in the AM and PM, take the evening dose of Metformin 12 hours after your AM dose.

If you have any procedure that require the use of IV contrast such as a CT scan, you should not take metformin on the morning that the procedure is planned and should only resume when instructed to do so by your physician/medical team.

You will continue to take metformin and vandetanib until your disease worsens, until you have intolerable side effects that require us to immediately stop your vandetanib. If your side effects require us to permanently discontinue metformin, you may be able to continue on the study, taking vandetanib alone.

**We will provide you with equipment and a diary to measure and record your blood pressure every day while you are on vandetanib. If you experience any worrisome side effects (e.g., headaches, chest pain, dizziness), or if your systolic blood pressure (upper or higher number) is above 140, or if your diastolic (lower number) is above 90 or above, you should call your doctors at the NIH or seek medical attention from your local doctors as soon as possible.**

We will also obtain/test the items below while you are on study medication. Some of these tests will be done more frequently during your first cycle. You will receive a calendar outlining what is to be done each cycle from your study nurse.

- History and physical examination
- Routine blood tests
- Routine urine tests
- Pregnancy test (if you are a woman who could become pregnant)
- Electrocardiogram (ECG)
- CT scans or MRI
- Bone scan
- PET scan
- Photographs of skin tumors in patients with HLRCC associated skin tumors
- 1 – 2 teaspoons of blood for research will be collected before you have taken any study medication, then at the end of each cycle through cycle 8. We will also collect blood for research if your disease worsens during the study.
- An optional CT- or ultrasound-guided tumor biopsy may be done before you begin treatment and approximately 8 weeks following start of treatment. We will only collect the biopsy if the tumor can be easily reached. The tumor samples we obtain will be used

to look for special markers that may be helpful in the study of kidney cancer and in understanding the effect of the study drugs on the tumor. We may also use the samples to grow tumor cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells). Results of research done on your specimens and data will not be available to you or your doctor. A separate consent form will be provided to you at the time of the biopsy for you to grant permission to that procedure if you agree to the biopsies.

During this study you will not be able to receive any other cancer treatments. You will be asked not to participate in any other clinical trials involving another experimental treatment while you are being treated in this study.

Several medications (both prescription and non-prescription), 'alternative/complementary' or herbal preparations, dietary supplements, and foods such as grapefruit juice, can have undesirable interactions with the medications provided as part of this study. You will not be allowed to take certain medications, supplements, and grapefruit juice during your participation in this study. Your doctor or the study staff will review the list of drugs that you are currently taking, as well as those that you took prior to participating in this study. Once you are on study, **please talk to your NIH doctors prior to starting any new drugs, dietary supplements or herbal or complementary medications**.

Drugs that affect the normal growth of blood vessels can delay or complicate wound healing following injury or surgical procedures. You should not schedule any elective surgeries while you are being treated in this study. **If you have an unplanned surgery, inform you doctor immediately, as you may not be able to continue study drug treatment.**

You will be asked not to wear contact lenses while on this study since vandetanib can lead to changes in your eye that may be worsened by wearing contact lenses.

*Pharmacogenetic Testing*

For this study approximately 1 teaspoon of blood will be drawn (4 mL) before you start the treatment. The purpose of this additional research study is to use the blood sample from you for research on genes, to see how genes and genetic variations are related to how the drug works and/or to learn more about your disease and the response to treatment. To do this, we will analyze your blood sample.

Pharmacogenetic research is an important way to try to understand the role of genetics in human disease and how genes impact the effectiveness of drugs. There are many differences, or variations, in genes from one person to another, which may affect a person's chances of suffering from a particular disease. These differences in genes can also change the way a person responds to a particular drug.

We would like to learn more about your type of tumor by measuring certain characteristics, so called "biological markers" in your blood sample. "Markers" refer to different types of genetic material (DNA or RNA) found in your blood that is associated with disease and/or your response to treatment. The aim is to find out if there are markers, which may help in predicting how well the treatment works.

This is voluntary and you are not required to participate in this blood study in order to be on this study. You will be given the opportunity to decide whether you want to participate in the pharmacogenetic study. The decision to participate in this part of the research is optional, and no matter what you decide to do, it will not affect your care.

*When you are finished taking the drugs (treatment)*

If you stop taking the study drug, we would like to perform the following tests if possible within approximately 60 days after your last dose. The tests may be done at NCI or by your local physician:

- History and physical exam
- Routine blood tests

If the tests cannot be performed, we would like to contact you by telephone to find out how you are doing.

In addition, after the 60 day follow up visit/contact, when possible we would like to contact you one a year by phone to find out how you are doing.

*Birth Control*

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 6 months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]

- tubal ligation
- vasectomy

**Risks or Discomforts of Participation**

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

*Possible Side Effects of Vandetanib*

| **COMMON, SOME MAY BE SERIOUS**<br>For every 100 people receiving Vandetanib, more than 20 and up to 100 may have: |
|---|
| • Diarrhea, nausea, loss of appetite, constipation<br>• Pain<br>• Tiredness<br>• Headache<br>• Acne, rash<br>• High blood pressure which may cause dizziness, blurred vision<br>• Changes in the ECG<br>• Weight loss<br>• Depression or anxiety<br>• Sleeplessness<br>• Dizziness<br>• Changes in measures of your kidney function, such as an increase in creatinine or increased protein in your urine<br>• Delayed wound healing |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br>For every 100 people receiving Vandetanib, from 4 to 20 may have: |
|---|
| • Severe blood or other infection<br>• Change in the heart rhythm, some of which may be life threatening<br>• Dehydration<br>• Changes in laboratory values of electrolytes and liver function tests<br>• Low platelet counts, white blood counts or anemia<br>• Itching<br>• Pain, including pain associated with tumor<br>• Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) |

**OCCASIONAL, SOME MAY BE SERIOUS**

For every 100 people receiving Vandetanib, from 4 to 20 may have:

- Damage to the lungs which may cause shortness of breath
- Scarring of the lungs
- Severe skin rash with blisters, ulcers can involve inside of mouth and other parts of the body
- Bleeding
- pain, redness, or peeling of the hands and feet
- increased blood levels of calcium, a mineral normally found in blood
- changes in levels of parathormone, a substance made in your body that regulates the levels of calcium and phosphorus
- Inflammation of the pancreas
- Inflammation/infection of the intestines
- Abnormal accumulation of fluid in the brain
- Development of an abnormal pathway between the esophagus (tube connecting the throat to the stomach) and trachea (windpipe) or surrounding structures
- Development of an abnormal communication between the intestines and surrounding structures, including the urinary bladder
- Decrease in thyroid function
- Stroke
- Mild nose bleeding
- Abnormal taste in mouth
- Dry or irritated eyes; vandetanib may also cause some visual changes or eye infections
- Formation of clots, such as in the lung or in the legs
- Lack of blood flow to heart (heart attack), brain (stroke), eye (blindness), legs, or bowel
- Serious or life-threatening complications from rashes
- Lung inflammation and stiffening, infections or fluid accumulation around the lungs
- Blockage or penetration of the bowel or gall bladder duct

| **RARE, AND SERIOUS**<br><br>For every 100 people receiving Vandetanib, 3 or fewer may have: |
|---|
| • Heart failure which may cause shortness of breath, swelling of ankles, and tiredness<br>• Stroke which may cause paralysis, weakness<br>• Kidney stones<br>• Life threatening problems resulting from abnormal heart rhythm<br>• Detached retina |

*Possible Side Effects of Metformin Hydrochloride*

| **COMMON, SOME MAY BE SERIOUS**<br><br>For every 100 people receiving Metformin Hydrochloride, more than 20 and up to 100 may have: |
|---|
| • Diarrhea, nausea, vomiting |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br><br>For every 100 people receiving Metformin Hydrochloride, from 4 to 20 may have: |
|---|
| • Heartburn, passing gas<br>• Headache<br>• Tiredness |

| **RARE, AND SERIOUS**<br><br>In 100 people receiving Metformin Hydrochloride, 3 or fewer may have: |
|---|
| • Lactic acid build up which may cause muscle aches, shortness of breath, or severe belly pain. If untreated this can lead to death |

*Tumor Biopsy Risks*

The biopsy procedure usually causes only brief discomfort at the site from which the biopsy is taken. Rarely, infection or bleeding may occur at the needle site.

*Research Radiation Risks*

This research study involves exposure to radiation from 1 FDG PET/CT scan of 10mCi of FDG on cycle 1 day 15 and up to 2 CT scans for CT guided biopsy. This radiation exposure is not required for your medical care and is for research purposes only. From participating in this, the total amount of radiation you will receive is 2.4 rem which is below the guideline of 5.0 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant you will not be permitted to participate in this research study. If you are breast feeding and the protocol involves injection of radioactive material, you will not be permitted to participate. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

## Potential Benefits of Participation

*Are there benefits to taking part in this study?*

The aim of this study is to establish a safe dose for the combination of vandetanib and metformin and also to determine whether this experimental combination will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

## Alternative Approaches or Treatments

*What other choices do I have if I do not take part in this study?*

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

## Stopping Therapy

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Sanofi Genzyme or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

*Research Subject's Rights*

*What are the costs of taking part in this study?*

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or
- paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

**Will your medical information be kept private?**

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Cancer Institute Institutional Review Board
- Qualified representatives from Sanofi Genzyme, the pharmaceutical company that produces vandetanib.

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.

**Certificate of Confidentiality**

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

**Conflict of Interest**

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study are using vandetanib developed by Sanofi Genzyme, through a joint study with your researchers and the company. The company also provides financial support for this study.

**Use of Specimens and Data for Future Research**

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

## OTHER PERTINENT INFORMATION

**1. Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

**2. Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**3. Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

**4. Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Ramaprasad Srinivasan, M.D., Building 10, Room 2-5950, Telephone: 240-760-6251. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

**5. Consent Document.** Please keep a copy of this document in case you want to read it again.

**COMPLETE APPROPRIATE ITEM(S) BELOW:**

**A. Adult Patient's Consent**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative — Date

Print Name

**B. Parent's Permission for Minor Patient.**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian — Date

Print Name

**C. Child's Verbal Assent (If Applicable)**

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian — Date — Print Name

**THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM APRIL 24, 2017 THROUGH APRIL 23, 2018.**

Signature of Investigator — Date

Print Name

Signature of Witness — Date

Print Name