INFORMED CONSENT FORM

**Name of Research Study: A Phase II Study Assessing Efficacy and Safety of NFL-101 as a Tobacco Cessation Therapy CESTO II trial)**

**Short Study Name: CESTO II**

**Sponsor: NFL BIOSCIENCES SAS**

**BB HREC Application ID: 2021-04-332**

**Principal Investigator: Professor Stuart Ferguson**

**Research Site Address(es):** **University of Tasmania Clinical Research Facility**

**17 Liverpool Street**

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**Tasmania 7000**

**Daytime telephone number(s): (03) 6226 4233**

You will be given a copy of this form to keep. If you have any questions or problems during the study, call the phone number above.

# What is the purpose of this form?

This form tells you about the research study, to help you decide if you want to participate. It explains why the study is being done, the tests and treatments involved as well as outlining the risks and benefits. If you sign this form, it means that you agree to take part in this study.

Participation in this research study is voluntary. If you do not wish to take part, you do not have to.

Before you decide if you want to take part in this research study, it is important that you read and understand the information in this form and ask the study doctor or the study staff to explain any words or procedures that you do not clearly understand.

You can change your mind about taking part in this study at any time. You may leave the study at any time, even if you have signed this form. You do not have to give a reason and it will not change your future medical care.

After reading this form and talking with the study staff, you should know which parts of the study are medical care and which are experimental. Please ask any questions you have.

You may talk with your family, friends, and your local doctor (GP) to help you make your decision. You can take as much time as you like to make this decision.

The sponsor is funding this research study. The University of Tasmania will be paid by the sponsor for your participation.

When deciding to take part in a research study you should know:

* The main goal of medical care is to help you.
* The main goal of a research study is to gain information to help others in the future.
* Being in this study does not replace your regular medical care.

# Why is this study being done?

You are being invited to take part in a research study of an investigational drug called NFL-101. This drug is being tested for use in tobacco cessation.

The aim of this investigational treatment is to help you to stop smoking. It is an additional aid in the process, which will require personal effort, you cannot count on the effect of this treatment alone. You must set an objective to stop smoking completely from the first administration of the treatment and not smoke even one cigarette more.

Smoking is one of the biggest public health problems in the world. There are currently more than a billion smokers in the world, half of whom risk dying from a disease linked to smoking if they do not quit. Various treatments are available to help smoking cessation, such as nicotine substitutes in the form of gum, transdermal patches, sublingual tablets, nasal sprays and inhalation systems. These treatments are associated with variable rates of success and side effects. It is essential to develop effective, better tolerated alternatives for this indication.

The company NFL Biosciences SAS developed a future drug with a view to use for smoking cessation. This new product, called NFL-101, has already been tested in a safety study in 24 smokers. NFL-101 is a tobacco leaf extract. It is injected at a low dose and thus provokes an immune reaction (the body’s natural defense mechanism against an external substance).

The purpose of this study is to assess the effectiveness, safety and tolerability of two different dose strengths of NFL-101 in helping smokers to stop and remain abstinent after attempting to stop smoking. This will be achieved by comparing the effects of those treatments with NFL-101 to a placebo. A placebo does not contain the study drug’s active ingredient, it is administered to some participants to compare the effects of the active agent administered to other participants.The term “study drug” refers to both NFL-101 and placebo in this form.

“Investigational” means that the drug is currently being tested. It is not approved by the Therapeutic Goods Administration (TGA) in Australia.

This study will involve about 318 participants and will be conducted at 1-3 different centers in Australia.

# investigationAL Study Drug

If you fulfil the conditions required to participate in this study and if you agree to take part, you will be randomized (assigned by chance) to receive one of three different treatments 1) NFL-101 at the dose of 100µg per administration / dose, 2) NFL-101 at the dose of 200µg per administration / dose, or 3) a placebo. During the study, neither you nor your study doctor will know whether you are getting NFL-101 or placebo. Your study doctor can find out in case of an emergency.

The two dose administrations will take place 7 days apart (each dose will comprise two sub-cutaneous injections).

If you are not able to stop your tobacco consumption after the first two doses of study drug, up to two additional doses could be offered to you. These two additional doses will be optional. They will be offered to you at the 3-month and 6-month follow-up visits, only if you have not stopped smoking.

The NFL-101 investigational product is an aqueous extract of tobacco leaves from which the nicotine has largely been eliminated. Nevertheless, some nicotine remains present and the dose of nicotine administered on Day 1 is 3,5µg or 7µg. The same dose is administered 7 days after the first administration and possibly during the additional administrations 3 and 6 months later. By way of comparison, the dose of nicotine contained in a nicotine substitute such as the Nicabate 1.5 mg lozenges is 1500µg per lozenge and the dose of nicotine contained in a cigarette (as indicated on cigarette packets) varies from 100µg to 1000µg depending on the cigarette type. The risk of over-exposure to nicotine is therefore limited if you continue to smoke or take nicotine substitutes.

# What are the study procedures?

If you agree to be in this study, you will sign this consent form before any study procedures are done.

The study consists of 10 x compulsory site visits which include:

* Screening visit - approximately 2 weeks before the first treatment administration visit
* Day 1, 1st Dose Day: A visit for the first treatment administration of the study drug
* Day 7, 2nd Dose Day: A visit 7 days after the first administration for the second administration of the study drug
* 7 x follow-up clinic visits at 2 weeks, 4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after the first treatment administration.

The duration of your participation in the study will be approximately 13 months with each study visit lasting a maximum of 4 hours.

For those participants that have not succeeded in stopping smoking following the first two doses of study drug will be offered a third (3rd) and fourth (4th) administration of the study drug. These dose will occur approximately 3 and/or 6 months from the first administration. Participants that elect to receive these extra doses of study drug will have additional clinic visits for these doses.

Before you can begin the study, you will need to complete a screening visit and have the following tests to find out if you are eligible for the study.

Screening visit:

* Sign the Informed Consent
* Urine and blood tests to check your liver and kidneys and other body systems
* A questionnaire will be completed in order to evaluate your tobacco consumption.
* An electrocardiogram (ECG) measurement of your heart’s electrical activity and rhythm
* Screening for illicit drugs (e.g., cannabis, opiates, cocaine) in urine will be performed in the case of positive results to these tests, you will not be able to participate in the study.
* A pregnancy test will be performed for women of child-bearing age.
* A prick test will be done. This test is used to check if you have an allergy to the studied product by injecting a small quantity of the product under the skin.

The exact procedures will differ from visit to visit, but study visits will includes activities such as:

* Physical examination comprising vital signs, weight, measurement of blood pressure and pulse.
* Evaluation of tobacco consumption
* Determination of exhaled CO (carbon monoxide), a marker for tobacco consumption
* A urine cotinine test (cotinine is a metabolite of nicotine)
* Blood tests

In addition, you will be asked to fill in a “self-reported” patient diary for 15 days after the first administration, where you will note the number of cigarettes smoked, your cigarette consumption, on a daily basis. The diary is completed by “self-reporting” which means that you will be asked to keep track of and to document between each of your clinic visits how much tobacco you use (how many cigarettes that you smoked). Your diary will take you only a few minutes each day to complete.

As part of your smoking cessation process, and until you no longer feel the need to smoke, you will be advised to stop consuming coffee, alcohol, and other psychotropic substances. Even if the treatment is working well consume these substances, the experience may make you want to smoke again. While this is not a requirement that you stop drinking coffee and alcohol as part of the study, limiting intake of these substances is encouraged.

During this study, you will need to visit the study site / clinic on a regular basis. All the tests noted above, will be repeated on a regular basis throughout this study. The following tables show when these tests and procedures will be done:

**Schedule of Events - Screening to Day 85**:

| **Phase II****CESTO trial** | D-36 to D-15Screening | D1,Adm. 1(TQD)1 | D8,Adm. 2+/-1 day | D15+/-1 day | D29+/-2 days | D43+/-4 days | D85 (M3)+/-7 days |
| --- | --- | --- | --- | --- | --- | --- | --- |
| *On site* | *On site* | *On site* | *On site* | *On site* | *On site* | *On site* |
| Signature of Informed consent | X |  |  |  |  |  |  |
| Demographics - medical history | X |  |  |  |  |  |  |
| Prick test | X |  |  |  |  |  |  |
| Eligibility Criteria | X |  |  |  |  |  |  |
| Clinical examination, Height and weight | X | X | X | X | X | X | X |
| Vital signs | X | X | X | X | X | X | X |
| Prior/Concomitant medications | X | X | X | X | X | X | X |
| 12-Lead ECG recording | X |  |  |  |  |  |  |
| Randomization |  | X |  |  |  |  |  |
| Study drug administration |  | X | X |  |  |  |  |
| Adverse events assessments |  | X | X | X | X | X | X |
| Urinary toxicology | X | X | X |  |  |  |  |
| Blood samples | X |  |  |  |  |  | X |
| Pregnancy test | X | x | x |  |  |  |  |
| Questionnaires | X | X | X | X | X | X | X |
| Urinary cotinine | X | X | X | X | X | X | X |
| Exhaled CO determination | X | X | X | X | X | X | X |

**Schedule of Events - Day 99 to Day 365**:

| **Phase II****CESTO trial** | D99 Adm. 3 (op.)+/-14 days | D113 14 days +/-1 Day after D99 visit | D182 (M6)+/-14 days | D196 Admin 3 or 4 (op)+/-14 days | D21014 days +/-1 Day after D196 visit | D274 (M9)+/-14 days | D365 (M12)+/-21 days |
| --- | --- | --- | --- | --- | --- | --- | --- |
| *On site* | *On site* | *On site* | *On site* | *On site* | *On site* | *On site* |
| Clinical examination, Height (at SCR only) and weight | X | X | X | X | X | X | X |
| Vital signs | X | X | X | X | X | X | X |
| Prior/Concomitant medications | X | X | X | X | X | X | X |
| Study drug administration | X |  |  | X |  |  |  |
| Adverse event assessment | X | X | X | X | X | X | X |
| Urinary toxicology | X |  |  | X |  |  |  |
| Blood samples |  |  | X |  |  |  | X |
| Urinary pregnancy test | X |  |  | X |  |  |  |
| Questionnaires |  | X | X |  | X | X | X |
| Urinary cotinine |  | X | X |  | X | X | X |
| Exhaled CO2 determination |  | X | X |  | X | X | X |

1CO = Carbon monoxide

Ask us if you have any questions about the tests and procedures for the study.

# What will I be asked to do in this study?

Before you decide whether to be in this study, you should think about how the tests and study visits will affect your time away from work and your schedule.

To be in this study, you must agree to:

* Follow directions from the study staff
* Make and keep study appointments
* Agree to receive the study drug as instructed
* Give blood samples and urine samples
* Tell the study staff about all of the medicines you take during the study
* Tell the study staff about any changes to your health during the study
* Not be part of any other research study while participating in this study
* Answer questions about your health and well-being
* Make an attempt to stop smoking starting on each of the days that you received a dose of the study drug, if you are still smoking

**Talk with your study doctor before starting any new medicine. This includes drugs you buy at the pharmacy and herbal or dietary supplements (vitamins). Some drugs could cause serious side effects if taken with the study drug.**

**Please ask your study doctor if you have any questions about the medicine(s) you are taking. He/she will tell you which medicine you cannot take during the study.**

# What will be done after the study?

Speak with your study doctor about your options for medical care when:

* You complete the study, or,
* You leave the study early.

The study drug will not be available to you after you complete the study.

# What are the risks or discomforts of the study?

You may not be able to stop smoking even if you participate in the study.

Blood samples will be taken using single-use needles. This procedure can sometimes cause bruising, pain, bleeding or a slight risk of infection.

The total quantity of blood taken will not exceed 450 ml.

During previous studies, participants received a series of single or multiple doses of NFL-101 for up to six (6) doses; the maximum dose administered was 200ug of protein which is the same highest dose to be administered during this study. The treatment of NFL-101 in those previous studies was found to be safe and well tolerated.

A total of 24 participants were dosed with NLF-101 at both the 100ug and 200ug dose levels and with only one (1) severe adverse event (an unwanted side effect) reported. The other adverse events that were reported were either mild (21%) or moderate (75%). The single severe event was reported as “dental pain” which was not thought to be related to the study drug.

The table below shows what percent of adverse events that were reported were scored as mild, moderate or severe at each of the two dose levels.

|  |  |  |  |
| --- | --- | --- | --- |
| **Maximum grade\*** | **Dose level 100ug** **(number of participants (N) =12)** | **Dose level 200ug** **(number of participants (N)=12)** | **Total****(number of participants (N)=24)** |
| **N** | **%** | **N** | **%** | **N** | **%** |
| Mild | 2 | 16.67 | 3 | 25 | 5 | 20.83 |
| Moderate | 10 | 83.33 | 8 | 66.67 | 18 | 75 |
| Severe | 0 | 0 | 1 | 8.33 | 1 | 4.17 |

* Mild = asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
* Moderate = minimal, local or non-invasive intervention indicated
* Severe = medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care

The participants who received the treatment with NFL-101 (up to a maximum dose of 200ug) as part of those studies reported the following adverse events: dry mouth, fatigue, drowsiness, nausea, dry eyes, insomnia, shivers, headache, taste modification, photophobia, diarrhoea, gastro-oesophageal reflux, weight gain, cramp in calf muscle, rhinitis, nasal dryness, productive cough, itching (arms, legs, nose, tongue).

The table below provides a listing of all the adverse events that were reported in the previous studies. The table lists the number of participants that reported that adverse event and the percentage of all the participants treated with NFL-101 reporting that same event.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Adverse Event Type** |  |  |  |  |  |
|  | **Maximum grade** | **Dose level 100ug**  | **Dose level 200ug**  | **Total** |
| **Adverse Event** |   |  |  |  |
|  |   | **(number of participants (N) =12 patients)** | **(number of participants (N) =12 patients)** | **(number of participants (N) =24 patients)** |
|  |   | **N** | **%** | **N** | **%** | **N** | **%** |
| **Cardiac disorders** | Bradycardia (slow heart rate) | Mild | 4 | 33,33 | 1 | 8,33 | 5 | 20,83 |
| **Ear and labyrinth disorders** | Tinnitus (ringing in the ears) | Mild | 1 | 8,33 | 2 | 16,67 | 3 | 12,50 |
| Vertigo (dizziness) | Mild | 2 | 16,67 | 0 | 0,00 | 2 | 8,33 |
| **Eye disorders** | Conjunctivitis (eye infection) | Mild | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
|  | Moderate | 1 | 8,33 | 1 | 8,33 | 2 | 8,33 |
| Dry eye | Mild | 3 | 25,00 | 3 | 25,00 | 6 | 25,00 |
| Chalazion (eyelid cyst) | Mild | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
|  | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Watering eyes | Mild | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Photophobia | Mild | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| **Gastrointestinal disorders** | Gastroesophageal reflux (heartburn) | Mild | 6 | 50,00 | 6 | 50,00 | 12 | 50,00 |
|   | Moderate | 0 | 0,00 | 2 | 16,67 | 2 | 8,33 |
| Dry mouth | Mild | 3 | 25,00 | 5 | 41,67 | 8 | 33,33 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Constipation | Mild | 5 | 41,67 | 2 | 16,67 | 7 | 29,17 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Diarrhea | Mild | 1 | 8,33 | 3 | 25,00 | 4 | 16,67 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| Dental pain | Mild | 0 | 0,00 | 3 | 25,00 | 3 | 12,50 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Nausea/Vomiting | Mild | 2 | 16,67 | 4 | 33,33 | 6 | 25,00 |
| Epigastralgia (stomach pain) | Mild | 0 | 0,00 | 2 | 16,67 | 2 | 8,33 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Hemorrhoids | Mild | 2 | 16,67 | 1 | 8,33 | 3 | 12,50 |
| Gastrointestinal disorders - Other | Mild | 2 | 16,67 | 7 | 58,33 | 9 | 37,50 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| **General disorders and administration site conditions** | Fatigue (feeling tired) | Mild | 9 | 75,00 | 6 | 50,00 | 15 | 62,50 |
|   | Moderate | 2 | 16,67 | 5 | 41,67 | 7 | 29,17 |
| Irritability | Mild | 4 | 33,33 | 6 | 50,00 | 10 | 41,67 |
|   | Moderate | 2 | 16,67 | 1 | 8,33 | 3 | 12,50 |
| Deltoid (upper arm)/Injection site pain | Mild | 11 | 91,67 | 9 | 75,00 | 20 | 83,33 |
| Edema (swelling) | Mild | 7 | 58,33 | 5 | 41,67 | 12 | 50,00 |
| Chills | Mild | 2 | 16,67 | 1 | 8,33 | 3 | 12,50 |
| Injection site reaction | Mild | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| **Hepatobiliary disorders** | Gallblader instability | Mild | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| **Infections and infestations** | Sinusitis (inflammation of the sinuses) | Mild | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
|   | Moderate | 1 | 8,33 | 1 | 8,33 | 2 | 8,33 |
| Infections and infestations - Other | Mild | 2 | 16,67 | 2 | 16,67 | 4 | 16,67 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| **Investigations** | Increased blood bilirubin | Mild | 4 | 33,33 | 3 | 25,00 | 7 | 29,17 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| Increased GGT | Mild | 3 | 25,00 | 2 | 16,67 | 5 | 20,83 |
| Increased creatinine | Mild | 3 | 25,00 | 1 | 8,33 | 4 | 16,67 |
| Increased ALAT | Mild | 3 | 25,00 | 0 | 0,00 | 3 | 12,50 |
| Weight gain | Mild | 4 | 33,33 | 1 | 8,33 | 5 | 20,83 |
| Investigations - Other | Mild | 1 | 8,33 | 4 | 33,33 | 5 | 20,83 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| **Metabolism and nutrition** | Hyperglycemia (high blood sugar level) | Mild | 5 | 41,67 | 2 | 16,67 | 7 | 29,17 |
| Hyperkalemia (high blood potassium level) | Mild | 6 | 50,00 | 3 | 25,00 | 9 | 37,50 |
| Hypercalcemia (high blood calcium level) | Mild | 2 | 16,67 | 3 | 25,00 | 5 | 20,83 |
| Metabolism and nutrition disorders - Other | Mild | 1 | 8,33 | 3 | 25,00 | 4 | 16,67 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| **Musculoskeletal and connective** | Musculoskeletal and connective tissue disorders - Other | Mild | 6 | 50,00 | 11 | 91,67 | 17 | 70,83 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| **Nervous system disorders** | Headache | Mild | 7 | 58,33 | 1 | 8,33 | 8 | 33,33 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| Somnolence (sleepiness) | Mild | 1 | 8,33 | 4 | 33,33 | 5 | 20,83 |
| Paresthesia (tingling) | Mild | 0 | 0,00 | 4 | 33,33 | 4 | 16,67 |
| Dysgeusia (altered taste) | Mild | 2 | 16,67 | 4 | 33,33 | 3 | 12,50 |
| Nervous system disorders - Other | Mild | 0 | 0,00 | 1 | 8,33 | 4 | 16,67 |
| **Psychiatric disorders** | Anxiety | Mild | 3 | 25,00 | 4 | 33,33 | 7 | 29,17 |
|   | Moderate | 3 | 25,00 | 2 | 16,67 | 5 | 20,83 |
| Insomnia (trouble sleeping) | Mild | 4 | 33,33 | 5 | 41,67 | 9 | 37,50 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| Agitation | Mild | 1 | 8,33 | 3 | 25,00 | 4 | 16,67 |
| Depression | Mild | 2 | 16,67 | 3 | 25,00 | 5 | 20,83 |
| Restlessness | Mild | 2 | 16,67 | 4 | 33,33 | 6 | 25,00 |
| **Renal and urinary disorders** | Nocturia (excessive urination at night) | Mild | 0 | 0,00 | 2 | 16,67 | 2 | 8,33 |
| **Reproductive system and breast disorders** | Reproductive system and breast disorders - Other | Mild | 1 | 8,33 | 2 | 16,67 | 3 | 12,50 |
| **Respiratory, thoracic and mediastinal disorders** | Cough | Mild | 10 | 83,33 | 11 | 91,67 | 21 | 87,50 |
| Rhinitis (nasal inflammation) | Mild | 4 | 33,33 | 3 | 25,00 | 7 | 29,17 |
| Bronchial infection | Mild | 1 | 8,33 | 1 | 8,33 | 2 | 8,33 |
| Viral ORL | Mild | 1 | 8,33 | 2 | 16,67 | 3 | 12,50 |
| Respiratory, thoracic and mediastinal disorders - Other | Mild | 1 | 8,33 | 4 | 33,33 | 5 | 20,83 |
|   | Moderate | 0 | 0,00 | 1 | 8,33 | 1 | 4,17 |
| **Skin and subcutaneous tissue disorders** | Erythema (reddening of the skin) | Mild | 1 | 8,33 | 3 | 25,00 | 4 | 16,67 |
| Pruritus (itchy skin) | Mild | 4 | 33,33 | 2 | 16,67 | 6 | 25,00 |
| Eczema (dry/itchy skin) | Mild | 1 | 8,33 | 2 | 16,67 | 3 | 12,50 |
| Skin and subcutaneous tissue disorders - Other | Mild | 1 | 8,33 | 3 | 25,00 | 4 | 16,67 |
|   | Moderate | 1 | 8,33 | 0 | 0,00 | 1 | 4,17 |
| **Vascular disorders** | Hot flashes | Mild | 1 | 8,33 | 1 | 8,33 | 2 | 8,33 |
| Vascular disorders - Other | Mild | 2 | 16,67 | 5 | 41,67 | 7 | 29,17 |

Furthermore, the following adverse reactions may occur in connection with nicotine reduction or cessation: depression, insomnia, irritability, anxiety, difficulties of concentration, agitation, increased appetite, weight gain, constipation and bradycardia.

# Allergic Reaction Risks

It is possible that the study product may cause allergic reactions in some participants due to its mechanism of action based on an immune response. You will also have an active control “skin-prick” test (using a small amount of histamine at the screening visit) which can cause a localized skin reaction at the location of the test. If you have a very bad allergic reaction, there is a possibility that you could die. Some signs that you may be having an allergic reaction are:

* Rash or hives
* Having a hard time breathing
* Wheezing when you breathe
* Sudden change in blood pressure (making you feel dizzy or lightheaded)
* Swelling around the mouth, throat or eyes
* Fast pulse
* Sweating

**In case of a medical emergency please call 000 immediately. If you experience any of the side effects noted above after any dose of study drug is administered, contact a study staff member as soon as possible to report the event.**

**ECG**

The procedure involves attaching small wires to your body with small adhesive patches in several locations for about 15 minutes. When the patches are removed, you may experience temporary discomfort as the adhesive patches pull on your skin or skin hair. Skin irritation and rashes have also been reported in association with ECG electrodes.

# Other Risks

When taking any new drug, you should be careful until you know how it affects you before you:

* Drive,
* Operate machinery, or
* Need to be alert.

These effects have not been observed with NFL-101 to date. If you have any feeling that your ability to perform these functions is not normal after dosing, you should inform your study team so that you can be observed and consider having somebody drive you home.

1. **PREGNANCY AND BIRTH CONTROL**

The effects of NFL-101 on the unborn child and on the newborn baby are not known. Because of this, it is important that study participants are not pregnant or breast-feeding and do not become pregnant during the research study. You must not participate in the research if you are pregnant, or believe you may be pregnant, or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the study. If you are male, you should not father a child or donate sperm for at least 30 days after the last dose of study drug.

Both male and female participants must use effective contraception during the study and for a period of 30 days after last dose of study drug of the study. You should discuss methods of contraception with your study doctor.

For female participants: Do not get pregnant or breastfeed while taking part in this study and for 30 days after your last dose of the study drug. In order to reduce the risk of pregnancy, you and your partner should use at least two effective methods of birth control. Acceptable methods of contraception for use in this study are abstinence, condoms a coil (intrauterine device), oral contraceptive pill, depot progesterone injections, progesterone implant, tubal occlusion or have a partner who has had a vasectomy. The Study Doctor or study staff will discuss this with you.

For male participants: Do not father a child while taking part in this study and for 30 days after your last dose of the study drug. You must also not donate sperm during the study and for 30 days after the last dose of study drug. In order to reduce the risk of pregnancy, you and your partner should use at least two effective methods of birth control. Acceptable methods of birth control for use in this study are abstinence, condoms or vasectomy or have a partner who has had tubal occlusion, a coil (intrauterine device), oral contraceptive pill, depot progesterone injections, or progesterone implant. The Study Doctor or study staff will discuss this with you.

# What if new information becomes available?

You will be told if we learn anything new that might affect your decision to stay in the study. You may be asked to sign a new consent form if this occurs.

# Are there any benefits?

Your participation in this study with therapeutic care and regular follow-up of your tobacco consumption could help you to either reduce, to stop for a certain period of time, or even to totally stop smoking. There may be no direct benefit for your participation, including being able to stop smoking; however, the knowledge learned from this study may be of benefits to others trying to reduce and/or stop smoking.

# Will I be paid to take part?

You will not receive any payment for taking part in this research study. However, in recognition of expenses associated with participation, including travel to the clinical site, parking, and meals, you will be provided up to $650. This will be provided to you in stages over the course of your participation; you do not need to retain receipts.

# Are there any costs?

You do not have to pay for the study drug, study visits, or any tests that must be done for the study.

# What are the alternatives?

You do not have to take part in this study to receive treatment and/or support to stop smoking. Your study doctor and/or a study staff member will discuss these options, and their risks and benefits, with you.

# How will my information be protected?

All information that you give will be kept strictly confidential. The information collected about you usually will not directly identify you (for example, by name, address, or personal identification number(s)). Instead, your initials and a code number will be used for your information. If you have any questions about how this will work, please contact your Study Doctor to discuss your concerns.

Your records may be reviewed by:

* the study sponsor,
* people who work with the sponsor on the study,
* government agencies, such as the Therapeutic Goods Administration (TGA), or
* Human Research Ethics Committees (HRECs). An HREC is a group of scientists and non-scientists who review the ethics of research. The goal of an HREC is to protect the rights and welfare of study participants.

These people may look at your records to make sure the study has been done the right way. They also want to make sure that your health information has been collected the right way, or for other reasons that are allowed under the law.

If information about this study is published, you will not be identified.

There is a risk of loss of confidentiality in research studies. Every effort will be made to protect you and your health information to the extent possible.

# What if I am hurt or get sick in the study?

If you are hurt or get sick while taking part in the study, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment.

If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

***Compensation for injury***

If you are injured as a result of your participation in this trial, you may be entitled to compensation. There are two avenues that may be available to you to seek compensation.

1. Sponsors of clinical trials in Australia have agreed that the guidelines developed by their industry body, Medicines Australia, will govern the way in which compensation claims from injured participants are managed by sponsors.

However, as guidelines, they do NOT in any way dictate the pathway you should follow to seek compensation. The sponsor is obliged to follow these guidelines.

These guidelines are available for your inspection on the Medicines Australia Website ([www.medicinesaustralia.com.au](http://www.medicinesaustralia.com.au)) under Policy – Clinical Trials – Indemnity and Compensation Guidelines.

1. You may be able to seek compensation through the courts.

It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice before taking any steps towards compensation for injury.

# Do I have to take part in the study?

Taking part in this study is your choice. There will not be any penalty or loss of benefits to you if you decide not to take part or if you leave the study early.

You may leave the study at any time. If you decide to leave the study early, there may be risks with this decision. You should discuss these risks with your study doctor. You may be asked to return to the clinic for tests.

# Could I be withdrawn from the study?

You Study Doctor, or the sponsor, may withdraw you from the study without your consent for the following reasons:

* if you have a side effect from receiving NFL-101,
* if you need a treatment not allowed in this study,
* if you do not follow the study procedures as instructed,
* if you become pregnant, or
* if the study is canceled by the TGA or the sponsor.

The sponsor, the government regulatory authority or the HREC may decide to stop the study at any time.

#

# What will happen to information about me?

By signing the consent form, you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Confidentiality will be maintained in accessing, keeping, processing and publication of information related to your taking part in the study, i.e. your name will not be revealed outside the clinic unless this is required by law.

Study staff are responsible for keeping a list of codes to make it possible to link your code to your name. This list will be kept in a safe place to make sure that in an emergency you can be identified and contacted. The list will be kept for at least 15 years from the end of the study and then for as long as necessary to keep to the legal, regulatory, scientific or other requirements. It will then be destroyed. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

If you do withdraw your consent during the study, the research team at the site will stop collecting personal information from you, but they will keep the information they have collected up to that point.

All study information will be stored securely at Study Centre for the duration of the study and then transferred to a secure storage facility.

The information will be kept until at least 15 years following the closure of the study. After this time, it will be securely destroyed.

Some of your coded study data will be sent overseas. The data protection laws governing data access and use in other countries may not be the same as those in Australia. If you have any questions about this, discuss them with a study staff member.

In accordance with relevant Australian *and/or* State specificprivacy and other relevant laws, you have the right to request access to your information collected and stored by the research team.

You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

# A description of this clinical trial will be available on the Australian New Zealand Clinical Trials Registry (ANZCTR) at https://www.anzctr.org.au/, as recommended by the Australian National Statement on Ethical Conduct in Human Research. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website anytime.

# Who do I call if I have questions?

If you have any questions, concerns, or complaints about this research study, you may call the study site. If you think you have an injury or illness from NFL-101, contact the site and, if necessary, they will contact the study doctor.

**Site Contact Person:**

|  |  |
| --- | --- |
| **Name** | Hannah Robert-Tissot |
| **Position** | Trial Coordinator |
| **Telephone** | (03) 6226 4233 |
| **Email** | hannah.roberttissot@utas.edu.au |

If you have any complaints about any aspect of the study, the way it is being conducted or any questions about being a study participant in general, then you may contact:

**Local HREC Office Contact:**

|  |  |
| --- | --- |
| **Name** | Bellberry HREC |
| **Position** | Operations Manager |
| **Telephone** | (08) 8361 3222 |
| **Email** | bellberry@bellberry.com.au  |

The Bellberry Human Research Ethics Committee has reviewed this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) incorporating all updates. Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact you may contact the Operations Manager, Bellberry Limited on 08 8361 3222.

This study has also been approved by the University of Tasmania Human Research Ethics Committee (HREC). If you have concerns or complaints about the conduct of this study, you can contact the Executive Officer of the HREC on (03) 6226 6254 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote H0024997.

PARTICIPANT’S Statement of Consent

**Name of Research Study: A Phase II Study Assessing Efficacy and Safety of NFL-101 as a Tobacco Cessation Therapy CESTO II trial)**

**Short Study Name: CESTO II**

**Sponsor: NFL BIOSCIENCES SAS.**

**BB HREC Application ID: 2021-04-332**

**Principal Investigator: Professor Stuart Ferguson**

**Research Site Address(es): University of Tasmania Clinical Research Facility**

**17 Liverpool Street**

**Hobart**

**Tasmania 7000**

**Daytime telephone number(s): (03) 6226 4233**

* I have read and understood the Participant Information Sheet.
* I am 18 years or older.
* I understand the purposes, procedures and risks of the research described in the project.
* I have had an opportunity to ask questions and I am satisfied with the answers I have received.
* I understand that the Study Doctor may contact my Local Doctor (GP) to inform him/her of my decision to participate in this study and the exchange of clinically relevant information. I consent to my Local Doctor (GP) being notified of my participation in this study and of any clinically relevant information noted by the Study Doctor in the conduct of the trial.
* I believe that my participation in this study is not contrary to my best interests.
* I freely agree to my participation in this research project as described and understand that I am free to withdraw my participation at any time during the research project without affecting my future health care.
* I understand that I will be given a signed copy of this document to keep on my own behalf.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
|  | Name of Participant (please print) |  |  |
|  |  |  |  |
|  |  |  |  |
|  | Signature of Participant |  | Date |  |  |
|  |

**Declaration by Investigator or Study Doctor/Senior Researcher†**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

|  |
| --- |
|  |
|  | Name of Study Doctor/Senior Researcher† (please print) |  |  |
|  |  |
|  | Signature |  |  Date |  |  |
|  |

† A senior member of the research team must provide the explanation of, and information concerning, the research project.