Participant Information Sheet/Consent Form for Adolescents to 17 Years

Southern Clinical Trials Ltd

Title	*A Phase III, Observer-Blind, Randomized, Controlled Multicenter Study to Evaluate the Safety of a Trivalent Subunit Influenza Vaccine Produced either in Mammalian Cell Culture or in Embryonated Chicken Eggs (Fluvirin®), in Healthy Children and Adolescents 4 to 17 Years of Age.*
Short title	*A study to evaluate the safety of a Novartis flu vaccine in children and adolescents aged 4 to 17 years.*
Protocol Number	*V58_31*
Project Sponsor	*Novartis Vaccines and Diagnostics Australia Pty Ltd*
Coordinating Principal Investigator / Principal Investigator	*Dr Simon Carson*
Location	*3 Strickland Street, Beckenham, Christchurch Ph: 03 337 1979*

Part 1

1 Introduction

You are being invited to participate in a clinical research project that is explained below.

This Information Sheet/Consent Form tells you about the research project. It explains to you clearly and openly all the procedures of the project. Knowing what is involved will help you decide if you want to take part in the research.
Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not you can take part, you might want to discuss it with a relative, friend or your doctor.
Participation in this research is voluntary. If you do not wish to take part, you don't have to.

If you decide you want to take part in the research project, you will be asked to sign the consent section before any study procedures are performed. By signing it you are telling us that you:
• Understand what you have read;
• Consent to taking part in the research project described below;
• Consent to have the procedures, which form part of the project;
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information Sheet and Consent Form to keep.

2 What is the purpose of this research?

Influenza (the 'flu) is a major cause of respiratory illness and death worldwide. Each year, many children are infected with flu. Symptoms are similar to a cold, including runny nose, sore throat, coughing, feeling unwell, headache and muscle aches. Most people recover within one to two weeks without requiring medical treatment. However, in the very young, the elderly, and those with serious health problems, infection with the flu virus can cause severe illness, and sometimes, death. Vaccination with a flu vaccine is the most effective way to prevent flu. Flu vaccines have been available for many years and can be effective in preventing infection and serious disease.

Generally, flu vaccines are made by growing the flu virus in chicken eggs, which means that hundreds of millions of high quality eggs are required each year to produce flu vaccines.

Novartis Vaccines and Diagnostics ('Novartis') is a pharmaceutical company (and is referred to in this Information Sheet as the 'Sponsor' of the research project) that has developed a flu vaccine called Flucelvax. Flucelvax does not require the use of chicken eggs during its manufacturing process, but is instead produced in a laboratory. A manufacturing process that is not dependent on eggs may allow a large number of vaccines to be produced very quickly, for example, in the event of a flu pandemic (when a large number of people may be infected with a new flu virus).

You are being asked to take part in this research study of a flu vaccine for the purpose of learning more about the safety of Flucelvax in children and adolescents. The study will compare Flucelvax with Fluvirin which is another flu vaccine made by the Sponsor using the traditional chicken egg-based manufacturing process. Results from this study will be provided to drug and vaccine regulatory authorities responsible for licensing vaccines.

Flucelvax is an experimental vaccine. This means that it has not yet been approved for use in Australia. However, it has been approved for use throughout Europe and the US for adults aged 18 years or older. It has been shown to increase the body's ability to fight flu infection. To date, Flucelvax has been given to nearly 6600 research participants older than 18 years and to approximately 2200 children and adolescents aged from 3 to 17 years.

Fluvirin® is approved in Australia to prevent flu and has been approved for use in the US and the UK for people aged 4 years and above, for many years.
This study will follow approximately 2040 children and adolescents aged 4 years to less than 18 years in Australia, Thailand the Philippines and New Zealand.

3 What does participation in this research involve?

If you decide to participate you will be in the study for approximately six months. During this period, you will need to follow all instructions given by the study staff. There are three scheduled study visits (Day 1, Day 29 and Day 183), two Diary completion reminder phone calls (Day 3 and Day 7) and four safety follow-up phone calls (Day 50, Day 91, Day 122 and Day 152) included in this study.

The procedures and activities described below will be performed to make sure you are able to participate in the study and to ensure that you can continue to participate for the duration of the study. These procedures will also be used to evaluate how safe the vaccine is.

Demographic and Medical History: During your first study visit (Day 1), and possibly during the following study visits and safety calls, you and your parent will be asked to provide information about your medical history. You and your parent will be asked to describe all medications and vaccinations you are currently taking or may have taken recently.

Physical Examination, Height and Weight: You will be given a brief physical examination at Day 1 and a brief physical examination one month and six months later if necessary. Your height, weight, temperature, blood pressure, heart rate and respiratory rate will also be measured at these three visits.

Pregnancy Test, Birth Control: If you are a female (aged from 9 to 17 years) who has started having periods, you will need to have a urine pregnancy test at the three study visits to confirm that you are not pregnant. For girls who have had their first period some questions will be asked about their period. The importance of adequate birth control will be discussed if research participants are, or may become sexually active during the study. Birth control must be used for at least 2 months before the study vaccine is given and used until the end of the study.

Vaccination: You will be given the study vaccine that is assigned to you. This will be done by chance (randomisation), like tossing a coin. You will have twice the chance of receiving Flucelvax compared to the chance of receiving Fluvirin. You will be given the vaccine in the upper muscle of (preferably) the arm you use the least. Neither you, your parent nor the study investigators will know which vaccine you receive. Only the person who gives you the vaccine will know which vaccine you have received. The study investigators will be able to find out if needed in an emergency.

30 Minutes After Vaccination (Post Injection Reactions): After the vaccination, you will be observed for approximately 30 minutes so that the study staff can look for any immediate side effects and measure your temperature.

Diary: Your parent (or someone they nominate) will be asked to report certain information following your study vaccination in a Diary provided to you. This is a booklet that reminds you to write down specific types of side effects that we look for after vaccination, any medications or vaccines you might have taken/received, and any changes to your health that occur during the time you will be using the Diary.

The study staff will explain to you and your parent how to make entries in the Diary and answer any questions you may have. You and your parent will also be asked to:

- look at the part of the arm where you received the vaccine and measure specific reactions you may see using a ruler provided;
- record and describe any other reaction you may experience that are sometimes seen after vaccination;
- measure your temperature by mouth using a digital thermometer provided;
- write down any medications and vaccinations you receive;
- describe any other illnesses you may have. You will also be asked questions about your health (including any serious medical problems such as hospitalization or any life-threatening medical problems);

- bring the Diary back with you at your next study visit.

The study staff will plan the visits as outlined in this form and remind you or your parent to complete the Diary for review and collection during the study visit at Day 29. During the reminder calls (on Day 3 and Day 7) the study staff will remind your parent (or someone they nominate) to write your reactions and events into the Diary given to them during your first study visit (Day 1).

If you experience any serious issue with your health, you will be monitored until the illness resolves or stabilises. After the last study visit (6 months after Day 1) you and your parent will also be instructed to contact the site in case you experiences any health event or change in your health which your parent thinks may be related to the study vaccine.

If you need to see your General Practitioner (GP) during the course of the study we would recommend that you inform the GP of your participation in this research project and we will send your GP a letter.

4 What do I have to do?

If you agree to participate in the study, you are agreeing to come to a clinic or be visited by study staff for the scheduled visits. You are also agreeing to follow the study doctor's and staff's instructions.

5 Other relevant information about the research project

There are no costs associated with participation in this research project, nor will you be paid for taking part. All flu vaccines used in this study are provided free of charge.

As you and your parent are required to attend a clinic study visit,you will be reimbursed for any reasonable travel, parking and other expenses associated with this. This is a set amount approved by the ethics committee.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you decide that you want to take part and later change your mind, you are free to withdraw from the study at any stage.

7 What are the alternatives to participation?

Your alternatives to taking part in this study may include being vaccinated against seasonal flu by your health care provider.

8 What are the possible benefits of taking part?

There may not be a direct medical benefit to you as a result of taking part in this study. You may be protected against flu or your body may have an improved ability to fight infection with flu. Information from this study will help us to learn more about the safety of the Flucelvax and Fluvirin.

9 What are the possible risks and disadvantages of taking part?

Based on what we know about seasonal flu vaccines and previous studies of Flucelvax and Fluvirin, the most likely side effects following vaccination with these vaccines are described below.

The injection site may ache; it may be red, bruised, swollen, or hard. You may also experience fever, chills/shivering, general discomfort, headache, muscle ache, aching of limbs, sweating, or a sense of fatigue. If such symptoms occur, they usually last for a very short period of time. Generalized skin reactions, including itching, non-specific rash and urticaria (hive like rash), flu-like symptoms, pain in the extremities, and muscular weakness are uncommon. Rarely, nerve pain, abnormal skin sensations, convulsions, swollen glands, high fever, a decrease in platelets (a type of blood cell), and allergic reactions which, in rare cases, can lead to shock, have been reported.

Digestive disorders such as diarrhoea, nausea, vomiting and abdominal complaints have also been reported. Inflammation of blood vessels associated, in rare cases, with transient kidney involvement, exudative erythema multiforme (a skin disorder resulting from an allergic reaction), neurological disorders such as dizziness, confusion, inflammation of the brain and spinal cord, inflammation of the nerves, Guillain Barré syndrome (inflammation of the nerves causing muscle weakness and sometimes paralysis), have been reported.

Occasionally cases of pain with swelling and redness of more than 10 cm in the injected arm, lasting more than one week have been reported.

As with all vaccines, in certain exceptional cases, severe allergic reactions may occur. Study staff will have access to equipment and medication to manage this rare event, should it occur.

If you have had an allergic reaction in the past after getting any vaccine, or if you are allergic to any part of the vaccine, chicken eggs, egg products or feathers) you must tell the study doctor or study staff before you decide to sign this informed consent form. If you have an allergy to any of these products, you will not be able to take part in this study as serious allergic reactions can be life-threatening.

Reproductive Risks:

The effects of cTIV (Flucelvax®) and TIVf (Fluvirin®) on an unborn child are not known. Because of this, both male and female participants must use effective contraception during the course of the research project.

It is important that research project participants are not pregnant or breast-feeding and do not become pregnant or father children during the course of the research project.

Females must not participate in this research project if they are pregnant or breast feeding or trying to become pregnant. If child-bearing is a possibility, female participants will be required to undergo a pregnancy test prior to commencing the research project.

Females who can become pregnant and who are sexually active must use an effective form of birth control for at least two months before getting the study vaccine and must be willing to use

effective birth control until the end of the study.

Male participants in this study should not father a child for the duration of the study.

We can advise whether you need to use contraception, what kind of contraceptive methods to use and how long to use them.

If you think you might be pregnant, you must contact the study doctor immediately.
If you become pregnant during the course of the study we will need to keep in touch with you and your parent until the end of the pregnancy to check on your health and the health of your baby.

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10 What if new information arises during this research project?

Sometimes during the course of a research project, new information about the risks and benefits of taking part in the study may become known to us. If this happens, the study staff will tell you about it in a timely manner and discuss with you whether you want to continue in the research project.

11 Can I have other treatments during this research project?

You can continue to take any medicines that you are currently on, or that are prescribed to you during the course of the study. It is important to inform the study staff about any medications you may be taking, including over-the-counter medications and to record any changes to them in the Diary during your participation in the research project.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify study staff before you withdraw.

If you do withdraw during the research project, we will not collect additional personal information, although personal information already collected will be retained to ensure that the results of the project can be analysed properly and to comply with law. However, you should be aware that any code-numbered data on you provided to the Sponsor up to the time of withdrawal will form part of the research project results. If you do not wish your code-numbered data to be supplied to the sponsor, you must tell us before you join the research project.

13 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
• Unacceptable side effects to either Flucelvax or Fluvirin;
• Flucelvax or Fluvirin being shown not to be effective;
• Flucelvax being shown to work and not need further testing;
• Decisions made in the commercial interests of the Sponsor or by local regulatory/health authorities.

Part 2

14 What will happen to information about me?

To ensure that your personal information is kept confidential, your name, and any other information that allows you to be identified, will not be entered on the forms/electronic systems or included in any records or samples the study investigators provide to the Sponsor. Instead, your data will only be identified by a code.
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.

The information obtained may be subject to an audit or inspection by the sponsor or by regulatory agencies (eg. Ethics committee).The results may be published, you will not be identified. A description of this trial will be available on http://www.ClinicalTrials.gov, as required by local health authorities

15 Complaints and Compensation

If you are injured as a direct result of a study related procedure or because you received the study vaccine, appropriate medical care for the treatment of the illness or injury will be given to you.

If you chose to participate in the study, you will not be able to claim injury compensation through the ACC (Accident Compensation Corporation).

However, if you suffer injury as a result of your participation in this trial, Novartis Pharmaceuticals Australia Pty Ltd will adhere to the Researched Medicines Industry Association of New Zealand Incorporated Guidelines on Clinical Trials Compensation for Injury Resulting from Participation in an Industry-Sponsored Clinical Trial.

A copy of these guidelines is available on request from your study doctor. If you think that you have suffered injury as a result of your involvement in this study, you must contact your study doctor immediately.

If you experience an injury or have any questions or concerns, you should contact the study doctor at: Southern Clinical Trials Ltd, ph 03 337 1979.

By signing this consent form you will not waive the legal rights you are entitled to as a participant in a research study.

16 Who is organising and funding the research?

This study is being funded by Novartis Vaccines and Diagnostics Pty Ltd who is referred to as the Sponsor of the study. Novartis manufacture both the investigational vaccine (Flucelvax) and Fluvirin that will be used in this study and they will provide funds to Southern Clinical Trials Ltd. to complete the study.

The Sponsor may benefit financially from this research project if, for example, the project assists them to obtain approval for Flucelvax. By consenting to taking part in this research project you agree that data generated from analysis of the collected data may be provided to the Sponsor who may directly or indirectly benefit financially from knowledge acquired through analysis of your collected data.

You will not benefit financially from your involvement in this research project even if, for example, the knowledge acquired from analysis of the collected information proves to be of commercial value to the Sponsor, the study investigators or their institutions, there will be no financial benefit to you, or your family from these discoveries.

No member of the research team will receive a personal financial benefit from your involvement in this research project.

17 Who has reviewed the research project?

This study has received ethical approval from the Northern A Health and Disability Ethics Committee, which reviews national and multi-regional studies.

18 Further information and who to contact

During this study, if you have any questions about the kind of research involved in this study or your child's rights as a research subject, you should contact Northern A Health and Disability Ethics Committee, Phone: 0800 4 384487 (ETHICS) or email: hdecs@moh.govt.nz.

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate: Free phone: 0800 555 050 Free fax: 0800 2 SUPPORT (0800 2787 7678)

You may also contact the Health and Disabilities Commissioner Phone: 0800 11 22 33 or email: hdc@hdc.org.nz .

For Maori Health Support; Please contact Peter Mason, Connections "Nga Kete E Rua", ph: 027 441 4312.

If you have any medical or study related questions or feel your child has been hurt or injured as a result of taking part in the study, you should contact: Dr Simon Carson, Southern Clinical Trials Ltd, ph 03 337 1979.

If you agree to have your child participate in this study, you will be given a copy of this consent form after both you and the study doctor have signed it.

Consent Form – Participant

Title	*A Phase III, Observer-Blind, Randomized, Controlled Multicenter Study to Evaluate the Safety of a Trivalent Subunit Influenza Vaccine Produced either in Mammalian Cell Culture or in Embryonated Chicken Eggs (Fluvirin®), in Healthy Children and Adolescents 4 to 17 Years of Age.*
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Coordinating Principal Investigator/	*Dr Simon Carson*
Location	*3 Strickland Street, Beckenham, Christchurch* *Ph: 03 337 1979*

Your rights as a participant are as described in the HDC Code of Rights

English	I wish to have an interpreter	Yes	No
Deaf	I wish to have a NZ sign language interpreter	Yes	No
Māori	E hiahia ana ahau ki tetahi kaiwhaka Māori/kaiwhaka pakeha korero	Ae	Kao
Cook Island Māori	Ka inangaro au i tetai tangata uri reo	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu	E	Nakai
Sāmoan	Ou te mana'o ia i ai se fa'amatala upu	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea	Io	Ikai
	Other languages to be added following consultation with relevant communities.		

- I have read and understand the information sheet dated **06 May 2013**
- I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
- I have had the opportunity to use whānau support or a friend to help me ask questions and understand the study.
- I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time, and this will in no way affect my future health care.
- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- I understand that information collected about me will be stored for 15 years.
- I understand that the treatment, or investigation, will be stopped if it should appear harmful to me.
- I understand the compensation provisions for this study and that Iwill not be able to claim injury compensation through the ACC (Accident Compensation Corporation).
- I have had time to consider whether to take part in the study.
- I know who to contact if I have any side effects from the study.
- I know who to contact if I have any questions about the medication used in this study or about the study in general.
- I may have to leave the study without my consent if I need other treatment, do not follow the study plan, have a study-related injury or for any other reason
- If I leave the study for any reason the study doctor may ask me to have some end-of-study tests
- I understand that by signing this consent form I am not giving up any of my legal rights.
- I will receive a signed copy of this consent form
- I agree to an approved auditor appointed by either the sponsoring pharmaceutical company, ethics committee or the regulatory authority or their approved representative and approved by the Multi-region Ethics committee reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
- I agree to my GP or other current provider being informed of my participation in this study. Yes No

Subject's name (print):

Subject's signature: Date (DDMMMYY):

Declaration by Investigator

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 Investigator/
(please print)

Signature Date

Note: All parties signing the consent section must date their own signature.