INFORMATION LETTER FOR PARENTS

Immunogenicity, molecular profiling and safety of a marketed quadrivalent influenza vaccine (Vaxigrip Tetra® administered by the intramuscular route in 6 to 8 months old infants.

Promotor of the study : Prof Arnaud Marchant, Institut d'Immunologie Médicale, ULB
Clinical Research Organiser *:* Harmony clinical research
Principal Investigator*: Dr Tessa Goetghebuer*
Sub Investigators*: Dr Lore Van Bruwaene*

1. Introduction

You are invited to take part in a clinical trial. The aim of this trial is to study the influenza vaccine Vaxigrip Tetra® that has been developed by Sanofi Pasteur Europe.

This informed consent form (ICF) describes the trial and what participating may mean for you. The trial staff will explain the trial in this informed consent form, please ask them about anything you do not understand.

Like for all clinical trials, the documents related to the trial have been reviewed and approved by the Belgian competent authorities and an independent Ethics Committee.

If you agree to join the trial, you will be asked to sign this informed consent form.

2. What is the purpose and the design of the trial?

Influenza or flu is caused by influenza viruses that circulate mainly in autumn and winter (flu season) and may vary from year to year. Symptoms of influenza can range from mild colds to severe infection of the airways and lungs. Complications are possible particularly in very young children.

The best protection against influenza is vaccination, but the composition of influenza vaccines needs to be adjusted annually and is often insufficiently effective to protect the most vulnerable. To remedy this, there is currently insufficient knowledge on how to obtain a long-term immunity with a broad protection against different flu viruses.

In order to develop a universal influenza vaccine, more insight into the immunological mechanism and which elements are necessary for protection is needed.

In 2019, the INCENTIVE project was launched with an EU-India collaboration with the aim of developing a new flu vaccine that can provide more long-lasting protection.

This project includes 3 studies addressing the elderly population, children and infants in Europe and India with the same commercial flu vaccine Vaxigrip Tetra®. This

vaccine is marketed in Europe and is an inactivated influenza vaccine that protects against four types of influenza viruses (season 2022-2023). Conducting the studies in parallel will allow us to compare immune responses after vaccination from both continents.

The study in Belgium will involve 50 infants . During the first visit, (D0) your baby will receive one dose of the vaccine in the thigh muscle after which he/she will remain at the centre for 15 minutes for observation. A second dose of vaccine will be given 1 month after the first dose. There will be follow up visits 3 days after the first dose and 28 days after the second dose. At each visit you child will be examined and weighted and blood sample will be taken for immunological tests at three of these visits: at D0, D3 and D58.

3. What will happen during the trial?

Your baby may participate in this study if:

- 6 to 8 months
- being healthy
- has not had influenza or viral respiratory infection since birth.

 you will come 4 times to the study center

  your baby will have a blood sample of 6 ml (= a table spoon) and receive the first dose of the vaccine on the first visit (D0). He/she will be observed for 15 minutes after vaccination.

 your baby will have a blood sample of 6 ml (= a table spoon) 3 days after the vaccination (D3)

your baby will receive the second dose of the vaccine on the first visit (D30), and be observed for 15 minutes

 A blood sample of 6 ml (= a table spoon) is taken 28 days after the second vaccination (D58)

approximately 1 month

	Visit 1 (D0)	Visit 2 (D3)	Visit 3 (D30)	Visit 4 (D58)
Questions on health status				
Physical examination				
Vaccination				
Sample collection	6 ml	6 ml		6 ml

4. What are the restrictions, as well as the potential risks and discomforts?

Your baby may also feel discomforts related to the procedures. The trial staff are trained to take the right measures to reduce risks and limit any discomforts such as applying cream to anesthetize the skin before the blood sampling.

It is also possible to have discomforts related to the vaccination. It includes local pain and/or local redness and fever. Some children may be more irritable or sleepy for a few hours after vaccination.

5. What are the potential benefits?

As the Flu Vaccine is not part of the usual vaccination calendar of childhood, your baby will benefit protection against Flu over the following year.
Moreover, the results of the trial will help learn about the mechanisms of immune response after influenza vaccination in infants.

6. Are there any alternative vaccines and/or treatments?

Currently for influenza several vaccines are available in Belgium. Vaxigrip Tetra® is one of them.

7. Will I receive compensation for my participation?

The sponsor has agreed to pay the trial site for the conduct of the trial and covers the costs of this trial. You or your health insurer will not need to pay anything to participate in this trial.

You will receive an amount of 50 euro cash for each visit to the study centre as compensation for the journey to the study centre and for any inconvenience that might arise from taking part in the study.

8. What if something goes wrong?

Even if there is no fault, the sponsor is liable for any damage you suffered that is directly or indirectly related to your participation in the trial. The sponsor has taken an insurance called ‘No Fault Insurance’ for this situation. This means you do not have to provide proof that the investigator or trial staff made a mistake.

In case you suffered any damage, you must inform the trial staff as soon as possible.

If the investigator believes a link between the damage you suffered and the trial is possible, he/she will inform the sponsor. The latter will officially inform the insurance company. The insurance company will then decide whether to appoint an expert to find out if there is a link between the damage you suffered and the trial.

At any point if you disagree with the investigator, you can contact the insurance company. If you disagree with the insurance company expert, you can sue the insurer directly. You can find the name and policy number of the insurer at the end of this form.

9. What will happen to my baby 'samples?

As part of the trial, 3 blood samples will be taken. Your samples will be given a unique code number (Ref. i). The code number will not identify your child directly and will not include his/her personal information (data).
The samples will be managed and stored at the Biobank of the Free University of Brussels, BB200002 managed by Prof. A. Marchant for a maximum of 25 years and will then be destroyed. They may be sent to the sponsor laboratories or other laboratories or institutions working with the sponsor. These institutions and/or laboratories may be outside the country where you live. The tracking of your samples will be ensured by the sponsor.
The samples will be used to learn more about the mechanisms of immune response after influenza vaccination and develop and improve tests related to the vaccine(s) or disease(s).

The remaining blood samples may be used for:

- Additional research related to the vaccine and/or disease. This means additional research conducted to better understand the vaccine and/or disease.

- Additional research NOT related to the vaccine and/or disease. This means additional research conducted to understand other vaccines and/or diseases or to develop new treatments or research methods. In this case, such research will always require ethics committee approval.

What happens in case of incidental findings?

During the trial new information about your baby's health might be discovered by chance. This is called "incidental findings". Such information may be important to you. If you agree, the investigator will discuss the results with you.

10. What happens to my data?

The trial staff will collect data about you including your name, address and phone number, and data about your baby's health. All your data collected for this trial will be stored in the trial medical records at the trial site. Each patient participating in the research will be identified by a code (which will not contain any personal identifiers (last name, first name, initials, full or partial date of birth, file number ...). This code will be used to identify the data and samples collected. Your child's identity will only be known to the hospital team where your child is treated. Processing these data in this trial is allowed because we are conducting scientific research and you have given your consent.

The person responsible for processing your coded data is the ULB, which is the Promoter of this study. The Hospital _____ remains responsible for the processing of your data included in your medical file.

Your data will be processed and protected in accordance with the General Data Protection Regulation (GDPR, Ref. ii) and the Belgian law on data protection of 30th July 2018 (Ref. iii).

What are your rights to access your data?

You can ask the investigator what data are being collected about you and your baby and how those data will be used in connection with the trial.

You have the right to access, receive and review your personal data and to request its correction if it is inaccurate. It is impossible to have all your data erased or to oppose or limit the processing of your data. This could lead to distorted study results.

How long will your data be kept?

The sponsor must keep the coded data from clinical trials for a minimum of 25 years after the end of the trial to ensure the validity of the research. This will also be the case if you stopped trial participation prematurely.

Where else can you find information about this trial?

There will be a description of this trial on the website of the study centre and/or other clinical trial registries. It may also appear in clinical trial registries in countries where the trial is conducted.

A description of this trial will be available on https://www.clinicaltrialsregister.eu. You can search this website(s) at any time.

After the trial is finished, the website https://www.clinicaltrialsregister.eu/ will include a summary of the results. Also, a description and the results of this trial may be published in specialised medical journals. A copy of a summary for laypersons or the scientific publication can be obtained from the investigator or the trial staff.

Who owns the trial results?

The sponsor, the Université Libre de Bruxelles, will own the trial results. The sponsor plans to use the results, and may get patents, or sell the vaccine in the future, or make profits in other ways.

Will my data be used for other purposes?

Your data might be used for:

- Further research related to the vaccine and/or disease. This means additional research conducted to understand the tested vaccine(s) and/or diseases(s) better.
- Further research NOT related to the tested vaccine and/or disease. This means additional research conducted to understand other vaccines and/or diseases or for the development of new treatments or research methods. In this case, this research will always have to be approved by an ethics committee.

11. Can my participation end prematurely?

Can you leave the trial?

Your participation is voluntary, and you can leave the trial at any time. You do not have to give a reason if you choose to leave. Tell the investigator if you no longer want to take part, so that your trial participation can be stopped safely. Your choice will not affect your relationship with the doctor.

If you decide to leave this trial, no new data will be collected. The data and samples that have been collected before you leave the trial will still be used as described in this form.

<u>You may be asked to leave the trial if:</u>
For example:

- You do not follow the trial instructions
- The entire trial may need to be stopped for all participants.

If any of this happens, the trial staff will explain the reason to you and ensure proper follow-up.

12. Who can I contact in case of questions?

Name	Function	In case of:	Contact details
Dr Tessa Goetghebuer	Principal Investigator of the trial site	Information and concerns about possible adverse events or your participation in the trial	02.535.48.56, tessa.goetghbuer@stpierre-bru.be
Katty Renard	The trial staff	Information, problems, concerns	02.535.48.56
Service des urgences pédiatriques	The trial staff urgency contact	Urgent questions	02.535.43.60
Pauline Etienne	Patient rights officer	Concerns relating to your rights as a participant in a trial	02.535.35.95
Deborah Duhoux	Data protection officer of the trial site	Questions relating to the confidentiality of your data	02.535.36.34 dpo@stpierre-bru.be
	Belgian Data Protection Authority	Complaints relating to the confidentiality of your data	+32 (0)2 274 48 00 contact@apd-gba.be

References

[1] Belgian Law of 19 December 2008 on the acquisition and use of human body material with a view to medical application to humans or scientific research, and the applicable royal decrees.

[1] General Data Protection Regulation No 2016/679 of the European Parliament and of the council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC.

[1] The Belgian Law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data.

INFORMED CONSENT FORM FOR PARENTS

Immunogenicity, molecular profiling and safety of a marketed quadivalent influenza vaccine (Vaxigrip Tetra®) administered by the intramuscular route in 6 months old infants.

1. I declare that Dr. …… has informed me of and that I understand the purpose of the clinical trial, its duration, possible risks and discomforts and what is expected of me and my child. My rights have been explained to me and I have understood those rights.

2. I have had enough time to think about taking part in this study and to discuss it with a trusted person (e.g. friends, relatives, treating physician).

3. I have had the opportunity to ask any questions that came to mind and have obtained a satisfactory response to my questions.

4. I understand that my participation (my child's participation) in this trial is voluntarily and free from any coercion and that I am free to stop at any time his trial participation.

5. I understand that data about my child will be collected and that they will be treated confidentially.

6. I understand that the sponsor has taken out an insurance in case my child should suffer any damage in connection with his participation in this trial.

7. I understand that when participating in this trial, I will not have any costs.

8. I declare that I will provide my child's general practitioner/treating pediatrician with the information letter given to me by the researchers.

9. I agree not to include my child in any other trial at the same time without first informing the investigator or the trial staff.

10. I understand that I need to cooperate and follow the investigator's and trial staff's instructions regarding the trial.

11. I understand that participation to the trial might end for me without my consent if I need other treatment, do not follow the trial plan, have a trial-related injury, or for any other justified reason.
12. I certify that all the information I have given about my child's medical history is correct. I understand that my failure to inform the investigator or designee about any exclusion criteria may harm my child.
13. I agree to the further use of the data for future research related and unrelated to the context of the study 0 Yes 0 No

    I agree to the storage of my excess sample in a biobank for future research under the conditions specified in the section "What happens to your sample" on page 5/10.
    0 Yes 0 No

    I consent to the use of my samples for future research limited to the scope of what has been presented to me in this document 0 Yes 0 No

    I consent to the use of my samples for future research NOT limited to the scope of what has been presented to me in this document 0 Yes 0 No

    I agree, in the context of a collaborative project, to the transfer of part of the sample collected to third party academic laboratories 0 Yes 0 No

    I agree, in the context of a collaborative project, to the transfer of part of the sample collected to third party laboratories linked to industry 0 Yes 0 No

    I agree to receive, via my referring physician, any information resulting from research carried out on my body material samples. 0 Yes 0 No

To be filled in by the parents / legal guardian, to sign and date personally:

Name or parents / legal guardian (as applicable):

1 : ……..

2 : ……..

Name child: ……..

Date of birth child: ……..

Date: ……../……../……

Signature parent / legal guardian 1 Signature parent / legal guardian 2

Declaration of the physician responsible for informed consent

The undersigned has informed, as described in the information form, the study to the parents / legal guardian (as applicable).

To be filled in by physician responsible for informed consent:

Date: ……../……../…… Stamp + signature:

[iii] The Belgian Law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data.