Informed consent 1: to participate in screening visit 1 of the Flu Air-shedding & Immunity Monitoring (FLAIM) Study

Official title of the study: ***FLAIM study: an open-label, single center influenza H3N2 controlled human infection model study of viral shedding, mucosal and systemic immunity***

Study number: CHIMFLU-M-001

Sponsor(s) of the study: Centre for the Evaluation of Vaccination (CEV) / Vaccinopolis, University of Antwerp

Contract Research organisation: Harmony Clinical Research BV, Brusselsesteenweg 159, 9090 Melle, Belgium.

Site name: Centre for the Evaluation of Vaccination (CEV), University of Antwerp

Address of site: Drie Eikenstraat 663, 2650 Edegem, Belgium

Document Revision History

Version	Date	Change
1	12 May 2025	NA
2	03 Jul 2025	Resolved inconsistency in wording eligibility criteria between protocol and ICF

Who can I contact in case of questions?

Name	Function	In case of	Contact details
Joren Raymenants	Principal Investigator of the site	Information, problems or concerns	+3232652652 vaccinopolis@uantwerpen.be
	The study staff	Information, problems, concerns	+3232652652 vaccinopolis@uantwerpen.be
	Emergency contact	Emergency	+32496230712
Amlin Insurance SE, Koning Albert II laan 37, 1030 Brussels, Belgium	Insurance Company of the sponsor	In case of disagreement or complaint on a damage claim	Policy N°: 199.535.692
	Patient rights ombudsman	Concerns relating to your rights as a participant in a study	+32 3 821 31 60, ombudsdienst@uza.be
	Data protection officer of the **site**	Questions relating to the confidentiality of your data	+3232655263 koen.pepermans@uantwerpen.be
	Belgian Data Protection Authority	Complaints relating to the confidentiality of your data	+32(0)2274 48 00 contact@apd-gba.be

- *To manage complaints not resolved by the investigator, you can contact the study centre ombudsman at the above address.*
- *According to the GDPR, you have the right to access the processing of your data. For questions about this, you can contact the Study Centre's Data Protection Officer at the above address.*
- *You also have the right to lodge a complaint about the way your data are processed with the Belgian supervisory authority responsible for compliance with data protection legislation: Data Protection Authority (GBA), above.*

Version No: 2

Dear Sir, Madam,

We would like to inform you with this brochure about the first screening visit of the FLAIM study. This consent form only relates to this first screening visit, where we will measure flu antibodies in your blood. If these are sufficiently low, you may, after a separate informed consent procedure, participate in a controlled human infection study. During such an infection study, you will be administered the Influenza virus to induce flu. We ask you to have a thorough read of this brochure.

Participation in this screening visit and the rest of the study are entirely voluntary, so you have the choice whether or not to participate.

This study was approved by an independent central ethics committee, the ethics committee of the University Hospital Antwerp (UZA, Belgian Registration Number: B3002023000030) on 26 May 2025. The study is conducted in accordance with Good Clinical Practice (ICH-GCP) and the 2013 Declaration of Helsinki regarding the protection of participants in clinical studies. Ethics committees are responsible for protecting participants in clinical studies according to Belgian law of May 7, 2004 (amended by the law of May 7, 2017) concerning studies involving humans. The approval of this study by the ethics committee should not influence your decision to participate in this study or not. Before you agree to participate in this study, we ask you to take note of what this study will entail in terms of organization, possible risks and benefits, so that you can make an informed decision. This is called 'informed consent'. We ask you to read the information brochure carefully. For any questions, you can contact the physician-researcher or their representative. This brochure consists of two parts: (1) the essential information you need to make your decision, (2) your written consent when you decide to participate.

Essential Information for your decision to take part in this first screening visit

Background

The influenza virus or "flu" still has an important health impact worldwide. Better interventions are needed for influenza control.

Human challenge studies (also known as controlled human infection models) involve deliberately exposing healthy volunteers to infectious organisms in a controlled manner. These studies allow better understanding of the impact of the organism on the exposed person (e.g. signs and symptoms), the body's response to infection (e.g. the development of immunity) and the risk of onward transmission.

This study plans to expose healthy, non-smoking volunteers of 18–55 years old to a measured amount of influenza A(H3N2) virus via nasal spray into the nose. This exact challenge virus has been used before in similar studies. ***Only individuals with low antibody levels can participate in this study.***

Purpose of the study

During the challenge study, we aim to reestablish the percentage of persons that become infected and which symptoms they develop. Also, we will study how many respiratory (viral) particles participants exhale before, during and after infection and the immune response they develop in airways and blood.

During the first screening visit, we only ask you to undergo a blood test to evaluate your blood antibody level against the administered virus. This is because, if your immunity is too strong, you are unlikely to become infected after virus exposure, and you will not be eligible to participate in the rest of the study. If your antibody levels are low enough, you will be invited for a second screening visit. At that point, a separate informed consent procedure will discuss the rest of the human challenge study. You can already review the second informed consent form and video presentation via https://www.uantwerpen.be/flaim.

Why am I being asked to take part?

You are being asked to take part in this study because, based on the pre-screening checklist you filled out, you:

- Are aged between 18 and 55 years old
- Are not currently participating in another clinical study where a vaccine, medication or another intervention is being tested
- Are not an employee or family member of the Investigator or study site personnel
- In good health with no significant medical conditions (including immune problems, lung problems or other chronic conditions)
- Don't have important allergies (e.g. pollen or egg products)
- Did not donate blood products in the last 30 days
- Are not pregnant or breastfeeding
- Are on effective contraception (if applicable)

- Are not a current smoker (including vaping) and haven't smoked more than 1 pack of cigarettes per day on average for a total of 5 years
- Are not a heavy drinker (>15 units per week or > 80 percent of days)
- Don't have a substantial history of drug abuse as judged by the investigator
- Highlighted that you were happy to stay in quarantine at Vaccinopolis for 13 days.

Any uncertainty related to your possibility to participate will be flagged during screening visit 1 and discussed in depth during screening visit 2.

What will happen during the study

We will invite up to approximately 180 individuals for the first screening visit for this study. Participants who are eligible based on the pre-screening checklist will be consented by a study physician (meaning they sign this form) and undergo a blood test to evaluate the 'microneutralization titer'. This is a blood antibody test that evaluates whether the antibodies in your blood can neutralize the challenge virus. We will draw no more than 10 milliliters of blood. Those with low antibody levels will be invited for screening visit 2 and – pending a second informed consent and further assessments – for the remainder of the study.

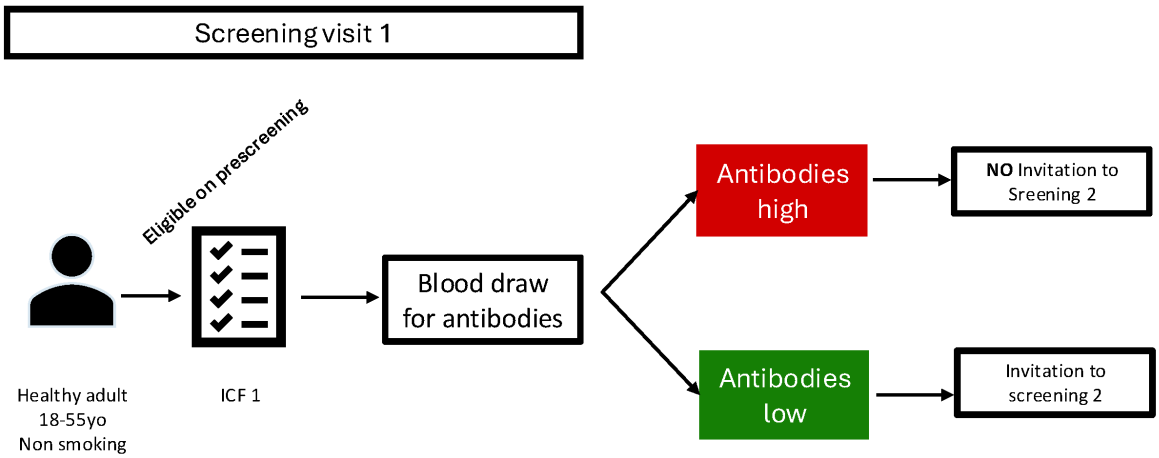

Figure 1 Flow of screening visit 1 and implications for further study participation

Voluntary Participation

Your participation in this study is entirely voluntary and there can be no form of coercion whatsoever. You have the right to refuse to participate in the study or to withdraw from the study without having to provide a reason, even if you previously agreed to participate. Your decision will in no way affect your relationship with the physician-researcher, nor the quality of your further care. If you wish to stop your participation in the study, you must inform your physician-researcher. If you withdraw your consent, the data collected up to the moment of your withdrawal will be retained. This is necessary to guarantee the validity of the study. If you agree to participate in screening visit 1 of this study, your signed consent is required (see part 2 of this information brochure).

End of the Study

The physician-researcher can also terminate your participation in the first screening visit of this study or beyond if they believe this is better for your health or if it is determined that you are not

complying with the participation requirements. Additionally, it sometimes happens that competent national or international authorities, the ethics committees that initially approved the study, or the sponsor may terminate the study.

Costs and Compensation

There will be no additional costs involved with this research for you as a healthy volunteer. You will need to travel to the research center for your visit. All medical costs (e.g. for sample collection and clinical tests on the samples) resulting from your participation in the screening visit of this study are covered by the sponsor.

A compensation of **€43.68** is provided for your participation in this screening visit.

Benefits and Risks

If you decide to participate to this screening visit, we can evaluate whether your antibody immunity is low enough to be eligible to join the influenza virus challenge study later.

There are no major risks associated with this screening visit itself. For the blood sampling, you may experience minor bruising at the site of the needle puncture and/or feel lightheaded during the procedure, but this risk is minimal as qualified personnel will be performing the blood draw. See informed consent 2 for the risks and benefits associated with the remainder of the study.

What If something goes wrong within the study?

The sponsor is liable for harm caused to you whether directly or indirectly related to your participation in this screening visit 1 and the remainder of the study. The sponsor has taken an appropriate insurance (a so called “NO FAULT INSURANCE”) for this liability (insurance company Amlin Insurance SE, policy number 199.535.692). A copy of the insurance certificate can be obtained from the investigator or study staff. If you experience damage as a result of your participation in the study, you or your beneficiaries will be compensated for this damage by the sponsor of this study, according to the applicable legislation. You do not need to prove fault for this.

Protection of Privacy and Data Coding

A unique code is used per participant of this screening visit and a possible later participation in the remainder of the study. To this unique code, we link data obtained from the pre-screening form and from the blood sample we take during the first screening visit.

This ensures confidentiality throughout the entire study. Your blood sample will be transferred in coded form to the laboratories where the antibody immunity test will be performed. Only the research team from UAntwerpen has access to the code list, which will be kept in a secure location. Only they can decode the data if additional information is needed. From the end of the research, the code list will be kept for at least 25 years according to Belgian legislation. After that, it will be kept as long as necessary to comply with legal, regulatory, scientific, or other requirements. After this, the code list will be destroyed. You will not be identified (neither by name nor in any other way) in results or publications related to this study.

For data handling, procedures follow the Belgian law for the protection of privacy with respect to the processing of personal data of December 8, 1992, and July 30, 2018. This Directive regulates the protection of natural persons with regard to the processing of personal data and the free movement of such data.

You have the right to ask the researcher what data about you is being collected during the study and why. You also have the right to ask the researcher to grant you access to your personal information and to have any necessary corrections made. By participating, you give permission to add the results of the blood sample to the study data and to pass them on to the principal investigator. The protection of personal data is legally determined by the validity of laws and regulations concerning the protection of privacy. If you agree to participate in this research, you also consent to the use of obtained coded data for the above purposes. If you stop your participation prematurely, the study data collected during the period you were included in the study will remain usable based on your initial consent. All parties involved in conducting the study will respect your privacy at all times.

What if new information becomes available during the course of the study?

During the course of the study, important new information might become available, possibly affecting your decision to participate to the first screening visit and/or the remainder of the study. For example, important new information on influenza challenge studies may become available. It is the duty of the investigator to discuss this new information with you and to give you the opportunity to re-consider your participation in the study.

Regardless of your (continued) participation, your investigator will see to it that you continue to receive the best possible medical care.

Biological Samples Collected During the Study

The sponsor of the study commits to using the samples only within the context of the study as mentioned in the 'Purpose' section above. Due to the continuous (technical) advances in the field of study, we would like to keep your samples for a maximum of 25 years for future research conducted by the sponsor of the study and by research groups and/or companies with which a collaboration agreement exists. This research will remain within the framework of the study and is therefore situated in the context of infectious diseases and immunology. Information that directly identifies you, such as your name, initials, address, will not be transferred. This will receive a code number where only the principal investigator and the research team (CEV/Vaccinopolis) know which name corresponds to it. Any research outside the context described in this document can only take place after approval by an ethics committee.

If after reading the first part of this information brochure you agree to participate in the first screening visit of the FLAIM study, please also read and sign the second part **'Consent Form'**. You also have the opportunity to first discuss your participation with your relatives and ask questions to the research team/treating physician.

On behalf of the researchers, we thank you for your time and possible participation in the study.

Informed consent form 1 to participate in the first screening visit of the Flu Air-shedding & Immunity Monitoring (FLAIM) Study

Principal Investigator: Dr Joren Raymenants

Co-investigators: Profs Pierre Van Damme, Ilse De Coster, Paolo Palma

PARTICIPANT

PREREQUISITES FOR YOUR PARTICIPATION IN THE STUDY

- I declare that I have read this form and understood its information.
- I declare that I have been informed of and that I understand the purpose of the clinical study visit, its duration, possible risks and discomforts, the precautions that I have to take and what is expected of me. My rights have been explained to me and I have understood those rights.
- I have had enough time to think about taking part in this study visit and to discuss it with a trusted person (for example friends, relatives, treating physician, …).
- I have had the opportunity to ask any questions that came to mind and have obtained a satisfactory response to my questions.
- I understand that my participation in this study visit is voluntarily and free from any coercion and that I am free to stop at any time my study participation.
- I understand that data about me will be collected and that they will be treated confidentially.
- I am aware that my personal data being processed as described in this document.
- I understand that representatives of the sponsor, the ethics committee, and competent health authorities have access to my medical record if authorised to do so (as described in this document).
- I understand that the sponsor has taken out an insurance in case I should suffer any damage in connection with my participation in this study visit.
- I understand that when participating in this study visit, I will not have any costs.
- I understand the importance of contraception and will adhere to the recommendations provided. I will also inform my partner(s) about my participation in a clinical study involving a medicinal product (influenza virus) that may be harmful to the fetus, and we will take the necessary contraceptive measures together.
- I will voice my wish to the investigators to inform my general practitioner of my participation in this study visit.
- If I take part in another interventional trial, I must inform the investigator or trial team about this. I agree not to take part in any other interventional trial (e.g. with a study drug, medical device, experimental surgical technique) at the same time without first informing the investigator or the trial staff, who might not permit me to participate for a good reason.
- I understand that I need to cooperate and follow the investigator's and study staff's instructions regarding the study.

- I understand that participation to the study might end for me without my consent if I need other treatment, do not follow the study plan, have a study-related injury, or for any other justified reason.

- I certify that all the information I have given about my medical history is correct. I understand that my failure to inform the investigator or designee about any exclusion criteria may harm myself.

OPTIONAL CONSENTS WHICH ARE NO PREREQUISITE FOR YOUR PARTICIPATION IN THIS STUDY.

1. As specified in this document, the sponsor would like to be able to use your data obtained from this study in connection with other research and development activities (and the associated scientific publications) on the condition that such research purposes have been approved by a Belgian recognized Ethics Committee.

   Do you agree with the use of your data obtained in this study for other research purposes?

   (Tick as appropriate. If you leave this question open, we assume the answer is 'I do not agree'.)

☐ **I agree**	☐ **I do not agree**

2. It may happen that incidental findings are discovered that may be important to your health or the health of your blood relatives.

   If this happens: do you want the investigator to inform you (directly or via your treating physician) of this result?

   (Tick as appropriate. If you leave this question open, we assume the answer is 'yes, I want to be informed'.)

☐ **No, I do not want to be informed**	☐ **Yes, I want to be informed**

I consent to take part in the study, with the above restrictions and I have received a signed and dated copy of all pages of this document.

Participant's surname and first name:

Date (DD/MMM/YYYY):

Participant's signature:

INVESTIGATOR

I, the undersigned investigator, confirm that

- the participant has been verbally provided with the necessary information about the first screening visit of the FLAIM study, has been explained the content and has been given an original signed document.
- I have verified that the participant has understood the proceedings of the screening visit of this study.
- I have given the participant sufficient time to agree to take part and to ask any questions.
- no pressure was applied to persuade the participant to agree to take part in the study.
- I operate in accordance with the ethical principles set out in the latest version of the "Helsinki Declaration", the "Good Clinical Practices" and the Belgian Law.

Investigator's delegate / Investigator, surname and first name:

Date (DD/MMM/YYYY):

Investigator's delegate / investigator signature: