Title of the study: *YAS open-label PoC study: IMEC breath analyser for capturing and detecting SARS-CoV-2 virus in exhaled air*

Sponsor of the study: *Imec vzw, Kapeldreef 75, 3001 Leuven, Belgium*

Medical Ethics Committee: *Ethische Commissie Onderzoek UZ / KU Leuven*

Local investigators: *Prof. Dr. Emmanuel André & Joren Raymenants, Universitair Ziekenhuis Leuven, Campus Gasthuisberg, Herestraat 49, B-3000 Leuven*

I Information vital to your decision to take part (5 pages)

Introduction

You are being invited to take part in a clinical study whereby you will be asked to breathe into a new device for the detection of the presence of COVID-19. This study is aimed at comparing a new detection method for COVID-19, which is based on exhaled air, with the existing method based on the nasopharyngeal swab. You will be asked that additionally to the standard nasopharyngeal swab, a second nasopharyngeal swab will be taken to perform a rapid COVID-19 test, and to perform a few breathing exercises in a new prototype which could serve as a novel tool to detect COVID-19 infection. As part of the study we will also consider the fact why you are performing a test for COVID-19: Presence of symptoms or contact tracing (i.e. having been in direct contact with someone that has tested positive for COVID-19 recently.)

This means that the (potential) treatment you will be offered will be prescribed in the usual manner, in accordance with the conditions of good medical practice and independently of your possible participation in this study.

Before you agree to take part in this study, we invite you to take note of its implications in terms of organisation, possible risks and benefits, to allow you to make a decision with full awareness of the implications. This is known as giving “informed consent”. Please read these few pages of information carefully and ask any questions you want to the investigator or his representative.

There are 3 parts to this document: (I) the information essential to your decision, (II) your written consent and (III) supplementary information (appendices) detailing certain aspects of the basic information.

If you take part in this study, you should be aware that:

- The treatment offered to you by the investigator in accordance with current recommendations will not be altered if you take part in the study.
- This clinical study is being conducted after having been reviewed by one medical ethics committee.
- Your participation is voluntary and must remain free from any coercion. It requires the signature of a document expressing your consent. Even after having signed this document, you can stop taking part by informing the investigator.
- The data collected on this occasion are confidential and your anonymity is guaranteed during publication of the results.
- Insurance has been taken out in case you should suffer any damage in connection with your participation in this clinical study.
- You may contact the investigator or a member of his team at any time should you need any additional information.

Further information about your “Rights as a participant in a clinical study” can be found on pages 8-10.

Objectives and course of the study

This clinical study has been organised to compare different detection methods to confirm the presence of COVID-19. The current nasopharyngeal method detects the genetic material of dead and living viruses in the nose. The method under investigation is based on the capturing and detection of the virus in exhaled breath. As the virus is mainly spreading through exhaled air, this new detection method can potentially also give an indication around infectiousness of transmission. The virus will be captured on a specially developed sieve and then be detected by specialised laboratory techniques. The new method will be compared with the conventional method whereby the presence of the virus is investigated through a nasopharyngeal swab. Dependant on the study phase in which you will participate, we will ask to take 2 different nasopharyngeal swabs: **one for the conventional detection** of COVID-19 and **one for the rapid antigen test** which gives an immediate indication of on-going infection. The goal of this study is to determine if the results from using the new method are sufficient to further develop this new technology. In order to being able to introduce a new methodology, the new method needs to be compared with the existing methods. This is what we would like to investigate in the current study.

We are inviting you to take part in this clinical study because you are showing COVID-19-related symptoms or because you have been in direct contact with someone that has tested positive for COVID-19 recently. As you will be tested at the COVID-19 testing centre Zeelstraat (KU Leuven) according to the standardised test procedure, we will also ask to have you tested through our new breath analyser test. This new test concerns a test where you will have to blow through a tube. Your breath will be captured in the device and examined for viral particles.

If you have decided to participate in the study, you will be assigned to one of the three parts of the study. In every part, you will be asked to take the conventional test and to take the new breathing test (see figure 1). How many times you will have to breathe into the new device will depend on what part of the study you are participating in. Also the amount of visits is determined by the specific part of the study you are involved in.

Figure 1 : Example of the test set-up and what to expect when participating in the study.

Part 1:

Your participation in this part of the study will last the length of a single visit, with an expected total duration of 1.5 hours. This will be the same visit as when you are attending the testing centre at Zeelstraat KU Leuven for the standard COVID-19 testing. During this visit the investigator will ask you questions to gather all the data and information required for the study, such as your demographic data (age and gender) as well as data concerning the reason for your need for a COVID-19 test (symptoms and/or direct contact with someone that has been tested positive for COVID-19). Two nasopharyngeal swabs will then be taken. 1 sample will be analysed straight away through the antigen test method to give an early indication if you are positive for COVID-19 or not (waiting time of around 20 minutes). The other sample will be sent to the bio-analytical lab to confirm this initial result. Based on the result of the rapid antigen test, a decision will be made on whether you can perform the breath analyser test or not. We will then also confirm what part of the study you are involved in and what is expected from your participation.

In part 1 of the study you will be asked to either:

- Blow in the tube of the breath analyser in four different ways, with a break of 5 minutes in between each test:
    1. Normal breathing for 4 minutes;
    2. Normal breathing for 2 minutes;
    3. Breathing for 1 minute whilst also vocalising (speaking or singing) into the sampler;
    4. 10 deep exhalations.
- Blow in the tube of the breath analyser, using the same method for 5 consecutive times with a break of 5 minutes in between each test.

Part 2:

In part 2 of this study, we will ask to take a nasopharyngeal swab as standard testing procedure and the breath analyser test. When you have tested positive for COVID-19, we will ask you to return to the testing centre around 72 hours later to repeat the breathing test.

Your participation in this part of the study will be a maximum of 3 visits: day 1, day 4 and day 8 (this can vary slightly depending on weekend closure). The first visit is expected to take an hour, while the follow-up visits are expected to take 20 minutes each. The first visit will be the same visit as where you are attending the testing centre at Zeelstraat KU Leuven for the standard COVID-19 test. During this visit the investigator will ask you questions to gather all the data and information required for the study, such as your demographic data (age and gender) as well as data concerning the reason for your need for a COVID-19 test (symptoms and/or direct contact with someone that has recently been tested positive for COVID-19). Then you will be asked to breathe through the breath sampler on just one occasion for a specified length of time. Once we have confirmed that you have tested positive for COVID-19, you will be asked to return to the study site 72h later (48-96h over the weekend) to repeat the breath analyser test. This process will also be repeated 7 days after the first test was taken (day 7-9). On this day another nasopharyngeal swab will be taken to compare the results of both testing methods.

Part 3:

This part is further subdivided in 2 phases:

- Phase 1: Only one visit will be needed with an expected duration of 1.5 hours. This will be the same visit as when you are attending the testing centre at Zeelstraat KU Leuven for the standard COVID-19 testing. After obtaining the data and information required for this study, a nasopharyngeal swab will be taken according to the standardised screening method, and you will be asked to breathe into the new breath analyser in four different ways (see Part 1).
- Phase 2: A maximum of 3 visits can be expected whereby the first visit will be the same visit as when you are attending the testing centre at Zeelstraat KU Leuven for the standard COVID-19 testing, and is expected to take 1 hour. The follow-up visits are expected to take 20 minutes and are designed to formulate an understanding of how long the infection persists (see Part 2).

This clinical study is to include a total of maximum 980 subjects.

To be able to take part in this study you must:

- Be willing and able to give informed consent for participation in the study.
- Be aged 18 years or above.
- Show COVID-19 related symptoms and/or had high-risk contact with a proven COVID-19 case during this case's infectious period [48 hours prior until 7 days after symptom onset if symptomatic or 48 hours prior until 7 days after the collection of a positive COVID-19 NP swab / RT-qPCR (if asymptomatic)]. *A high-risk contact is defined as having spent 15 minutes in within a 1.5 meters distance while at least one of both did not wear a mask over nose and mouth. Also 'extended close contact' e.g., sharing facilities in a residence will be considered.*
- Able (in the Investigators opinion) and willing to comply with all study requirements.

Description of risks and benefits

As indicated above, neither the treatment that has been proposed nor the diagnostic and monitoring procedures for your clinical situation go beyond good medical practice. Very little risk, in terms of health, can be linked to your participation in this study.

Similarly, you should not expect any personal benefits as a result of taking part in the study. Know only that your participation will allow us to better understand the principle of the new breathing test, and to develop a faster and less cumbersome test for COVID-19. You will be compensated for the time you spent on the study (see page 8 for more information).

You will be asked to perform a sort of breathing exercise; this in itself should not pose any risks. However, if you were to feel unwell while performing the test, you need to inform the investigator / study nurse promptly. He/she can then decide to stop the testing. Off course you also have the right to stop the test at any moment in time.
There is no infection risk when breathing into the sampling device: the device is equipped with a one-way valve and a HEPA filter. As for the tube in which you will have to blow, this will be changed in between every testing person. The overall set-up of the devices will also be disinfected every single time, so you have no risk of obtaining the infection from another test person.

Withdrawal of consent

Your participation is voluntary and you are entitled to withdraw your consent to take part in the study for any reason, without having to justify your decision.

If you withdraw your consent to take part in the study, to guarantee the validity of the research, the data encoded up to the point at which you withdraw will be retained. No new data may be sent to the sponsor.

The sponsor responsible for the study may also decide to stop the study because the data collected provide a faster response than originally expected.

If you take part in this study, we ask you:

- To cooperate fully in the smooth running of this study.
- Not to conceal anything such as information relating to your state of health, the medication you are taking or the symptoms you are experiencing.
- To inform your doctor if you are asked to take part in another study to discuss with him/her the possibility of taking part in this study and to see whether you should then stop taking part in the present study.

Contact

If you need further information, but also if you have problems or concerns, you can contact the investigator (André, Emmanuel) or a member of his research team (Raymenants, Joren) on the following telephone number: +32 16 379373. Email addresses: emmanuel.andre@UZLeuven.be and joren.raymenants@UZLeuven.be.

If you have any questions relating to your rights as a participant in a clinical study, you can contact the patient rights ombudsman of your institution on this telephone number: +32 16 34 48 18. If necessary, he/she can put you in contact with the ethics committee.

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II Informed consent (1 page)

Participant

- I declare that I have been informed of the nature of the study, its purpose, its duration, the possible side effects and what is expected of me. I have taken note of the information document and the appendices to this document.
- I have had sufficient time to think about it and discuss it with a person of my choice (e.g., GP, relative).
- I have had the opportunity to ask any questions that came to mind and have obtained a favourable response to my questions.
- I understand that my participation in the study is voluntary and that I have the right to withdraw at any time. My decision will not affect my relationship with the investigator or the quality of future therapeutic care.
- I understand that data about me will be collected throughout my participation in this study and that the investigator and the sponsor of the study will guarantee the confidentiality of these data in accordance with applicable European and Belgian legislation.
- I agree to my personal data being processed as described in the section dealing with confidentiality guarantees (page 8-10).
- I agree / do not agree (delete as appropriate) that the sponsor of this study can store my biologic material during 10 years to be used in other studies, as long as the study is limited to the context of the current study, and the study has been approved by an ethics committee.
- I have received a copy of the information to the participant and the informed consent form.

Surname, first name, date and signature of the volunteer:

Investigator

I, the undersigned, [surname, first name] investigator/clinical research assistant, confirm that I have verbally provided the necessary information about the study and have given the participant a copy of the information document.

I confirm that no pressure was applied to persuade the patient to agree to take part in the study and that I am willing to answer any additional questions if required.

I confirm that 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 of 7 May 2004 related to experiments on humans.

Surname, first name, date and signature of the investigator’s representative	Surname, first name, date and signature of the investigator

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III Supplementary information

1: Supplementary information on the protection and rights of the participant in a clinical study

Ethics Committee

This study has been reviewed by an independent Ethics Committee, namely the Ethics Committee of Onderzoek UZ / KU Leuven, which has issued a favourable opinion. It is the task of the Ethics Committees to protect people who take part in a clinical trial. They make sure that your rights as a participant in a clinical study are respected, that based on current knowledge, the study is scientifically relevant and ethical.

You should not under any circumstances take the favourable opinion of the Ethics Committee as an incentive to take part in this study.

Voluntary participation

Before signing, do not hesitate to ask any questions you feel are appropriate. Take the time to discuss matters with a trusted person if you so wish.

Your participation in the study is voluntary and must remain free of any coercion: this means that you have the right not to take part in the study or to withdraw without giving a reason, even if you previously agreed to take part. Your decision will not affect your relationship with the investigator or the quality of your future therapeutic care.

If you agree to take part in this study, you will sign the informed consent form. The investigator will also sign this form to confirm that he/she has provided you with the necessary information about the study. You will receive a copy of the form.

Costs associated with your participation

The sponsor has arranged to compensate the hospital for the time devoted to the study by the investigator and his team. The study will not involve any additional costs for you. You will receive compensation for your participation in this study. The total will depend on how many visits you will complete (min. 35 euro and up to 65 euro):

- You will receive a gift card with a value of 35 euro when you participate in the first visit taking approximately 1,5 hours of your time;
- You will receive a gift card of 10 euro when you have tested positive and you will attend the testing centre on day 4;
- You will receive a gift card with a value of 20 euro when you attend the testing centre on day 8 and participate in the breathing test and undergo an additional nasopharyngeal test.

The biological material obtained is considered a “gift” and you need to be aware that you will not receive any financial advantage (i.e. royalties) in the event that a new testing tool will be developed based on the data from this study.

Guarantee of confidentiality

Your participation in the study means that you agree to the investigator collecting data about you and to the study sponsor using these data for research purposes and in connection with scientific and medical publications.

Your data will be processed in accordance with the European General Data Protection Regulation (GDPR) and with the Belgian legislation on the protection of natural persons with regard to the processing of personal data. Imec vzw shall act as data controller for your data.

You are entitled to ask the investigator what data are being collected about you and what is their use in connection with the study. You have the right to inspect these data and correct them if they are incorrect[1].

The investigator has a duty of confidentiality vis-à-vis the data collected. This means that he undertakes not only ever to reveal your name in the context of a publication or conference. The personal data transmitted will not contain any combination of elements that might despite everything allow you to be identified[2].

For the study data manager designated by the sponsor, the data transmitted will not allow you to be identified. The latter is responsible for collecting the data gathered by the investigator, processing them and protecting them in accordance with the requirements of the Belgian law on the protection of privacy. Also for the biologic material, data will be encoded as is done for your personal data.

These (encoded) data could be sent to Belgian or other regulatory authorities, to the relevant ethics committees, to other doctors and/or to organisations working in collaboration with the sponsor.

Your consent to take part in this study therefore also implies your consent to the use of your encoded medical data for the purposes described in this information form and to their transmission to the aforementioned people and authorities.

The sponsor undertakes only to use the data collected within the context of the study in which you are taking part.

The sponsor will use the data collected only within the context of the present study in which you are taking part.

If you withdraw your consent to take part in the study, to guarantee the validity of the research, the data encoded up to the point at which you withdraw will be retained (both personal data and biologic material). No new data may be sent to the sponsor.

The biological material obtained is considered a “gift” and you need to be aware that you will not receive any financial advantage (i.e. royalties) in the event that a new testing tool will be developed based on the data from this study.

If you have any questions relating to how your data are being processed, you may contact the investigator. The data protection officer in your hospital can be contacted as well: DPO - UZ Leuven, Herestraat 49, 3000 Leuven, e-mail dpo@uzleuven.be.

1 These rights are guaranteed by the European Data Protection Regulation (GDPR), by the Belgian legislation on the protection of natural persons with regard to the processing of personal data and by the Law of 22 August 2002 on patient rights.
2 The database containing the results of the study will therefore not contain any combination of elements such as your initials, your gender and your full date of birth (dd/mm/yyyy).

Finally, if you have a complaint concerning the processing of your data, you can contact the Belgian supervisory authority, which ensures that privacy is respected when personal data are processed.

The Belgian supervisory authority is called:
Data Protection Authority (DPA)
Drukpersstraat 35,
1000 Brussels
Tel. +32 2 274 48 00
e-mail: contact@apd-gba.be
Website: https://www.dataprotectionauthority.be

Insurance

In a clinical study, the possible risk would be a flaw in the measures taken to protect the confidentiality of the private information about you. Even without fault, the sponsor accepts responsibility for damage caused to the participant (or his/her dependants) and linked directly or indirectly to participation in this study. In this context, the sponsor has taken out an insurance contract (Strict Liability Policy nr 390/01319140-14221;
HDI Global SE, Avenue de Tervueren 273 /1, B-1150 Brussels)[3].

[3] In accordance with Article 29 of the Belgian Law related to experiments on humans (7 May 2004)