“Testing a New CT Scan Technique to Find Heart Problems in Cardiac Arrest Survivors”

Official title of the trial: Diagnostic Accuracy of ECG-less gated Cardiac CT in Resuscitated Cardiac Arrest Survivors

EU number: *N/A*

Trial number: /

Sponsor(s) of the trial: UZ Brussel - Universitair Ziekenhuis Brussel.

Site name: UZ Brussel - Universitair Ziekenhuis Brussel.

Main address of site: Laarbeeklaan 101, 1090 Jette, Belgium.

Document Revision History

Not applicable.

Who can I contact in case of questions?

Name	Function	In case of	Contact details
Dr. Bert Popelier	Principal Investigator of the site	Information, problems or concerns	Bert.Popelier@uzbrussel.be 024 74 96 54
	The trial staff	Information, problems, concerns	024 74 91 38
	Emergency contact	Emergency	024 74 33 60
	Patient rights ombudsman	Concerns relating to your rights as a participant in a trial	024 77 60 09
Name and address of insurance company of the sponsor & contact of insurer	Insurance Company of the sponsor	In case of disagreement or complaint on a damage claim	Policy N°: will be added
	Data protection officer of the site	Questions relating to the confidentiality of your data	024 77 69 20 E-mail: dpo@uzbrussel.be
	Belgian Data Protection Authority	Complaints relating to the confidentiality of your data	E-mail : contact@apd-gba.be

Version No: *2.0*

Table of contents

THE STUDY AT A GLANCE

For the attention of the legal representative:
The person you represent is currently unable to make an informed decision about participation in this study due to their clinical condition. You are therefore invited to make a decision regarding participation in this clinical study, taking into account what this person would likely want themselves.

1. **Why is the participant being asked to take part? What is the purpose of the study?**
   You are a survivor of a cardiac arrest. In a significant portion of these patients, the cardiac arrest is caused by a heart attack, due to narrowing or blockage of one or more coronary arteries (the blood vessels that supply blood to the heart). In some people, this is immediately evident from basic tests; in others, it is more difficult to predict with the currently available examinations. We are investigating a technique that allows us to also assess the coronary arteries on the CT scan that is performed in all these patients, so that in the future we can better identify who needs a traditional coronary angiography. In most cases, any issues identified during a traditional coronary angiography can be treated immediately. We aim to determine whether the CT scan provides accurate information about the condition of the coronary arteries, and this will be verified with the traditional coronary angiography.
2. **What is the purpose of this document?**
   To inform you about the opportunity to participate in the study, the study's purpose and concept, and the costs.
3. **Will the participant benefit from the study?**
   At this moment, there is no expected benefit for the patient.
4. **How will the study be conducted?**
   The CT scan is medically indicated based on the patient's condition, regardless of participation in this study. The brain, chest, and sometimes abdomen are typically scanned to detect common causes of cardiac arrest. The current standard technique does not allow for good visualization of the coronary arteries, but a recent development has made this possible.
5. **What are the main (most frequent, most painful) procedures the patient will undergo?**
   For the CT scan, the main potential side effects are related to the administration of contrast dye—namely, reduced kidney function and allergic reactions ranging from mild to (rarely) severe. This contrast dye would be administered anyway; no extra dose is needed to examine the coronary arteries. Additionally, X-rays are used, with a small increase in radiation dose. Even with this, the total dose remains below the limit set by the Federal Agency for Nuclear Control (FANC).
   For the traditional coronary angiography, the main discomfort is associated with puncturing the blood vessel (usually in the wrist, rarely in the groin). This is done under local anesthesia but can still be unpleasant or painful. During the procedure, there is a small risk of complications, primarily stroke or heart rhythm disturbances. A full list of possible side effects and risks from the studies performed can be found in section 6 of this document.
6. **What is the duration of the study?**

The patient will not be hospitalized or followed for longer than would be the case without participation in the study. The CT scan and traditional coronary angiography are performed shortly after the cardiac arrest (the CT scan as soon as possible, the angiography within 24 hours of the scan). Finally, a physician will assess certain data about the patient's condition and blood results using the electronic medical record 90 days after the cardiac arrest; the patient does not need to come to the hospital for this.

7. **Has insurance been arranged in case something goes wrong during the study?**
   Yes, insurance has been arranged. More information can be found in the table above.
8. **Who pays for study-related costs and what must the participant pay or not pay?**
   All procedures that are performed would also take place if the patient were not participating in the study, except for the part of the CT scan that examines the coronary arteries. This part is not billed to the patient. In other words, the costs are the same whether or not the patient participates in the study.
9. **Will the data be handled confidentially?**
   Yes, a specific computer program is used for this.
10. **Is participation in the study voluntary?**
    Yes, there is no obligation to participate.
11. **Who reviewed the study documents?**
    The ethics committee of the University Hospital Brussels reviewed the documents.
12. **What is expected of the participant?**
    If you participate, you agree that the investigator informs the treating physicians of your participation. You cannot take part in another clinical study while enrolled in this one. The patient or their representative must provide relevant information about their health status.
13. **Who will provide the participant with more information about the study?**
    The investigator or one of their representatives.

CHAPTER I – DESCRIPTION OF THE TRIAL AND YOUR RIGHTS WHEN PARTICIPATING

1. Why are we doing this trial

The purpose of this trial is to investigate whether a specialized CT scan can effectively detect problems in the coronary arteries (the blood vessels supplying blood to the heart) after a cardiac arrest. In some patients, currently available tests clearly indicate such problems, but in others, the results are less conclusive.

For these unclear cases, there is currently no reliable method to determine whether a coronary issue is present. We aim to evaluate whether we can obtain high-quality CT images of the heart during the routine CT scan performed to rule out other causes of cardiac arrest. Specifically, we want to assess whether these images can be successfully acquired and whether they provide accurate diagnostic information.

To verify the accuracy of this approach, the CT findings will be compared with results from invasive coronary angiography. This procedure involves puncturing an artery—usually in the wrist, but sometimes in the groin—and guiding catheters through the blood vessels to the coronary arteries, allowing to obtain images from these blood vessels.

The CT technique being tested is called "ECG-less," but the scanner itself is the same as the one used for other post-cardiac arrest scans.

2. Why am I being asked to take part?

You survived a cardiac arrest. The most common cause of cardiac arrest is a problem with the coronary arteries, that is why it is useful to find the best way to detect them.

Your eligibility is determined by meeting the following criteria:

Inclusion Criteria:
- Adult (≥18 years) cardiac arrest survivor with return of spontaneous circulation.
- Informed consent provided before invasive coronary angiography.

Exclusion Criteria:
- Patients on VA-ECMO (veno-arterial extraporeal membrane oxygenation, which gives organ support for heart and lungs).
- Patients with ST elevation myocardial infarction (a clear case of myocardial infarction, that requires emergent invasive coronary angiography).
- Severe hemodynamic instability (dangerously low or unstable blood pressure) precluding CT imaging.
- Known or likely pregnancy or lactation.
- Absolute contraindications to iodinated contrast (patients not tolerating the contrast dye used during a CT scan or invasive coronary angiography).
- Participation in another study that may interfere with this research.

3. Do I have to take part in a trial?

Your participation in a trial is voluntary and must remain free of any coercion. This means that you have the right not to take part in the trial or to withdraw at any time without giving a reason, even if you previously agreed to take part. Your decision will not affect your relationship with the investigator or your treating physician nor will it affect the quality of your future medical care.

4. What will happen during the trial?

This trial will include about 30 participants, all of them in the Brussels university hospital (UZ Brussel).

If you agree to participate, the following procedures will take place:

- A head and chest (and in some cases abdominal) CT scan will be performed as early as possible. During this CT scan, an ECG-less gated cardiac CT will be performed, the technique under investigation during this clinical study. This requires no additional contrast dye administration, about 2 minutes of time and a small amount of radiation exposure.
- A standard invasive coronary angiography (ICA) will be conducted within 24 hours of admission.
- Relevant medical data, including baseline health status and test results (e.g. laboratory data), will be collected.
- A follow-up assessment by the investigator by interrogation of the computer system will be conducted 90 days after inclusion to evaluate health outcomes. This assessment is specific to the study, but you do not need to take any action yourself.

The only exam that is performed additional to the standard of care, is the cardiac CT scan, which is in fact done at the same time as the CT scan that is already performed.

Since all examinations performed during the study—except for the cardiac CT scan—are clinically indicated and would be conducted even without participation in the study, the cost of these exams will be covered by the patient.

Participation in the trial will last no longer than the usual clinical course after a cardiac arrest. There are no extra study visits after the initial hospitalisation.

If you meet all the conditions required to be enrolled in the trial and agree to take part in the trial, you will undergo the above-mentioned tests and examinations. If you have any important side effects, the investigator might determine that it is necessary to perform additional tests which will be considered as specific to the trial.

5. Will I benefit from the trial?

The information obtained during a trial may contribute to a better understanding of the use of the investigational medicinal product (referred to as “IMP”) or to the development of a new medicinal product for the treatment of yourself or future patients.

6. What are the possible risks and discomforts of taking part?

Potential risks of the trial include:
- Exposure to low supplementary dose of ionizing radiation from the CT scan.

- Potential adverse reactions to iodinated contrast used in the CT scan and ICA, yet the type and amount of contrast used is identically the same as for people not participating in this trial.

6.1. What are the possible risks or discomforts of the examinations during the trial?

Participation in a trial involves some risk.

Both a **CT scan** and an **invasive coronary angiography** use iodinated contrast media and ionizing radiation. The side effects are very well known. Even if previous studies have shown that these are normally well tolerated, you may still experience the following side effects:

The **radiation exposure** gives a minimal risk of cancer, cumulative exposure over time may increase this risk. Modern CT scanners minimize radiation dose. This scan system uses on average a Dose Length Product (DLP) between 150 and 200 mGy.cm. The diagnostic reference level (DRL) as set by the Federal agency for Nuclear Control (FANC) for a coronary CT angiography is 300 mGy.cm, which means the CT scan we use is far under this limit. The amount of radiation is comparable or a bit more than the annual background radiation dose.

Allergic reactions to **contrast** may vary from mild (skin rash, itching, and flushing) to more severe and rare events such as low blood pressure and difficulties breathing.

The exposure to iodinated contrast can cause impaired kidney function. This is called contrast-induced nephropathy (CIN). This occurs mostly in patients with pre-existing kidney disease, diabetes, or dehydration. Its risk can be lowered by adequate hydration, reducing the amount of contrast used and avoiding other drugs that can cause kidney dysfunction. This new CT system allows to obtain images on both pulmonary and aortic and coronary arteries with one single contrast bolus, thus reducing the total amount of contrast used. Our protocol includes the administration of 60-80 ml of contrast.

If the IV line is not properly placed or if the vein is damaged, the contrast agent can leak from the vein into the surrounding tissues. This may cause pain and swelling. In rare cases, this can lead to the death of the surrounding tissue (tissue necrosis).

Coronary angiography requires puncture of an artery. This can lead to local complications such as a hematoma at the puncture site, pseudoaneurysm (rare, damage with bulging of the blood vessel wall), or arteriovenous fistula (rare, connection between the vein and the artery). Bleeding may occur at the puncture site, but this is usually stopped by applying pressure, either manually or with the help of compression devices. Access via the femoral artery can be complicated by bleeding in the lower abdomen. Access via the radial artery can lead to occlusion of this artery in 3 to 5% of cases. This is usually asymptomatic due to collateral circulation via the other, but it does prevent future use of this artery for interventional procedures.

During coronary angiography, slow heart rate, dizziness and nausea may occur. When using the artery in the wrist, this blood vessel can become constricted (spasm), causing pain in the arm during insertion and manipulation of the catheter.

Especially when performing a percutaneous coronary intervention (PCI), dissection (tearing of a layer of the blood vessel wall) or perforation (rupture of the coronary artery) can occur, which can lead to a heart attack or cardiac tamponade (fluid accumulation in the pericardium). These are rare but serious complications that must be treated during the procedure, for example with a drug-eluting stent in case of dissection, or a covered stent or embolization device in case of perforation.

Life-threatening arrhythmias (ventricular fibrillation or ventricular tachycardia) are rare, but are life-threatening complications.

Manipulating the catheter can in rare cases lead to thrombosis or gas embolism. This can cause an ischemic cerebrovascular accident (stroke) or peripheral embolism (movement of the clots to other blood vessels).

The risk of death during invasive coronary angiography is very low (<0.1%) and is more common in seriously ill or high-risk patients.

Because this IMP is still under investigation, other currently unknown risks and discomforts could occur. **Therefore, it is very important that you report <u>any</u> new or worsened health problems immediately to the investigator, regardless of whether you think it has to do with the trial, and even when it is already described in this document. If, for any reason, you consult another treating physician during the trial you must inform him/her that you are taking part in a trial and present your emergency card. This could be important in determining a diagnosis and giving you the correct treatment if needed.**

The **taking of blood** is always done after a cardiac arrest and the frequency/amount taken is not influenced by participation in the study (around 20-30 ml of blood per day). It may cause pain, bleeding, bruising or infection localised around the injection site. Similarly, some participants may feel dizzy or even faint during the procedure. The staff who take the blood will do all they can to minimize these discomforts.

6.2. Can I take <u>other medicines</u> during the trial?

There is not any restriction to medication use when participating in the trial.

6.3. Will my participation to the trial have an <u>impact on my daily activities</u>?

There will be no impact on daily activities during hospitalisation or after discharge.

7. What If something goes wrong within the trial?

Even if there is no fault, the sponsor is liable for harm caused to you whether directly or indirectly related to your participation in the trial. The sponsor has taken an appropriate insurance (a so called “NO FAULT INSURANCE”) for this liability (Ref. 1). A copy of the insurance certificate can be obtained from the investigator or trial staff.

If you (or in the event of death, your rightful claimants) seek compensation for a harm to your health as a direct or indirect result of participating in the trial, you must inform your investigator or trial staff promptly.

If the investigator believes that a link between the new or worsened health problem(s) and the trial is possible, he/she will inform the trial sponsor. The sponsor will then immediately initiate the declaration procedure to its insurance company. If the company considers it necessary, it will appoint an expert to assess whether there is a link between your reported health problem(s) and the trial. The insurance does not cover the natural progression of your disease/condition or the known side effects of the treatment you would have received without taking part to the trial (*that is* your standard treatment).

Whenever you feel it is appropriate or if you or your rightful claimants disagree either with the investigator or with the expert appointed by the insurance company, you may contact the insurance company or proceedings may be brought against the insurance company. You will find the contact details on the front page of this form.

8. What if other treatment options or new information on the IMP become available during the course of the trial?

During the course of the trial, important new information might become available, possibly affecting your decision to (further) participate. For example other treatments for your condition or important new information on the IMP 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 trial.

If you decide to stop taking part in the trial or if you are no longer able to participate, your investigator will see to it that you continue to receive the best possible medical care.

9. Can my participation in the trial end prematurely?

As explained in detail below, your trial participation may end prematurely when

- you decide to withdraw your consent,
- the investigator decides to end your trial participation, or
- other entities interrupt or end the trial.

In any case, if your trial participation ends prematurely, the investigator will discuss your future medical care with you. The sponsor can continue to retain and use any data that have already been collected before the end of your participation. This is to avoid skewing / biasing results of the trial (as described in I. § **Fout! Verwijzingsbron niet gevonden.**., page **Fout! Bladwijzer niet gedefinieerd.**).

If you experience a side effect at the moment of stopping the IMP, the investigator may contact you in the future to see if it has resolved or not after the end of the trial participation.

If you experience a new side effect after the end of your trial participation you may contact the investigator to ask for a follow-up.

9.1. You decide to withdraw your consent

You are entitled to withdraw your consent for any reason, at any time, without having to justify your decision. However, for your safety, you should inform the investigator of your decision. Although it is not mandatory, it may be useful for the investigator and

for the sponsor to know the reason of your decision (for example side effects, frequency of clinical visits,…).

If you withdraw your consent, this means you decide to stop

- the treatment with the IMP, and
- all trial-related visits and examinations.

Please discuss with your investigator to evaluate the practical modalities of your withdrawal (in light of your situation), including any follow up-visits or procedures.

In any case, no new data will be sent to the sponsor.

In this study, only blood samples are taken, which is part of standard care after cardiac arrest. So if you decide to withdraw your consent, this will not affect the collection or analysis of blood samples.

9.2. The investigator decides to end your trial participation

The investigator may end your trial participation because

- it is better for your health,
- he/she determines that you are not following the instructions given to participants, or
- any other reason that will be explained.

9.3. Other entities may interrupt or end the trial

The sponsor and the competent Belgian health authorities may interrupt or end the trial because

- the information gathered shows that the IMP is not effective (does not deliver a sufficient level of improvement in the health of the trial participants),
- the IMP causes more (serious) side effects than anticipated, or
- any other reason that will be duly motivated by such party.

10. Which treatment will I get after my participation in the trial?

After you stopped the treatment with the IMP, the investigator will assess your health. If necessary, he/she will prescribe you the best standard treatment available or refer you to another treating physician of your choice.

11. Will my participation in the trial involve extra costs for me?

11.1. Examinations and treatments paid by the sponsor

Examinations and treatments will be payed for by the patient since all of the examinations (CT scan, invasive coronary angiography, blood samples) are done as standard of care. The extra scan of the heart during the CT scan will not be charged separately.

The visits and treatments which are a consequence of a side effect are also considered as trial specific.

12. Which data are collected about me during the trial and what will happen with them?

12.1. Which data are collected and processed during the trial?

The collected and processed personal data concern information about your health and medical condition. This includes your medical history, some of your background information (for example your age, sex, and ethnic origin) and the results of examinations required by the trial.

12.2. How will the investigator treat my personal data?

The investigator is bound by professional secrecy about the data collected.

This means that he/she will never reveal your identity, including in a scientific publication or a lecture and that he/she will encode your data (*that is* by replacing your identity by an identification code in the trial) before sending them to the sponsor.

Therefore, the investigator and the trial staff under the responsibility of the investigator, will be the only ones able to establish a link between your identity and the data transmitted during the trial, with the exceptions listed under section 12.6.

The data transmitted to the sponsor will not allow the sponsor to identify you.

12.3. What will happen to information about me collected during the trial?

Your participation in the trial means that your personal data

- are collected by the investigator, and
- are used in an encoded form by the trial sponsor.

The investigator and the sponsor can only use the encoded personal data for research purposes in connection with scientific publications within the context of the trial that you participate in, or for a broader use of the encoded data if described below.

In addition, the sponsor may provide access to the encoded data to external researchers (that are not involved in this trial). In the event an external researcher wants to use the data in a project not yet described in this document, this project will have to be approved by an Ethics Committee. If your encoded trial data are sold, you will not benefit from this.

12.4. How will my data be handled

Your data will be handled in compliance with the General Data Protection Regulation (GDPR). All personal information will be anonymized before analysis. Only authorized personnel will have access to your data, and it will not be shared outside the study without your consent.

Your trial data will be processed in accordance with the General Data Protection Regulation (GDPR, Ref. 2) and the Belgian law on data protection of 30th July 2018 (Ref. 3). The sponsor is responsible for this processing.

Processing your personal data in this trial is allowed because we are conducting scientific research and you have given your consent.

12.5. Do I have access to my data collected and processed during the trial and can I rectify them ?

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

You have the right

- to inspect and access these data
- to receive the personal data that are collected
- to ask for correction if they are incorrect
- to object to the processing of your personal data
- to withdraw your consent for the processing of personal data. However, personal data collected before withdrawal will be kept to avoid skewing of results in the trial.

12.6. Who, other than the Investigator and his staff, has access to my personal data?

To verify the quality of the trial, it is possible that your personal **un**coded data or information in your medical records relevant for the trial, will be examined by people outside the trial staff but under the responsibility of the investigator. These persons must be subject to professional secrecy or a confidentiality agreement. The following might be considered:

- the personnel designated by the sponsor of the trial (MONITORS and AUDITORS), and people or organisations providing services for or collaborating with the sponsor. They will however never transfer your name and contact details to the sponsor.
- inspectors of competent health authorities worldwide
- an independent audit group
- people designated by the Ethics Committee

For the needs of the trial, the encoded trial data may be sent to other EU and non-EU countries and may be reviewed by

- personnel (other than the inspectors) of competent health authorities of Belgium (Federal agency for medicines and health products, FAMHP) and other EU and non-EU countries,
- the evaluating Belgian Ethics Committee(s),
- external researchers,
- the sponsor of the trial, personnel designated by the sponsor, and people or organisations providing services for or collaborating with the sponsor, and/or
- group companies of the sponsor in Belgium, and in other EU and non-EU countries.

The European regulation and the Belgian legislation on data protection have requirements for transferring data to non-EU countries. The sponsor must ensure equivalent guarantees regarding personal data protection standards before

transferring the encoded data to non-EU countries. If for this purpose, there is a data protection agreement, a copy of this agreement may be obtained via the investigator. You can always contact your investigator to obtain more information about any such transfers.

12.7. What will happen to the results of the trial?

After trial closure, a description and the results of this clinical trial will be published in specialised medical journals. A copy of the scientific publication [if applicable:] or a summary for laypersons can be obtained from the investigator or the trial staff.

A description of the trial will also be available on https://www.clinicaltrialsregister.eu/ and/or https://www.Clinicaltrials.gov. You can search these websites at any time using the trial number given on the front page of the informed consent form. The websites will include a summary of the results within 1 year after the end of the trial (Ref. 4).

These websites or publications will not include information that can identify you.

12.8. Will my data be used for other purposes than for the trial in which I take part?

The results of the trial will only be used to answer the scientific questions of the trial.

Any additional research outside of the trial, must be approved by a Belgian recognized Ethics Committee.

At the end of this form you agree or disagree to the use of your trial data for other purposes by ticking the appropriate check-box in Chapter II, page 18.

12.9. How long will my data be kept?

After the end of the trial your encoded data will be retained for at least 25 years (Ref. 5) to ensure the validity of the research. This will also be the case if you stopped trial participation prematurely.

13. Which biological samples are collected from me during the trial and what will happen with them?

13.1. Which biological samples are collected from me during the trial?

Biological samples are samples of human body material (for example blood, tissue, urine, faecal stool, ….)

In this trial, only blood samples will be taken, as mentioned above, which is standard of care after a cardiac arrest.

13.2. What will happen to the collected biological samples?

The collected blood samples will be managed by the hospital laboratory in just the same way as usually.

13.3. Will any additional biological samples be collected and used for additional research?

In this trial, no additional biological samples will be collected.

14. Who has reviewed and approved the trial documents?

The documents of the trial have been reviewed by

- The Belgian competent health authorities (FAMHP) or if applicable by the competent national health authorities of other EU members states and
- An independent Belgian Ethics Committee

It is the task of the competent health authorities and the Ethics Committees to protect people who take part in a trial. The health authorities will ensure that the trial is conducted in accordance with the applicable legislation.

You should not under any circumstances take their approval as an incentive to take part in the trial.

15. What happens in case of incidental findings?

If by chance and in addition to the trial objectives a result is discovered during the trial that may be important to your health or the health of your blood relatives (called ”incidental findings”), the sponsor will inform the investigator. With your consent the investigator will notify you and your treating physician about your results and potential consequences. If necessary, the investigator and/or the treating physician will advise you on the next steps.

You agree or disagree to being informed of it by ticking the appropriate check-box in Chapter II, page 17.

CHAPTER II - INFORMED CONSENT

PARTICIPANT

PREREQUISITES FOR YOUR PARTICIPATION IN THE TRIAL

- I declare that I have been informed of and that I understand the purpose of the clinical trial, its duration, possible risks and discomforts, 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 trial 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 trial is voluntarily and free from any coercion and that I am free to stop at any time my trial participation.
- I understand that data about me will be collected and that they will be treated confidentially.
- I agree to my personal data being processed as described in Chapter I, § 12, page 13.
- I understand that the sponsor has taken out an insurance in case I should suffer any damage in connection with my participation in this trial.
- I understand that when participating in this trial, I will not have any costs except those related to the standard of care treatment of my disease.
- I agree to my treating physician(s) being informed of my participation in this trial.
- I agree not to take part in any other trial 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 trial staff's instructions regarding the trial.
- 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.
- 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 TRIAL.

1. As specified in Chapter I, § 12.8, page 15, the sponsor would like to be able to use your data obtained from this trial 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 trial 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. As described in Chapter I, § 13, page 15, and § 15, page 16, 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**

Participant's surname and first name:

Date (DD/MMM/YYYY):

Participant's signature:

LEGAL REPRESENTATIVE (REF. 6)

I declare that I have been informed that I am being asked to take a decision on whether or not to take part in the clinical trial for the person I represent, considering his/her best interests and taking into consideration his/her likely wishes. My consent applies to all the items listed in the consent of the participant.

I have also been informed that as soon as the clinical situation allows, the person I represent will be made aware of his/her participation in a clinical trial and from that point will be free to continue with this participation or end it by signing or refusing to sign this consent form.

I have received a signed and dated copy of this document.

Legal representative's surname and first name:

Relationship to the participant:

Date (DD/MMM/YYYY):

Legal representative's signature:

IMPARTIAL WITNESS / INTERPRETER (REF. 7)

I, the undersigned (Tick as appropriate),

☐ Impartial Witness

☐ Interpreter

was present during the entire process of informing the participant and I confirm that the information on the objectives and procedures of the trial was adequately provided, that the participant (or his/her legal representative) apparently understood the trial and that consent to participate in the trial was freely given.

I declare furthermore that acting as an impartial witness, I am independent of the sponsor and the investigator.

Impartial Witness / Interpreter surname and first name:

Impartial Witness / Interpreter qualification:

Date (DD/MMM/YYYY):

Impartial Witness / Interpreter signature:

INVESTIGATOR

I, the undersigned investigator, confirm that

- the participant has been verbally provided with the necessary information about the trial, has been explained the content and has been given an original signed document.
- I have verified that the participant has understood the trial.
- 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 trial.
- 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 (Ref. 8).

Investigator's delegate, surname and first name:

Investigator's delegate, qualification:

Date (DD/MMM/YYYY):

Investigator's delegate signature:

Investigator's, Surname and first name:

Date (DD/MMM/YYYY):

Investigator's signature:

GLOSSARY

DPA: The Data Protection Authority ensures that personal data are handled with care and thoroughly protected, and that your future privacy also remains guaranteed.

FAMHP: Federal agency for medicines and health products

IMP: investigational medical product

NO FAULT INSURANCE:

The sponsor is liable for any injury or any damage that the participant has suffered, and which is directly or indirectly related to the clinical trial. You do not have to prove any mistake in this respect.

MONITOR and AUDITOR

Both the monitor and auditor work for the sponsor.
The monitor takes care of a continuous quality check during the course of a trial. The auditor performs a quality check after the trial. They verify if the trial is being/was conducted according to the protocol, if the reported data are liable and if the clinical trial was conducted according the applicable rules.

REFERENCES

[1] This is in accordance with Article 12 of the Belgian Law of 7 May 2017 on clinical trials with medicinal products for human use.

[2] 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.

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

[4] In accordance with section 4.3. of the Commission Guideline: Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 - (2012/C 302/03). [From the moment the Clinical trial regulation enters into force : In accordance with article 37 of the Clinical trial regulation No 536/2014 of the European Parliament and of the council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC; sponsor have to provide summary results of clinical trials in a format understandable to laypersons.]

[5] In accordance with article 58 of the Clinical trial regulation No 536/2014 of the European Parliament and of the council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

[6] When a person of full age is incapable of expressing his will, legal representation must be used which is determined in successive order (administrator, or failing that, the spouse, the legal cohabiting partner, de facto cohabiting partner, an adult child, a parent, an adult brother or sister). The regulation is laid down in article 11 of the law of Belgian Law of 7 May 2017 on clinical trials with

[7] Use of an impartial witness is necessary when either the subject or the subject's legally authorized representative speaks and/or fully understands the language of the approved informed consent form, but cannot read and write due to any physical impairment or is visually impaired. An interpreter is necessary when the investigator doesn't speak the language of the patient.

[8] Belgian Law of 7 May 2017 on clinical trials with medicinal products for human use, and the applicable royal decrees.