Subject Information sheet and Informed Consent Form

Titel of the study: COVID-19 National Survey for Assessing Viral Spread by Non-Affected Carriers

Acronym: *CON-VINCE*

Sponsor: Luxembourg Institute of Health (LIH)

Principal Investigator: Prof. Dr Rejko Krüger, MD

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1 INTRODUCTION and GOAL OF THE STUDY?

COVID-19 is an infectious disease caused by the most recently discovered coronavirus (SARS-CoV-2). This new virus and disease were unknown before their appearance in Wuhan, China, in December 2019. Due to the rapid virus spread all over the world, the World Health Organization (WHO) declared the state of a pandemic on January 30th 2020, attesting to the global emergency. Generally, coronaviruses (CoVs) form a large family of viruses that cause manifestations ranging from the common cold to more serious illnesses such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) that triggered several global emergencies in the past 20 years.

The coronavirus (SARS-CoV-2) can cause asymptomatic (manifesting no symptoms) or very mild symptoms such as a runny nose or pink eye, and the infection remains mild in 80% of cases. However, there is a vulnerable population at higher risk of developing a more severe disease course, such as the elderly or those affected by chronic disorders – for more information see the Ministry of Health website: https://msan.gouvernement.lu/fr/dossiers/2020/corona-virus.html.

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The Luxembourg Institute of Health (LIH) and the University of Luxembourg (UL)/Luxembourg Centre for Systems Biomedicine (LCSB) are joining forces to better understand the disease course and spread of the virus in the population. Therefore, they are carrying out a national survey on the prevalence of the novel coronavirus (SARS-CoV-2) in the healthy (having no respiratory symptoms or fever) or oligosymptomatic (with few symptoms such as runny nose or sore throat) populations in Luxembourg. The main goal of the study is the assessment of the prevalence, dynamics, and penetrance of the SARS-CoV2 infection within the Luxembourgish population. Secondary analyses include focus on epidemiological, socio-economic and psychological aspects of the confinement during the pandemic.

This study, together with parallel national efforts currently being put in place, will provide essential insight on the prevalence (i.e., how many virus-positive people are in the population), the evolution of clinical symptoms, and on the impact and spread of the COVID-19 disease in Luxembourg. Further to this, it is important to capture aspects on vaccination for individual participants due to its expected impact on the spread of the virus. These precious insights will enable to perform simulations and short- and medium-term

projections of the virus spread to facilitate decision-making on the restrictions, when to lift them, and at what speed, aiming to prevent further virus spread as well as alleviate socio-economic burden. In the second phase of the project, the biosamples (e.g., blood) and data collected in the framework of this study may, with your consent, be used for other research projects authorised by the competent authorities.

To identify a representative sample of the adult population in Luxembourg, a selection of people was performed by an epidemiologist and statistician to include adults of all age groups, gender, geographical areas, and nationalities. You have been contacted, among more than 1500 other people residing in Luxembourg. There is no other reason for those mentioned above why *you* have been contacted.

The purpose of this document is to inform you about the study details, including what you will need to do if you decide to participate. Based on this information, you will be able to decide whether or not you wish to participate. Your participation is entirely voluntary. If you choose to participate in this study, you may withdraw at any time without giving your reason. This study has been authorized by the Ministry of Health and by the National Research Ethics Committee (CNER) on 10/04/2020.

2 CONDUCT OF THE STUDY

The national CON-VINCE survey referred to as the "study" in the rest of the document, is based on your voluntary participation. It has different levels of participation, but if you wish to participate, **the collection of certain information and samples is mandatory**. Additionally, we propose a flexible participation model, meaning that there is the *standard set of information* we will ask you and *basic samples* we will collect. However, you can opt for an optional part, where you can contribute even more (see below). In case you want to participate, but for any reason you wish to keep it as short as possible, a reduced set of questions is possible with the basic set of sampling.

If you are enrolled in the study, you will be asked to fill out the initial questionnaires (appr. 35 minutes) and undergo a sample collection (for the exact samples that are required or optional, see below). If you have no disease-symptoms (COVID-19) this procedure will be repeated every two weeks during 2 months after your inclusion in the study, five times in total, where the questionnaires are shorter (appr. 20 minutes). Finally, you will be asked to fill out the questionnaire one year after your enrollment in the study with a standard sample collection.

Flexible participation principle: standard set of information, minimal set of information, and optional biosampling

The first contact via the company TNS-Ilres will be via email to invite you to participate in the study. In order for you to agree to participate, you are receiving this information sheet. For the next steps, we use a secured online interface to ask you to provide some personal information (name, surname, date of birth, phone number, email, and postal address), and your consent will be requested. If you have any questions about the study and your involvement, you can contact the study team by phone or email, as indicated on the top of this document.

Once you agreed to take part in this study and provided the above information, you will receive another email to complete an online questionnaire. Therefore, the company TNS-Ilres will provide you with an appropriate link and instructions on how to log in. An account will be created specifically for you and answers will be treated confidentially and separate from your personal information. The questions will concern the following domains (duration app. 35 minutes to complete):

- Epidemiological factors and travel history
- Demographics and socio-economic questions
- Symptoms onset
- Current clinical symptoms
- **SARS-CoV-2 vaccine**
- Following of the government recommendations during COVID-19 pandemic
- Home and social contact + socio-economic status
- Environmental conditions at home with a diagnosis of COVID-19
- Psychological questionnaire

In case you wish to participate in the most reduced form, a minimal data set will be proposed to you (duration max. 20 minutes) comprising questions related to the following domains:

- Epidemiological factors and travel history
- Demographics and socio-economic questions
- Current clinical symptoms and onset
- **SARS-CoV-2 vaccine**

Additionally, after you complete filling out the questionnaire, you will be asked to go to a laboratory near you to provide the following samples:

- Blood
- Spit-up (induced sputum)
- A nasal swab
- An oropharyngeal swab

You will also be asked to do a simple quick and non-invasive smell test and qualified personal will measure your blood pressure, heart rate and ventilation frequency.

You will have the possibility, if you wish, to donate the following samples for the research as well:

- A stool sample (you will receive a special collection kit to take home, and you will take a small amount of stool in the days following your visit. You should then send the kit by post.)
- A urine sample

All samples will be stored in the LIH's biobank, the Integrated Biobank of Luxembourg (IBBL) for research purposes.

Long-term follow-up:

In order to capture the dynamics and impact of the virus spread in the Luxembourgish population in the following months, you will be re-contacted to complete a questionnaire and give samples every 2 weeks during the next 2 months (5 times in total) with a final follow-up 1 year after your inclusion in this study.

Important: At any time during your participation in this study, if you develop symptoms typical to COVID-19 (cough and fever), you are asked to contact your treating physician and keep us informed by calling the number listed at the top of this document. If you develop symptoms and test positive for the novel coronavirus, you will have to leave this study. However, you will have the option of participating in another

study (Predi-COVID) of the Luxembourgish Research Task Force, dedicated to patients with clinical symptoms of COVID-19 related to the novel coronavirus.

The implementation of app-based questionnaires for the follow-up assessments over the study period are envisioned, giving you the choice to answer to the follow-up questionnaires also via the CON-VINCE app.

3 USE OF MY SAMPLES

As part of this research project, specific tests are foreseen on your samples; e.g.: virology (to check if the virus is present, and which virus variant is present) and, serology (analysis of your blood antibodies that indicate if your immune system encountered and reacted against the coronavirus).

New knowledge about the SARS-CoV-2 infection is gained daily through the efforts of researchers at the international level. For this reason, it is currently impossible to list precisely which tests will be performed on the samples you donate, however, all future analysis and testing on these samples will be limited to projects focusing on infectious diseases and immunology.

If you give consent for other research as well, your samples may be used for other medical research programs conducted by the LIH or other duly authorized national or international research organizations or biobanks, for academic and/or commercial purposes, whether in the field of COVID-19 research or in the field of infectious diseases and immunology, depending on the options you choose in the consent form.

The principles described in this document will therefore also apply to future medical research projects as long as they are scientifically relevant, except that for future third party research projects:

- information on such future medical research may not be available, and the Data Controller, Principal Investigator, sponsor and approving authority may be different;
- in case of withdrawal of consent, you will not be able to request the destruction of your samples or data already transferred to biomedical research projects.

Your samples and data will only be used for research projects that have received the formal approval from the Comité National d'Ethique de Recherche (CNER) and the Ministry of Health, and that do not contradict the choices you have expressed in the informed consent form. In any case, the recipients of the data will not have access to information that allows your identity to be associated with these samples and data.

4 WHAT ARE THE GENETIC ANALYSES?

Genes are present in every cell of the body. They give the body the instructions it needs to function and repair itself, and they are passed from parents to children and from cell to cell as new cells are created in the body. Sometimes the genes in the body can change, and if this change can be passed from parents to children, it is called a germline mutation.

Researchers want to understand how diseases can be linked to the genes we all carry. In this case, the question is to know whether the genetic make-up of individuals can influence the susceptibility towards the coronavirus or the course of COVID-19 disease. Understanding these links may lead to the development of more effective and personalized tests and treatments for each patient. For this type of research to be carried out, it is necessary to analyse and compare the genes of healthy and sick people. In this context, the use of

Next Generation Sequencing (NGS) techniques allows a precise and exhaustive analysis of the genome that will contribute to the discovery of genetic modifications, even subtle ones.

If you also agree, genetic analyses may be carried out in the framework of secondary use of your samples. In this context, a fortuitous discovery of a germline mutation (mutations or aberrations that could not only affect my future health, but also that of my children, siblings, parents) could also be discovered. Therefore, you are asked to authorize the genetic analysis of your samples.

In this context, it's possible that we encounter incidental findings. An Incidental Finding (IF) can be defined as a "finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study." Genetic and clinical IFs can be of potential importance for the health of the participant. IFs are not specifically targeted and there is no obligation of the researcher to search for such findings actively. It is also of importance to stress out, that methods used in the research study are prima facie intended concerning the research questions of the study.

In such cases, we follow the guidelines published by the Comité National d'Ethique de Recherche (CNER) of Luxembourg, where, if the researcher discovers an IF, he/she will inform the principal investigator (PI) of the study, who will act according to your preference "to be informed" or "not to be informed". If you indicate in the consent form that you prefer "to be informed" the PI (who in this case is the study physician) will communicate the finding to tou within 15 working days. If you indicate that you prefer "not to be informed", no action is required in case of an IF. Your decision is fully respected. Finally, at any time during the study, you can change your mind and communicate the decision to the study team.

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5 WHAT ARE THE POSSIBLE RISKS AND DRAWBACKS?

There are no significant risks associated with this study. The table below lists all of the risks associated with the collection procedures associated with taking your samples, but these risks are **RARE**.

Procedure – Collection of samples	Associated risks.
Blood sampling	Pain, bruising, tiredness or fainting, infection
Nasal swap	Discomfort while brushing, bleeding, infection
Oropharyngeal swab	Discomfort while brushing, bleeding, infection
Stool sampling	No known risks
Urine sampling	No known risks
Saliva/sputum sampling	No known risks
Entering data on an online application	Minimal risks* associated by entering data on an online application

* there are risks associated with the fact that the study involves the recording of data online (hacking, risk of endangering the confidentiality of health and other personal data). This risk is low, but there is no such thing as zero risks. The LIH has implemented extensive data protection measures to minimize this risk. These measures are explained in the section "Confidentiality and Protection of Personal Data".

6 WHAT ARE THE BENEFITS OF PARTICIPATING IN THE STUDY?

You may not benefit directly from participating in this study. However, in case you were tested positive for the coronavirus, we will inform you and your treating physician and advise regular diagnostic confirmation and appropriate sanitary and healthcare measures. There is a possibility that your test for the virus is inconclusive, which usually means that virus is in the low range for positivity. In this case, we will contact you and ask you to repeat the test in a regular diagnostic lab for a final assessment of your status.

Moreover, our study will inform you about your immune status, which can inform about your personal risk to be (re)infected by coronavirus. Please be aware that the presence of antibodies against the new coronavirus in your blood does not necessarily mean that you are immune. Since the SARS-CoV-2 is a new virus, further research is needed to better understand whether, and if so, for how long antibodies protect against the virus.

Your participation in this study is voluntary. You will not receive any compensation for your participation in this study, nor further developments resulting from this study. Your participation is important because you are the source of the information we need to improve our understanding of infectious diseases such as the current COVID-19.

7 CONFIDENTIALITY AND PROTECTION OF PERSONAL DATA

As part of this study, your personal data will be collected and analysed to achieve the scientific objectives of the study.

The LIH and LCSB/UL are jointly responsible for the collection, analysis, and processing of your personal data, and ensure their protection in accordance with the General Data Protection Regulation (EU) 2016/679 of 27 April 2016, applicable as of 25 May 2018 known as the "GDPR" and any subsequent text replacing or supplementing this text (in particular the law of 1 August 2018 on the organisation of the National Commission for Data Protection and the implementation of the GDPR).

What data do we collect?
Your participation in the study involves only the collection of personal data that is necessary for answering the objectives of this scientific study.

In particular:

- At the time of your registration, the following data will be collected to verify that you meet the criteria to participate in the study and create your account in the application: date of birth, contact details (name, first name, phone number, email, postal address). The personal identification information will be collected only for the purpose of recontacting you in case you were tested coronavirus positive. In this case, we will refer you for a diagnostic validation of the results by an accredited laboratory. We have the legal obligation to inform the competent authorities of any coronavirus-positive tests for taking the necessary procedures. The personal identification information will also be used to recontact participants regarding future studies but only if the participant has agreed to be contacted regarding future studies.

On what legal basis do we process your data?
The use of your personal data is necessary to achieve the objectives of the study, which we are conducting in the public interest and for the purposes of scientific research (art. 6.1e and art. 9.2j of the GDPR.).

Who has access to your data?
Only the following categories of people will be able to access your data:

- the investigating physician involved in the study and restricted number of authorized members of his team acting under his responsibility,
- the scientific leader of the study at LIH/IBBL and LCSB/UL, the team acting under his responsibility,
- other researchers or research organizations in the private or public sector will have access to your pseudonymized data to meet the objectives of the study or for future scientific research purposes if

you have consented to this (under no circumstances do we provide them with data revealing your identity).

We may also provide access to your pseudonymised data to service providers who perform services on our behalf. Finally, in the context of certain controls or audits, the competent authorities may also have access to your personal data for the purpose of controlling the quality of data.

What are your rights?

You have the right to access and rectify your personal data. In certain cases (according to the conditions laid down by law), you have additional rights to object to the way your data is used, to request the deletion of your data, to request the restriction of certain aspects of the processing of your data, to retrieve your data with a view to passing it on to a third party (right of portability). If you wish to exercise your rights, you may contact the investigating doctor or his designated representative.

Finally, you have the right to lodge a complaint with the National Commission for Data Protection (CNPD) concerning the processing of your personal data.

For any request for information concerning the processing of your personal data by the LIH or LCSB/UL, you can contact the Data Protection Officer by e-mail at dpo@lih.lu ordpo@uni.lu, or by post at the following address:

LUXEMBOURG INSTITUTE OF HEALTH
Protection des données
1A-B, rue Thomas Edison
L-1445 Strassen
Luxembourg

Or

UNIVERSITÉ DU LUXEMBOURG
Protection des données
Maison du Savoir
2, Avenue de l'Université
L-4365 Esch-sur-Alzette

How do we protect your personal data?

LIH and LCSB/UL implement appropriate security measures, depending on the sensitivity of the data concerned, to protect your data against the risk of unauthorised access, loss, fraudulent use, disclosure, alteration, or destruction of your data.

Your data will be treated in a strictly confidential manner. They will be pseudonymised, i.e., a confidential reference code will be used instead of your name. This code alone does not allow you to be directly identified and will only be used for the scientific processing of your data. At no time will your identity appear in a document intended for the public or other institutions. The correspondence table establishing the link between the reference code and your name will be kept by the Principal Investigator in a confidential manner.

The LIH and LCSB/UL also apply the principle of data segregation, i.e., identification data on the one hand and research data, on the other hand, are stored on different secure servers in order to minimize the

potential risks of re-identification. Despite all security efforts, the risk of a data breach is not zero but can be described as very low.

How long do we keep your data?

Your personal data that are not directly identifiable (pseudonymised data) will be kept for a period of 10 years from the end of the sample and data collection scheduled for April 2021. Thereafter, the need for further retention of this data for further processing for research purposes (in the area of infectious diseases and immunological research as you choose in the informed consent form) will be reassessed upon submission to the National Ethics Committee (CNER) by April 2031.

Concerning your directly identifying personal data (e.g., first name, surname or contact details):

- If you do not wish to be recontacted for possible participation in future research/clinical studies, the link between your identification number in the study and this personal data will be removed 5 years after the end of the sample and data collection.
- If you agree to be recontacted for possible participation in future research/clinical studies, the need to keep this personal data will be evaluated every 5 years.

In the event that you no longer wish to participate in the study, your samples collected prior to the withdrawal of your consent may be retained and used in the study unless you object. In this case, they will be destroyed. However, if any of your samples has already been used in the study, they can no longer be removed from the study.

Data transfers outside the European Union.

Your data may be transferred outside the European Union when this is necessary for the implementation of the research or the exploitation of its results. Only anonymous data or data that does not allow you to be directly identified (coded or pseudonymised data) will be transmitted outside the European Union.
It is possible that certain countries outside the European Union/European Economic Area do not offer the same level of privacy protection as your country. In such cases, LIH and LCSB/UL will put in place appropriate measures to ensure the protection of your personal data (for example, by including standard data protection clauses in its contracts, by complying with codes of conduct or by complying with a certification scheme) or will rely on your explicit consent.

For more detailed information on the appropriate measures implemented by the LIH, you can send a written request to the LIH Data Protection Officer by e-mail to dpo@lih.lu.

For more detailed information on the appropriate measures implemented by the LCSB/UL, you can send a written request to the Data Protection Officer of the University of Luxembourg by e-mail to dpo@uni.lu.

8 COSTS ASSOCIATED WITH YOUR PARTICIPATION

If you decide to participate in this study, there will be no additional cost to you or your insurance company. Visits and procedures identified as being specific to the study are the responsibility of the promoters.

9 INSURANCE

As the promoter, the Luxembourg Institute of Health (LIH) has taken out civil liability insurance for this study (Zurich Insurance plc, Belgium Branch, Da Vincilaan 5, B-1930 Zaventem).

10 YOUR DECISION TO PARTICIPATE

Your decision whether or not to participate in this study will not affect the quality of care you receive. If you decide to take part in this study, you may end your participation at any time, and you will not be required to give reasons for your decision.

In order to participate in the study, we are seeking your consent online. Please read the consent form and tick the boxes that correspond to your wishes. You can download this document at any time.

If you decide to participate in this clinical study, we ask that you:

- Cooperate fully in the conduct of this study.
- Not withhold any information about your health condition, the medications you are taking, or any symptoms you may have.

If you would like more information about the study, you can contact the research team at the number indicated at the beginning of this form.

Informed Consent Form

Validated by Prof. Dr. Rejko Krüger :

_____

Signature

- I declare that I have read and understood the information described above.
- I understand that I have the possibility to download a copy of this document, as well as the general information for participants.
- I declare that I have received a clear description of the purpose and nature of the study and am aware of what is expected of me as a participant in this study.
- I attest to have had sufficient time to think about it and to discuss it with a person of my choice.
- I understand that I can call the number mentioned in the Information leaflet to ask all the questions about the study that came to my mind
- I agree that my treating physician will be informed about my participation in the study (in case you don't have a treating physician, write *none*):

  Name and address of my treating physician: _____
- I fully understand that I am free to leave the study at any time without having to justify my decision and without suffering any material or moral prejudice. I will simply inform the Principal Investigator or the investigative team via the contact options indicated in the top of this questionnaire.
- I understand that any personal information collected in the context of this study will be treated in a strictly confidential manner, in accordance with the General Data Protection Regulation (EU) 2016/679 of 27 April 2016, applicable as of 25 May 2018 (known as the RGPD) and any subsequent text replacing or supplementing this text (in particular the law of 1 August 2018 on the organisation of the National Commission for Data Protection and implementation of the RGPD).
- I accept that the results of this study may be the subject of scientific communications or publications. I am aware that presentation of the study results can in no way allow my direct or indirect identification.
- I voluntarily consent to participate in this study on the basis of the terms and conditions described in the attached information leaflet, and I understand what type of data will be collected during this study.*

  ❑ YES ❑NO
- **If you select "no", you are not eligible to participate in the study.*

- I agree that my samples may be collected and given to LIH/IBBL.*

  ❑ YES ❑NO

  **If you select "no", you are not eligible to participate in the study.*

- I authorise the LIH/IBBL and LCSB/UL to use my samples and pseudonymized data for further research in the broader field of infectious disease and immunological research:

  ❑ YES ❑NO

- I agree that my data and samples may be transmitted in an anonymized form outside the European Union where the legislation in force concerning the protection of personal data may be less strict than that of the European Union:

  ❑ YES ❑NO

- I agree to be recontacted for possible participation in future studies:

  ❑ YES ❑NO

- I am aware that no genetic analysis on my sample is foreseen in the frame of this study, but I agree to the genetic analysis by a Next Generation Sequencing techniques (NGS) on my samples in an amendment to the primary study, targeting on COVID-19 subjected to the approval of the Ministry of Health and Ethics Committee (CNER) in Luxembourg.

  ❑ YES ❑NO

- I am aware that no genetic analysis on my sample is foreseen in the frame of this study, but I agree to the genetic analysis by a Next Generation Sequencing techniques (NGS) on my samples in future research projects related to infectious diseases and immunology subjected to the approval of the Ministry of Health and Ethics Committee (CNER) in Luxembourg.

  ❑ YES ❑NO

  - In case of fortuitous discovery of a germline mutation (mutations or aberrations that could not only affect my future health, but also that of my children, siblings, parents etc.), I consent to this information being communicated to me by my treating physician, to discuss the possible implications and to be referred to a local geneticist if necessary.

    ❑ YES ❑NO

  In making my decision, I confirm that I have been fully informed and understand that the researcher is under no obligation to actively search for genetic mutations in my sample(s) and that the discovery of such a mutation does not constitute a diagnosis. It is also at this time that I will be contacted again if I checked "yes" above. Finally, I confirm that I have been informed that I may reconsider my decision at any time.

→ Consequences of my decision:

If I answer "no", I will not receive any information about these chance discoveries, nor will my relatives be informed.

If I answer "yes", I will be informed of the incidental finding(s) by my treating physician / the study physician / a geneticist. I will then be invited to discuss the possible implications and be referred to a local geneticist if necessary.

- If the answer to the previous question is 'yes', and in the event that a germline mutation is identified and I am unable to receive this information personally (including if I am deceased at the time this information is identified), I wish to designate a family member (representative) to whom these results could be communicated, who could discuss the implications with my treating physician, and be referred to a local geneticist

  ❑ YES ❑NO

Name of my representative: _____

If I answer "yes", it means that I agree that my representative can receive such information, discuss the implications with my treating physician, and be referred to a local geneticist.