Title of the study: International randomised study comparing personalised screening, according to individual risk of breast cancer, to standard screening, in women aged 40 to 70

Name of the study: MyPeBS

Protocol number: UC-0109/1805

Study sponsor: UNICANCER 101, rue de Tolbiac – 75654 Paris CEDEX 13 – FRANCE
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Medical Ethics Committees: _____

Local study doctors-investigators: _____

ESSENTIAL INFORMATION ……..1

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ESSENTIAL INFORMATION

Dear Madam,

You have been invited to take part in the clinical study entitled **"International randomised study comparing personalised screening, according to individual risk of breast cancer, to standard screening, in women aged 40 to 70"** (MyPeBS).

This study aims to evaluate the benefit of more personalised breast cancer screening compared to current standard screening practices.

As the study sponsor, UNICANCER (Hospital network devoted to cancer care in France) is responsible for the set-up, management and funding of this clinical study.

The study is conducted in compliance with the applicable Belgian national legislation and international guidelines and regulations.

This document describes the study and summarises its procedure, its objectives, its potential benefits and possible disadvantages to you. Before you decide whether to take part in MyPeBS or not, we advise you to read this information leaflet carefully and take the time to understand the objectives of the study, what it entails and the potential benefits, risks and constraints that it is liable to cause for you, so that you can make a fully informed decision. This is known as giving "informed consent". Nevertheless, there is no guarantee that you will benefit from taking part in this study.

Feel free to talk about MyPeBS with your family, your friends and your general practitioner. Please contact the study doctor-investigator at the participating centre of your choice, if you would like more details on certain aspects.

This study is funded by the European Union. Five countries (France, Italy, United Kingdom, Belgium and Israel) are participating in the MyPeBS study. The study will include a total of 85,000 women aged 40 to 70 who will each take part in the study for 4 years. In Belgium, the study envisages to include approximately 10,000 women.

MyPeBS was designed and is conducted by a group of doctors, researchers, and scientists, all experts in breast cancer prevention and screening, along with patient representative associations. Their objective is to improve standard breast cancer screening. This study is supervised and monitored by the executive committee of the MyPeBS project, by the study steering committee which handles the day-to-day management of the study, and by a study execution and data monitoring committee (EDMC) which ensures good ethical practice and monitors participant data. The executive committee of the project supervises project progress, responds to partners' queries, acts as the main point of contact for the EDMC and defines the publication policy, database access and collaborations. More information about MyPeBS can be found on the website: www.mypebs.eu.

This document contains 3 parts: the essential information to make your decision, your written consent form and additional information (annexes) detailing certain aspects of the basic information.

<u>If you take part in this clinical study, you should be aware that:</u>

- This clinical study is executed following a review by several ethics committees in Belgium.
- Your participation is voluntary and should remain free from all constraints. It requires the signature of a document expressing your consent. Even after you have signed this document, you may withdraw your participation at any time by notifying the investigator. Your decision not to or to no longer take part in the study at any time will have no impact on the quality of your care or on your relationship with the study doctor-investigator.
- The data collected at this time are confidential and your anonymity will be guaranteed at all times including when the findings are published.
- Insurance has been taken out by the sponsor (UNICANCER) in the event of you being subjected to harm associated with your participation in this clinical study.

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- You will not be charged for the visits and imaging exams specific to the protocol of this study (for more details, see section 3.5 and Annex II).
- You may contact the study doctor-investigator or a member of his/her team at any time if you need further information.

You will find further information on your "Clinical study participant rights" in Annex III (Additional information).

1. What is the objective of the research?

The MyPeBS study was devised to assess, in women aged 40 to 70, whether personalised breast cancer screening based on individual risk of developing breast cancer in the next 5 years (risk-based screening) is at least as effective as current standard screening. In both groups, the occurrence of advanced-stage (stage 2+) invasive (capable of infiltrating surrounding tissue) breast cancer will be assessed, Stage 2+ cancer denotes tumours greater than or equal to 2 cm in diameter or with involvement of axillary lymph nodes (lymph nodes located under the armpits). MyPeBS will also assess whether this personalised screening strategy can reduce the potential adverse effects of conventional screening (see section 2.2). In addition, the sociopsychological and socioeconomic impact of both screening strategies will be compared, by assessing the satisfaction of women, their anxiety, etc. There is currently no comparison in literature between the standard breast cancer screening as organised in Belgium and the personalised breast cancer screening based on individual risk.

After analysis of the study results, the European MyPeBS study will put forward general recommendations for more effective organisation of breast cancer screening in Europe.

2. Advantages and the disadvantages of current breast cancer screening, and estimation of individual breast cancer risk

Breast cancer is the most common cancer in Western women. It is a serious disease, as around one in 5 women with breast cancer die from it.

The purpose of breast cancer screening is to detect potential cancer as early as possible, as the treatment is, in principle, less aggressive and the likelihood of recovery greater than when cancer is diagnosed at a more advanced stage.

Breast cancer screening has been offered in most Western countries for around fifteen years. At the present time in Belgium, organised breast cancer screening is aimed at women aged 50 to 69, who are called for a mammogram (X-ray examination of the breasts) every 2 years. Only a small number of women, with very high specific risk factors, undergo more intensive screening.

2.1 Breast cancer screening: known benefits

- In Western countries, breast cancer screening consists of regular mammograms.

- Except for the very high risk, age is currently the only entry criterion for the organised screening programme.

- These screening guidelines are based on large-scale studies which have demonstrated that screening reduced breast cancer-related deaths by around 20%, meaning that it prevented one in 5 deaths. The benefit of screening between the age of 40 and 50 years is controversial and each country is currently trying to decide on this point. Mammogram-based screening also reduces the number of cases of cancer diagnosed at stage 2 and higher in women over the age of 50. Stage 2+ cancer denotes tumours greater than or equal to 2 cm in diameter or with involvement of axillary lymph nodes (lymph nodes located under the armpits).

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2.2 Current standard mammogram-based breast cancer screening: disadvantages

Mammogram-based screening as performed in current practice comes with disadvantages:

- 1 to 2 breast cancers out of 1000 women examined occur between 2 screening mammograms. These as known as "interval cancers".

- Around one-quarter of breast cancers occurring in women undergoing regular screening have already reached stage 2 or higher at the time of diagnosis.

- In a small percentage of cases, screening mammograms give rise to further assessments (clinical breast examination, ultrasound) or biopsies (tumour tissue samples) which eventually detect a benign, or non-cancerous, lesion ("false positive" results).

- On average, 1 case of breast cancer in 10 diagnosed by screening develops so slowly that it would never cause problems during the lifetime of the woman concerned. These cases are called "overdiagnoses".

- Finally, the mammogram exposes women to a low dose of X-rays which in the long-term can increase the risk of breast cancer. However, the risk of radio-induced cancers (caused by long-term exposure to low X-ray doses) appears to be extremely low (around 1 in 1000 women undergoing screening for 30 years) compared to the benefits of early diagnosis. In addition, the radiation doses currently delivered are very closely monitored.

2.3 Estimating individual breast cancer risk for better "targeting" the screening population: for whom and which screening programme?

Our ability to identify women at high or low risk of developing breast cancer should enable better targeting of cancer screening. The outcome would be to be able to offer more intensive (more frequent) screening to women with a high risk and less frequent screening for those with a low risk.

To do this, we need to estimate the risk of breast cancer in the general female population. This risk is calculated on the basis of straightforward personal and clinical data, such as the woman's age, family history of cancer, personal previous history of benign/non-cancerous breast disease, and exposure to natural hormones (age of first period/menstrual cycle, pregnancy, age of menopause, etc.) and/or medical hormones (hormone replacement therapy, contraceptive pill, etc.) as well as a breast density score (i.e. a mammogram-based assessment of the density of your breasts) and a genetic polymorphism analysis of your DNA. Genetic polymorphisms are variations in the DNA sequence of certain genes. DNA (deoxyribonucleic acid) is a biological molecule found in all cells of the human body. It contains genetic information in the form of tens of thousands of genes coding for proteins that enable the development, function and reproduction of human beings.

3. What is the methodology and the procedure?

This is a randomised study, which means that if you wish to take part in the study, you will be assigned at random (computer randomisation) to one of the two screening programmes: either standard screening (group 1), or risk-based screening (group 2). Neither you nor the study doctor-investigator will be able to choose your group. The likelihood of undergoing standard screening is the same as that of undergoing risk-based screening (1:1 randomisation).

If you are randomised to group 1, you will undergo the standard organised screening programme in Belgium. If you are randomised to group 2, you will have a personalised screening programme based on your estimated individual risk of developing breast cancer (within the next 5 years). This "risk-based screening" may include a mammogram, carried out at various frequencies, and in some cases, a Magnetic Resonance Imaging (MRI) examination. MRI is used to record two- or three-dimensional images of the breast and provides information on lesions which are not visible on conventional X-rays or ultrasounds. In certain women with dense breast tissue, an additional ultrasound may be offered.

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You will find below a summary of all the tests/procedures that you will be required to undergo if you decide to take part in MyPeBS (see annex II for more details).

3.1 Inclusion and randomisation visit – for ALL women taking part in the study:

During this visit, your study doctor-investigator or his/her assigned nurse will check your eligibility to take part in MyPeBS via the study inclusion/exclusion criteria. The primary inclusion criteria are 1) being a woman aged between 40 and 70, and 2) being registered with a mutual health insurance provider, 3) do not have a predisposition to or have a personal history of breast cancer. If you agree to take part in the study, you will need to sign the consent form to take part in the study.

During this visit, you will also be requested to complete a questionnaire on 1) your personal and family medical history, and your lifestyle, 2) your knowledge of screening for breast cancer and its risk factors, and on your anxiety level and comprehension of the information received.

Your personal data will be input by the study doctor-investigator or his/her assigned nurse in a centralised web platform which will handle all the study data. A computer tool will then perform randomisation. You will then be assigned to one of the 2 study screening groups.

3.2 If you are randomised to the "standard screening" group

Your screening schedule, i.e. the schedule of your mammograms, will follow the standard screening programme applicable in Belgium for the next 4 years (follow-up period). There will be no further visits within the scope of the MyPeBS study. You will receive a reminder by e-mail near the date of your mammograms. **It is important for the findings of the study that you comply with your screening schedule as closely as possible, over the 4 years of participation. You will be requested to enter the dates and results of each of your imaging tests in your secure private space in the web platform.**

During this follow-up period, you will also be requested to complete on-line questionnaires in the MyPeBS web platform, accessible from your PC, and update your personal data.

A mammogram is required at the end of the study, i.e. 4 years after the start of your participation. The date and the result must be entered in the web platform. The end-of-study mammogram will be shown on your screening schedule.

3.3 If you are randomised to the "personalised risk-based screening" group

You will need to undergo the following procedures:

3.3.1 Saliva test

During the inclusion visit, you will be requested to provide a saliva sample which will be used to analyse your DNA. This test will verify a set of genetic polymorphisms associated with breast cancer risk. Your saliva sample will be sent to a specialised testing laboratory located in France for analysis. Your risk level, including the results for the polymorphisms, will be available after a few weeks. This risk score will be disclosed and explained to you by your study doctor-investigator or his/her assigned nurse at your second visit (see section 3.3.2).

3.3.2 Second visit

Around 12 weeks after the inclusion visit, the time required to complete the genetic polymorphisms analysis which is used to estimate your risk score (see section 3.4.3 for more details), you will be requested to attend a second visit with your study doctor-investigator.

During this visit, the study doctor-investigator will provide you with information on your individual risk level (low, moderate, high or very high) and will give you your personalised screening programme, i.e. the schedule of your imaging tests over the next 4 years (see 3.3.3 Personalised follow-up period).

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Below you will find more information about the different risk levels:

- low: in this risk category, less than 1 in 100 women may develop breast cancer within the next 5 years.
- moderate: in this risk category, about 1 in 70 women may develop breast cancer within the next 5 years.
- high: in this risk category, 1 in 20 to 60 women may develop breast cancer within the next 5 years.
- very high: in this risk category, more than 1 in 17 women may develop breast cancer within the next 5 years.

3.3.3 Personalised follow-up period

The follow-up period lasts 4 years from your initial mammogram. During this period, you will be requested via your personal portal in the study web platform to complete on-line questionnaires and update your personal data, once a year. You will also be required to undergo imaging tests based on the screening schedule adapted to your estimated risk level: the higher your risk, the higher the screening frequency (see table below). A mammogram is required at the end of the study, i.e. 4 years after the start of your participation in MyPeBS. The date and the result must be entered in the web platform. You will receive a reminder by e-mail near the date of your scheduled visit(s)/test(s). **It is important for the findings of the study that you comply with your screening schedule as closely as possible, over the 4 years of participation. You will be requested to enter the dates and results of each of your imaging tests or any important event (knowledge of cancer in the family, pregnancy, etc.) in your secure private space in the web platform.**

The table below summarises the tests required according to the risk categories:

Estimated 5-year risk	Low risk	Moderate risk	High risk	Very high risk
Mammogram#	After 4 years	Every 2 years	Each year	Each year
Further test	-	Ultrasound in the event of high breast density	Ultrasound in the event of high breast density	MRI-scan each year up to the age of 60

#Or tomosynthesis* for centres using this technique

3.4 Description of study procedures

3.4.1 Imaging tests

Mammograms: in both groups, the radiologists may use, depending on the guidelines in the centres, either "2D" mammography, or a new technique, called digital breast tomosynthesis (DBT). This new technology produces images of the breast in 3 dimensions (3D) and reconstructed (synthetic) 2D images. It was recommended by European Guidelines as an alternative to conventional mammography (recommendations from the European Commission Initiative on Breast Cancer Guidelines).

Your doctor will receive the test results, or tomosynthesis (if it is available), as this would have been the case within the scope of standard organised screening in Belgium.

Image storage during the study:

The mammogram images taken during the study will be stored, as far as possible, for other potential research applications, at the hospital where the imaging tests were carried out.

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These images will be made available for potential future research projects, either as part of the MyPeBS study or in other studies related to breast cancer screening, for example studies seeking to better assess breast density or refine risk prediction potential. They may also be used to develop or test mammogram diagnostic tools in the future. Any use of your images outside the context described in this document is subject to ethics committee approval.

3.4.2 Collection and updating of your personal data

Each of the participants will have private secure access to the MyPeBS study web platform.

Once you have joined the study, the study doctor-investigator or his/her assigned nurse will create your private access to your secure personal space on the study web platform participant portal. This will provide you with access to your personal space, your screening programme, questionnaires, study information, letters to be printed for your various doctors if needed, etc. This web platform will also be used by the sponsor for sharing with you any new information arising during your participation that would be liable to affect your decision to continue to take part.

Your personal space on the web platform is private, confidential and secure; All your personal data collection for the purposes of the study will be pseudonymised, i.e. all data identifying you will be replaced by an artificial identifier, such that it will be absolutely impossible to identify you outside this secure personal space. The artificial identifier will be composed as follows: country code (0032) – centre code (XXXX) – subject number (XXXXX) (5 digits, defined by the order of your arrival in the centre). Only your doctor will know your first and last names and contact details. No researchers or any other people will be able to do so.

We would be grateful if you could update your data during the 4 years of your participation in the study. **It will be particularly important to notify any changes in your personal or family history of cancer**. Similarly, any change of lifestyle or home address should be notified as it may impact your participation in the study (for example, moving to another region not taking part in MyPeBS). More generally, any new personal information that you deem relevant may be input in the platform.

We would also be grateful if you could complete the psychological follow-up and satisfaction questionnaires: after 3 months, 1 year and 4 years from the first visit, and enter the following items over the 4-year study period:

- Your radiological test (mammograms, MRIs, etc.) dates and results
- Reporting of medical or personal events likely to occur during the four-year follow-up period, such as the need for a breast biopsy or serious events, such as cancer diagnosis pertaining to you or your family.

If you have been randomised to the "risk-based screening" group: your estimated individual breast cancer risk may change over time, according to the changes in your personal characteristics and your family history; this is why it is very important that you continuously update the information in the secure web platform for the study. Your personal risk will be re-evaluated and updated if required. If your risk category/level changes after a significant event (such as a new case of breast cancer in the family or a breast biopsy, etc.), you will be sent or given a new screening programme. Please follow the new screening programme. If you have any questions, feel free to ask your study doctor-investigator. Your personal portal will contain information on your updated screening programme.

3.4.3 DNA analysis of your saliva

If you are randomised to the "personalised risk-based screening" group (group 2), you will be requested to provide a saliva sample at the inclusion visit to screen for genetic breast cancer predisposition factors. Your sample collected in a specific tube will be identified by a bar-code on the tube (without your last and first names), and will be sent to the centralised platform located in France (Centre d'Etude du

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Polymorphisme Humain (CEPH) in Paris and to Centre National de Recherche en Génomique Humaine (CNGRH) in Evry) for genetic polymorphism testing.

The full results of the polymorphism tests will be stored confidentially and may be used during the study to re-evaluate your risk. For example, if new polymorphisms of major interest are identified during the study, your risk score will be re-evaluated using the results of the saliva test from the first visit. If this gives rise to a change in your risk score, you will be notified and will be provided with a new personalised screening schedule. However, this is very unlikely.

No other routine genetic testing will be carried out for this study. In particular, we will not screen for very rare breast cancer predisposition gene abnormalities (i.e. BRCA1 or BRCA2). However, if you (or your doctor) think you may have a hereditary predisposition due to your family history of breast cancer, you will be advised to attend an oncogenetic consultation. Your study doctor-investigator can provide you with further information if necessary.

Residual DNA storage:

If you agree to donate the DNA remaining after your saliva test, it will be stored in an pseudonymised and fully secure DNA bank (Centre d'Etude du Polymorphisme Humain (CEPH), Paris, France), opened specially for the MyPeBS study. This residue may be used for the purposes of future research, for example to test for other genes causing cancerous diseases. In this case, neither you nor your doctor will receive the results of this testing.

3.5 Payment of tests

If you decide to participate in the study, this will not create extra costs for you nor for your insurance company in regards to the standard breast cancer screening in Belgium. This means that you will only be billed the amount that a standard screening procedure would cost you. Any procedures specific to the study will be paid for by the sponsor of the study. If by chance these extra procedures are billed to you, and you pay them, you can ask to be reimbursed by your site. If, depending on the results of the imaging scheduled in your screening programme, other further tests are required (ultrasound, biopsy, additional mammogram and/or MRI-scan, or even treatment if a lesion requiring treatment is identified), they will be paid for in accordance with the usual conditions in Belgium. Therefore, you/your private mutual health insurance provider may be required to pay for a portion of the cost of these tests.

3.6 What happens if the results of the tests carried out during the study are not normal?

If an abnormal result is confirmed during your tests and requires further tests (another mammogram or ultrasound, additional MRI-scan, biopsy), all measures will be taken by your radiologist and/or attending doctor in accordance with standard practice.

If tests of this type are necessary, please complete the relevant section in your personal space in the web platform for the study. It is very important that this information be reported to ensure that the study data are reliable and complete. **Your cooperation is essential for the study to be conclusive**.

What happens if you find something unusual in your breasts?

Regardless of your screening programme, if you notice something unusual in one of your breasts (deformation, nipple discharge, lumps, etc.), you must consult your attending doctor as soon as possible. He/she will arrange for further tests/examinations as required. **Even in women with a low estimated breast cancer risk, this type of event may occur; Similarly, a negative screening test does not mean that you are completely free from risk. Therefore, it is important to monitor these signs**.

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What happens in the event of the onset of breast cancer?

Should you be diagnosed with breast cancer during the study, your attending doctor would be responsible for organising your care and you would be treated in the same way as if you were not taking part in this study, and in accordance with the national regulations in force and best practice guidelines. Should this scenario arise, you would be requested to report it in the web platform along with the proposed treatment(s).

3.7 What will happen at the end of the study?

At the end of the study, you will continue to follow the standard screening programme in Belgium, regardless of the screening strategy to which you were assigned. However, if screening practices were to change in Belgium and elsewhere following the MyPeBS study, you may subsequently access or return to personalised risk-based screening after the end of the study.

You can discuss your continuing follow-up with your attending doctor in accordance with currently applicable health care standards.

When all the findings of the study are available, they will be sent to you as soon as possible, as well as to all the study participants, and to all the doctors-investigators.

Certain long-term medical follow-up data are very important to assess the impact of personalised screening on women's health and survival. However, the study follow-up period is merely 4 years. For this reason, we request **your consent for us to collect your follow-up data for up to 15 years after your inclusion in the MyPeBS study.** If you agree, these data will be forwarded confidentially by your screening coordination centre and/or your mutual health insurance provider. You can change your mind at any time.

4. What are the expected benefits relating to participation in this study?

If you are randomised to the "standard national screening programme" group, no specific individual benefit is expected. However, you will regularly receive information about breast cancer screening that we will update during the study in the web platform and on the study website. **The data collected from the study participants, including your data, may affect future breast cancer screening in Europe. When we publish the results of the MyPeBS study, and if risk-based personalised screening becomes the norm, it may be offered to you after the study.**

If you are randomised to the "personalised risk-based screening" group and your risk category involves more frequent tests than standard screening, and **you unfortunately develop breast cancer, it may be detected at an earlier stage than under normal conditions.** We estimate that, in this group, around 50 women will be diagnosed with breast cancer at an earlier stage, as such theoretically preventing around 50 cancers at stage 2 or higher. Cancer diagnosed at an earlier stage is associated with a better prognosis and less intense treatment. Also, in this group, we hope to see fewer "interval cancers", cancers which develop between two negative screening results.

If you are randomised to the "personalised risk-based screening" group and you are in the low breast cancer risk category, you will undergo less tests than for standard screening. This could reduce the risk of mammogram false positives, overdiagnosis, radiation-induced cancers and stress or anxiety induced by the associated tests.

5. What are the potential risks and adverse effects associated with taking part in this study?

The medical risks from the radiological tests (mammograms, ultrasound and MRI-scans) carried out during the study are identical to the risks from these tests when carried out as part of standard practice.

If you are randomised to the "standard screening" group, no additional risk and no adverse effects are expected if you are aged 50 or over. The advantages and disadvantages of standard screening were

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described above (sections 2.1 and 2.2). If you are under 50, you will need to undergo an end-of-study mammogram. This additional mammogram, which is not standard practice in Belgium, may give rise to "false positive" results, or overdiagnosis as explained above.

If you are randomised to the "personalised risk-based screening" group, the potential risks and adverse effects include:

- For women over the age of 50 presenting with a low breast cancer risk, there is a risk, in the event of breast cancer development, that it is diagnosed later than with standard screening. The probability of this occurring is very low (around 1 in 1,000 women).

- Women categorised as high-risk will undergo more frequent screening than with standard screening. This can lead to an increased risk of mammogram false positives and to overdiagnoses. This can lead to needless anxiety and even emotional trauma.

6. Withdrawal from the study

Your participation is voluntary and you are entitled to stop taking part regardless of the reason, at any time, without having to provide justification. This will not affect your medical care or any other benefits to which you may be entitled. Nevertheless, it may be useful for the study doctor-investigator and for the study sponsor (Unicancer) to know the reasons for your withdrawal. This information could be useful when designing future studies. If you so wish, you may inform your study doctor-investigator of these reasons.
If you decide to withdraw from the study, previously collected data pertaining to you may be used for analysis.
There is also a possibility that the study doctor-investigator may withdraw you from the study because he/she deems that it is best for your health or has observed that you are not following the instructions given to participants correctly.

7. Discussion of protocol with your attending doctor:

For your safety, it is advisable for your attending doctor, if you have one, to be notified of your participation in this study. We will request you to confirm your consent, but will respect any wish you may have not to notify your doctor.

8. Publication of findings of the study

A description of this clinical study is available on the U.S. website http://www.ClinicalTrials.gov. You may access this site at any time. The findings of the MyPeBS study may be published in scientific/medical publications. However, this will only occur in several years' time (generally several months after the end of the study), as it will take time to collect, analyse and interpret the data. Individual participants' findings will not be published, only the overall findings of the study will be published.

You will be notified of all the findings of the study by contacting your study doctor-investigator.

9. Contact

Should you require further information, or in the event of any problems or concerns, you can contact the study doctor-investigator _____ at the following telephone number _____.
If you have any questions relating to your rights as a participant in a clinical study, you can contact your institution's patients' rights mediator _____ via the telephone number _____. If required, the latter may place you in contact with the ethics committee.

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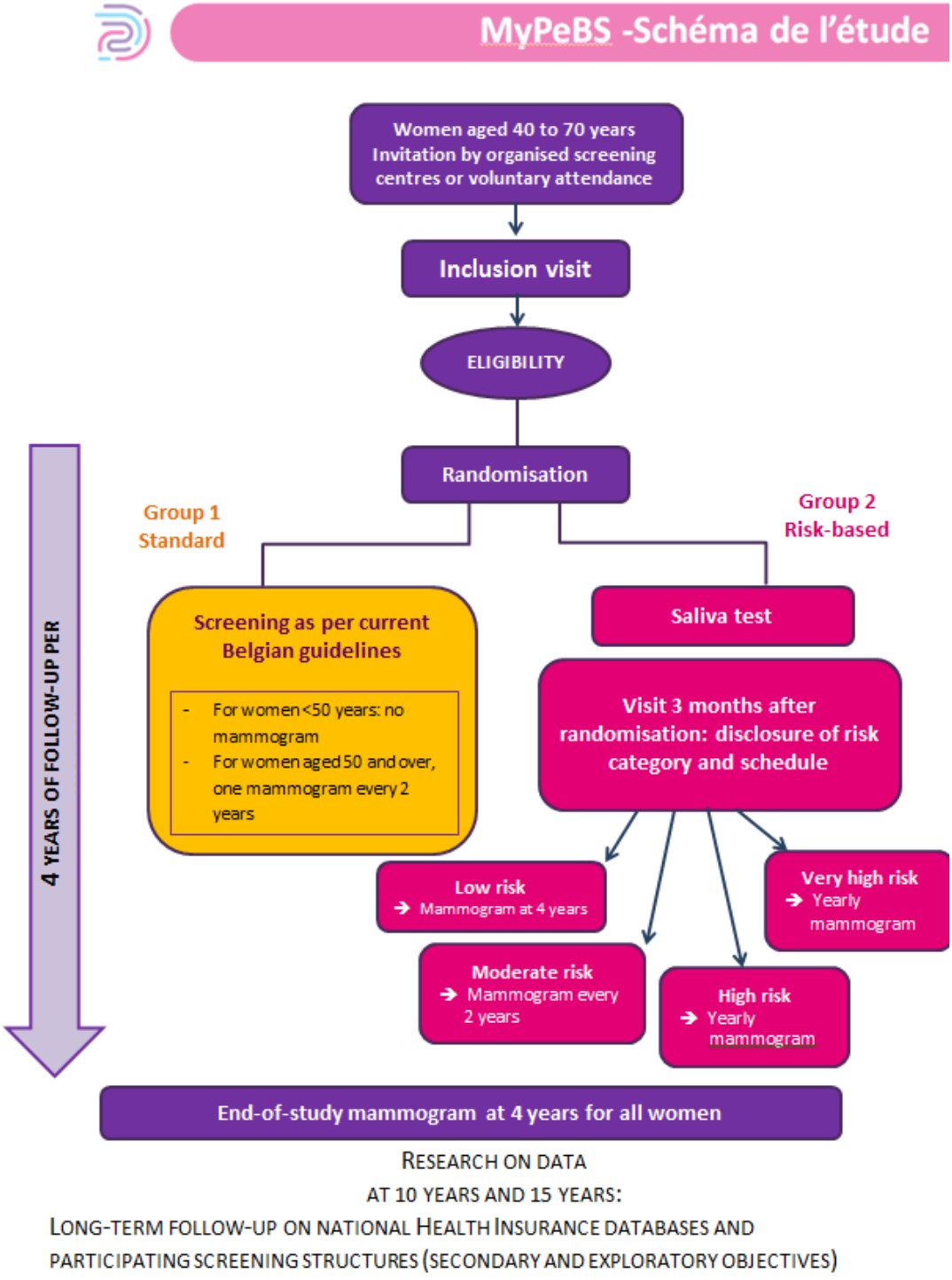
Annex 1: Additional information on study organisation



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Annex II: Organisation of study procedures

Table 1: Schedule of visits with your study doctor-investigator and tests:

VISITS	Inclusion visit (V1)	Second visit (for group 2 only)	Follow-up for both groups (1 & 2)			
Visit dates	**D0**	**8 to 12 weeks after V1**	**1 year (±6 months) after V1**	**2 years (±6 months) after V1**	**3 years (±6 months) after V1**	**4 years (±6 months) after V1**
Type of visit	Physical	Physical	On-line on the web platform			
Inclusion/exclusion criteria	X					
Consent form signature	X					
Mammogram (if not yet available)	X					
Minimum medical data collection	X					
Randomisation	X					
Provision of schedule for group 1 women	X					
SALIVA SAMPLE	X (for group 2 only)					
Information on your risk level and provision of screening schedule		X (for group 2 only)				
IMAGING TEST: Mammogram and if recommended: ultrasound and/or MRI	Necessity and frequency determined according to your programme					
COMPLETION OF QUESTIONNAIRES (on-line on the web platform)	X	X	X			X
UPDATE OF YOUR DATA (on-line on the web platform)			X	X	X	X

Annex III: Additional information on clinical study participant protection and rights

a. Ethics Committee

This study was reviewed by an independent Ethics Committee who approved the study after consulting the local ethics committees of the Belgian institutions participating in the study. The independent Ethics Committee is responsible for protecting subjects taking part in a clinical study. It ensures that your rights as a participant in a clinical study are respected, that, in the light of current knowledge, the balance between risks and benefits remains favourable for participants, and that the study is scientifically relevant and ethical. Under no circumstances should you take Ethics Committee approval as an incentive to take part in the study.

b. Voluntary participation

Before signing the informed consent form, feel free to ask any questions that you deem necessary. Take the time to discuss it with a trustworthy person if you so wish.
Your participation in the study is voluntary and should remain free from any constraints: this means that you are entitled not to take part or to withdraw without any justification even if you previously agreed to take part. Your decision will in no way affect your relationship with the study doctor-investigator and the quality of your future therapeutic care.
However, for your safety, you are advised to notify the study doctor-investigator if you have decided to withdraw your participation from the study.
If you agree to take part, you will sign the informed consent form. The study doctor-investigator will also sign this form and thereby confirm having provided you with the necessary information on the study. You will receive a copy of the consent form.

Within the scope of MyPeBS, we have not placed any restriction on participation in other clinical trials; nevertheless, we request that you contact your study doctor-investigator who will check the compatibility of your participation in this clinical trial with the sponsor.

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c. *Costs associated with your participation*

The sponsor has envisaged to compensate the hospital for the time devoted to the study by the study doctor-investigator and his/her team and for the study-specific visits.

Your participation is unpaid. In addition, it will not incur **any additional costs relative to the standard screening for you or your insurance provider.**

If you agree to participate, you must have social security cover. At the end of the study, the clinical study databases, and those of the national social insurance will be linked. Your NISS number (Belgian national registration number) will be used for this purpose unless you refuse.

d. *Protection of your personal data*

Your medical record, which is subject to professional secrecy, will remain **confidential** and can only be consulted under the supervision of the doctor-investigator responsible for your follow-up, or by the Health Authorities and persons duly appointed by the trial sponsor.

Processing of data pertaining to you is necessary for the purposes of this scientific conducted in the public interest in the field of public health (articles 6.1.e, and 9.2j of the General Data Protection Regulation (European Regulation. 2016/679) of the European Parliament and of the Council of 5 May 2018 (General Data Protection Regulation) and by the law in force on 30 July 2018 concerning the protection of privacy. These rights are also guaranteed by the law of 22 August 2002 concerning the rights of patients. Hence, the health and administrative data required to address the scientific questions of this research, will be collected, sent and processed by UNICANCER (France), the sponsor, and its service providers strictly within the framework of the execution of their duties. These data will be processed confidentially to enable the analysis of the findings of the research. The sponsor (UNICANCER, Paris, France) is the data controller of your encoded data. The investigator and the hospital are, on the one hand, subcontractors of the sponsor with regard to the processing of your encoded data and, on the other hand, data controllers of your unencoded data collected both as part of the study and outside it.

If you agree, the data collected during the trial may be used by UNICANCER or its partners in a confidential and secure manner in order to continue research to combat cancer or improve access to therapies.
To this end, your personal medical data will be sent to the research Sponsor, or persons or companies working on their behalf, to their partners and to the competent authorities, in France and abroad. In the event of transfer of your encoded data outside the European Union, to countries with a lower level of personal data protection or no data protection legislation, particularly to service providers or researchers with whom the sponsor collaborates, the sponsor will take the necessary measures, such as contracts or other means reinforced by data protection authorities, to ensure that an equivalent level of protection is provided as stipulated by Regulation (EU) 2016/679 of the European Parliament and of the Council of 25 May 2018 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 (General Data Protection Regulation) and by the law in force of 30 July 2018 concerning the protection of privacy. These rights are also guaranteed by the law of 22 August 2002 concerning the rights of patients. You have the right to obtain a copy of the contract or other reinforced means that has been taken to ensure an adequate level of protection.

In case of future research conducted by Unicancer or its partner, further information and the possibility to exercise your rights will be available on the information website: http://mesdonnees.unicancer.fr/.

Your data will be kept for not more than two years after the latest scientific publication associated with the research projects. They will subsequently be archived, with very restricted access, for not more than twenty-five years. It is not out of the question for the findings of this research to enable the development of new diagnostic tools: for example a new predictive test for cancer risk could be developed by means of the data collected within the scope of MyPeBS (therefore by means of your data) and subsequently marketed to enable its distribution.

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Regarding the data pertaining to you, you have the following rights, in accordance with the conditions provided for by the regulation in force:

- a right of access to your personal data,
- a right to rectification of inaccurate personal data,
- a right to request the erasure of your personal data,
- a right to restrict the processing of your personal data, particularly if the processing is called into question.
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You also have the right to oppose data processing. In particular, this prevents any subsequent collection of data by the processing manager.

If you exercise your right to oppose or your right to deletion of your data, Unicancer may keep and analyse data collected previously if their deletion was likely to make it impossible or seriously compromise achieving the objectives of the research, or in case of overriding legitimate reason for processing these data, such as guaranteeing the reliability of the research results, to comply with a request from public authorities or to fulfil a legal obligation.

It is recommended, but not required, prior to exercising your rights, to contact the doctor-investigator who follows you in the research so that he/she may provide you with your identification number and the centre identifier which are specific to the research.

If you wish to exercise one of your rights relating to data pertaining to you, please submit your request to the study doctor-investigator or to the data protection manager at the study hospital: _____ .

If, despite UNICANCER's undertaking to protect your rights and your personal data, you were not satisfied with the protection of your data, you are also entitled to submit a complaint concerning the mode of processing of your data to the Belgian supervisory authority responsible for ensuring compliance with data protection legislation:

Data Protection Authority (DPA)
Rue de la Presse 35,
1000 Brussels - Belgium
Tel. +32 2 274 48 00
e-mail: contact@apd-gba.be
website: https://www.dataprotectionauthority.be

You can also access all medical data pertaining to you directly or through a doctor of your choice.

The data collected during this study may be used for other research, such as research for furthering understanding or more effectively preventing cancer risk. We will ask you whether you allow us to use your pseudonymised data for other research. This research may lead to potential commercial operation: for example a new predictive test for cancer risk could be developed by means of the data collected within the scope of MyPeBS (therefore by means of your data) and subsequently marketed to enable its distribution. We will therefore also ask you whether you agree or not to your personal pseudonymised data being used for such research which could lead to potential commercial operation. Any use of your data outside the context described in this document is subject to Belgian ethics committee approval.

If you wish to know more about the measures to protect your personal data, you should first contact the investigator. You can also contact the data protection officer of the site of the study either by mail or by e-mail

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e. *Insurance*

Your participation in a clinical study involves a risk, however small. The sponsor accepts, even in the absence of fault, liability for any harm caused to you (or in the event of death, your beneficiaries) and directly or indirectly associated with your participation in the research.

The sponsor has taken out an insurance policy (policy No. 390/01321386-30010) covering this liability from HDI-GLOBAL SE, Branch for Belgium (Avenue de Tervueren 273/1 1150 Brussels; 02 773 09 50). This insurance certificate can be consulted at your centre on request.

If the study doctor-investigator deems that there is a possible link between the harm caused to you and the study, he/she will undertake to notify the study sponsor who will undertake to initiate the reporting procedure to the insurer. The insurer will appoint - if deemed necessary - an expert to assess the relationship between your new health problems and the study.

In the event of disagreement either with the study doctor-investigator, or with the expert appointed by the insurer, as well as whenever deemed necessary, you or - in the event of death - your beneficiaries may cite the insurer directly in Belgium.

The law envisages that the insurer may be cited either in the jurisdiction of the location where the event causing the harm took place, in the jurisdiction of your residence, or in the jurisdiction of the insurer's head office.

f. *Rights relating to biological samples*

Use of your saliva for genetic tests in this study (evaluation of polymorphisms specific to breast cancer risk) requires your prior written consent.
In addition, if you give your consent, these samples may be stored by a centre guaranteeing their protection and confidentiality for use by UNICANCER or its partners for the purpose of future genetic research in the field of health, and in particular on cancer, prevention or nutrition, previously approved by a Belgian ethics committee. This will be carried out in compliance with the legislation in force as long as the samples retain scientific interest for improving cancer screening or care. You may nonetheless oppose this use at any time by informing your doctor-investigator. The samples will be destroyed after 20 years but, you can request, at any time, your study doctor-investigator to destroy the samples earlier.

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