GRAIL NHS-interface supplementary information document pack

This document pack includes useful supportive information about the NHS-Galleri study. The documentation specifically focuses on the NHS-interface and approved pathways as per the study protocol. It includes supplementary information for clinicians and example 2ww referral documentation that would be attached to each referral.

Contents

NHS-Galleri: Supporting information for clinical teams/ Cancer Alliances.

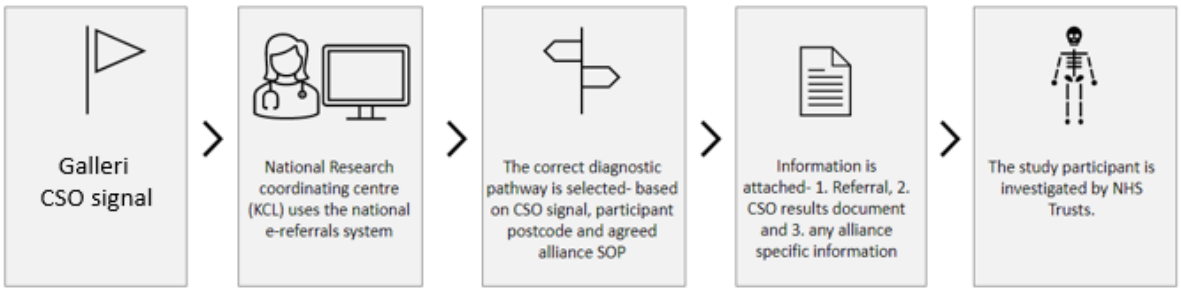
Introduction

The NHS-Galleri trial is investigating a new blood test to see if it can help the NHS detect cancer earlier than standard pathways. The test can detect more than 50 types of cancer, often before symptoms occur.

NHS England is working with King's College London and GRAIL (the company who developed the test) on this study, which is inviting men and women aged 50-77 without signs or symptoms of cancer from eight Cancer Alliance areas in England to take part. GRAIL's Galleri™ test is a qualitative, next-generation sequencing (NGS)-based screening test for the detection of DNA methylation signals using cell-free DNA isolated from adult human peripheral whole blood.

The NHS-Galleri trial will demonstrate the clinical utility of the multi cancer early detection (MCED) test in a general screening population in a real-world NHS setting. Participants with a cancer signal detected are at significantly elevated risk of cancer. The test will give an indication of the likely location(s) of the tumour reported as Cancer Signal Origins (CSO)s. Participants with a cancer signal detected will require NHS diagnostic assessment following a 2-week wait (2ww) referral (via eRS).

Process Map



NHS-Galleri trial supplementary information

As part of the NHS-Galleri study, participants will have blood taken to perform the Galleri test. They will then be randomised to either i) intervention arm – blood immediately analysed and those (1-2%) with a cancer signal detected, referred via 2ww to NHS cancer diagnostic services or ii) control arm - NHS standard of care (blood is stored and may be subsequently tested). The test will be performed three times at 12m intervals, over a period of 2 years for the majority of participants.

If a cancer signal is identified, participants and will enter the appropriate NHS diagnostic pathway(s). These investigations are within the 2-week wait referral pathway and are carried out outside the NHS-Galleri study.

Clinical teams receiving a referral for a participant in the pathway should perform clinical diagnostic evaluations for the reported cancer signal origins within their appropriate 2ww or RDC pathways. Once

these investigations are complete, providing no cancer is found, participants are returned to the community to follow NHS standard care and will continue in the trial. Where a cancer is found any further diagnosis, staging or follow-up is carried out in the NHS.

Processes

Galleri™ test results will be sent directly to the trial nurses at the national research coordinating centre at King's College London. Participants with a Cancer Signal Detected will be contacted by phone, the results explained to them and a 2ww referral made by trained nursing staff. The research coordinating centre will have responsibility for making the national referrals using the NHS e-referral system (e-RS) for suspected cancer to ensure these participants get followed-up with appropriate diagnostic tests and no unnecessary burden is placed on primary care. As part of the referral, up to three documents will be attached. This will include a Galleri CSO test report and a national NHS-Galleri 2ww referral form. Additional cancer alliance specific information may be appended if required by the alliance.

Depending on the alliance area, the referral will either be sent via i) Trust co-ordinating centre (MODEL A), or ii) direct to trusts providing diagnostic services (MODEL B).

MODEL A: Trust NHS-Galleri co-ordinating centre requirements

A trust co-ordinating centre is a model whereby there is a single point of entry for individuals with a positive test at the level of a trust. It embeds the NHS-Galleri study into existing local pathways and enables local GRAIL co-ordinators to monitor patient attendances in the trust referral pathway. This model has been pioneered by the Cheshire and Merseyside Cancer Alliance using Warrington as an example. The requirements of this model are: -

- Creation of a new virtual Trust/RDC triage point on e-RS.
- A Trust NHS-Galleri coordinator lead who will have responsibilities for triage and referring into local NHS trust 2ww clinics

MODEL B: Direct to Trust requirements

The Direct to Trust model will minimise impact on Cancer Alliances, whilst still providing the ability to embed the NHS-Galleri study into existing regional pathways. The requirements of this model are: -

- To develop regional guidance for the national research co-ordinating centre at King's College London. This may include addition of more information on the e-RS and/or guidance on appropriate clinics to refer to.
- An NHS-Galleri support lead to liaise with the Trust diagnostic centre to ensure patients get access to appropriate diagnostic tests.

Frequently asked questions

How will a referral be made to the NHS by the study team?

A referral will be made electronically via the national e-referral system (e-RS) 'any-to-any' process, into a suspected cancer 2ww pathway. The referral will be made for participants with a Galleri™ CSO detected. The referral will include patient details, the recommended cancer diagnostic pathway, the Galleri test report (Appendix 1) and information about the study. A national NHS-Galleri 2ww referral form will be utilised.

Where will the referral be made to?

All NHS-Galleri referrals should be seen by the team who are clinically trained to investigate the first CSO reported. The referral will be made by the agreed referral model for that Cancer alliance (Model A/Model B). Patients will be informed of their results and referral options by the research team nurses.

What happens if the referral document does not contain all the information I normally require?

While the NHS-Galleri study is designed to work well alongside established local/regional processes, the referrals are being made from a national trial centre and there will be differences in the format of the information appended to the referral compared to that usually provided to NHS trusts when referring on a symptomatic 2ww pathway. Additional information is provided in both the Galleri test report and the 2ww referral form.

Please also consider that additional supporting patient information in the form of summary care records is available on the NHS spine.

If clinically indicated, please arrange a virtual review of the patient to gain additional background information and/or to formulate a diagnostic plan. It is important to note that the number of participants who are expected to be seen in any referral clinic/pathway over the course of the study is expected to be very small.

What is a summary care record and how can I access it?

Summary Care Records are an electronic record of important patient information, created from GP medical records. They can be accessed by most NHS secondary care trusts and be accessed through local electronic patient record systems or by the national NHS spinal web portal (https://portal.national.ncrs.nhs.uk/portal/)

How many referrals are likely to be made across the trial?

The study aims to recruit 140,000 participants ***across eight Cancer Alliances*** in England. Of the ~70,000 in the intervention arm, 1-2% are expected to have a cancer signal detected (therefore requiring referral and investigation) within the first year.

What diagnostic tests should be performed for individuals with any given CSO?

Participants in the study may receive a report with one or two CSO results. If there are two CSOs reported, these should sequentially undergo NHS diagnostic tests according to the clinical indications reported. NHSE does not mandate specific tests for each CSO result, however this document sets out the usual suggested primary and secondary tests for the given cancer sites. If no tumour is identified

in the suggested site(s) after investigation, a CT chest/abdo/pelvis is recommended prior to return to the community if not already performed as part of the routine diagnostics.

What happens if two abnormal CSO are identified?

For some trial participants two abnormal CSOs will be identified. These will be reported in order of probability (see Appendix 1 example), with the first CSO site being a more likely cancer origin than the second CSO site. The NHS-Galleri referral protocol advises that both signals are investigated, but that these are done sequentially. If no tumour is identified in either of the suggested site(s) a CT chest/abdo/pelvis is recommended, if not previously undertaken, prior to return to the community.

Should NHS-Galleri referrals be included in trust metrics and performance for diagnostic pathways?

The number of NHS-Galleri referrals is expected to make up a tiny proportion of total referrals for any given diagnostic pathway. Depending on local/regional processes and the impact on these clinics, NHS trusts may or may not choose to include these referrals in their diagnostic pathway metrics. Taking part in this national NHS study should not adversely impact Trust performance.

What happens if a patient does not attend clinic follow up or is lost to follow up?

Trusts are not expected to make specific additional attempts, beyond usual NHS care, to encourage patients to attend clinics once booked. Please follow standard Trust protocols for DNAs. However, alliance and trust clinical teams may contact the research nurses at King's if they are concerned. A trial pathway facilitator can help to ensure that all participants get the diagnostic follow-up they need.

What happens if diagnostic tests performed do not identify a cancer?

In some cases, the Galleri™ test produces a CSO result, but diagnostic tests do not identify a cancer. This could mean:

i) that the individual has a cancer which was not identifiable by the diagnostic tests used

ii) that the cancer is present in some other part of the body, not explored by the CSO-directed tests

iii) that the result of the Galleri test was a false positive and the individual does not have cancer.

A CT chest/abdo/pelvis is therefore recommended prior to return to the community if not already performed. Participants should be investigated in a similar manner to any individual in a 2ww/RDC pathway and once investigations are complete, they are returned to continue NHS standard care.

Is it possible to map a CSO positive test result to a 2ww pathway?

Most CSO results map clearly to NHS 2ww pathways. The recommended mapping is enclosed (Appendix 2).

For individuals who have been referred to the 2ww, is it required/mandated to involve an MDT?

Clinical teams are not mandated/required to involve an MDT. However, if appropriate to consult an MDT, teams are free to do so.

Can alliances append additional information to this document or create alliance-specific clinical guidance documentation to help clinical care.

Participants with a cancer signal detected in the NHS-Galleri trial are offered NHS follow-up as part of the 2ww clinical pathway. The aim is that investigations do not deviate significantly from existing diagnostic pathways. Additional alliance-specific supporting information can be appended to the referral documentation, but there should not be significant deviation from usual 2ww diagnostic processes.

What if Straight to Test (STT) would usually be most appropriate?

For most individuals, a preliminary virtual/telephone consultation is recommended to develop a diagnostic plan for trial participants.

Are GPs informed of participation/positive results?

GPs are informed of GRAIL results. This will be done at the time the referral is made to the 2ww pathway. Additional, GPs are also informed of 2 week wait referrals and results of the investigations.

How should GRAIL referrals be considered for alliance cancer waiting time performance metrics?

Referrals from GRAIL should be classified as a 2 week/Urgent Suspected Cancer Referral to ensure patients are recorded as being on this pathway. Total numbers of individuals referred by this pathway are forecasted to be low and will have minimal impact in terms of performance metrics.

How should we be recording the referral source for these referrals

In terms of alliance performance reporting, referrals from GRAIL should be recorded under the other (97) option. More detailed information is planned for release in the next Cancer Waiting Times guidance document.

How would I report an adverse event?

Use the MHRA Yellow Card reporting site to report medical device and diagnostic adverse incidents (https://yellowcard.mhra.gov.uk/). Further information about adverse medical device and diagnostic adverse incidents can be raised to GRAIL Customer Service - customerservice@grail.com or the trial team.

Appendix 1: Example document with GRAIL CSO test result

Galleri

Firstname Last | GRAIL ID ID1234567890

Multi-cancer early detection test report

Patient
Name: Firstname Lastname
Patient ID: StudyPar123456
Age: 56
Bio Sex: Female

Sample
GRAIL ID ID123456789
Report Date: 15-OCT-2019 / 18:13 PT
Collection Date: 20-DEC-2019 / 21:39 PT

Ordering Provider
Name: Firstname Lastname, MD
Location: Academic Hospital - Clinic 1
Address: 123 Maple St. Unit 321
Rainbow Town, CA 94000

Results

Cancer Signal Detected

The GalleriTM test detected DNA methylation signals associated with cancer in the analyzed cell-free DNA obtained from the patient sample. **Diagnostic evaluation for cancer should be conducted.**

In some cases, the Galleri test may produce a "Cancer signal detected" result, but follow-up diagnostic evaluation may not result in a cancer diagnosis. This could mean that the individual has a cancer that was not identified by the selected follow-up diagnostic evaluation, or that the result of the Galleri test is a false positive and that the individual does not have cancer.

In the Circulating Cancer Genome Atlas (CCGA) clinical validation study, Galleri detected cancer signals across more than 50 cancer types.

Top Predicted Signal Origin

Head & Neck

Signal Origin(s) Score

This chart displays the two top scores of Cancer Signal Origin predicted by the Galleri test. This chart does not provide an indication of the overall likelihood of cancer. The Cancer Signal Origins reported can help guide next steps in the diagnostic evaluation.

Cancer signals are organized into 21 Cancer Signal Origins, which are listed in the Method section. For more information, please visit www.galleri.com/test-report.

Included sub-categories of the predicted origins:

Head & Neck: Oropharynx, Hypopharynx, Nasopharynx, Larynx, Lip and Oral Cavity (including Oral Tongue), Nasal Cavity, Paranasal Sinuses, Major Salivary Glands

Cervix: Cervix

When a cancer signal is detected, even if the diagnostic evaluation of the Cancer Signal Origin(s) is negative, the likelihood that the individual has cancer remains elevated and may warrant further evaluation. Please visit www.galleri.com/test-report for more information. Healthcare providers may contact GRAIL clinical support services at 833-694-2553.

Comments:
Tur tem qui corum quam fugia qui am temporem et. Con eum ea porror sequi odiosae simin es evelestis delictio test eos ressimusdam hicipsandae sunt volor accatem nobisimpos aut maximet que et.

GRAIL
Laboratory Director: Rita Shaknovich MD, PHD | CLIA #05D2154430 | CAP #8149563
1525 O'Brien Dr., Menlo Park, CA 94025 | 833-MY-GALLERI (833-694-2553) | FAX 650-999-9000 | customerservice@grail.com

DRAFT

Note that this is an example document only. The contact details and website for GRAIL should be obtained from the GRAIL CSO test result document received with each referral.

APPENDIX 2: - Recommended mapping of CSO to NHS 2WW pathways

Cancer Signal Origin (CSO)	Suitable 2WW pathway
Head and Neck	2WW head and neck
Oesophagus, Stomach	2WW upper GI
Colon, Rectum	2WW lower GI
Anus	2WW lower GI
Liver, Bile Duct	2WW upper GI
Pancreas, Gallbladder	2WW upper GI
Lung	2WW Lung
Melanocytic Lineage	2WW Skin
Breast	2WW urgent breast
Cervix	2WW gynaecological
Uterus	2WW gynaecological
Ovary	2WW gynaecological
Prostate	2WW Urology
Kidney	2WW Urology
Bladder, Urothelial Tract	2WW Urology
Thyroid Gland	2WW head and neck
Myeloid Lineage	2WW haematology
Lymphoid Lineage	2WW haematology
Plasma Cell Lineage	2WW haematology
Bone and Soft Tissue	2WW sarcoma
Neuroendocrine cells of lung or other	2WW Lung/2WW other. If an organ site is indicated the referral should be considered to that pathway. If there is a known local NET MDTs, a referral may be made to this service.

Anus CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	ANAL CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Anus Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. Primary Investigation(s):

- Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
- Direct visualisation of anus and anal canal and rectum (anoscopy or flexible sigmoidoscopy or colonoscopy).
- At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
    - CT chest, abdomen and pelvis.

2. Further Investigations:

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. No Cancer Diagnosis:

If no cancer is confirmed following primary investigations and following investigation of the second CSO if relevant, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. Discharge:

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Breast CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	BREAST CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Breast Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Triple assessment (physical examination, imaging with mammography or US, and biopsy of identified lesions).
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - Further imaging with MRI.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Bladder, Urothelial tract CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	BLADDER & UROTHELIAL TRACT

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Bladder, Urothelial Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Flexible cystoscopy.
   - CT abdomen/pelvis (e.g. triple phase or pre- and post- contrast)
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT chest

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Bone & Soft tissue CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	BONE & SOFT TISSUE CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Bone and Soft Tissue Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - MRI with contrast or CT of chest, abdomen, pelvis
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis: radionuclide bone scan.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Cervix CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	CERVICAL CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: Suggested Investigation Pathway for Cervix Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Speculum exam +/- biopsy +/- cervical screening (HPV test +/- cytology if overdue).
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT chest, abdomen and pelvis.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Colon, rectum CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	COLORECTAL CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Colon, Rectum Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Direct visualisation of the colon (colonoscopy or CT colography, colon capsule endoscopy).
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - Liver ultrasound and chest X-ray
     - CT chest, abdomen and pelvis.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Head and Neck CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	HEAD & NECK CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Head and Neck Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Direct visualization of oropharynx, nasopharynx and hypopharynx - endoscopy, imaging (fibre-optic panendoscopy, ultrasound of neck).
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT neck, chest, abdomen and pelvis.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Kidney CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	KIDNEY/RENAL CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Kidney Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation. Test urine for blood.
   - CT renal, pre and post contrast
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT chest, abdomen and pelvis

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Liver & bile duct CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	LIVER/BILARY CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Liver, Bile Duct Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation. Tumour markers.
   - CT Triple Phase of the Liver to include Pancreas
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT chest, abdomen and pelvis.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Lung CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	LUNG CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Lung Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Contrast enhanced CT scan of the thorax.
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - 6 month follow up CT.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Lymphoid lineage CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	LYMPHOID LINEAGE CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Lymphoid Lineage Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - History and clinical examination, routine bloods –FBC, peripheral blood film, biochemistry screen, LDH, viral serology (Hep B, C HIV), Immunoglobulins and protein electrophoresis.
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT chest, abdomen and pelvis.
     - Bone marrow biopsy.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Melanocytic Lineage CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	MELANOCYTIC LINEAGE CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Melanocytic Lineage Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate prior to further consultation
   - Skin inspection including vulva and anus, fundoscopy,
   - Panendoscopy of oropharynx.
   - CT chest, abdomen and pelvis

2. Further Investigations:
If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. No Cancer Diagnosis:
If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. Discharge:
Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:
email: clinical_help@nhs-galleri.org,
NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

CANCER RESEARCH UK | KING'S COLLEGE LONDON CANCER PREVENTION TRIALS UNIT

GRAIL

Myeloid lineage CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	MYELOID LINEAGE CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Myeloid Lineage Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - History and clinical examination, routine bloods – FBC, peripheral blood film biochemistry screen, LDH.
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - Bone marrow biopsy.
     - Consider CT chest, abdomen and pelvis

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Neuroendocrine cells of lung or other organs CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	Neuroendocrine cells of lung or other organs

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Neuroendocrine Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - CT of neck, chest, abdomen and pelvis.
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis: Ga68 Dotatate PET

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Oesophageal CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	OESOPHAGEAL/GASTRIC CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Oesophageal/Stomach Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Upper gastrointestinal endoscopy
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - CT chest, abdomen and pelvis.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. CT of the chest, abdomen and pelvis was listed as a possible primary investigation in Step 1, but if this has not been undertaken already, it should be considered now to exclude a cancer in site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Ovary CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	OVARIAN CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Ovary Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - CA125 blood test and transvaginal ultrasound scan (must include views of both ovaries).

2. **Further Investigations:**
   If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**
   If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**
   Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:
email: clinical_help@nhs-galleri.org,
NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Pancreas CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	PANCREATIC CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Pancreas Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Pre-imaging: complete/comprehensive blood panels including CA19.9, HbA1c
   - Primary imaging: Dual phase contrast enhanced CT of the abdomen and pelvis, covering the pancreas, liver, bile ducts and gallbladder in detail.
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - Endoscopic ultrasound of pancreas with view of duodenum and ampulla of Vater
     - MRI with MRCP component.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

CANCER RESEARCH UK | KING'S COLLEGE LONDON CANCER PREVENTION TRIALS UNIT

GRAIL

Plasma Cell CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	PLASMA CELL CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Plasma Cell Lineage Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - History and clinical examination, routine bloods – FBC, peripheral blood film, biochemistry screen, Beta 2 microglobulin, Immunoglobulins including protein electrophoresis, Serum free light chains, urine protein electrophoresis.
   - At the discretion of the clinician/MDT, if the primary investigation does not confirm a cancer diagnosis:
     - Bone marrow biopsy.
     - Skeletal survey or MRI.

2. Further Investigations:
If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. No Cancer Diagnosis:
If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. Discharge:
Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:
email: clinical_help@nhs-galleri.org,
NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Prostate CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	PROSTATE CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Prostate Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - PSA level
   - Digital Rectal Examination
   - Multi-parametric MRI of the prostate

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Thyroid CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	THYROID CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Thyroid Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Ultrasound imaging of the thyroid by thyroid-trained sonographer or radiologist.

2. **Further Investigations:**

If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**

If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**

Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

Contacts for the trial research nurses:

email: clinical_help@nhs-galleri.org,

NHS-Galleri trial call centre 0800 030 9245 -- request to be put through to the research nurses at KCL

Further information on the MCED test and the NHS-GRAIL study can be found at www.nhs-galleri.org.

Uterus CSO signal NHS-interface documents

Suspected Cancer for assessment on 2WW/RDC

National NHS-Galleri Referral form

Date of referral

Forename:		Surname:		NHS ID:	
DOB:		Address:			
Telephone:					

□ The patient has been told that a 2WW/RDC referral for suspected cancer has been completed.
□ The patient is available and willing to attend hospital for tests/appointments within 14 days.
□ The patient has received all information about MCED DNA blood tests and the NHS-GRAIL study

SUSPECT CANCER SIGNAL (S):	UTERINE CANCER

Reason for referral:

The patient being referred is part of the NHS-Galleri trial and has had a positive Galleri screening test. The test is a blood based MCED test and has a Positive Predictive Value (PPV) estimated to be in excess of 40%. The test report will indicate 1 or 2 potential origins for a cancer signal.

If one cancer origin is reported, please investigate the patient as a 2ww suspected cancer referral for the cancer site reported (See Grail test report) and consider 2ww diagnostic tests.

If two cancer signal origins are reported and no cancer is detected at the first site, please refer within your trust to the 2ww pathway for the second cancer site reported. If there are any difficulties making this referral according to local referral pathways, please contact the research team (see below).

If no tumour is identified in the cancer site(s) reported, a CT chest/abdo/pelvis may be appropriate before discharge with advice to continue screening and to be alert for changing or new symptoms.

If the response to questions below is yes, please give details

Is the patient suitable for telephone review/triage? y/n
Are there any language needs? y/n
Are there any travel needs? y/n
Have you identified any special needs? y/n
Any other important information:

Patient's GP details:

NHS-Galleri Trial: SUGGESTED Investigation Pathway for Uterus Cancer Signal Origin

This information is advisory: Clinical judgement should be applied at all steps, including consideration of the patient's overall fitness and their likelihood of benefit from further investigation or treatment.

1. **Primary Investigation(s):**
   - Review and discuss diagnostic plan with patient, including specific initial tests if appropriate to further consultation.
   - Transvaginal ultrasound
   - Pipelle biopsy
   - Hysteroscopy if indicated by ultrasound findings

2. **Further Investigations:**
If investigation does not confirm a cancer diagnosis, the patient should be referred for investigation of the second CSO if one is reported. Urgent Referral should be made to the relevant local clinical team for the second CSO. Study team at KCL should be informed. If direct local referral cannot be made, patient management should be handed back to the KCL study team who will make the referral for the second CSO.

3. **No Cancer Diagnosis:**
If no cancer is confirmed following primary investigations and following investigation of the second CSO *if relevant*, given the overall high positive predictive value of the Galleri test, the patient is still likely to have a residual risk of cancer in excess of NICE urgent referral thresholds for people with symptoms. The clinician/MDT should therefore consider CT of the chest, abdomen and pelvis at this point, if this has not already been done, to rule out cancer in a site other than the first or second CSO.

4. **Discharge:**
Having undertaken steps 1 to 3, if no cancer is confirmed, unless the clinician/MDT feel there is a clinical reason to investigate further, the patient can be discharged. The study team at KCL should be informed that the patient can be re-entered into the trial for the next blood sample in approx. 12 months. The patient should be reassured but reminded to continue with routine cancer screening appointments and to report any new or unusual symptoms to their GP. The patient's GP should be informed of the extent of investigation undertaken.

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