Date: 03/05/2022 Version 4.1

PHENOTYPING SEROCONVERSION FOLLOWING VACCINATION AGAINST COVID-19 IN PATIENTS ON HAEMODIALYSIS

Sponsor Reference No:

Date and Version No: 03/05/2022 Version 4.1

IRAS: 292716

Chief Investigator:	Dr Matthew Graham-Brown – NIHR Academic Clinical Lecturer in Renal medicine, Department of Cardiovascular Sciences, University of Leicester, and Honorary Specialist Registrar Renal Medicine, John Walls Renal Unit, University Hospitals Leicester.
Investigators:	Professor Nigel Brunskill Dr Richard Baines Professor James Burton Dr Rupert Major Dr Haresh Selvaskanden Dr Katherine Hull Miss Rosey Billany Dr Sherna Adenwalla
Sponsor:	University of Leicester
Funder:	Leicester Charity Hospitals
Signatures:	The approved protocol should be signed by author(s) and/or person(s) authorised to sign the protocol

Confidentiality Statement

Date: 03/05/2022 Version 4.1

Authors

List here all authors / collaborators that have assisted with the writing of the protocol

Dr Matthew Graham-Brown
Professor Nigel Brunskill
Professor James Burton
Dr Rupert Major
Dr Haresh Selvaskanden
Dr Katherine Hull
Miss Rosey Billany
Dr Sherna Adenalla

Date: 03/05/2022 Version 4.1

Signature Page

Chief Investigator Name: Dr Matthew Graham-Brown

Chief Investigator signature: _____

Date: **06/05/2022**

Sponsor Representative Name: **__Yasmin Godhania__**

Sponsor Representative signature: _____

Date: **06/05/2022**

Principal Investigator Name: Dr Matthew Graham-Brown

Principal Investigator signature: _____

Date: **06/05/2022**

(In cases of Multi-centre studies, this must be replicated for each site)

Date: 03/05/2022 Version 4.1

TABLE OF CONTENTS

Date: 03/05/2022 Version 4.1

1. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
Pre-approval	**2**	**22.01.2021**	**Miss R Billany Dr M Graham-Brown**	**1. Samples will now be taken 1 month after the first vaccine dose and 1 month after the second vaccine dose**
SA01	**2**		**Miss R Billany Dr M Graham- Brown**	**These changes were made at the same time as the response to REC above: 1. Addition of a baseline sample and a 6 month post second vaccine dose sample 2. Access to stored clinical samples for patients (to prevent having to take the baseline sample) 3. An increase in the amount of blood taken at each timepoint 4. Analysis and storage of samples at University of Leicester 5. Transfer of samples to the CRICK Institute**
SA02	**3**	**19.02.2021**	**Miss R Billany**	**1. Addition of a survey pack for patients and controls**
SA03	**4**	**16/08/2021**	**Miss R Billany Dr M Graham- Brown**	**1. Addition of additional time points for blood sampling, including before and following any subsequent booster doses. 2. Addition of the ability to transfer samples collaborating centres for analyses that cannot be completed in Leicester under the terms of material transfer agreements agreed between UoL and collaborating centres, 3. Extend the study time period for a further 24 months to allow us to collect the additional blood samples above**
NSA01	**4.1**	**03/05/2022**	**Miss R Billany**	**1. Reduction of the sample size to 115**

Date: 03/05/2022 Version 4.1

2. SYNOPSIS

Study Title	**PHENOTYPING SEROCONVERSION FOLLOWING VACCINATION AGAINST COVID-19 IN PATIENTS ON HAEMODIALYSIS**
Internal ref. no.	0810
Trial Design	Prospective observational
Trial Participants	End Stage Kidney Disease on Haemodialysis and Healthy volunteers
Planned Sample Size	95 patients with end stage kidney disease on haemodialysis and 20 healthy volunteers
Planned Trial Period	3 years (36 months)
Primary Objective	• To phenotype the 1 month seroconversion following the first vaccination dose and the 1 month and 6 month seroconversion following the second vaccination dose against COVID-19 in haemodialysis patients
Secondary Objectives	• To compare rates of 1 month seroconversion following the first vaccination dose and the 1 month and 6 month seroconversion following the second vaccination dose against COVID-19 between patients on maintenance haemodialysis and healthy control volunteers • To assess antibody levels 12, 18 and 24 months post second vaccination. • Assess the antibody response before and 1 month after any booster vaccinations

3. ABBREVIATIONS

AE	Adverse event
AR	Adverse reaction
CI	Chief Investigator
CKD	Chronic Kidney Disease
CRO	Contract Research Organisation
EC	Ethics Committee (see REC)
eGFR	Estimated Glomerular Filtration Rate
ESKD	End Stage Kidney Disease
GCP	Good Clinical Practice
GP	General Practitioner
ICF	Informed Consent Form
NHS	National Health Service
NRES	National Research Ethics Service
PI	Principal Investigator
PIL/S	Participant/ Patient Information Leaflet/Sheet
R&D / R&I	NHS Trust Research &Development / Innovation Department
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
TMF	Trial Master File

4. BACKGROUND AND RATIONALE

Patients with end stage kidney disease (ESKD) on haemodialysis are more likely to suffer poorer outcomes following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (1). This is likely to be because these patients have higher levels of co-morbid diseases and they are relatively immunosuppressed due to the effects of advanced kidney disease. The humoral response against common viral vaccination is known to be blunted in patients with ESKD (2) and there are data to suggest seroconversion following infection with COVID-19 is blunted in patients with kidney disease (3). A successful programme of vaccination will undoubtedly improve outcomes for patients on haemodialysis, but vaccine testing programmes have not included patients with ESKD. Whilst initial press-coverage of the efficacy of vaccines which are available for use is promising, they are untested in patients on haemodialysis who are known to be relatively immunosuppressed as a result of their renal disease and as such the efficacy for this patient group is not known.

This study will phenotype the IgG antibody response to vaccination for COVID-19 in 95 patients on haemodialysis compared to 20 healthy volunteers. Antibody testing will be conducted at 1 month post first vaccination dose and 1 month and 6 months post second vaccination dose. This will give crucial information as to the efficacy of the vaccine and inform possible requirements for re-vaccination.

5. OBJECTIVES

This study will:

1. Phenotype the 1 month IgG antibody response to the first vaccination dose and the 1 month and 6 month response to the second vaccination dose for COVID-19 in patients on haemodialysis
2. Compare the 1 month IgG antibody response to the first vaccination dose and the 1 month and 6 month response to the second vaccination dose for COVID-19 between patients on haemodialysis and healthy volunteers
3. Assess the antibody response immediately before and 1 month after any booster vaccinations
4. Measure antibody levels 12, 18 and 24 months after their second vaccination

Date: 03/05/2022 Version 4.1

6. STUDY DESIGN

6.1 Summary of study design

This will be a prospective observational study. Following vaccination as part of the National COVID-19 vaccination programme, consecutive patients on haemodialysis (n=95) and healthy volunteers (n=20, NHS workers who are likely to be vaccinated in the first wave of vaccination) will attend for IgG antibody testing to COVID-19 1 month after the first dose and 1 month and 6 months after the second dose of vaccine. Antibody tests will also be done immediately before and 1 month after any booster vaccination and 12, 18 and 24 months after second vaccination dose.

6.2 *Outcome measures:*

IgG seroconversion at 1 month after the first dose and 1 month and 6 months after the second dose of vaccine.

Antibody levels immediately before and 1 month after any booster vaccination and 12, 18 and 24 months after second vaccination.

A survey pack containing: Section 1: General Practice Physical Activity Questionnaire (GPPAQ), Section 2: PROMIS Global Health Scale, Section 3: Pittsburgh Sleep Quality Index (PSQI)

Details of outcome measures are discussed below:

Participants with ESKD on haemodialysis will have blood sampling 1 month following the first vaccination dose and 1 month and 6 months following the second vaccination dose when they attend for their regular haemodialysis slot on the dialysis unit. Additionally, blood will be sampled in the same way from haemodialysis patients immediately before and 1 month after any booster doses of the vaccine and 12 months, 18 months and 24 months after second vaccination dose. Serum samples from all participants will be tested for the presence of spike protein antibodies using the Siemens Centaur platform currently used at the University Hospitals of Leicester NHS Trust. In order to obtain a baseline sample we will access routinely stored clinical samples to prevent the need for additional samples to be taken.

Participants who are healthy volunteers will attend the blood room at the Leicester General Hospital for samples to be taken at baseline, after the first vaccination dose and 1 month and 6 months following the second vaccination dose. Additionally, blood will be sampled in the same way for healthy volunteers immediately before and 1 months after any booster doses of the vaccine and 12 months, 18 months and 24 months after second vaccination dose.

Participants recruited to the study will be contacted via telephone to collect relevant details of medical history and demographics and their medical records will be accessed to collect recent blood test results and historic tests results for COVID-19 (both antigen and antibody tests).

Date: 03/05/2022 Version 4.1

7. TRIAL PARTICIPANTS

7.1 Overall Description of Trial Participants

95 prevalent patients on maintenance haemodialysis and 20 healthy volunteers will be recruited following vaccination for COVID-19.

7.2 Inclusion/Exclusion Criteria (ESKD patients on haemodialysis)

Inclusion Criteria

- Age>18 years
- ESKD on maintenance haemodialysis
- Able and willing to give informed consent
- Have completed or due to complete vaccination against COVID-19

Exclusion Criteria

- Acute kidney injury requiring temporary haemodialysis
- Unable to give informed consent
- Pregnancy

7.3 Healthy Controls Inclusion/Exclusion criteria

Inclusion Criteria

- Age>18 years
- Able and willing to give informed consent#
- Have completed or due to complete vaccination against COVID-19

Exclusion Criteria

- History of immunosuppression
- Use of immunosuppressive medications in prior 12 months
- Known history of chronic kidney disease
- Pregnancy

Date: 03/05/2022 Version 4.1

8. STUDY PROCEDURES

Patients on haemodialysis are currently being vaccinated by invitation in secondary care. As part of routine clinical care, patients are being asked when they attend dialysis whether they have been called for vaccination or whether they have been vaccinated. When they have been vaccinated this is routinely recorded by the clinical staff on the University of Leicester renal database (PROTON). The clinical team will identify people who have been vaccinated through this database and members of the study team (who will also be members of the clinical team) will approach the patients to discuss the study and to give them a PIS should they want to take part. These patients will be followed up at their next dialysis session and if they wish to participate will be consented by a member of the research team.

Healthy volunteers will be identified as members of the clinical team who are having the vaccine or those who contact the study team directly in response to posters advertising the study to healthy volunteers. Once healthy volunteers have been identified in these ways they will be given a PIS by a member of the study team and contacted after 48 hours by a member of the study team. If they wish to take part they will then be consented by a member of the study team.

8.1 *Informed Consent*

In both cases, participants will have a minimum of 48 hours to consider the patient information sheet, and the opportunity to question the study team, or other independent parties to decide whether they will participate in the study.

Written informed consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent will be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator as detailed on the Delegation of Authority and Signature log for the study. The original signed form will be retained at the study site within the Trial Master File (TMF) or Investigator Site File (ISF). A copy of the signed informed consent will be given to participants (or emailed to participants at their request) and a copy retained in the participant medical notes. Written informed consent will be taken prior to any assessments.

8.2 *Screening and Eligibility Assessment*

Potential participants who are patients on haemodialysis will be screened prior to initial telephone contact by a member of the clinical team involved in patient care based on the

inclusion/exclusion criteria against patients. The clinical team will also screen clinic lists and the COVID-19 vaccination log on PROTON (see above) to identify and approach potential participants at routine dialysis sessions.

Potential participants who are healthy volunteers will be NHS workers at the University Hospital of Leicester. It is anticipated that NHS workers will be amongst the first groups of people to receive the vaccine and these people will be made aware of the study through local poster advertisements in the department of renal medicine at the University Hospitals. Those interested in participating will be asked to contact the study team via email and the study team will then make contact to screen for eligibility, send the PIS and invite to take part as required.

8.3 *Assessments*

For patients on haemodialysis, blood sampling for IgG antibody response to COVID-19 vaccination will take place when the patient attends a routine dialysis appointment 1 month post first vaccination dose and 1 month and 6 months post second vaccination dose (3 samples total). A baseline sample will be obtained from routinely stored clinical samples. Blood will be taken during the patients dialysis at the same time as bloods for routine clinical care with no additional procedures needed when blood is taken. Vaccines currently available or soon to be available require 2 doses before immunity is achieved and the blood antibody tests will be taken 1 month after the first immunisation has been administered and 1 month and 6 months after the second. Blood will be taken from the arterial dialysis line at the start of dialysis so no additional venepuncture is required and no additional visits to a clinical environment are required.

Healthy volunteers will be working in a clinical environment within UHL and will have their blood taken by a trained member of the research team (all of whom are working on the clinical service at UHL) at baseline, 1 month post the first vaccination dose and 1 month and 6 months after the second vaccination dose. This will be arranged in the most practical way and will conform to Hospital protocols on the wearing of personal protective equipment in the clinical environment the blood is taken.

Some of each sample will be processed in the laboratories at the University Hospitals of Leicester, and some will be processed and stored at the University of Leicester. One aliquot

of the stored samples will be transferred in accordance with a Material Transfer Agreement to the Francis Crick Institute (London).

Clinical Information

With the participant's consent, the researcher team will access their clinical records and extract relevant medical and demographic information including:

- Age
- Gender
- Ethnicity
- Primary cause of renal failure
- Previous history of transplantation
- Time on dialysis
- Co-morbidities
- Blood test results
- Medication
- Smoking Habits
- The specific vaccine administered (make/type)

Past medical history, patient demographics, medications and relevant test results will be recorded for healthy volunteers in the same way through access of medical records.

All information will be entered into a case report form (CRFs) which will be stored in a locked filing cabinet in the locked office of the Chief Investigator at the Leicester General Hospital. Data will be extracted from the CRF and entered into an excel spreadsheet that is a coded and anonymised with no patient information which is stored on the UHL CardioRenal Research drive on NHS servers only accessible by members of the research team with specific access.

Laboratory Tests

30 ml (2 tablespoons) of venous blood samples will be taken from the arm by a trained member of the research team/clinical phlebotomy service at 1 month after the first vaccination dose and 1 month and 6 months after the second vaccination dose and using the Monovette System. A baseline sample will also be taken from healthy controls (the patient baseline sample will be extracted from routinely stored clinical samples).

Blood samples from each participant will be sent to the pathology labs for analysis and will be destroyed after the test is completed by the UHL pathology staff.

Additional serum will be separated and stored in aliquots at -80°C at the University of Leicester (Maurice Shock Building, Level 1 Renal Research Laboratory).

One aliquot per time point of the stored samples will be transferred in accordance with the details of a Material Transfer Agreement to the Francis Crick Institute (London) for further antibody analysis. Routinely stored clinical samples for patients (baseline) will also be transferred to the Francis Crick Institute. Any aliquots that have been transferred to the Francis Crick Institute will be disposed of after analysis is completed not stored or transferred back to the University of Leicester.

Aliquots of stored samples will be transferred to additional collaborating sites with ethical approval to conduct analyses that cannot be completed locally in accordance with details of the Material Transfer Agreements drawn up between the University of Leicester and the collaborating centre. Any samples that are transferred externally will be disposed of after analysis is complete, not transferred back to the University of Leicester.

Questionnaires

A short survey pack will be administered at the point of consent containing the following: This will take less than 5 minutes to complete.

Section 1: General Practice Physical Activity Questionnaire (GPPAQ)

Section 2: PROMIS Global Health Scale

Section 3: Pittsburgh Sleep Quality Index (PSQI)

8.4 *Definition of End of Trial*

National Research Ethics Service (NRES)/Health Research Authority (HRA) standard operating procedures advise that the end of the research should be defined in relation to the collection of all data required to answer the research questions in the protocol. In the current study, this will be once all outcome measures have been analysed.

8.5 *Discontinuation/Withdrawal of Participants from Study Treatment*

Each participant has the right to withdraw from the study at any time without giving a reason. In addition, the investigator may discontinue a participant from the study at any time if the investigator considers it necessary for any reason including:

- Significant protocol deviation
- Significant non-compliance with treatment regimen or study requirements
- An adverse event which requires discontinuation of the study or results in inability to continue to comply with study procedures
- Disease progression which requires discontinuation of the study or results in inability to continue to comply with study procedures
- Consent withdrawn
- Lost to follow up

If the participant is withdrawn due to an adverse event, the investigator will arrange for follow-up visits or telephone calls until the adverse event has resolved or stabilised.

8.6 *Source Data*

Source documents are original documents, data, and records from which participants' CRF data are obtained. In this trial, these will include:

- Hospital records (from which medical history and previous and concurrent medication may be summarised into the eCRF)
- Questionnaire pack

In this study the eCRF will be used as the source document to store data extracted from:

- Clinical and demographic data
- Clinical blood results
- IgG Antibody results

All documents will be stored safely in confidential conditions on the UHL Renal Research drive. On all study-specific documents, other than the signed consent, the participant will be referred to by the study participant number/code, not by name.

Date: 03/05/2022 Version 4.1

9. TREATMENT OF TRIAL PARTICIPANTS

9.1 *Description of Study Treatment*

As described in section 6 this is a prospective observational study

9.2 *Storage of Study Equipment or Related apparatus*

No storage of equipment will be required for this study as blood taking will be done

Date: 03/05/2022 Version 4.1

10. SAFETY REPORTING

10.1 Definitions

10.1.1 Adverse Event (AE)

An AE or adverse experience is any untoward medical occurrence in a patient or clinical investigation participants, which does not necessarily have to have a causal relationship with this treatment.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the study, whether or not considered related to the study.

10.1.2 Adverse Reaction (AR)

All untoward and unintended responses related to the study.
All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the study qualify as adverse reactions.

10.1.3 Severe Adverse Events

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided: The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

10.1.4 Serious Adverse Event or Serious Adverse Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- Results in death,
- Is life-threatening,

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity, or
- Is a congenital anomaly/birth defect.
- Other important medical events*

*Other events that may not result in death, are not life threatening, or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

10.1.5 Expected Serious Adverse Events/Reactions

We do not expect any SAEs related to either study assessments. Any SAE (defined above) will be recorded and reported within 24 hours of knowing about the event (see below 10.3). We will only report SAEs that are a direct result of the study intervention or protocol.

10.1.6 Anticipated Adverse Events/Reactions

We do not anticipate any adverse events/reactions related to study procedures

10.1.6 Suspected Unexpected Serious Adverse Reactions

A serious adverse reaction, the nature or severity of which is not consistent with the applicable product information.

10.2 Reporting Procedures for All Adverse Events

All AEs occurring during the study observed by the investigator or reported by the participant, whether or not attributed to study, will be recorded in the site-file. The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to study, other suspect device and action taken. Follow-up information should be provided as necessary.

AEs considered related to the study as judged by a medically qualified investigator or the sponsor will be followed until resolution or the event is considered stable. All related AEs that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs.

It will be left to the investigator's clinical judgment whether or not an AE is of sufficient severity to require the participant's removal from treatment (see section 7.7). A participant may also voluntarily withdraw from treatment due to what he or she perceives as an intolerable AE. If either of these occurs, the participant must undergo an end of study assessment and be given appropriate care under medical supervision until symptoms cease or the condition becomes stable.

The severity of events will be assessed on the following scale: 1 = mild, 2 = moderate, 3 = severe. The relationship of AEs to the study will be assessed by a medically qualified investigator. Only AEs that are judged to be related to the study intervention or procedures will be reported to the Sponsor.

10.3 Reporting Procedures for Serious Adverse Events

Any SAEs related to the study procedures will be reported to the Sponsor within one working day of discovery or notification of the event. The Sponsor will perform an initial check of the information and ensure that it is reviewed at the next R&I Management meeting. SAEs that meet these criteria for reporting will be recorded on an SAE form and sent to the Sponsor using the appropriate reporting form with the contact details on there. Additional information received for a case (follow-up or corrections to the original case) needs to be detailed on a new SAE form which must be sent to the Sponsor using the appropriate reporting form and the contact details on there.

The Sponsor will report all SUSARs to the Research Ethics Committee concerned. Fatal or life-threatening SUSARs must be reported within 7 days and all other SUSARs within 15 days. The CI will inform all investigators concerned of relevant information about SUSARs that could adversely affect the safety of participants.

In addition to the expedited reporting above, the CI shall submit once a year throughout the study or on request an Annual Report to the Ethics Committee which lists all SAEs / SUSARs that have occurred during the preceding 12 months.

Date: 03/05/2022 Version 4.1

11. STATISTICS

11.1 Description of Statistical Methods

Quantitative Analysis:
To investigate the differences between groups in rates of 1 month seroconversion post the first vaccination dose and 1 month and 6 months post the second vaccination dose we will use analysis of covariance, adjusting for relevant baseline differences between groups. Suitable omnibus tests will be used to evaluate differences within groups.
Similar analysis will be performed to look at the association between physical activity levels, sleep and vaccine seroconversion rates.
A Statistical Analysis Plan will be drafted prior to analysis of the data. Analysis will be conducted in line with the SAP.

11.2 The Number of Participants

This study will include 115 participants. 95 patients with ESKD on haemodialysis and 20 healthy volunteers

11.3 The Level of Statistical Significance
$\alpha = 0.05$

11.4 Procedure for Accounting for Missing, Unused, and Spurious Data.
Missing data will be handled by imputation of last variable carried forward (assumption of no change).

11.5 Procedures for Reporting any Deviation(s) from the Original Statistical Plan
Any deviation(s) from the original statistical plan will be described and justified in the final report.

12. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections. Participants will be asked to consent for this to occur if required.

13. QUALITY CONTROL AND QUALITY ASSURANCE PROCEDURES

The study will be conducted in accordance with the current approved protocol, ICH GCP, relevant regulations and standard operating procedures. Regular monitoring will be performed according to ICH GCP. Data will be evaluated for compliance with the protocol and accuracy in relation to source documents. Following written standard operating procedures, the monitors will verify that the clinical trial is conducted and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements.

14. CODES OF PRACTICE AND REGULATIONS

14.1 Ethics

Blood sampling - in this study we will collect 30mL of blood from each participant at each specified time point. This will be taken from dialysis lines for patients on haemodialysis and using venepuncture for healthy volunteers. As is always the case when using venepuncture, there is a small risk of pain and bruising. To minimise these risks venepuncture will be performed by a trained member of the research team.

14.2 Sponsor Standard Operating Procedures

All relevant Sponsor SOPs will be followed to ensure that this study complies with all relevant legislation and guidelines

14.3 Declaration of Helsinki

The Investigator will ensure that this study is conducted in full conformity with the current revision of the Declaration of Helsinki (last amended October 2000, with additional footnotes added 2002 and 2004).

14.4 ICH Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.

14.5 Approvals

Once Sponsor authorisation has been confirmed, the protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), regulatory authorities (MHRA in the UK), and host institution(s) for written approval.

Once Sponsor authorisation has been confirmed, the Investigator will submit and, where necessary, obtain approval from the above parties for all substantial and non-substantial amendments to the original approved documents.

14.6 Participant Confidentiality

The trial staff will ensure that the participants' anonymity is maintained. The participants will be identified only by initials and a participant's ID number on the CRF and any electronic database. All documents will be stored securely and only accessible by trial staff and authorised personnel. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

15. DATA HANDLING AND RECORD KEEPING

All study data will be entered into an SPSS database on a secure University of Leicester system. This database will only be assessable on password protected University of Leicester or UHL computers. The participants will be identified by a study specific participants number and/or code in this database. The name and any other identifying detail will NOT be included in any study data electronic file. Original identities will be kept in the trial site file, accessible only to researchers on the study. All documents containing source data will be kept in a locked office.

Date: 03/05/2022 Version 4.1

16. STUDY GOVERNANCE

16.1 Trial Steering Committee (TSC)

The TSC consists of: Dr Matthew Graham-Brown, Professor Nigel Brunskill, Prof James Burton, Dr Rupert Major and Miss Roseanne Billany. The TSC will aim to meet every 3 months throughout the study to review progress and ensure results are disseminated appropriately and in a timely fashion.

17. FINANCING AND INSURANCE

Research Costs - the costs of the R&I itself that end when the research ends. They relate to activities that are being undertaken to answer the research questions.

Research costs are being funded by Leicester Hospitals Charity

Major outgoings from the study

Costs of IgG Antibody tests - £9000 (£30 per test, 150 participants with 2 tests each)

Printing and posting - £500

Date: 03/05/2022 Version 4.1

18. PUBLICATION POLICY

Research outputs will be in line with the University of Leicester Publication policy (https://www2.le.ac.uk/offices/researchsupport/integrity/code-of-conduct/5-after-research/5-1-publishing-outputs accessed 19/06/2019).
The results of this study will be presented in abstract form at relevant scientific and medical conferences, and will be published in appropriate peer-reviewed journals. The Chief Investigator as custodian of the data will oversee preparation and submission of abstracts and journal articles, and his permission must be obtained prior to preparation of any reports including reference to the study, data or results. Authorship will include all individuals who have made significant contributions to study design and execution, data analysis and interpretation and manuscript preparation. Authors and order will be at the discretion of the Chief Investigator. Individuals who have had involvement in the study but made insufficient intellectual contribution for authorship will be acknowledged in manuscripts. All authors will be given ample opportunity to review and approve all abstracts and manuscripts before submission, and those acknowledged will be asked for approval of their inclusion before publication.

If a collaborator fails to provide agreed and timely contributions to or review of an abstract or manuscript, the Chief Investigator reserves the right to alter the authorship order, or to remove an individual from the author list in order to meet deadlines and avoid delays in dissemination and publication.

Date: 03/05/2022 Version 4.1

19. REFERENCES

1. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al.: Factors associated with COVID-19-related death using OpenSAFELY. Nature 584: 430–436, 2020, In press doi:10.1038/s41586-020-2521-4 pmid:32640463

2. P. Martin and L. S. Friedman, “Chronic viral hepatitis and the management of chronic renal failure,” Kidney International, vol. 47, no. 5, pp. 1231–1241, 1995.

3. Prendecki M, Clarke C, Gleeson S, Greathead L, Santos E, McLean A, Randell P, Moore LSP, Mughal N, Guckian M, Kelleher P, Mcadoo SP, Willicombe M. Detection of SARS-CoV-2 Antibodies in Kidney Transplant Recipients. J Am Soc Nephrol. 2020 Oct 29:ASN.2020081152. doi: 10.1681/ASN.2020081152. Epub ahead of print. PMID: 33122285.

Date: 03/05/2022 Version 4.1

20. STUDY VISIT TABLE

Visit Name	Haemodialysis patients	Healthy volunteers
Baseline	Extraction of routine clinical and demographic information and previous relevant investigation, including telephone call if required Extraction of baseline sample from stored clinical samples.	Extraction of routine clinical and demographic information and previous relevant investigation, including telephone call if required Attend UHL blood room for IgG antibody testing for COVID
1 month post first vaccine dose visit	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
1 month post second vaccine dose	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
6 months post second vaccine dose	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
Immediately before any planned booster vaccine	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
1 month after any booster doses of COVID vaccine	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
12 months after second vaccination	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
18 months after second vaccination	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID
24 months after second vaccination	Blood taken from arterial line at the start of dialysis when patient attends for regular dialysis session	Attend UHL blood room for IgG antibody testing for COVID