

Welcome to the Integrated Research Application System**IRAS Project Filter**

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)

PROTECT-CH

1. Is your project research?

☒ Yes ☐ No

2. Select one category from the list below:

- ☒ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☐ Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
- ☐ Basic science study involving procedures with human participants
- ☐ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- ☐ Study limited to working with data (specific project only)
- ☐ Research tissue bank
- ☐ Research database

If your work does not fit any of these categories, select the option below:

☐ Other study

2a. Is this a commercially sponsored Phase 1 or Phase 1/2a trial involving healthy volunteers?

☐ Yes ☒ No

2b. Will the study involve the use of any medical device without a UKCA/CE UKNI/CE Mark, or a UKCA/CE UKNI/CE marked device which has been modified or will be used outside its intended purposes?

☐ Yes ☒ No

2c. Please answer the following question:

Is this trial subject to advice from the Expert Advisory Group on Clinical Trials and the Commission on Human Medicine prior to authorisation from MHRA?

☐ Yes ☒ No

2d. Please answer the following question:

Is this a trial of a gene therapy medicinal product?

☐ Yes ☒ No

2e. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation?

☐ Yes ☒ No

b) Will you be taking new human tissue samples (or other human biological samples)?

☐ Yes ☒ No

c) Will you be using existing human tissue samples (or other human biological samples)?

☐ Yes ☒ No

3. In which countries of the UK will the research sites be located?(Tick all that apply)

- ☒ England
☒ Scotland
☒ Wales
☒ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ☒ England
☐ Scotland
☐ Wales
☐ Northern Ireland
☐ This study does not involve the NHS

4. Which applications do you require?

- ☒ IRAS Form
☒ Medicines and Healthcare products Regulatory Agency (MHRA) – Medicines
☐ Confidentiality Advisory Group (CAG)
☐ Her Majesty's Prison and Probation Service (HMPPS)

5. Will any research sites in this study be NHS organisations?

☒ Yes ☐ No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out the research e.g. NHS support costs) for this study provided by a NIHR Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), NIHR Patient Safety Translational Research Centre (PSTRC), or an NIHR Medtech and In Vitro Diagnostic Co-operative (MIC) in all study sites?

Please see information button for further details.

☐ Yes ☒ No

Please see information button for further details.

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) Support and inclusion in the NIHR Clinical Research Network Portfolio?

Please see information button for further details.

☒ Yes ☐ No

The NIHR Clinical Research Network (CRN) provides researchers with the practical support they need to make clinical studies happen in the NHS in England e.g. by providing access to the people and facilities needed to carry out research "on the ground".

If you select yes to this question, information from your IRAS submission will automatically be shared with the NIHR CRN. Submission of a Portfolio Application Form (PAF) is no longer required.

6. Do you plan to include any participants who are children?

☐ Yes ☒ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

☒ Yes ☐ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

☐ Yes ☒ No

9. Is the study or any part of it being undertaken as an educational project?

☐ Yes ☒ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

☐ Yes ☒ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

☐ Yes ☒ No

Integrated Research Application System

Application Form for Clinical trial of an investigational medicinal product

IRAS Form (project information)

Please refer to the E-Submission and Checklist tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting [Help](#).

Please define any terms or acronyms that might not be familiar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
PROTECT-CH

Please complete these details after you have booked the REC application for review.

REC Name:

REC Reference Number:

Submission date:

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

COVID-19: Prophylactic therapy in care homes trial-CH

A3-2. National coordinating investigator (for a multicentre trial) or principal investigator (for a single centre trial)

☒ National coordinating investigator

☐ Principal investigator

Given name	Philip
Family name	Bath
Qualification (MD...)	FRCP, FRCPATH, MD, DSc, FMedSci
ORCID ID	0000 0003 2734 5132
Institution name	University of Nottingham
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** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?

This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

Title Forename/Initials Surname
 Ms Angela Shone
 Address Research and Innovation, East Atrium,
 Jubilee Conference Centre, Triumph Road
 Nottingham
 Post Code NG8 1DH
 E-mail angela.shone@nottingham.ac.uk
 Telephone 01158467906
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A5-1. Research reference numbers. Please give any relevant references for your study:

Applicant's/organisation's own reference number, e.g. R & D (if available):

Sponsor's/protocol number: 21001

Protocol Version: 1.0

Protocol Date: 21/04/2021

Funder's reference number (enter the reference number or state not applicable): NIHR133443

Project website: www.protect-trial.net

Registry reference number(s):

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

International Standard Randomised Controlled Trial Number (ISRCTN):

ClinicalTrials.gov Identifier (NCT number):

European Clinical Trials Database (EudraCT) number: 2021-000185-15

Additional reference number(s):

Ref.Number	Description	Reference Number

A5-2. Is this application linked to a previous study or another current application?

☐ Yes ☒ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.*

The COVID-19 pandemic has had a devastating effect in care homes causing illness and death in residents and staff. Measures to reduce viral spread into care homes (e.g. limiting family visits) have had a significant impact on the health and wellbeing of residents. Additional action beyond public health measures to prevent infection (hygiene, masks, personal protective equipment, maintaining distance) is urgently needed to minimise the impact of COVID-19 on residents.

The PROTECT-CH trial is a large "platform" trial that will test several treatments intended to reduce the spread of COVID-19 within care homes and reduce the risks of hospitalisation and death. A trial platform allows multiple treatments to be tested at the same time with results analysed regularly. As soon as a treatment is shown to be effective or ineffective, it is removed from the platform. This makes space for new treatments to be added and rapidly tested. The treatments to be tested will be chosen by Government scientific advisors and may be for pre-exposure prophylaxis (PrEP, i.e. before the care home has a case) and/or post-exposure prophylaxis (PEP, once the care home has a new case to control an outbreak).

Each comparison of a treatment with standard care will require 200 care homes i.e. in the region of a total of 6,400 residents. Care homes will be randomised (like a toss of a coin) to treatment or usual care (no additional treatment). It is expected that most of the treatments will be given for up to two months before it is known whether they have worked, and whether the treatments are cost-effective.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

Inclusion of residents lacking capacity

It is expected that approximately 76% of residents within care homes will not have capacity to consent to the trial. Assessment of capacity will be carried out by the resident's usual care team who are familiar with the resident. Where a resident lacks capacity to consent, a personal legal representative (as defined by the relevant national legislation) will be approached to give consent on their behalf. Residents lacking capacity to consent and without a personal legal representative will not be able to take part in the trial.

Assessment of trial eligibility

The medical management of care home residents is the responsibility of their general practitioner (GP). In accordance with CTIMP legislation, eligibility to take part in the trial must be assessed by a medically qualified doctor. Following consent, the participant's GP will be required to perform an initial assessment of eligibility based on their knowledge of the participant and the trial treatment inclusion and exclusion criteria. The GP's eligibility assessment will be recorded within the trial database. The GP will also upload the participant's summary care record (SCR) to a secure storage vault. Immediately prior to randomisation, the Medical Administration Record (MAR) of all consented residents will be uploaded by the care home and reviewed by the PROTECT-CH PI (or delegate) alongside the SCR and complete the final eligibility checklist.

Care home staff unfamiliar with clinical research and Good Clinical Practice (GCP)

While some care homes are familiar with the research environment, for many this will be their first experience of working on a clinical trial. We will be designing and implementing a comprehensive suite of training courses for staff in care homes that will be working on the study. Training will be targeted to specific roles in the trial and will cover the

necessary aspects of GCP to perform that role alongside the trial-specific functions including full training in safety reporting requirements.

Challenges with taking consent

Taking consent within a care home is challenging for many reasons –residents have a variety of ailments, may have hearing or vision difficulties, be unable to read/write for themselves and/or unable to digest complex trial information. A patient and public involvement (PPI) group has led the development of all consent documentation to ensure that this is comprehensible to the target audience, and with consideration of care home resident ailments. A variety of media formats will be used to ensure full comprehension of the trial as part of the consent process.

Due to the ongoing COVID-19 pandemic personal legal representatives will be provided with trial information electronically (via e-mail) or via the post if they have indicated they are unable to access resources electronically. Consent discussions will take place with trained members of the PROTECT-CH research team (via tele/video conference) and personal legal representatives will be asked to give their consent remotely using electronic consent. A paper postal option will be available where the electronic option is not suitable or possible for the residents' personal legal representative.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. Please tick all that apply:

- ☐ Case series/ case note review
- ☐ Case control
- ☐ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☐ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis
- ☒ Qualitative research
- ☐ Questionnaire, interview or observation study
- ☒ Randomised controlled trial
- ☐ Other (please specify)

A8. Type of medicinal trial:

- ☒ Clinical trial of an unlicensed investigational medicinal product
- ☐ Clinical trial of a licensed medicinal product in new conditions of use (different from those in the SmPC, i.e. new target population, new dosage schemes, new administration route, etc.)
- ☐ Clinical trial of a licensed medicinal product used according to the SmPC
- ☐ Other (please specify)

A9. Phase of medicinal trial: (Tick one category only)

Human pharmacology (Phase I)

☐ Yes ☒ No

Therapeutic exploratory trial (Phase II)

☒ Yes ☐ No

☒ Therapeutic exploratory trial (Phase II)

☐ Therapeutic exploratory trial including comparison with the standard treatment regimen (Phase II/III)

Therapeutic confirmatory trial (Phase III)

☐ Yes ☒ No

Therapeutic use trial (Phase IV)

☐ Yes ☒ No

A10. What is the principal research question/objective? Please put this in language comprehensible to a lay person.

In residents in a UK care home setting, which treatments when compared to usual care are effective and safe to prevent or reduce the symptoms and poor outcomes associated with COVID-19?

A11. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.

To assess the cost-effectiveness of treatments to prevent death, hospitalisation and healthcare referrals for COVID-19 infection.

To collect information on the process of introducing and delivering treatment into a care home setting.

A12. What is the scientific justification for the research? Please put this in language comprehensible to a lay person.

The COVID-19 pandemic has had a profound impact on the UK population, and this has been particularly true for residents of care homes and nursing homes.

Since the start of the pandemic, the lives of care home residents and their relatives have been greatly affected by COVID-19. Efforts to reduce spread of the virus into care homes, such as limiting family visits, have had a significant impact on the health and wellbeing of residents. Although the COVID-19 vaccines may prevent symptomatic COVID-19, care home residents have a need for additional treatments as the vaccines may not work as well in older people. This is due to older people whose immune system may not work as well as it once did and often have other diseases that may increase their risk of getting seriously ill from the virus.

Government health ministers have asked us to set up this study to find out how we can protect care home residents from COVID-19. We will test different treatments to see which ones may help, so that residents can stay well and resume a more normal life.

A13. Please summarise your design and methodology. It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.

The aim of the PROTECT-CH trial is to see if we can find treatments to prevent or reduce the spread and impact of COVID-19 in residents of care homes.

To understand which treatments might work we need to compare these to usual care. Government health advisors will tell us which treatments to test. Treatment may either be pre-exposure prophylaxis (PrEP, i.e. before a care home has a COVID-19 case) and/or post-exposure prophylaxis (PEP, once the care home has a new case to control an outbreak).

Care home residents, or their personal legal representative if they lack capacity, will be provided with written information about the trial and (where necessary/practicable) a video briefing outlining the trial by care home staff. The information provided will include details of the different treatment(s). Consent will be taken by a member of the PROTECT-CH research team (typically a Research Nurse or Principal Investigator) by tele/video call.

Residents or their personal legal representative will be asked to provide informed consent for the research team to contact their GP. The resident's GP will perform an initial assessment of eligibility for the trial and provide the participant's summary care record to the research team.

When the trial treatments are known the care home will be assigned to an arm of the trial at random (like the tossing of a coin). The trial arm will either be a trial treatment plus usual care or usual care only. This process is called randomisation and this is to make sure that this trial is doing a 'fair comparison' of the new trial treatment(s). All residents within the same care home who are eligible and agree to take part in the trial will be assigned to the same trial arm.

For trials of PrEP the care home will be randomised once an trial treatment has been identified and the necessary

processes have been implemented. The care home must have no evidence of SARS-CoV-2 infection for at least 4 weeks. For trials of PEP, care home will only be randomised once they have an indication of a developing infection, e.g. recent positive PCR or lateral flow test (or equivalent) in a resident or member of staff (index case). The care home must have had no evidence of SARS-CoV-2 infection for at least 4 weeks prior to the index case.

Immediately prior to a care home being randomised, the Medication Administration Record (MAR) of all consented residents will be provided by the care home to the PROTECT-CH PI (or delegate) who will assess the participant's eligibility. The care home will then be randomised to one of the trial arms.

The care home staff involved in administration of trial treatment will be trained and supported to give the trial treatment as part of normal day-to-day care. Care home staff will help residents with capacity to fill in questionnaires relating to their health and quality of life (or will be asked to complete these on the resident's behalf) before they commence trial treatment and again after 60 days (or a relevant time point depending on trial treatment).

The researchers will collect some information from the care home about the trial treatment the resident is receiving and whether this has made a difference to the overall health of the resident. The research team will also collect information from national databases (routine data) about their general health. This will allow the researchers to understand if the trial treatment(s) can prevent or reduce the impact and spread of COVID-19 in care homes.

We will interview a sub-set of care home residents, staff and other individuals involved in delivering treatment to gain insight about those contextual factors which support or inhibit effective delivery. We will consider acceptability of the treatment to staff, residents and their families. We will reflect upon trial processes to support the on-going delivery of the trial.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- ☒ Design of the research
- ☒ Management of the research
- ☒ Undertaking the research
- ☒ Analysis of results
- ☒ Dissemination of findings
- ☐ None of the above

Give details of involvement, or if none please justify the absence of involvement.

A Patient and Public Involvement (PPI) team has been formed specifically for this trial. The lead member of this group, who led PPI in a large care home trial (FinCH), is also a co-applicant on the grant from the funder. The PPI team contributed to the development of the grant application and design of the trial. Throughout the trial the PPI team will specifically advise on trial processes and documentation, and will support involvement with the care homes including training. They will also advise on interpretation of results. The membership of the PPI team will be representative of the communities the care homes serve. Members of the PPI group have provided guidance on issues related to consent with residents and proxy consent by personal legal representatives.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A15. What is the sample group or cohort to be studied in this research?

Select all that apply:

- ☐ Blood
- ☐ Cancer
- ☐ Cardiovascular
- ☐ Congenital Disorders

- ☐ Dementias and Neurodegenerative Diseases
- ☐ Diabetes
- ☐ Ear
- ☐ Eye
- ☒ Generic Health Relevance
- ☒ Infection
- ☐ Inflammatory and Immune System
- ☐ Injuries and Accidents
- ☐ Mental Health
- ☐ Metabolic and Endocrine
- ☐ Musculoskeletal
- ☐ Neurological
- ☐ Oral and Gastrointestinal
- ☐ Paediatrics
- ☐ Renal and Urogenital
- ☐ Reproductive Health and Childbirth
- ☐ Respiratory
- ☐ Skin
- ☐ Stroke

Gender: Male and female participants

Lower age limit: 65 Years

Upper age limit: 115 Years

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Care Home criteria:

- 1) Location: UK care homes for older people, with and without nursing.
- 2) Size: ≥20 beds in the care home in total

Resident criteria at trial entry

- 1) Resident in a Care Home.
- 2) Age ≥ 65 years
- 3) Able to give informed consent for participation or a personal legal representative has been identified who can give consent, if resident lacks capacity.

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Care home criteria:

- 1) Care Quality Commission quality: Inadequate or equivalent in devolved administrations

Resident criteria at trial entry:

- 1) Identified by care home staff to have entered end-stage palliative care
- 2) Resident in care home for short-term respite care
- 3) Resident's general practitioner is unable to support their involvement in the trial

Resident criteria at treatment phase:

- 1) Currently taking all* of the trial interventions
- 2) Contraindication to all* trial interventions
- 3) In treatment phase of another COVID-19 prevention or treatment trial

* A resident will be eligible if they can take at least one intervention at the point of randomisation. Residents allocated to an intervention which they are already taking (or another drug in the same class), or to which they have a contraindication, must not be given the trial IMP. Residents in all trial arms will be excluded from all comparisons involving IMPs that were contraindicated or being taken at the time of randomisation, except for a limited number of supplementary analyses based on all residents or all residents who consented to participation.

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. These include seeking consent, interviews, non-clinical observations and use of questionnaires.

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Informed Consent	1	0	30-60mins	For residents with capacity to consent an informed consent discussion about the trial will take place with a member of the PROTECT-CH research team by video call. For residents lacking capacity to consent this will be done with the personal legal representative.
QoL Questionnaires	2	0	15mins	Trained care home staff at the care home will administer questionnaires to residents with capacity to consent (approx 30% of participants).
Process evaluation resident interview	1	0	20-40mins	A PROTECT-CH researcher via video call (sub-set of residents only).
Process evaluation staff/stakeholder interview	1	0	30-60mins	A PROTECT-CH researcher via video call (for a sub-set only).

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Taking prescribed Ciclesonide (once daily for 6 weeks)	1	0	5 mins	In the care home either by resident or by staff trained to administer the inhaler. 5 mins per administration.
Taking prescribed Niclosamide (twice daily for 6 weeks)	2	0	5 mins	In the care home either by resident or by staff trained to administer. 5 mins per administration.

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

☐ Yes ☒ No

A21. How long do you expect each participant to be in the study in total?

The trial will test both pre-exposure prophylaxis treatments (PrEP, i.e. before the care home has a case) and/or post-exposure prophylaxis (PEP, once the care home has a new case to control an outbreak). The length of time each participant will be in the trial will depend on the time between consent and randomisation and the IMP received.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

Participants at a care home randomised to receive a trial treatment will be required to take an additional treatment to any existing treatments they are on. This is expected to take around 5 minutes per administration. Depending on the treatment selected this may be an inconvenience to the participant. The selected treatment and how this will be administered will be explained to the resident (or personal legal representative) before they agree to take part in the trial.

Participants could experience side effects from the trial treatment. The side effects of the selected treatments will be reviewed prior to selection and information on potential side effects will be provided to the participant/legal representative and care home.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

☐ Yes ☒ No

A24. What is the potential for benefit to research participants?

The trial may not help participants directly but the information from this trial may help us to improve the future care of care home residents during the COVID-19 pandemic.

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.

Once a participant finishes their trial treatment they will continue to receive usual medical care which may or may not include the IMP depending on Government policy.

A26. What are the potential risks for the researchers themselves? (if any)

There are no perceived risks to the researchers themselves.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used? For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).

Care homes will be identified from the private (including chains and individual homes), charity and council sectors

using multiple ascertainment methods including care home registers, social media and email lists, and media promotion of the trial.

Within a participating care home, potential participants will be identified and approached by care home staff. Residents will be provided with written information about the trial by care home staff, and (where necessary/practicable) a video briefing outlining the trial. Consent will be taken by a member of the PROTECT-CH research team (typically a Research Nurse or Principal Investigator) by tele/video call, this will include consent to contact their GP, consent for a copy of their summary care medical record to be provided to the research team and consent to obtain information from national databases (routine data).

Informed consent will comprise either:

- a) Consent by the resident, either written or witnessed verbal consent for residents with capacity but unable to physically write or sign. Residents will be asked to make a mark if able to do so.
- b) Consent by the personal legal representative for residents who lack capacity. This will either be electronic or a paper form returned to the Nottingham Clinical Trials Unit or the Care Home.

As part of the consent process a member of the PROTECT-CH research team (typically a Research Nurse or Principal Investigator) will ensure that they adequately explain the aim, trial treatment, anticipated benefits and potential hazards of taking part in the trial to the resident or personal legal representative. The resident or personal legal representative must give explicit consent for the regulatory authorities, members of the research team and representatives of the Sponsor to be given a copy of the resident's summary care record.

Following resident or personal legal representative consent, the resident's GP will decide if the resident is eligible to join the study and provide the residents summary care record to the research team.

Immediately prior to a care home being randomised, the Medication Administration Record (MAR) of all consented residents will be provided to the PROTECT-CH PI (or delegate) who will do a final review and confirm the residents are still eligible. The care home will then be randomised to one of the trial arms. The resident's GP will be informed that their patient has entered the treatment phase of the trial and if applicable will be provided information on the IMP.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

☒ Yes ☐ No

Please give details below:

Care home staff will identify potential participants within the care home and provide them with written information about the trial. Each resident that has consented or has been consented by their personal legal representative to be included in the trial will have their summary care record (including their medication administration record) reviewed by their GP and the PROTECT-CH PI (or delegate) to assess their eligibility to enter the trial.

A27-3. Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants. Indicate what steps have been or will be taken to inform patients and service users of the potential use of their records for this purpose. Describe the arrangements to ensure that the wishes of patients and service users regarding access to their records are respected. Please consult the guidance notes on this topic.

The resident or personal legal representative must give explicit consent for the regulatory authorities, members of the research team and representatives of the Sponsor to be given direct access to the resident's summary care records. After consent has been obtained, the summary care records will be stored in a secure central location, accessible by restricted VPN. The transfer of summary care records will be via secure upload to this location.

Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the Data Protection Act 2018.

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

☒ Yes ☐ No

A27-5. Has prior consent been obtained or will it be obtained for access to identifiable personal information?

☒ Yes ☐ No

If Yes, please give details below.

Those outside the usual care team will only have access to personal information once initial consent has been obtained from the resident. Where the care home identifies a personal legal representative for a resident without capacity a member of the care home staff will directly contact the personal legal representative to advise them that the care home is taking part in the trial and specifically request their permission for their contact details to be passed to the research team so that they can contact them directly to discuss the trial and what taking part would involve. This will be detailed within the consent documentation.

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

☒ Yes ☐ No

If Yes, please give details of how and where publicity will be conducted, and enclose copy of all advertising material (with version numbers and dates).

Care homes will be identified from the commercial (including chains and individual homes), charity and council sectors using multiple recruitment methods including care home registers, social media (such as Facebook, LinkedIn and Twitter) email lists, and media promotion of the trial. Any advertising material for recruitment will be submitted for approval prior to use.

If residents/relatives who are interested in taking part make contact with the research team as a result of media coverage they will be advised that their care home will need to sign up firstly and directed to speak to their care home manager.

A29. How and by whom will potential participants first be approached?

Care home staff will complete the expression of interest form on the trial website. If selected to take part on the basis of eligibility, a care home will be provided with the necessary training and resources to recruit residents into the trial. A care home pack (this is expected to include information about the trial, information sheets, consent forms, stamped envelopes, information DVDs) will be sent to the care home.

Once a care home is open to recruitment, care home staff will approach residents and provide them with information about the trial which can be provided in various formats as appropriate to the resident e.g. verbally (read out from the PIS), written information sheets, videos/animations. The wording in the PIS will also be used to generate the resident facing frequently asked questions on the trial website.

Care home staff will assess which residents have capacity to consent and which residents do not. Where it is unclear whether the resident has capacity, a Three Question Test will be used by the care home staff (e.g. the resident is given a statement; "the study is trying to reduce COVID-19 with a medicine that reduces the chance of infection"; the potential participant is only deemed to have capacity if all three bits of information are correctly fed back to the Staff member). The resident must be able to Understand, Retain, Weigh the information in order to decide and then communicate their decision (Mental Capacity Act).

For residents who do not have capacity to consent, the care home will contact their personal legal representative and request their permission for their contact details to be passed to the research team to contact them with information about the trial by e-mail or post and an appointment with a member of the research team to discuss the trial and take informed consent. If a resident, whom lacks capacity to consent for themselves, has not previously identified a personal legal representative then they will be excluded from the study

Once consent has been obtained for a resident, their GP will be contacted and they will be asked to assess the residents eligibility and provide a copy of their summary care record. Immediately prior to a care home being randomised, the Medication Administration Record (MAR) of all consented residents will be provided to the PROTECT-CH PI (or delegate) who will do a final review and confirm the residents are still eligible.

A30-1. Will you obtain informed consent from or on behalf of research participants?

☒ Yes ☐ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

Written informed consent for each participant will be obtained prior to performing any trial related procedure; this will be collected electronically or on paper. The potential participant will be given the opportunity to ask questions throughout the process.

Informed consent will comprise either:

- Consent by the resident, either written or witnessed verbal consent for residents with capacity but unable to physically write or sign. Residents will be asked to make their mark wherever possible.
- Consent by the personal legal representative (person who holds power of attorney for health matters) for residents who lack capacity. This will either be electronic or a paper form that they would return to the Nottingham Clinical Trials Unit or the care home for processing.

The PROTECT-CH research team (this will typically be a Research Nurse or Principal Investigator) will ensure that they adequately explain the aim, trial treatment, anticipated benefits and potential hazards of taking part in the trial to the resident. They will also stress that participation is voluntary and so the potential resident is free to decline participation and may withdraw from the trial at any time. The potential participants will be given time to consider the trial information and to discuss their participation with others (i.e. family members if they wish). The residents shall give explicit consent for the regulatory authorities, members of the research team and representatives of the Sponsor to be given access to the residents summary care records.

The above process will be followed for residents who lack capacity except that a personal legal representative will provide consent. In most cases, residents who permanently do not have capacity will already be known to care home staff and will have a nominated legal representative in place for decisions on their usual care, such as COVID-19 vaccination.

If a personal legal representative cannot be identified for the resident they will not be recruited into the trial. A personal Legal representative Information Sheet (LIS) will be provided to facilitate this process. The legal representative will be given time to read the LIS and to discuss their relative's participation with others (i.e. family members, GP or other healthcare professionals outside of the site research team, if they wish). The personal legal representative shall give explicit consent for the regulatory authorities, members of the research team and representatives of the Sponsor to be given direct access to the residents summary care records.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

☒ Yes ☐ No

A31. How long will you allow potential participants to decide whether or not to take part?

After the PROTECT-CH research team (research nurse or principal investigator) have adequately explained the aim, trial treatment, anticipated benefits and potential hazards of taking part in the trial to residents with capacity to consent, the potential resident will be given enough time to consider the trial information and to discuss their participation with others (i.e. family members if they wish).

For residents who lack capacity, a personal Legal representative Information Sheet (LIS) will be provided to facilitate this process. The legal representative will be given time to read the LIS and to discuss their relative's participation with others (i.e. family members, GP or other healthcare professionals outside of the site research team, if they wish).

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

☒ Yes

- ☐ No
- ☐ Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

Care home residents who are currently taking part in other research will be given the opportunity to participate in PROTECT-CH if they are willing and unless there are any contraindications to either trial that would make them ineligible. Residents taking part in another COVID-19 prevention or treatment trial are excluded.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?(e.g. translation, use of interpreters)

Written information about the trial will be available in several languages. A variety of media formats will be used to ensure full comprehension of the trial as part of the initial consent process. Information sheets can be read to the residents and visual pictorial aids (including animations) may be used. Videos explaining the trial will be available on the trial website and provided to the care homes on a DVD. It is assumed that care homes who have residents where English is not their first language will have adequate translation services in place in order to communicate with their residents.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

Where requested, information sheets will be made available in Welsh. In addition it is assumed that care homes who have residents where English is not their first language will have adequate translation services in place in order to communicate with their residents.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

Throughout the trial the resident or personal legal representative will have the opportunity to ask questions about the trial. Any new information that may be relevant to their/their relatives continued participation will be provided. Where new information becomes available which may affect the resident or their personal legal representative's decision to continue, they will be given time to consider and if happy to continue will be re-consented. Re-consent will be documented in the care home notes.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?(Tick as appropriate)

- ☒ Access to medical records by those outside the direct healthcare team
- ☐ Access to social care records by those outside the direct social care team
- ☒ Electronic transfer by magnetic or optical media, email or computer networks
- ☒ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☒ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☒ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☒ Use of audio/visual recording devices
- ☒ Storage of personal data on any of the following:

- ☒ Manual files (includes paper or film)
- ☒ NHS computers
- ☐ Social Care Service computers
- ☐ Home or other personal computers
- ☒ University computers
- ☐ Private company computers
- ☐ Laptop computers

Further details:

All transported data to and from the University clinical trials databases servers is encrypted using SSL.

Access to the data servers is strictly controlled, and access to the data via the application is limited to approved users only.

A37. Please describe the physical security arrangements for storage of personal data during the study?

All data is to be stored on a secure server in the University of Nottingham.

All personally identifiable data (names, address, contacts etc) is stored separately from clinical trial data, linked by an identifying number (pseudonymisation).

All access to the data is limited by application role to restrict to that commensurate with the user's role. For example, statisticians will not be able to access identifiable data, and care home staff will only be able to see identifiers of residents at their own care homes.

A38. How will you ensure the confidentiality of personal data? Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.

All trial data is to be stored on a secure server in the University of Nottingham.

All personally identifiable data (names, address, contacts etc) is stored separately from clinical data, linked by an identifying number (pseudonymisation).

All access to the data is limited by application role to restrict to that commensurate with the user's role. For example, statisticians will not be able to access identifiable data, and care home staff will only be able to see identifiers of residents at their own care homes.

A40. Who will have access to participants' personal data during the study? Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.

1. Staff within the coordinating centre at the University of Nottingham, with consent from participant/personal legal representative.

2. PROTECT-CH health care professionals involved in consenting and checking eligibility, with consent from the participant/personal legal representative

3. Members of the Dundee Trusted Research Environment (TRE) team responsible for linking national healthcare research data and trial data, with consent from the participant/personal legal representative.

4. Statisticians will have access to pseudonymised clinical trial data only.

Storage and use of data after the end of the study**A41. Where will the data generated by the study be analysed and by whom?**

Data collected on the eCRF will be analysed by a blinded statistician at the Nottingham Clinical Trials Unit, University of Nottingham.

No data will be transferred outside the UK.

A42. Who will have control of and act as the custodian for the data generated by the study?

	Title	Forename/Initials	Surname
	Professor	Philip	Bath
Post	Stroke Association Professor of Stroke Medicine/Head of Division of Clinical Neuroscience		
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Work Email	philip.bath@nottingham.ac.uk		
Work Telephone	07798670726		
Fax			

A43. How long will personal data be stored or accessed after the study has ended?

- ☐ Less than 3 months
☐ 3 – 6 months
☐ 6 – 12 months
☒ 12 months – 3 years
☐ Over 3 years

If longer than 12 months, please justify:

Personal data will be stored for dissemination of trial results and audit purposes.

A44. For how long will you store research data generated by the study?

Years: 7

Months: 0

A45. Please give details of the long term arrangements for storage of research data after the study has ended. Say where data will be stored, who will have access and the arrangements to ensure security.

Study documentation and source documentation (e.g. signed informed consent forms, investigator site files, completed paper CRFs etc.) at sites will be securely archived for at least 7 years.

Raw data sets for analyses will be retained indefinitely with all other electronic data retained for at least 7 years.

INCENTIVES AND PAYMENTS**A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?**

☐ Yes ☒ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

☐ Yes ☒ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

☐ Yes ☒ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

☒ Yes ☐ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

☒ Yes ☐ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

☒ Yes ☐ No

Please give details, or justify if not registering the research.

Trial registered on EudraCT and will be registered on ISRCTN

Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? Tick as appropriate:

- ☒ Peer reviewed scientific journals
- ☒ Internal report
- ☒ Conference presentation
- ☒ Publication on website
- ☐ Other publication
- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when

publishing the results?

N/A

A53. How and when will you inform participants of the study results?

If there will be no arrangements in place to inform participants please justify this.

Results of the trial will be made available via the trial website and results newsletters to care homes.

5. Scientific and Statistical Review**A54. How has the scientific quality of the research been assessed? Tick as appropriate:**

- ☒ Independent external review
- ☐ Review within a company
- ☒ Review within a multi-centre research group
- ☒ Review within the Chief Investigator's institution or host organisation
- ☒ Review within the research team
- ☐ Review by educational supervisor
- ☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:

The study underwent rigorous peer review from topic and methodological experts as part of the grant application process for the NIHR. The funding board peer review comments and our responses are available. The protocol will be reviewed by the chairs of the Platform Steering Committee and Data Monitoring Committee prior to use.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? Tick as appropriate:

- ☒ Review by independent statistician commissioned by funder or sponsor
- ☐ Other review by independent statistician
- ☐ Review by company statistician
- ☒ Review by a statistician within the Chief Investigator's institution
- ☒ Review by a statistician within the research team or multi-centre group
- ☐ Review by educational supervisor
- ☐ Other review by individual with relevant statistical expertise
- ☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

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Institution	University of Nottingham	

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Mobile	
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Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

A four-level ordinal outcome will be used to capture the ability of the drug candidate(s) to prevent/reduce morbidity and mortality from COVID-19 in care home residents, and to reduce transmission in care home settings during the 60 days post-randomisation (or at a relevant time point dependent on intervention – see IMP Appendix for further details). Participants will be classified according to the highest level, that is, the most serious event they experience during the 60-day period (or relevant time point) following randomisation:

1. No SARS-CoV-2 infection.
2. SARS-CoV-2 infection but resident remains in care home.
3. Admission to hospital, all-cause.
4. Death, all-cause.

SARS-CoV-2 status (positive or negative) will be diagnosed using PCR or lateral flow testing (or equivalent) in accordance with the care home's usual testing schedule.

A58. What are the secondary outcome measures?(if any)

1. Individual components of the primary outcome
2. Healthcare referral for COVID-19, e.g. discussion outside of care home with GP (excluding routine visit), 111, 999 paramedic or Emergency Department assessment (without admission), remote hospital consultation
3. Participant receives dexamethasone in the care home for COVID-19
4. Participant receives oxygen in the care home for COVID-19
5. Time to SARS-CoV-2 infection- positive PCR or lateral flow test (or equivalent) (i) with symptoms of COVID-19 (ii) without symptoms of COVID-19 (iii) total i.e. either with or without symptoms of COVID-19.
6. Time to first admission to hospital
7. Cause specific hospital admission
8. Time to death
9. Days alive and not in hospital
10. Cause-specific mortality, including COVID-19, stroke, pulmonary embolism, myocardial infarction
11. Frailty index at 60 days
12. Ordinal outcome for the most serious event experienced during the 120 days post-randomisation with the following levels: 1. No SARS-CoV-2 infection, 2. SARS-CoV-2 infection but resident remains in care home, 3. Admission to hospital, all-cause, 4. Death, all-cause.

Safety

1. Serious Adverse Reactions (SAR, excluding primary and secondary outcomes) and Suspected Unexpected SARs (SUSARs)
2. Adverse Events relevant to the intervention

Clinical- care home level

Number of SARS-CoV-2 infections in residents in the care home (aggregate data including residents not participating in PROTECT-CH).

Economic evaluation

1. EQ-5D-5L utilities and EQ-VAS at 60 days
2. Quality Adjusted Life Years
3. Healthcare resource use and costs
4. Incremental cost-per QALY and Net Monetary Benefit

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size: 9600
 Total international sample size (including UK): 9600
 Total in European Economic Area: 0

Further details:

N=3,200 participants per arm (average of 32 participants from 100 care homes), with at least one intervention arm plus control (N=6,400), and potentially up to three intervention arms plus control (N=12,800) for each of two types of prophylactic intervention (pre-exposure prophylaxis and post-exposure prophylaxis) (maximum total N=25,600). This range in sample size is due to the platform design and depends on the number and type of interventions to be tested.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

Without any adjustment for clustering, a total of 530 residents per group are required to detect an odds ratio of 0.67 for a 4-level ordinal primary outcome (no infection proportion 60%, infection remain in care home 15%, all cause hospitalisation 10%, all-cause mortality 15%), assuming a two-sided significance level of 5% and 90% statistical power.

Care homes of varying size will be included, and the number of residents recruited per care home will likely be in the range 20–60. Assuming an intra-cluster correlation of 0.11, a coefficient of variation for care home size of 0.49 (Lothian population analysis in 189 care home) and an average of 32 residents per care home in the study (assuming that the average number of beds per care home is 40 [Competition and Markets Authority. Care Homes Market Study. London: 2017] and that not all residents will take part in the study), this gives rise to a design effect or inflation factor of 5.25.

Therefore, to compare a single active treatment versus standard care, in the region of 174 care homes is needed i.e. in excess of 5,500 residents. Allowing for the uncertainty surrounding the parameters listed above (e.g. levels of mortality and transmission rates are expected to be different in the second wave due to improved preparedness, better treatments and the potential impact of the expected vaccination programme, therefore it is possible that the observed proportions in the Standard Care group may differ), we propose a sample size of 200 care homes and a total number of residents in the region of 6,400 per comparison, with sample size re-estimation during the trial (once 60-day outcome data are available for at least 75% of residents randomised to standard care).

Therefore, comparing three active (unrelated) treatments versus standard care (in a 1:1:1:1 allocation ratio) would require 400 care homes in total, corresponding to around 13,000 residents.

A61. Will participants be allocated to groups at random?

☒ Yes ☐ No

If yes, please give details of the intended method of randomisation:

This trial will use cluster randomisation, therefore care homes will be randomised, not individual participants. Residents within the same care home will all receive the same treatment.

The randomisation programme will allocate care homes 1:1 to each available treatment arm or standard care arm.

The dynamic randomisation will use a probabilistic minimisation algorithm to ensure balance across:

- Care home type (residential vs nursing vs nursing and residential)
- Prior COVID-19 in care home at any time (yes vs no)
- Size of Care Home - Total number of residents in care home (small (≤ 30 residents), medium (>30 , <50 residents), large (>50 residents))
- Care home has capacity to give oxygen and/or dexamethasone (yes vs no)

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Statistical analyses

The analysis and reporting of the trial will be in accordance with CONSORT guidelines for adaptive and cluster designs with the primary comparative analyses being conducted according to randomised allocation with due

emphasis on confidence intervals for between-arm comparisons. All comparative analyses will be based on contemporaneously randomised care homes. A full statistical analysis plan will be developed and agreed with the Platform Steering Committee (PSC) prior to the first release of treatment allocations for final pairwise comparison. The primary approach to between-group comparative analyses will be by intention-to-treat (i.e. including all residents according to randomised allocation regardless of adherence to trial allocation). Cluster-level and resident-level descriptive statistics will be used to illustrate balance between the groups at baseline.

Primary comparative analyses will employ a multi-level ordinal logistic regression model. The model will adjust for the minimisation factors, plus the individual-level covariates age, sex and vaccination status. A random effect to adjust for clustering within care homes will be used. The treatment comparison will be presented as an adjusted common odds ratio for a shift in the direction of a better outcome on the ordinal scale together with 95% confidence intervals.

Secondary outcomes will be analysed using appropriate multi-level regression models dependent on data type (binary, categorical, continuous etc.), adjusted similarly and including a random effect to adjust for clustering within care homes.

Economic evaluation

A cost-utility analysis will be conducted from an NHS and PSS perspective, based on within-trial data collection from routine sources, or eCRF where not possible. Resource use data will be gathered on primary care (including GP and nurse contacts) and secondary healthcare usage (including A&E attendance, hospital admission and critical care hospital stay) and 111(119)/999 services. Unit costs will be applied based on national sources to increase generalisability.

Health related quality of life questionnaires (EQ-5D-5L) will be administered to residents at baseline and follow-up and completed by proxy if necessary, with response patterns explored and reporting subgroups (self-report vs proxy) examined in sensitivity analysis. The UK crosswalk tariff will be used to derive utility scores from responses and combined with survival data using the area under the curve approach to compute quality adjusted life years (QALYs).

Group mean costs (including prophylaxis acquisition and administration costs), utilities and QALYs will be analysed in line with other outcomes, using linear mixed effects models to take account of clustering and key baseline prognostic factors, with QALYs adjusted for baseline EQ-5D utility scores and presented with associated 95% confidence intervals. Cost-effectiveness will be expressed as Incremental Cost Effectiveness Ratios and Incremental Net Monetary Benefit at various cost-effectiveness thresholds, accompanied by cost-effectiveness acceptability curves, produced using non-parametric bootstrapping techniques that take account of clustering. If between arm differences in costs and QALYs are observed at 60 days post randomisation, parametric modelling will be conducted to perform simple extrapolations of costs and QALYs to incorporate a lifetime horizon. A Health Economic Analysis Plan (HEAP) will be produced to present planned analyses in more detail.

Process evaluation

All interview data will be transcribed in full, anonymised and handled using the NVivo software package.

Data will be coded and analysed concurrently with data collection to inform the management of the process evaluation – early analysis will inform the development of the interview topic guide and will guide subsequent sampling and recruitment decisions. An inductive thematic approach to data analysis will be utilised.

Thematic analysis will seek to identify those mechanisms which care home residents, staff and others involved in the delivery of the treatment recognise as facilitating effective delivery or hampering the delivery of the treatment in the care home.

Thematic analysis will primarily be developed at the level of the individual care home, i.e. constructing multiple, detailed case studies of treatment delivery in distinct care home settings. Subsequent analyses may bring together data from similar stakeholders across multiple sites, i.e. synthesising staff perspectives or care home resident perspectives from multiple settings.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. Please include all grant co-applicants, protocol co-authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.

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Post	Head Digital Research Service		
Qualifications	BSc (Hons) Applied Computing, PhD AI in Biomedical Datasets		
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Work Email	Philip.Quinlan@nottingham.ac.uk		
	Title	Forename/Initials	Surname
	Ms	Maureen	Godfrey
Post	Public Patient Involvement representative		
Qualifications	N/A		
Employer	N/A		
Work Address	8 Danehurst Drive		
	Gedling		
	Nottingham		
Post Code	NG4 3GA		
Telephone	0115 9614504		
Fax			
Mobile	07709508780		
Work Email	maureengodfrey47@gmail.com		
	Title	Forename/Initials	Surname
	Ms	Valerie	Leyland
Post	Public Patient Involvement representative		
Qualifications	N/A		
Employer	N/A		
Work Address	46 Valmont Road		
	Bramcote		
	Nottingham		
Post Code	NG9 3JB		
Telephone	07929 662351		
Fax			
Mobile	07929 662351		
Work Email	vmleyland@gmail.com		

A64. Details of research sponsor(s)

A64-1. Sponsor

SP1

Status: ☐ NHS or HSC care organisation☒ Academic☐ Pharmaceutical industry☐ Medical device industry☐ Local Authority☐ Other social care provider (including voluntary sector or private organisation)☐ Other

Commercial status: Non-Commercial

*If Other, please specify:***Contact person**

Name of organisation University of Nottingham

Given name Angela

Family name Shone

Address Research and Innovation, East Atrium, Jubilee Conference Centre, Triumph Road

Town/city Nottingham

Post code NG8 1DH

Country United Kingdom

Telephone 0115 8467906

Fax

E-mail angela.shone@nottingham.ac.uk

Legal representative in the European Economic Area for the purpose of this trial

A legal representative must be appointed for a clinical trial of an investigational medicinal product if the sponsor is not established within the European Economic Area (EEA) (see article 19 of Directive 2001/20/EC). If this applies, please enclose evidence that the legal representative is established within the EEA and has accepted the role of legal representative.

Legal representative**Contact person**

Name of organisation

Given name

Family name

Address

Town/city

Post code

Country

Telephone

Fax

E-mail

A65. Has external funding for the research been secured?

Please tick at least one check box.

- ☒ Funding secured from one or more funders
☐ External funding application to one or more funders in progress
☐ No application for external funding will be made

What type of research project is this?

- ☒ Standalone project
☐ Project that is part of a programme grant
☐ Project that is part of a Centre grant
☐ Project that is part of a fellowship/ personal award/ research training award
☐ Other

Other – please state:

Please give details of funding applications.

Organisation National Institute for Health Research
Address Evaluation, Trials and Studies Coordinating Centre
 University of Southampton
 Alpha House, Enterprise Road, Southampton
Post Code SO16 7NS
Telephone 023 8059 5586
Fax 023 8059 5639
Mobile
Email netsmonitoring@nihr.ac.uk

Funding Application Status: ☒ Secured ☐ In progress

Amount: £1,726, 187.91

Duration

Years: 2

Months: 0

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?

NIHR Health Technology Assessment

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? Please give details of subcontractors if applicable.

☐ Yes ☒ No

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

☐ Yes ☒ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title Forename/Initials Surname
	Mr Kiran Mistry
Organisation	NIHR CRN East Midlands
Address	First floor
	Knighton Street Outpatients Building
	Leicester Royal Infirmary
Post Code	LE1 5WW
Work Email	kiran.mistry@nihr.ac.uk
Telephone	07960875039
Fax	
Mobile	07960875039

Details can be obtained from the NHS R&D Forum website: <http://www.rdforum.nhs.uk>

A68-2. Select Local Clinical Research Network for NHS Organisation identified in A68-1:

East Midlands

For more information, please refer to the question specific guidance.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 05/05/2021

Planned end date: 31/12/2022

Total duration:

Years: 1 Months: 7 Days: 27

A69-2. How long do you expect the study to last in all countries?

Planned start date: 05/05/2021

Planned end date: 31/12/2022

Total duration:

Years: 1 Months: 7 Days: 27

A70. Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial ⁽¹⁾

The end of the scheduled treatment phase is defined as the date of the last follow-up visit of the last participant. The end of individual comparisons within the platform will be the date of the final data extraction from NHS Digital. This will allow sufficient time for the completion of protocol procedures, data collection and data input.

A71-1. Is this study?

☐ Single centre

☒ Multicentre

A71-2. Where will the research take place? (Tick as appropriate)

- ☒ England
☒ Scotland
☒ Wales
☒ Northern Ireland
☐ Other countries in European Economic Area

Total UK sites in study 300

Does this trial involve countries outside the EU?

☒ Yes ☐ No

- ☐ USA
☒ Other international (please specify)

United Kingdom

A72. Which organisations in the UK will host the research? Please indicate the type of organisation by ticking the box and give approximate numbers if known:

- ☐ NHS organisations in England
☐ NHS organisations in Wales
☐ NHS organisations in Scotland
☐ HSC organisations in Northern Ireland
☒ GP practices in England
☒ GP practices in Wales
☒ GP practices in Scotland
☒ GP practices in Northern Ireland
☐ Joint health and social care agencies (eg community mental health teams)
☒ Local authorities 20
☐ Phase 1 trial units
☐ Prison establishments
☐ Probation areas
☒ Independent (private or voluntary sector) organisations 280
☐ Educational establishments
☐ Independent research units
☐ Other (give details)

Total UK sites in study: 300

A73-1. Will potential participants be identified through any organisations other than the research sites listed above?

☐ Yes ☒ No

A74. What arrangements are in place for monitoring and auditing the conduct of the research?

Monitoring will be carried out as required following a risk assessment and as documented in the monitoring plan.

Routine monitoring will be carried out centrally and will include informed consent form review and site metrics review from eCRF data.

Due to the nature of the trial within care home settings, on site monitoring for this trial is not expected, however if feasible on site monitoring may be performed if necessary. Additional monitoring may be carried out remotely should the need arise from monitoring triggers or site performance metrics. Any monitoring carried out in such a manner will be detailed in a monitoring report, a copy of which will be provided to the Sponsor. Any issues noted will be followed up to resolution. Triggers will be detailed in the monitoring plan but may include for example, lack of data entry, poor data quality, lower or higher than expected safety reporting rates. Remote monitoring may include telephone/video calls to site and remote source data verification.

The eTMF and associated documents will be subject to audit by NCTU as part of the biennial NCTU audit programme if required or selected.

A75-1. What arrangements will be made to review interim safety and efficacy data from the trial? Will a formal data monitoring committee or equivalent body be convened?

An independent Data Monitoring Committee (DMC) will be convened for the trial and they will meet prior to commencement of the project and then at regular intervals. Interim analyses will be supplied in confidence to the DMC, which will be asked to give advice on whether the accumulated data from the trial, together with the results from other relevant research, justifies the continuing recruitment of further participants. The DMC will operate in accordance with a trial specific charter based upon the template created by the Damocles Group.

If a formal DMC is to be convened, please forward details of the membership and standard operating procedures to the Research Ethics Committee when available. The REC should also be notified of DMC recommendations and receive summary reports of interim analyses.

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

The Sponsor reserves the right to discontinue this trial at any time for failure to meet expected enrolment goals, for safety or any other administrative reasons. The Sponsor shall take advice from the Platform Steering Committee (PSC) and Data Monitoring Committee (DMC) as appropriate in making this decision.

A76. Insurance/ indemnity to meet potential legal liabilities

Note: in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? Please tick box(es) as applicable.

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- ☐ NHS indemnity scheme will apply (NHS sponsors only)
- ☒ Other insurance or indemnity arrangements will apply (give details below)

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non-negligent harm.

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? Please tick box(es) as applicable.

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- ☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- ☒ Other insurance or indemnity arrangements will apply (give details below)

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non-negligent harm.

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

- ☐ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
- ☒ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non-negligent harm.

Care homes will be indemnified by their own insurance providers. Confirmation that their insurance covers research activity will be requested prior to opening to recruitment.

Principal Investigators will be indemnified by negligence insurance from their protection society/defence union or their associated NHS employer.

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

- ☐ Yes ☒ No

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

- ☐ Yes ☒ No ☐ Not sure

Part B Section 1: Investigational Medicinal Products

Information on each IMP.

Information on each 'bulk product' before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator, if applicable.

If the trial is performed with several products please create a separate set of the following questions for each product. If the product is a combination product please give separate information for each active substance. Click on the first row and enter details of the product in the following screens. When you have completed the details, click on the navigate button or the "See All" link and return to this section to enter details of the next product. When you have completed details of all products please move to question 13 using the navigation screen.

Investigational medicinal products

PR1 [Ciclesonide](#)

PR3 [Niclosamide Ethanolamine](#)

13. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR1**

Investigational medicinal product category:

Test IMP

14. STATUS OF THE IMP

If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to question 14-.2

14-1. Does the IMP to be used in the trial have a marketing authorisation?

☐ Yes ☒ No ☐ Not Answered

14-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☐ No ☒ Not Answered

14-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☒ Yes ☐ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

14-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

14-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

14-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

Description of IMP**15-1. Description of IMP**

Product name where applicable Ciclesonide

Product code where applicable N/A

ATC codes, if officially registered RO3BA08

Pharmaceutical form (use standard terms) Inhalation solution

Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

Maximum duration of treatment of a subject according to the 6 weeks

protocol

Dose allowed

First dose for first-in-human clinical trial

N/A

Specify per day or total:

☒ per day ☐ total ☐ Not Answered

Specify total dose (number and unit)

480 μ g
microgram(s)

Route of administration (relevant to the first dose):

Inhalation use

Maximum dose allowed

480 microgram(s) per day (3 actuations of 160 micrograms)

Specify per day or total

☒ per day ☐ total ☐ Not Answered

Specify total dose (number and unit)

480 μ g
microgram(s)

Route of administration (relevant to the maximum dose): Inhalation use

Routes of administration for this IMP

Inhalation use

Nasal use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

15-2. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available):

Ciclesonide

CAS number:

141845-82-1

Current sponsor code:

Other descriptive name:

Full Molecular formula

C32H44O7

Chemical/biological description of the Active Substance

Ciclesonide is an inhaled corticosteroid used in the prophylaxis of asthma (80 μ g od with maximum 320 μ g bd; British National Formulary, accessed 28/12/2020); in North America it is also licensed for hay-fever and allergic rhinitis. It is a safe and effective inhaled corticosteroid (ICS) in asthma. Potential advantages over other ICS are activation in the lung only with low oral and high pulmonary deposition, high first pass effect in the liver and high protein binding in the bloodstream.

Strength

Concentration unit:

 μ g microgram(s)

Concentration type:

up to

Concentration number (only use both fields for range):

480

15-3. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Ciclesonide is an inhaled corticosteroid used in the prophylaxis of asthma (80 µg od with maximum 320 µg bd; British National Formulary, accessed 28/12/2020); in North America it is also licensed for hay-fever and allergic rhinitis. It is a safe and effective inhaled corticosteroid (ICS) in asthma. Potential advantages over other ICS are activation in the lung only with low oral and high pulmonary deposition, high first pass effect in the liver and high protein binding in the bloodstream.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

13. Indicate which of the following is described below then repeat as necessary for each:This refers to the IMP number: **PR3**

Investigational medicinal product category:

Test IMP

14. STATUS OF THE IMP*If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to question 14-2***14-1. Does the IMP to be used in the trial have a marketing authorisation?**☐ Yes ☒ No ☐ Not Answered**14-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered*If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1*

Other :

☐ Yes ☒ No ☐ Not Answered**14-3. IMPD submitted:**

Full IMPD

☒ Yes ☐ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☐ Yes ☒ No ☐ Not Answered**14-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**☐ Yes ☒ No ☐ Not Answered**14-5. Has the IMP been designated in this indication as an orphan drug in the Community?**☐ Yes ☒ No ☐ Not Answered

14-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

Description of IMP**15-1. Description of IMP**

Product name where applicable Niclosamide Ethanolamine

Product code where applicable N/A

ATC codes, if officially registered P02DA01

Pharmaceutical form (use standard terms) Nasal spray, solution

Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

Maximum duration of treatment of a subject according to the protocol 6 weeks

Dose allowed

First dose for first-in-human clinical trial N/A

Specify per day or total: ☒ per day ☐ total ☐ Not Answered

Specify total dose (number and unit) 560 μ l microlitre(s)

Route of administration (relevant to the first dose): Nasal use

Maximum dose allowed 560 microlitre(s) per day

Specify per day or total ☒ per day ☐ total ☐ Not Answered

Specify total dose (number and unit) 560 μ l microlitre(s)

Route of administration (relevant to the maximum dose): Nasal use

Routes of administration for this IMP

Nasal use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

15-2. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Niclosamide ethanolamine salt

CAS number: 1420-04-8

Current sponsor code:

Other descriptive name:

Full Molecular formula C₁₃H₈Cl₂N₂O₄.C₂H₇NO

Chemical/biological description of the Active Substance Niclosamide anhydrous is a salicylanilide introduced as an oral anthelmintic in the early 1960s. Niclosamide ethanolamine is the slightly higher water-soluble salt of the compound niclosamide anhydrous. The major metabolites of niclosamide, identified in the Wistar rat after oral administration, are the O-glucuronide of niclosamide in bile (hydrolysed by β glucuronidase in the intestines), the 4'-nitro- reduced metabolite, (2',5-dichloro-4'-amino-salicylanilide) in the urine, and unchanged niclosamide in the faeces.

Strength

Concentration unit: μ l microlitre(s)

Concentration type: up to

Concentration number (only use both fields for range): 560

15-3. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Niclosamide inhibits SKP2 activity, which enhances autophagy and reduces MERS-CoV replication and a similar mechanism may explain inhibition of SARS-CoV-2 infection. Recent studies suggest anti-viral activity with IC50 0.042-0.26 µM in Vero cells, e.g. 0.28 µM.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

Information on Placebo**13. Is there a placebo:**☐

Yes

☒

No

Index of Sites where the qualified person certifies batch release

14. IMPs and placebos for which no responsible site needs to be identified:

This section is used to identify IMPs and placebos which:

- Have an MA in the EU **and**
- Are sourced from the EU market **and**
- Are used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labeling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive).

If all the conditions above are met, then select below the IMPs and placebos to which this applies.

This section is dedicated to finished IMPs, i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. In the case of multiple sites indicate the product certified by each site.

15. Identify who is responsible in the Community for the certification of the finished IMPs.

Where the product does not have a MA in the EU, but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2. of Directive 2005/28/EC (GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial.

RS1

Manufacturer

Organisation Mono chem-pharm Produkte GmbH
 Address Leystrassa 129
 Town/city Wien
 Post code 1200
 Country Austria

Give the manufacturing authorisation number
 481218

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
 PR3

RS3

Manufacturer

Organisation Pharmaserve (North West) Limited
 Address 9 Arkwright Road, Astmoor Industrial Estate
 Town/city Runcorn

Post code WA7 1NU

Country United Kingdom

Give the manufacturing authorisation number

32169

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP

PR1

RS4

Both

Organisation BCM Specials Ltd

Address D10 Fourth Floor, Thane Road

Town/city Nottingham

Post code NG90 2PR

Country United Kingdom

Give the manufacturing authorisation number

34777

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP

PR1

IMP

PR3

Part B: Section 6 - Adults unable to consent for themselves

A. Clinical trials of investigational medicinal products

In this sub-section, an adult means a person aged 16 or over.

A1. What clinical condition(s) will the participants have? *The trial must relate directly to this condition.*

Participants will be residents in a care home setting who are at risk of COVID-19 infection due to a positive case identified in their care home.

A2. Could the trial be carried out equally effectively if confined to adults capable of giving consent?

☐ Yes ☒ No

A3. Who in the research team will decide whether or not the participants have the capacity to give consent? What training/experience will they have to enable them to reach this decision?

In most cases, residents who permanently do not have capacity will already be known to care home staff and will have a nominated legal representative for decisions on their usual care such as COVID-19 vaccination. Where it is unclear whether the resident has capacity, an assessment of capacity will be carried out by care home staff who are familiar with the resident. The Three Question Test will be used (e.g. the resident is given a statement; the trial is trying to reduce COVID-19 with a medicine that reduces the chance of infection; the potential participant is only deemed to have capacity if all three bits of information are correctly fed back to the Staff member. Training on this will be included in the training package provided to care home staff.

A4. What benefit is the administration of the investigational medicinal product expected to produce for these participants? *You may refer back to your answer to Question A24.*

The trial IMP may reduce COVID-19 infection and severity in care homes.

A5. Will the trial involve any foreseeable risk or burden for these participants, or interfere in any way with their freedom of action or privacy?

☒ Yes ☐ No

If Yes, please give an assessment below. You may refer back to your answers to Questions A22 and A23. Highlight any risk, burden or discomfort specific to these participants. Justify in relation to the potential benefits.

Participants at a care home randomised to receive the trial treatment will be required to take an additional medicine as well as any existing treatments they are on. The selected treatment and how this will be administered will be explained to the participant before they agree to take part in the trial.

Participants could experience side effects from the trial treatment. Depending on the treatment selected this may be an inconvenience to the participant and may cause some distress. The side effects of the selected treatments will be reviewed prior to selection and information on potential side effects will be provided to the participant/legal representative and care home.

A6. What arrangements will be made to identify and seek informed consent from a legal representative?

In most cases the legal representative will already be known to the care home staff. They will be provided with the Legal Representative Information Sheet (LIS) and will represent the potential participant during the consent process. The consent process will comprise of proxy consent by the personal legal representative for residents who lack capacity. If no legal representative is identified then a resident will not be eligible to join the trial.

A7. Is it possible that a participant requiring urgent treatment might need to be recruited into the trial before it is possible to identify and seek consent from a legal representative?

☐ Yes ☒ No

If Yes, outline how decisions will be made on the inclusion of participants and what arrangements will be made to seek consent from the participant (if capacity has been recovered) or a legal representative as soon as practicable thereafter.

A8. What arrangements will be made to continue to consult legal representatives during the course of the research where necessary?

Throughout the course of the research if it is necessary to consult the legal representatives e.g. if new information becomes available which may affect the legal representatives decision for a participant to continue, they will be contacted by care home staff or a member of the research team.

A9. Will steps be taken to provide information about the trial to participants, according to their capacity of understanding, and to consider the wishes of participants capable of forming an opinion?

☒ Yes ☐ No

If Yes, give details.

A variety of media formats will be used to ensure full comprehension of the trial as part of the initial consent process. This will include giving of information by DVD, reading of information sheets to the residents, visual pictorial aids (including animations) and paper information sheets; the mode of information giving will be at the discretion of the care home manager who is familiar with their resident's needs.

The information sheets and consent forms have been prepared and reviewed by lay members of the public to ensure the information is provided in language that is appropriate to care home residents. Personal legal representatives will be asked to consider the wishes of the resident in taking part in research.

A10-1. What will be the criteria for withdrawal of participants?

Participants may be withdrawn without a reason by themselves, their personal legal representative, the care home manager, their GP or the PI.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For further information please refer to guidance.*

Investigator identifier	Research site	Investigator Name	
IN1	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Forename	
		Middle name	
		Family name	
		Email	
	Organisation name Address	NIHR CRN: North East and North Cumbria Regent Point Regent Farm Road Gosforth Newcastle upon Tyne	Qualification (MD...) Country
	Post Code	NE3 3HD	
	Country	ENGLAND	
IN2	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Forename	
		Middle name	
		Family name	
		Email	
	Organisation name Address	NIHR CRN: North West Coast Royal Liverpool and Broadgreen University Hospitals NHS Trust Prescot Street Liverpool	Qualification (MD...) Country
	Post Code	L7 8XP	
	Country	ENGLAND	
IN3	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Forename	
		Middle name	
		Family name	
		Email	
	Organisation name Address	NIHR CRN: Yorkshire and Humber 8 Beech Hill Road SHEFFIELD	Qualification (MD...) Country

IN4

Post Code S10 2SB
Country ENGLAND

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename
Middle name
Family name
Email

Organisation name NIHR CRN: Greater Manchester
Address 2nd Floor
Citylabs
Nelson Street
Manchester
Post Code M13 9NQ
Country ENGLAND

Qualification (MD...)
Country

IN5

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename
Middle name
Family name
Email

Organisation name NIHR CRN: East Midlands
Address Knighton Street
Outpatients
1st Floor
Leicester Royal Infirmary
Post Code LE1 5WW
Country ENGLAND

Qualification (MD...)
Country

IN6

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename
Middle name
Family name
Email

Organisation name NIHR CRN: West Midlands
Address James House
Newport Road
Albrighton
Wolverhampton

Qualification (MD...)
Country

IN7

Post Code WW7 3FA
Country ENGLAND

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename
Middle name
Family name
Email

Organisation name NIHR CRN: West of
 England
Address Whitefriars
 Lewins Mead
 Bristol
Post Code BS1 2NT
Country ENGLAND

Qualification
(MD...)
Country

IN8

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename
Middle name
Family name
Email

Organisation name NIHR CRN: Thames
 Valley and South
 Midlands
Address John Radcliffe Hospital
 Headley Way
 Headington Oxford
Post Code OX3 9DU
Country ENGLAND

Qualification
(MD...)
Country

IN9

☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Forename
Middle name
Family name
Email

Institution name All Care Homes
Department name
Street address
Town/city
Post Code
Country

Qualification
(MD...)
Country

IN11

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NIHR CRN: Wessex

Qualification
(MD...)

Address

Unit 7, Berrywood
Business Village
Tollbar Way
Hedge End Southampton

Country

Post Code

SO30 2UN

Country

ENGLAND

IN12

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameNIHR CRN: South West
PeninsulaQualification
(MD...)

Address

F7
Bowmoor House
Royal Devon and Exeter
Hospital (Wonford) Exeter

Country

Post Code

EX2 5DW

Country

ENGLAND

IN13

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameNIHR CRN: North
ThamesQualification
(MD...)

Address

3rd floor
170 Tottenham Court
Road
London

Country

Post Code

W1T 7HA

Country

ENGLAND

IN14

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameNIHR CRN: South
LondonQualification
(MD...)

Address

16th Floor BRC Faculty
Guy's Tower
Guy's Hospital Great
Maze Pond London

Country

Post Code

SE1 9RT

Country

ENGLAND

IN15

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameNIHR CRN: North West
LondonQualification
(MD...)

Address

Imperial College
Healthcare NHS Trust
3rd Floor Administrative
Block South
Hammersmith Hospital
Du Cane Road London

Country

Post Code

W12 0HT

Country

ENGLAND

IN16

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameANEURIN BEVAN
HEALTH BOARDQualification
(MD...)

Address

DENTAL DEPARTMENT
PSS BUILDING
LLANFRECHFA
CWMBRAN GWENT

Country

Post Code

NP44 8YN

Country

WALES

IN17

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameBETSI CADWALADR
UNIVERSITY LHBQualification
(MD...)

Address

EXECUTIVE OFFICES,
YSBYTY GWYNEDD
PENRHOSGARNEDD
BANGOR GWYNEDD

Country

Post Code

LL57 2PW

Country

WALES

IN18

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameCARDIFF & VALE
UNIVERSITY LHBQualification
(MD...)

Address

WOODLAND HOUSE
MAES-Y-COED ROAD
CARDIFF

Country

Post Code

CF14 4HH

Country

WALES

IN19

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameCWM TAF MORGANNWG
UNIVERSITY LOCAL
HEALTH BOARDQualification
(MD...)

Address

DEWI SANT HOSPITAL
ALBERT ROAD
PONTYPRIDD MID
GLAMORGAN

Country

Post Code

CF37 1LB

Country

WALES

IN20

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameHYWEL DDA
UNIVERSITY LHBQualification
(MD...)

Address

CORPORATE OFFICES,
YSTWYTH BUILDING
HAFAN DERWEN
ST DAVIDS PARK,
JOBSWELL ROAD
CARMARTHEN DYFED

Country

Post Code

SA31 3BB

Country

WALES

IN21

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

POWYS TEACHING LHB

Qualification
(MD...)

Address

GLASBURY HOUSE
BRONLLYS HOSPITAL
BRECON POWYS

Country

Post Code

LD3 0LS

Country

WALES

IN22

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameSWANSEA BAY
UNIVERSITY LOCAL
HEALTH BOARDQualification
(MD...)

Address

ONE TALBOT GATEWAY,
SEAWAY DRIVE
SEAWAY PARADE
INDUSTRIAL ESTATE
BAGLAN PORT TALBOT
WEST GLAMORGAN

Country

Post Code

SA12 7BR

Country

WALES

IN23

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Ayrshire and Arran

Qualification
(MD...)

Address

PO Box 13, Boswell
House

Country

10 Arthur Street

AYR Scotland

Post Code

KA7 1QJ

Country

SCOTLAND

IN24

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Borders

Qualification
(MD...)

Address

NEWSTEAD

Country

MELROSE

ROXBURGHSHIRE

Post Code

TD6 9DB

Country

SCOTLAND

IN25

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Fife

Qualification
(MD...)

Address

Springfield House

Country

CUPAR Scotland

Post Code

KY15 5UP

Country

SCOTLAND

IN26

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
nameNHS Greater Glasgow
and ClydeQualification
(MD...)

Address

J B Russell House
Gartnavel Royal Hospital
1055 Great Western
Road Glasgow
Glasgow Scotland

Country

Post Code

G12 0XH

Country

SCOTLAND

IN27

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Highland

Qualification
(MD...)

Address

Reay House
17 Old Edinburgh Road
INVERNESS Scotland

Country

Post Code

IV2 3HG

Country

SCOTLAND

IN28

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Lanarkshire

Qualification
(MD...)

Address

14 Beckford Street

Country

HAMILTON Scotland

Post Code

ML3 0TA

Country

SCOTLAND

IN29

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Grampian

Qualification
(MD...)

Address

Summerfield House
2 Eday Road
ABERDEEN Scotland

Country

Post Code

AB15 6RE

Country

SCOTLAND

IN30

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Orkney

Qualification
(MD...)

Address

GARDEN HOUSE
NEW SCAPA ROAD
KIRKWALL ORKNEY

Country

Post Code

KW15 1BQ

Country

SCOTLAND

IN31

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

Family name

Email

Organisation
name

NHS Lothian

Qualification
(MD...)

Address

Waverley Gate
2-4 Waterloo Place
Edinburgh Scotland

Country

Post Code

EH1 3EG

Country

SCOTLAND

IN32

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename

Middle name

		Family name
		Email
	Organisation name	Qualification (MD...)
	Address	Country
	Post Code	
	Country	
IN33	<input checked="" type="radio"/> NHS/HSC Site	
	<input type="radio"/> Non-NHS/HSC Site	
		Forename
		Middle name
		Family name
		Email
	Organisation name	Qualification (MD...)
	Address	Country
	Post Code	
	Country	
IN34	<input checked="" type="radio"/> NHS/HSC Site	
	<input type="radio"/> Non-NHS/HSC Site	
		Forename
		Middle name
		Family name
		Email
	Organisation name	Qualification (MD...)
	Address	Country
	Post Code	
	Country	
IN35	<input checked="" type="radio"/> NHS/HSC Site	
	<input type="radio"/> Non-NHS/HSC Site	
		Forename
		Middle name
		Family name
		Email

	Organisation name	NHS Dumfries and Galloway	Qualification (MD...)
	Address	Grierson House The Crichton Bankend Road DUMFRIES Scotland	Country
	Post Code	DG1 4ZG	
	Country	SCOTLAND	
IN36	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site		Forename Middle name Family name Email
	Organisation name	NHS Shetland	Qualification (MD...)
	Address	BREVIK HOUSE SOUTH ROAD LERWICK, SHETLAND	Country
	Post Code	ZE1 0RB	
	Country	SCOTLAND	
IN37	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site		Forename Middle name Family name Email
	Organisation name	NICRNPC	Qualification (MD...)
	Address	4th Floor Dunluce Health Centre 1 Dunluce Avenue BELFAST	Country
	Post Code	BT9 7HR	
	Country	NORTHERN IRELAND	
IN38	<input type="radio"/> NHS/HSC Site <input checked="" type="radio"/> Non-NHS/HSC Site		Forename Middle name Family name Email
	Institution name	Care Homes throughout the UK	Qualification (MD...)

Department name		Country	
Street address			
Town/city			
Post Code			
Country			
IN39			
<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site			
		Forename	Adam
		Middle name	L.
		Family name	Gordon
		Email	Adam.Gordon@nottingham.ac.uk
Organisation name	UNIVERSITY HOSPITALS OF DERBY AND BURTON NHS FOUNDATION TRUST	Qualification (MD...)	Honorary Consultant Geriatrician, Professor of the Care of Older People - University of Nottingham Vice President (Academic Affairs) - British Geriatrics Society
Address	ROYAL DERBY HOSPITAL UTTOXETER ROAD DERBY	Country	United Kingdom
Post Code	DE22 3NE		
Country	ENGLAND		
IN40			
<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site			
		Forename	Elizabeta
		Middle name	
		Family name	Mukaetova-Ladinska
		Email	eml12@leicester.ac.uk
Organisation name	UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST	Qualification (MD...)	Chair/Professor in Old Age Psychiatry, University of Leicester
Address	LEICESTER ROYAL INFIRMARY INFIRMARY SQUARE LEICESTER	Country	United Kingdom
Post Code	LE1 5WW		
Country	ENGLAND		
IN41			
<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site			
		Forename	Emma
		Middle name	
		Family name	Vardy
		Email	Emma.Vardy@srft.nhs.uk
Organisation name	SALFORD ROYAL NHS FOUNDATION TRUST	Qualification (MD...)	Consultant Geriatrician and Honorary Senior lecturer, Clinical Dementia Lead Salford ICO
Address	SALFORD ROYAL STOTT LANE	Country	United Kingdom

IN42

SALFORD GREATER
MANCHESTER

Post Code M6 8HD

Country ENGLAND

- ☒ NHS/HSC Site
- ☐ Non-NHS/HSC Site

Forename Amy

Middle name

Family name Heskett

Email amy.heskett@nhs.net

Qualification (MD...) Community Trust Associate
Specialist Doctor, West Kent Urgent
Home Treatment Service

Country United Kingdom

Organisation name KENT COMMUNITY
HEALTH NHS
FOUNDATION TRUST

Address UNIT D
THE OAST
HERMITAGE LANE
MAIDSTONE

Post Code ME16 9NT

Country ENGLAND

IN43

- ☒ NHS/HSC Site
- ☐ Non-NHS/HSC Site

Forename Shelagh

Middle name

Family name O'Riordan

Email shelagh.o'riordan@nhs.net

Qualification (MD...) Consultant Geriatrician, Clinical
Director Frailty in East Kent and Chair
of the Community Geriatrics Special
Interest Group

Country United Kingdom

Organisation name KENT COMMUNITY
HEALTH NHS
FOUNDATION TRUST

Address UNIT D
THE OAST
HERMITAGE LANE
MAIDSTONE

Post Code ME16 9NT

Country ENGLAND

IN44

- ☒ NHS/HSC Site
- ☐ Non-NHS/HSC Site

Forename Miles

Middle name D.

Family name Witham

Email Miles.Witham@newcastle.ac.uk

Qualification (MD...) Professor of Trials for Older People,
Newcastle University, Honorary
consultant geriatrician

Country United Kingdom

Organisation name THE NEWCASTLE UPON
TYNE HOSPITALS NHS
FOUNDATION TRUST

Address FREEMAN HOSPITAL

FREEMAN ROAD
HIGH HEATON
NEWCASTLE UPON
TYNE
Post Code NE7 7DN
Country ENGLAND

IN45

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Asangaedem

Middle name

Family name Akpan

Email asan.akpan@nhr.ac.uk

Organisation name LIVERPOOL UNIVERSITY
HOSPITALS NHS
FOUNDATION TRUST

Address ROYAL LIVERPOOL
UNIVERSITY HOSPITAL
PRESCOT STREET

LIVERPOOL

Post Code L7 8XP

Country ENGLAND

Qualification
(MD...)

Consultant Geriatrician, Liverpool
University Hospitals NHS FT / Deputy
Chair British Geriatrics Society
England Council
Visiting Professor, University of
Cumbria / Honorary Associate
Professor, University of Liverpool

Country United Kingdom

IN46

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Tania

Middle name

Family name Kalsi

Email tania.kalsi@gstt.nhs.uk

Organisation name GUY'S AND ST THOMAS'
NHS FOUNDATION
TRUST

Address ST THOMAS' HOSPITAL
WESTMINSTER BRIDGE
ROAD

LONDON

Post Code SE1 7EH

Country ENGLAND

Qualification
(MD...)

Consultant Geriatrician, Department
of Ageing and Health/ Honorary
Clinical Senior Lecturer, King's
College London

Country United Kingdom

IN47

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename David

Middle name Graeme

Family name Smithard

Email david.smithard@nhs.net

Organisation name	LEWISHAM AND GREENWICH NHS TRUST	Qualification (MD...)	Consultant in Elderly and Stroke Medicine Queen Elizabeth Hospital
Address	UNIVERSITY HOSPITAL LEWISHAM LEWISHAM HIGH STREET LONDON	Country	United Kingdom
Post Code	SE13 6LH		
Country	ENGLAND		

IN48

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Divya

Middle name

Family name Tiwari

Email divya.tiwari@uhd.nhs.uk

Organisation name	UNIVERSITY HOSPITALS DORSET NHS FOUNDATION TRUST
-------------------	--

Qualification (MD...)	Consultant physician in General and Geriatric Medicine
-----------------------	--

Address	MANAGEMENT OFFICES POOLE HOSPITAL LONGFLEET ROAD POOLE
---------	--

Country	United Kingdom
---------	----------------

Post Code	BH15 2JB
-----------	----------

Country	ENGLAND
---------	---------

IN49

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Jay

Middle name

Family name Amin

Email jay.amin@soton.ac.uk

Organisation name	SOUTHERN HEALTH NHS FOUNDATION TRUST
-------------------	--------------------------------------

Qualification (MD...)	Associate Professor in Psychiatry of Older Age, University of Southampton / Honorary Consultant in Older People's Mental Health
-----------------------	---

Address	TATCHBURY MOUNT HOSPITAL CALMORE SOUTHAMPTON
---------	--

Country	United Kingdom
---------	----------------

Post Code	SO40 2RZ
-----------	----------

Country	ENGLAND
---------	---------

IN50

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Andrew

Middle name

IN51

Organisation name	BRADFORD TEACHING HOSPITALS NHS FOUNDATION TRUST	Family name	Clegg
Address	BRADFORD ROYAL INFIRMARY DUCKWORTH LANE BRADFORD	Email	a.p.clegg@leeds.ac.uk
Post Code	BD9 6RJ	Qualification (MD...)	Professor of Geriatric Medicine & Honorary Consultant Geriatrician/ Theme Lead, NIHR ARC Yorkshire & Humber Improving Care for Older People with Frailty theme/ Associate Director, HDRUK North Academic Unit for Ageing & Stroke Research, University of Leeds
Country	ENGLAND	Country	United Kingdom

<input checked="" type="radio"/> NHS/HSC Site	Forename	Liz	
<input type="radio"/> Non-NHS/HSC Site	Middle name		
	Family name	Graham	
	Email	liz.graham@bthft.nhs.uk	
Organisation name	BRADFORD TEACHING HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	Senior Research Fellow Academic Unit for Ageing and Stroke Research Bradford Institute for Health Research
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IN52

<input checked="" type="radio"/> NHS/HSC Site	Forename	Ilaria	
<input type="radio"/> Non-NHS/HSC Site	Middle name		
	Family name	Bellantuono	
	Email	i.bellantuono@sheffield.ac.uk	
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IN53

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Forename Sarah

Middle name J

Family name Mitchell

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Organisation
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HOSPITALS NHS
FOUNDATION TRUSTQualification
(MD...)GP & Yorkshire Cancer Research
Senior Research Fellow, Dept of
Oncology and Metabolism, University
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IN54

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Forename Susan

Middle name Deborah

Family name Shenkin

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Organisation
name

NHS Lothian

Qualification
(MD...)Senior Clinical Lecturer and Honorary
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IN55

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Terence

Middle name J

Family name Quinn

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Organisation
nameNHS Greater Glasgow
and ClydeQualification
(MD...)Senior Lecturer and Honorary
Consultant,
NHS Greater Glasgow and Clyde and
University of Glasgow

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1055 Great Western
Road Glasgow
Glasgow Scotland

Country

United Kingdom

Post Code

G12 0XH

Country

SCOTLAND

IN56

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Jonathan

Middle name

Family name Hewitt

Email hewittj2@cardiff.ac.uk

Organisation name ANEURIN BEVAN
UNIVERSITY LHB

Qualification (MD...) Honorary Consultant Physician

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CADO'S HOSPITAL
LODGE ROAD
CAERLEON NEWPORT
GWENT

Country United Kingdom

Post Code NP18 3XQ

Country WALES

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.
3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.
10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
 - ◊ Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
 - ◊ May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
 - ◊ May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
 - ◊ Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
 - ◊ May be sent by email to REC members.
11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.
12. I understand that the main REC or its operational managers may share information in this application or supporting documentation with the Medicines and Healthcare products Regulatory Agency (MHRA) where it is relevant to the Agency's statutory responsibilities.
13. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

HRA would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- ☐ Chief Investigator
- ☐ Sponsor
- ☐ Study co-ordinator
- ☐ Student
- ☐ Other – please give details
- ☐ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Philip Bath on 28/04/2021 10:51.

Job Title/Post: Chief Investigator/Professor of Stroke Medicine

Organisation: University of Nottingham

Email: philip.bath@nottingham.ac.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.
7. The statutory responsibilities of sponsors set out in the Medicines for Human Use (Clinical Trials) Regulations 2004 will be undertaken in relation to this trial.

Please note: The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.

8. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.
9. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by ANGELA SHONE on 28/04/2021 10:54.

Job Title/Post: Head of Research Governance

Organisation: University of Nottingham

Email: