



Health Research Authority

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16 September 2021

Prof Christopher Butler
Chief Investigator
University of Oxford
Nuffield Department of Primary Care Health Sciences, Radcliffe Observatory Quarter,
Woodstock Road
Oxford
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Dear Professor Butler

Application title:	Platform Randomised Trial of Treatments in the Community for Epidemic and Pandemic Illnesses
CAG reference:	21/CAG/0122
IRAS project ID:	281958
REC reference:	20/SC/0158

Thank you for submitting a research application for the purpose of transferring the lawful basis for processing confidential patient information without consent from the 'COPI Notice' issued under Regulation 3(4) to Regulation 5 of the Health Service (Control of Patient Information Regulations) 2002.

The role of the Confidentiality Advisory Group (CAG) is to review applications submitted under Regulations 5 and to provide advice to the Health Research Authority on whether application activity should be supported, and if so, any relevant conditions. This application was considered at the CAG meeting held on 02 September 2021.

Health Research Authority decision

The Health Research Authority, having considered the advice from the Confidentiality Advisory Group as set out below, has determined the following:

1. The application to transition from the COPI Notice to Regulation 5 of the Health Service (Control of Patient Information Regulations) 2002 is conditionally supported. This support automatically comes into effect only when the COPI Notice expires. While the COPI Notice is in effect that should be relied upon

2. Support allows the disclosure of confidential patient information from NHS Digital to the University of Oxford, so that the research team can contact eligible patients by telephone to recruit into the study.
3. Support is subject to compliance with the standard and specific conditions of support.

Context

Purpose of application

This application from the University of Oxford set out the purpose of medical research that seeks to assess the effectiveness of trial treatments in reducing time to recovery and hospitalisation and/or death for patients aged 18 years and over with confirmed COVID-19 infection during time of prevalent COVID-19 infections.

This Clinical Trial of an Investigative Medicinal Product (CTIMP) began in March 2020 in order to identify interventions that may favourably modify progression of COVID-19 infection. The trial will be run as an open, prospective, individually randomised, platform, controlled clinical trial in community care. The design will be flexible to allow the addition of further interventions into the trial while it is in progress, should such suitable interventions become available. In the first instance, a drug called hydroxychloroquine will be evaluated.

Patients will be recruited in a variety of ways. Patients who are concerned about Covid-19 may contact their GPs and participating GP practices will be asked to record whether a patient contacting them about Covid-19 is eligible for the study. The practice will then ask if patients are interested in participating in the study. The GP practice will then provide information or pass patient contact details to the trial team to provide information. Participating GP practices will also screen their practice list to identify suitable patients and will make contact with information about the study and request that they contact the practice or study team, in the event that they develop relevant symptoms and test positive for Covid-19. The study will also be promoted via press releases, social media, etc, and patients interested in participating may contact the study team directly.

NHS Digital will provide the study team with a list of patients who have recently tested positive for Covid-19 and who fit the eligibility criteria for the trial. The applicants have been conducting this recruitment method under Regulation 3 of the Control of Patient Information (COPI) Regulations, and are now seeking support to continue this method of recruitment under Regulation 5 of COPI. NHS Digital upload confidential patient information for patients who test positive for Covid-19 to the TIBCO MFT Internet Transfer Client account on a daily basis. The PRINCIPLE Trial Manager at the University of Oxford will download the data each day and send the contact details of eligible patients to the study team. The study team will then use this list, known as the NHS Digital Pillar 2 call list, to telephone patients to provide information about the trial and invite them to take part. Should patients consent, their participation will proceed on a consented basis. The outcome of each call will be logged on a password protected online tracker for statistical and monitoring purposes. Patients details will be deleted from the call list on a monthly basis.

A recommendation for class 3 and 6 support was requested to cover access to the relevant unconsented activities as described in the application.

Confidential patient information requested

The following sets out a summary of the specified cohort, listed data sources and key identifiers. Where applicable, full datasets and data flows are provided in the application form and relevant supporting documentation as this letter represents only a summary of the full detail.

Cohort	Patients aged 18 years and over who have tested positive for Covid-19 via a home test or at a test centre.
Data sources	1. NHS Digital Pillar 2 call list, provided by NHS Digital.
Identifiers required for linkage purposes	1. NHS Number 2. Name 3. NHS Number 4. Date of birth 5. Postcode – unit level 6. Patients Covid-19 test result date 7. Telephone number
Identifiers required for analysis purposes	1. Date of birth 2. Date of death 3. Postcode – unit level 4. Gender 5. Ethnicity

Confidentiality Advisory Group advice

The following sets out the Confidentiality Advisory Group advice which formed the basis of the decision by the Health Research Authority to transition the study to support under Regulation 5.

Scope

The CAG noted that the application is currently relying on an alternative legal basis to process confidential patient information without consent, under the 'COPI notice' and that this will continue for its duration. The group therefore considered the elements of the project that are expected to be continuing following expiry of the 'COPI notice', and which require support under Regulation 5.

The CAG noted that it was unclear how long support under Regulation 5 will be required for and asked that the applicants advised when they anticipated that confidential patient information will cease to be processed, so that the duration of support can be estimated.

The CAG noted that the research will be carried out in all 4 nations of the UK. Although the CAG remit does not extend to Northern Ireland and Scotland, the CAG remit does extend to processing of confidential patient information generated within Wales. Members advised that an amendment would be needed to add processing of confidential patient information generated in Wales, as this also falls under the CAG remit.

The application explained that information may be obtained from other bodies, such as NHS 111. If this required processing of confidential patient information without consent

by those outside the direct care, an amendment would also need to be submitted to the CAG.

The participating trusts will supply the study team with confidential patient information so that patients can be contacted and invited to take part in the trial. It was not clear if a limit had been placed on the number of times patients could be contacted and members suggested that contact attempts were limited to 3-4 calls.

Public interest

The CAG noted that this activity fell within the definition of medical research and was therefore assured that the application described an appropriate medical purpose within the remit of the section 251 of the NHS Act 2006. The CAG agreed the application was in the public interest and had a clear medical purpose.

Practicable alternatives

Members considered whether a practicable alternative to the disclosure of confidential patient information without consent existed in accordance with Section 251 (4) of the NHS Act 2006, taking into account the cost and technology available.

- Feasibility of consent

The applicants explained that, due to the urgent nature of the research, consent was not feasible. Eligible patients needed to be contacted as soon as possible after diagnosis, as they are only suitable for the trial if their symptoms started within the previous 14 days. Using the NHS Digital Pillar 2 call list will allow the research team to contact patients within 24-28 hours of their positive test. The CAG agreed that consent was not feasible.

- Use of anonymised/pseudonymised data

NHS Digital had also considered whether the patients should be contacted directly by the trial staff or whether recruitment could be managed by the Test and Trace service. It was determined that Test and Trace service could not undertake the recruitment in the timescale required by the study. The CAG agreed that the research could not be undertaken in any other way.

Justification of identifiers

The CAG noted that patients' dates of birth and postcodes will be collected before the recruitment telephone call is made. Members requested clarification on why these items of information were required at this point, or whether these data items could be collected from patients after they had been consented.

The CAG asked the applicants to clarify where patients' dates of death will be obtained from and when they will be obtained.

'Patient Notification' and mechanism for managing dissent

It is part of the CAG responsibility to support public confidence and transparency in the appropriate sharing and use of confidential patient information. Access to patient information without consent is a privilege and it is a general principle of support for reasonable measures to be taken to inform the relevant population of the activity and to

provide a right to object and mechanism to respect that objection, where appropriate. This is known as 'patient notification'. This is separate to the local obligation to comply with the principles of the General Data Protection Regulation and Data Protection Act 2018.

Patients will be contacted by telephone and a script for the call was provided. Patients will be able to dissent to inclusion during this call. This explained that patients' data had been provided by NHS Digital. A Patient Information Leaflet and Privacy Notice were also provided. The Patient Information Leaflet was also included in the screening link, which patients are directed to access during the call with the research team.

The Privacy Notice will be displayed prominently on the trial website for the general public to access at any time. The Patient Information Sheet also provides information on the use of patient identifiable information without consent following expiry of COPI and use of Regulation 5 of the Health Service Regulation 2002.

The applicants are currently maintaining an NHS Digital call log with information on call outcomes with patients, such as those who do not wish to be contacted again. Patients who do not consent to the trial have their details deleted. If patients are recruited but later withdraw from the trial, the applicants will record whether they no longer consent to the use of their records for research purposes on a discontinuation CRF.

If patients dissent from the use of their data, they will not be contacted again and this will be clearly highlighted on the contact call list to prevent further contact. Patient identifiers will be deleted from the contact list on a monthly basis. Patient identifiers will be obtained from COVID-19 positive test result data provided to NHS Digital, therefore patients are not expecting contact from the PRINCIPLE trial team. Filters will be applied when processing the data to remove patients who have registered a national opt-out, as well as special categories of people for whom the data should not be disseminated.

The CAG agreed that further patient notification needed to be undertaken to inform patients about the study before they are telephoned. The information provided described what happened if patients consented but was less clear over what happened to patients' data if they dissented. The CAG suggested that making information about the study available on the NHS Digital website was explored.

The application design allows for other medications to be added, should evidence suggest that they are effective in treating covid-19. The CAG asked that reassurance was provided that patients who have previously registered dissent, either before or after contact, are not re-contacted if different medications are added.

The CAG commended the applicant for providing pictorial information, but noted that this information could be simplified.

Patient and Public Involvement

Meaningful engagement with patients, service users and the public is considered to be an important factor for the CAG in terms of contributing to public interest considerations as to whether the unconsented activity should go ahead.

The applicants advised that the HDR UK had conducted a patient and public panels and networks survey, requesting feedback from the public on the use of contact details without consent for patients who have tested positive for Covid-19. 92 patients were involved in this survey. 97% of respondents agreed that this would be an ethical use of data. 68% of respondents stated they would be comfortable or very comfortable with

their test result and contact information being provided to researchers so that they could be invited to participate in a clinical trial into treatments for COVID-19.

The NIHR Clinical Research Network Thames Valley and South Midlands had conducted a survey of PRINCIPLE participants to obtain feedback on their experience of taking part in the study.

An independent Trial Steering Committee had also been set up to ensure that the study team deliver on time and that the research plans provide good value to the public. Two members of the public were included on the Trial Steering Committee. The Steering Committee approved the use of a list of COVID positive contacts, to allow the recruitment of participants quickly, within 24-48 hours of them receiving a positive test.

The applicants noted that recruitment via contacting patients directly using the NHS Digital Pillar 2 call list had been running under the COPI Notice. Over the 5 week period between 16 November and 20 December 2020, up to 87 additional patients per week were registered via this recruitment method, accounting for 31% of weekly registrations to the trial.

The CAG was largely satisfied with the patient and public involvement conducted. Members noted that 68% of those consulted were comfortable or very comfortable with their test result and contact information being provided to researchers, and that this seemed to be a relatively low percentage. Members asked that further details were provided on the comments on or objections to the use of confidential patient information raised by those consulted during patient and public involvement.

Exit strategy

Eligible patients will be contacted by telephone by the research team. Their participation will proceed on a consented basis. The applicants stated that patients' details, including those who did not consent to participate or who were not called, will be deleted from the call list on a monthly basis. The CAG raised no queries over the exit strategy.

Confidentiality Advisory Group advice conclusion

The CAG agreed that the minimum criteria under the Regulations appeared to have been met, and therefore advised recommending support to the Health Research Authority, subject to compliance with the specific and standard conditions of support as set out below.

The CAG also provided the below advice:

1. An amendment will need to be submitted should confidential patient information obtained from other bodies, such as NHS 111, is included in the research.
2. An amendment will be needed to add processing of confidential patient information generated in Wales, as this also falls under the CAG remit.

Specific conditions of support

1. The below conditions are to be responded to within three months of the issuing of this outcome letter.

- a. Contact attempts are to be limited to 3 – 4 calls.
 - b. Provide the date that it is anticipated that confidential patient information will cease to be processed, so that the duration of support can be estimated.
 - c. Clarify why patients' dates of birth and postcodes are required prior to making the recruitment telephone call.
 - d. Clarify where patients' dates of death will be obtained from and when they will be obtained.
 - e. Further patient notification needs to be undertaken to inform patients about the study before they are telephoned. Making information about the study available on the NHS Digital website should be explored. The patient notification also needs to explain what will happen to patients' data when they dissent.
 - f. The information provided in the Pictorial PIS needs to be revised for simplicity and clarity.
 - g. Provide details on the objections to the use of confidential patient information raised by those consulted during patient and public involvement.
 - h. Provide reassurance that patients who have previously registered dissent are not re-contacted if different medications are added.
2. Support under Regulation 5 Health Service (Control of Patient Information) Regulations 2002 will come into effect automatically following expiry of the COPI notice.
 3. The National Data Opt-Out will apply to processing of Confidential Patient Information under Regulation 5.
 4. Favourable opinion from REC **Issued 24 March 2020.**
 5. Continual achievement of 'Standards Met' in relation to the relevant DSPT submission (or any future security assurance changes) for the duration of support. Evidence to be provided (through NHS Digital confirmation they have reviewed and confirmed the DSPT submission as standards met' for the duration of support, and at time of each annual review. **The applicant must ensure that NHS Digital confirmation of 'standards met' for the University of Oxford – Nuffield Department of Primary Care Health Services is in place once support under Regulation 5 is active.** See below for further details.

Security Assurances

It is a policy position of the Department of Health and Social Care that all bodies that process patient information in England under Regulation 5 have their DSPT submissions reviewed by NHS Digital to provide assurances that the DSPT self-assessed submission has achieved the appropriate 'standards met' status. Similar policy positions apply when the processing is undertaken within the devolved nations.

As such each applicant, **no less than 4 weeks prior to expiry of the COPI notice**, should ensure that all organisations that will be processing confidential patient information without consent under this support have the necessary assurances in place. Full guidance on how to request these assurances, depending on which nation the organisation lies can be found on the [HRA website](#). For further information please contact the Confidentiality Advice Team.

Reviewed documents

The documents reviewed at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
CAG application from (signed/authorised) [CAG_Form_ReadyForSubmission]		
Covering letter on headed paper [CAG cover letter]		
Other [Data Flow Diagram]		
Other [21CAG0122 CAT COPI notice transition assessment form template KC]		
Other [Sponsor_approval_10.08.2021]		
Patient Information Materials [PRINCIPLE PIS_v4.3 20.08.2021_tracked]	4.3	20 August 2021
Patient Information Materials [PRINCIPLE PIS_v4.3 20.08.2021_clean]	4.3	20 August 2021
Patient Information Materials [PRINCIPLE_PositiveResult_Script_v2.0_21Jul2021_clean]	2.0	21 July 2021
Patient Information Materials [PRINCIPLE Consent Form V2.3 27.01.2021_Clean]	2.3	27 January 2021
Patient Information Materials [PRINCIPLE_Pictorial PIS v2.6_12.07.2021_clean]	2.6	12 July 2021
Patient Information Materials [Privacy Notice v1.3_05.08.2021_clean]	1.3	05 August 2021
REC favourable opinion letter and all correspondence [281958_Substantial Amendment 17_]		
REC favourable opinion letter and all correspondence [IRAS 281958 SL44_Acknowledgement_for_documentation_received_following_a_FO_FIFO_AC-2]		
REC favourable opinion letter and all correspondence [281958_Letter_of_HRA_Approval_26032020]		26 March 2020
Research protocol or project proposal [PRINCIPLE Protocol v9.1 24.07.2021_tracked]	9.1	24 July 2021
Research protocol or project proposal [PRINCIPLE Protocol v9.1 24.07.2021_clean]	9.1	24 July 2021

Membership of the Committee

The members of the Confidentiality Advisory Group who were present at the consideration of this item are listed below.

There were no declarations of interest in relation to this item.

User Feedback

The Health Research Authority is continually striving to provide a high-quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please

use the feedback form available on the HRA website: <http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>

HRA Training

We are pleased to welcome researchers and R & D staff at our training days – see details at <http://www.hra.nhs.uk/hra-training/>

Please do not hesitate to contact me if you have any queries following this letter. I would be grateful if you could quote the above reference number in all future correspondence.

With the Group's best wishes for the success of this project.

Yours sincerely

Kathleen Cassidy
Confidentiality Advisor

On behalf of the Health Research Authority

Email: cag@hra.nhs.uk

Included: List of members who considered application
Standard conditions of support

Copy to: berkshire.rec@hra.nhs.uk

**Confidentiality Advisory Group meeting attendance
02 September 2021**

Members present:

<i>Name</i>	
Dr Tony Calland MBE	CAG Chair
Ms Sophie Brannan	CAG member
Dr Patrick Coyle	CAG vice-chair
Mr David Evans	CAG member
Mr. Myer Glickman	CAG member
Professor Jennifer Kurinczuk	CAG member
Ms Clare Sanderson	CAG alternative vice-chair
Dr Pauline Lyseight-Jones	CAG member
Ms Rose Payne	CAG member
Mr Umar Sabat	CAG member

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Ms Katy Cassidy	HRA Confidentiality Advisor
Ms Natasha Dunkley	HRA Head of Confidentiality Advice Service
Mr Michael Pate	HRA Confidentiality Advisor
Ms Caroline Watchurst	HRA Confidentiality Advisor
Ms Emma Marshall	HRA Confidentiality Specialist

Standard conditions of support

Support to process the specified confidential patient information without consent, given by the Health Research Authority, is subject to compliance with the following standard conditions of support.

The applicant and those processing the information under the terms of the support will ensure that:

1. The specified confidential patient information is only used for the purpose(s) set out in the application.
2. Confidentiality is preserved and there are no disclosures of information in aggregate or patient level form that may inferentially identify a person, nor will any attempt be made to identify individuals, households or organisations in the data.
3. Requirements of the Statistics and Registration Services Act 2007 are adhered to regarding publication when relevant, in addition to other national guidance.
4. All staff with access to confidential patient information have contractual obligations of confidentiality, enforceable through disciplinary procedures.
5. All staff with access to confidential patient information have received appropriate ongoing training to ensure they are aware of their responsibilities and are acting in compliance with the application detail.
6. Activities must be compliant with the General Data Protection Regulation and Data Protection Act 2018.
7. Audit of data processing by a designated agent is facilitated and supported.
8. The wishes of patients who have withheld or withdrawn their consent are respected.
9. Any significant changes (for example, people, purpose, data flows, data items, security arrangements) must be approved via formal amendment prior to changes coming into effect.
10. An annual review report is submitted to the CAG every 12 months from the date of the final support letter, for the duration of the support.
11. Any breaches of confidentiality around the supported flows of information should be reported to CAG within 10 working days of the incident, along with remedial actions taken/to be taken. This does not remove the need to follow national/legal requirements for reporting relevant security breaches.