NOTTINGHAM CLINICAL TRIALS UNIT

PROTECT-CH

Prophylactic Therapy in Care Homes Trial

Platform Steering Committee (PSC) Charter

EudraCT Number:	2021-000185-15
ISRCTN Number:	N/A
SPONSOR'S Name and Reference Number:	University of Nottingham (21001)
FUNDER'S Name and Reference Number:	NIHR 133443
PSC Charter Version Number and Date:	1.0 08-Jun-2021

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1. Introduction	
Full name of the platform.	PROTECT-CH - PROphylactic ThErapy in Care homes Trial
Objectives of the platform.	To set in place an overarching platform for the efficient delivery of a suite of randomised comparisons to provide reliable evidence on the efficacy of candidate therapies for preventing SARS-CoV-2 infection and transmission in care homes.
Objectives of trial, including interventions being investigated.	Primary objective: To provide reliable estimates of the effect of study treatments for each pairwise comparison with the standard care arm on SARS-CoV-2 infection, morbidity and mortality at 60 days after randomisation. Secondary objectives: To assess the effects of study treatments on mortality (all-cause and cause specific), hospitalisation, healthcare referrals for COVID-19, infection (asymptomatic, symptomatic), time to symptomatic infection and serious adverse reactions. Tertiary objectives: To assess the cost-effectiveness of study treatments and evaluate processes/formative learning in the platform trial and contextual variation in outcomes.
Outline of scope of Charter.	The purpose of this document is to describe the membership, roles, responsibilities, authority, decision-making and relationships of the Platform Steering Committee (PSC) for this trial, including the timings of meetings, methods of providing information to and from the PSC, frequency and format of meetings and relationships with other trial committees.
Facilitation.	A member of the platform management team at the coordinating centre (Nottingham Clinical Trials Unit (NCTU)) will facilitate the organisation of meetings and attend all the meetings for minute taking. The Facilitator will be responsible for the organisation of meetings and should be copied into all communications with and between the PSC.
2. Roles and responsibilities	
Role of the PSC.	The role of the PSC is to provide oversight for the platform study encompassing the randomised comparisons on behalf of the Sponsor and Funder and to ensure that (i) the project is conducted to the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice, and (ii) appropriate ethical and other approvals are obtained in line with the project plan. It should also provide advice through its independent Chair to the Platform Management Group (PMG), the Funder (National Institute for Health Research; NIHR), Sponsor (University of Nottingham), the Chief Investigator (CI) and NCTU on all aspects of the study.

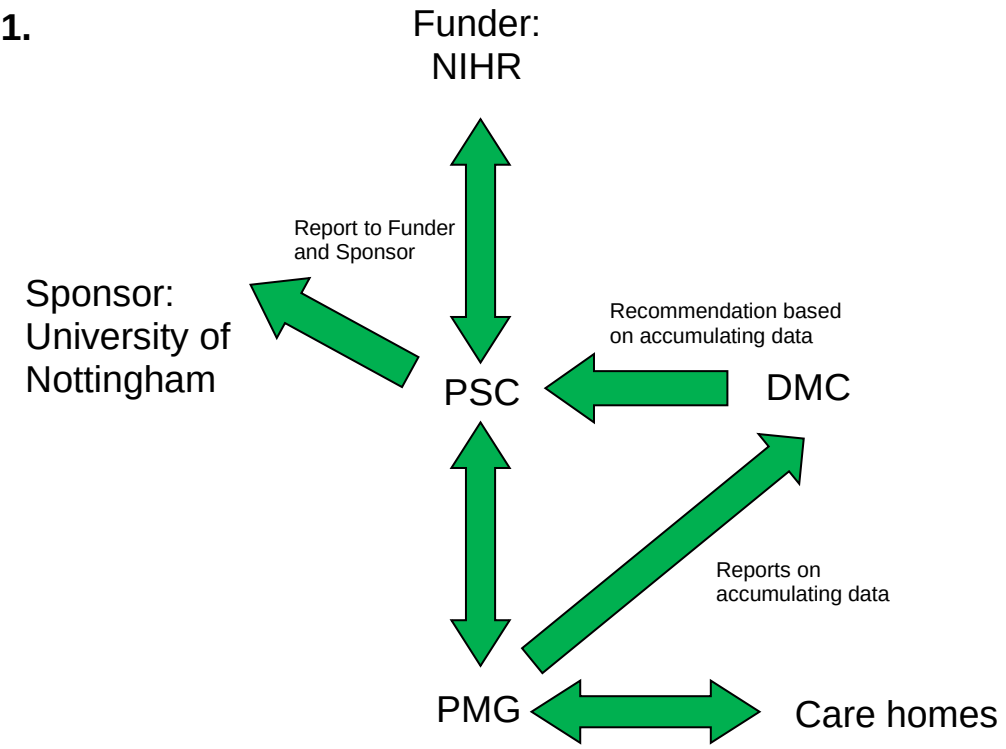
	The PSC will review progress, including adherence to the Protocol, participant safety, and considerations for new information of relevance to the research question and will receive and consider recommendations made by the independent Data Monitoring Committee (DMC).
Role of the PSC Chair.	The Chair of the PSC is directly answerable to the relevant NIHR programme, as Funder. The Chair's responsibilities include: • Liaising with the CI to arrange a meeting to finalise the Protocol and to set up a schedule of meetings to align with the project plan. • Establishing clear reporting lines to the Funder, Sponsor, etc. • Being familiar with relevant guidance documents and with the role of the DMC if appropriate. • Providing an independent, experienced opinion if conflicts arise between the needs of the research team, the Funder, the Sponsor, the participating organisations and/or any other agencies. • Leading the PSC to provide regular, impartial oversight of the study, especially to identify and pre-empt problems. • Ensuring that changes to the Protocol are debated and endorsed by the PSC; letters of endorsement should be made available to the project team when requesting approval from the Funder and Sponsor for matters such as changes to Protocol. • Being available to provide independent advice as required, not just when PSC meetings are scheduled. • Commenting on any extension requests and, where appropriate, providing a letter to the Funder commenting on whether the extension request is supported or otherwise by the independent members of the PSC. • Commenting in detail (when appropriate) regarding the continuation, extension or termination of the project. NB: The PSC Chair does not need to be a content expert himself but needs to ensure that sufficient content expertise is available for the group to perform its oversight function effectively.
Responsibilities of the PSC.	The responsibilities of the PSC include the following: • provide expert oversight of the study and each of the randomised comparisons • review and approve the platform Master Protocol • maintain confidentiality of all trial information provided to them that is not already in the public domain • monitor recruitment against target and encourage the PMG to develop strategies to deal with any recruitment problems • review regular progress reports of the trial from NCTU (sent on behalf of the PMG) • receive letters of feedback from the Chair of the DMC and consider their recommendations

	• make decisions as to the continuation of each comparison or other adaptation within the platform study • assess the impact and relevance of any accumulating external evidence • monitor the completeness and quality of data collection, and comment on strategies from the PMG to encourage high quality completion • monitor follow-up/retention rates and review strategies from the PMG to deal with problems • review any substantial amendments to the Protocol, where appropriate (e.g. fundamental change in design of the study, addition of new comparison, etc.) and provide advice to the Sponsor and Funder regarding approvals of such amendments • approve any proposals by the PMG concerning any change to the design of the trial, including additional sub-studies • review and approve the Statistical Analysis Plan • comment on the publication policy • oversee the timely reporting of trial results • review/comment on the manuscript reporting the trial results for each of the randomised comparisons • consider external or early internal requests for release of data or subsets of data or samples including clinical data and stored biological samples
3. Before or early in the platform	
Whether the PSC will have input into the Protocol.	All PSC members will have had an opportunity to review the Master Protocol before agreeing to join the Committee and, where appropriate, have passed comments to the CI. The Master Protocol has undergone review by the Funder and Sponsor, and the favourable opinion of a Research Ethics Committee will be in place prior to commencement of recruitment. PSC members should be constructively critical of the on-going platform, but also supportive of the aims and methods.
Will the PSC meet before the start of the platform?	The PSC will usually meet before the platform starts or early in the course of the study to discuss the Master Protocol, the comparison(s), and future meetings. Where a meeting is not possible prior to the establishment of the platform, PSC members will be given an opportunity to review the Master Protocol prior to recruitment commencing.
Any specific regulatory issues.	The PSC is aware that this platform is established to evaluate Clinical Trials of Investigational Medicinal Products (CTIMPs) and requires a Clinical Trials Authorisation from the Medicines and Healthcare products Regulatory Agency and is governed by UK legislation.

Any other issues specific to the intervention under study.	None.
Whether members of the PSC will have a contract.	PSC members will be asked to sign a contract and formally confirm their agreement (1) to be a member of the PSC and (2) with the contents of this Charter. Any potential competing interests should be declared at the same time. Members should complete and return the form at the end of this charter to confirm their agreement (Annexe 3). Any observers (attendees who are not members) will be asked to sign a confidentiality agreement following agreement by the PSC Chair for their attendance (Annexe 4).
4. Composition	
Membership and size of the PSC	This PSC is larger than usual to take into account the specific circumstances, urgency and frequency of meetings, due to the pandemic. The majority of members of the PSC, including the Chair, should be independent (i.e. are not involved with the platform in any other way and will not have competing interests that could impact on the randomised comparisons). Non-independent members will also be part of the PSC but cannot comprise more than 25% of membership. Observers are not formal members of the PSC but may be invited to provide expert input or to represent the funding and Sponsorship bodies involved; other observers will be at the discretion of the PSC. The members of the PSC are detailed in Annexe 1. Any competing interests, both current and potential, should be declared on the Annexe 3 form returned by the PSC members to the NCTU. Attendance at PSC meetings by non-members is at the discretion of the Chair and should be agreed in advance of the meeting.
The Chair (and Vice-Chair), how they are chosen and their role.	The Chair and members of the PSC were nominated by the investigators. The funding body (NIHR) subsequently approved the membership. The Chair has previous experience of serving on trial committees and experience of chairing meetings and should be able to facilitate and summarise discussions. A Vice-Chair should be appointed prior to, or at the first meeting.
The responsibilities of the Facilitator.	The Facilitator will be responsible for arranging meetings of the PSC, coordinating reports, producing and circulating minutes and action points. The Facilitator will be the central point for all PSC communications between the PSC and other bodies, will be copied into all correspondence between PSC members and will be kept aware of study issues as they arise.
The responsibilities of the trials unit team.	NCTU will produce a short report on trial progress prior to each meeting. The structure of this report will be agreed with the PSC at their first meeting and amended as necessary.
The responsibilities of the CI and other members of the PMG.	The CI (or their deputy or a nominated representative if the CI is unable to attend) is an important member of the PSC and no major decisions should be made without their involvement.

The responsibilities of the observers.	Additional observers may be in attendance through (parts of) the PSC meetings in order to provide input on behalf of NCTU, or the Sponsor/Funder or to provide specific relevant expertise.
5. Relationships	
Relationships with CI, other trial committees (e.g. PMG and DMC), Sponsor/Funder, regulatory bodies.	The responsibilities of each trial committee are detailed in the Protocol and in the respective Charters. The relationships between these groups are summarised in Figure 1.

Figure 1.



Advisory and executive bodies.	The PSC is the executive body and is delegated the roles and responsibilities in Section 2 by the Sponsor. All substantial issues regarding the platform must go to the PSC for consideration. The DMC is advisory to the PSC.
Payments to PSC members	Standard travel and subsistence costs will be paid to members of the PSC. No other payments or rewards will be given to professional members. Lay members will be paid expenses, subsistence costs and for their time, both to review documents and prepare for the meetings and to attend meetings, at standard INVOLVE guideline rates.
The need for PSC members to disclose information about any real or potential competing interests.	Any competing interests, real or potential, should be disclosed. These are not restricted to financial matters – involvement in other trials or intellectual investment could be relevant. Although members may well be able to act objectively despite such connections, complete disclosure enhances credibility. Competing interests of PSC members should be recorded on their PSC Charter signature page (Annexe 3) and a standard item on the agenda will address any emerging competing interests.
6. Organisation of PSC meetings	
Expected frequency of PSC meetings.	The exact frequency of meetings will depend upon the stage and progress of the individual comparisons, a minimum of 3–4 times a year, more often as appropriate. Combined meetings for multiple comparisons will take place, whenever possible. Major study issues may need to be dealt with between meetings, by videoconference ideally, or by email. PSC members should be prepared for such instances.
Attendance of PSC members at meetings	It is anticipated that most meetings will be virtual, at least for the foreseeable future. Every effort will be made to ensure that all members can attend. The Facilitator will arrange dates that enable this. One of the Co-CIs is expected to attend all meetings. If, at short notice, any PSC members cannot attend then the PSC may still meet if quorate (See Section 8). If the PSC is considering a major action after such a meeting the PSC Chair should communicate with the absent members, including the Co-CIs, as soon after the meeting as possible to check they agree. If they do not, a further tele/videoconference should be arranged with the full PSC.
How PSC meetings will be organised?	PSC meetings will be organised by the Facilitator (a member of the of the platform trial management team), in conjunction with the Chair of the PSC. Where possible they should be timed to be shortly after each DMC meeting. Notes will be taken by the Facilitator (or another member of the NCTU) for circulation to the PMG and Funder. If confidential or sensitive information, or information with the potential to unblind non-independent members is discussed, the Chair

	will ordinarily ask members to leave whilst such information is discussed.
Can PSC members who cannot attend the meeting provide input?	PSC members who will not be able to attend the meeting may pass comments regarding the PSC report (circulated prior to the meeting) to the PSC Chair, the CI, their deputy or a nominated representative, or a member of the PMG for consideration during the discussions.
What happens to independent members who do not attend meetings?	If an independent member does not attend a meeting or provide comments when requested between meetings, it should be ensured that the independent member is available for the next meeting. If an independent member does not attend the next meeting or provide comments when next requested, they should be asked if they wish to remain part of the PSC. If an independent member does not attend a third meeting, strong consideration should be given to replacing this member.
Absence of Chair	Should the Chair be unexpectedly unavailable to attend a meeting, the Vice Chair (as appointed at the first meeting) should act as Chair. The meeting should only take place if the PSC remains quorate (defined in section 8). Should both the Chair and Vice Chair be unavailable, an alternative date should be sought where possible.
7. Platform documentation and procedures to ensure confidentiality and appropriate communication	
Intended content of material to be considered during meetings.	A PSC report will be prepared by the PMG following a standard template. This will report on accrual and any matters affecting the platform. Additionally, the material to be considered during the meeting may include a report/recommendations from the DMC, requests from the PMG or draft publications. No trial outcome measure data will be presented by allocation unless explicitly authorised by the DMC. Where relevant, accrual, compliance with follow-up and adherence to treatment may be presented by care home.
Whether reports to the PSC will be available before the meeting or only at/during the meeting.	The PSC will receive the report at least 48 hours and preferably at least 1 week before any meetings. Different procedures may apply to interim teleconference meetings.
Who will see the accumulating data and interim analysis?	The accumulating trial data by arm and any interim analyses will be confidential. These will be viewed only by the DMC. The PSC will not routinely have access to these interim reports. The DMC will make recommendations to the PSC based on the interim data.
Who will be responsible for identifying and circulating external evidence (e.g. from other trials/ systematic reviews)?	Identification and circulation of external evidence (e.g. from other trials, platforms and systematic reviews) is not the responsibility of the PSC members. This is the responsibility of the PMG.
What will happen to the papers after the meeting?	All documentation should be considered confidential. The PSC members will store their copies of the meeting papers securely after each meeting so they can check future reports against them. At the end of the study PSC members will destroy all papers. A central record of all

	minutes, reports and correspondence by the PSC will be filed in the eTMF.
8. Decision making	
What decisions will be open to the PSC?	Based on recommendations from the DMC, and other issues that may arise, possible decisions include:- • No action needed, the comparison under evaluation continues as planned • Early stopping due, for example, to clear benefit or harm from a treatment, futility or external evidence (this should generally involve a recommendation from the DMC to unblind the PSC to these data) • Temporarily pausing recruitment allowing further follow-up data to be received • Stopping one or more comparison(s) in a multi-arm trial • Stopping recruitment within a comparison i.e. subgroup (this should generally involve a recommendation from the DMC to unblind the PSC to these data) • Modifying target sample size, based on any changes to the assumptions underlying the original trial sample size calculation (but not on any emerging differences) • Sanctioning and/or proposing Protocol changes The rights, safety and well-being of the participants are the most important considerations and should prevail over the interests of science and society. Based on other factors, possible decisions include the decisions above and:- • Approving proposed Protocol amendments for new comparisons • Approving requests for early release of (subsets of) data • Approving presentation of comparative results during evaluation or soon after the end of follow-up • Approval of new care homes or strategies to improve follow-up
The role of formal statistical methods.	Formal statistical methods may have been considered by the DMC in making their recommendations to the PSC. These methods are usually used as guidelines rather than absolute rules. This is because formal statistical methods generally only consider one dimension of the study and the DSMC will consider all dimensions when making their recommendations. Where appropriate, the DMC will record reasons for disregarding a stopping guideline in the notes of their meetings and may choose to also note this in their report to the PSC, if necessary.

How will decisions or recommendations be reached within the PSC?	Every effort should be made to achieve consensus. The role of the Chair is to summarise discussions and encourage consensus; therefore, it is usually best for the Chair to give their own opinion last. Implications (e.g. ethical, statistical, practical, financial and consideration as to whether a definitive answer has been reached) for the trial will be considered before any decision/recommendation is made.
When is the PSC quorate for decision-making?	At least 66% of independent members of the PSC should be present including the Chair or Vice-Chair, plus a representative of the PMG (or other appropriate NCTU representative). The Funder's guidelines for quoracy will always be adhered to, which state the minimum quoracy for the PSC meeting to conduct business is 66% of the appointed membership. If major action is to be considered, the CI (or their deputy or a nominated representative if the CI is unable to attend) and a representative of the PMG (or other appropriate NCTU representative) should be present. If the Chair is unable to attend, they should confirm in writing their agreement with action as soon as possible after the meeting, or else call a further meeting.
Specific issues relating to the trial design that might influence the proceedings.	Given that the sample size parameters were estimated using data from the first COVID-19 wave, it is anticipated that the unblinded trial statisticians will conduct a review of the parameters during the trial, with a view to sample size re-estimation, for review by the DMC. In addition, given the nature and urgency of the pandemic in care homes, it is anticipated that the trial committees (PSC, DMC and PMG) will meet regularly, the frequency dictated by the recruitment rate.
9. Reporting	
To whom will the PSC report their recommendations/decisions, and in what form?	The PSC will report their decisions (via the Facilitator) within 48 hours to the CIs who will be responsible for implementing any actions resulting, together with the PMG. The PSC may also provide feedback to the DMC and, where appropriate, to the Sponsor/Funder. Copies of communications must pass through the Facilitator using a secure mailbox.
Will minutes of the meeting be made and, if so, by whom and where will they be kept?	Notes of key points and actions will be made by the Facilitator. This will include details of whether potential competing interests have changed for any attendees since the previous meeting. The draft minutes will be initially circulated for comment to those PSC members who were present at the meeting. The PSC Chair will sign off the final version of minutes or notes.
What will be done if there is disagreement between the PSC and the other study committees?	The PSC is the oversight body for the platform. However, the PSC should have good reason before deciding not to accept requests from the PMG or recommendations from the DMC. If there are serious problems or concerns with the PSC decision following a DMC recommendation, a joint meeting of the PSC and DMC should be held, if possible face-to-face. The information to be shown would depend upon the action proposed and each committee's concerns. Depending on the reason for

	the disagreement, confidential data by trial allocation may have to be revealed to all or some of those attending such a meeting: this would be minimised where possible. The meeting would be chaired by a senior member of the Sponsor or an external expert who is not directly involved with the trial, and agreeable to the CIs, PSC Chair and DMC Chair.
10. After the trial	
Publication of results.	The PSC will oversee the timely analysis, writing up and publication of the main comparison results. The independent members of the PSC will have the opportunity to review the proposed main publications of trial data prior to submission, and on conference abstracts and presentations during the study. This review may be concurrent to that of the investigators and the DMC.
What information about the PSC will be included in published trial reports?	PSC members will be named, and their affiliations listed in the main report, unless they explicitly request otherwise.
Are there any constraints on PSC members divulging information about their deliberations after the main comparison(s) has/have been published?	Unless permission is agreed with the DMC, the PSC will not discuss confidential information to what they have been privy to as a result of their involvement in each comparison study until 12 months after the primary study results have been published for each comparison.

Figures and Appendices

Annexe 1 - Committee membership

Platform Steering Committee (PSC) member	Membership status
Name, Title, Institute	
Prof Alistair Burns, Prof of Old Age Psychiatry, University of Manchester	Chair, Independent member
Prof Shaun Treweek, Professor of Health Services Research, University of Aberdeen	Independent member
Prof James Wason, Professor of Biostatistics, Newcastle University	Independent member
Prof Anne Forster, Professor of Stroke Rehabilitation, University of Leeds	Independent member
Prof Azhar Farooqi, General Practitioner, East Leicester Medical Practice	Independent member
Prof Martin Vernon, Consultant Geriatrician, Manchester University NHS Foundation Trust	Independent member
Mr Peter Pratt, Pharmacist, NHS England/NHS Improvement	Independent member
Ms Vic Rayner, Executive Director, National Care Forum	Independent member
Ms Linda Hamlin, Patient and Public Involvement representative	Independent member
Prof Philip Bath, Prof of Stroke Medicine, University of Nottingham	Non-independent member
Prof Adam Gordon, Professor of the Care of Older People, University of Nottingham	Non-independent member
Prof Alan Montgomery, Professor of Medical Statistics, University of Nottingham	Observer
Prof Ed Juszczak, Professor of Clinical Trials & Statistics in Medicine, University of Nottingham	Observer
Dr Christopher Partlett, blinded trial statistician, University of Nottingham	Observer
Ms Lucy Bradshaw, blinded trial statistician, University of Nottingham	Observer
Dr Caroline Rick, Associate Professor of Clinical Trials, University of Nottingham	Observer

Data Monitoring Committee (DMC) member	Membership status
Name, Title, Institute	
Prof Kennedy Lees, Emeritus Professor of Cerebrovascular Disease, University of Glasgow	Chair, Independent member
Prof Tim Peters, Professor of Primary Care Health Services Research, University of Bristol	Independent member
Dr Ben Carter, Senior Lecturer in Biostatistics, King's College London	Independent member
Prof Finbarr Martin, Emeritus Professor of Medical Gerontology, King's College London	Independent member
Dr Eileen Burns, Consultant in Care of the Elderly, Leeds Teaching Hospitals NHS Trust	Independent member
Prof Philip Bath, Prof of Stroke Medicine, University of Nottingham	Non-independent member (open session only)
Prof Adam Gordon, Professor of the Care of Older People, University of Nottingham	Non-independent member (open session only)
Dr Reuben Ogollah, unblinded trial statistician, University of Nottingham	Observer
Mr Martin Law, unblinded trial statistician, University of Cambridge	Observer
Prof Alan Montgomery, Professor of Medical Statistics, University of Nottingham	Observer (open session only)
Prof Thomas Jaki, Professor of Statistics, University of Cambridge	Observer (open session only)
Dr Christopher Partlett, blinded trial statistician, University of Nottingham	Observer (open session only)
Ms Lucy Bradshaw, blinded trial statistician, University of Nottingham	Observer (open session only)
Dr Caroline Rick, Associate Professor of Clinical Trials, University of Nottingham	Observer (open session only)

Annexe 2 - Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
DMC	Data Monitoring Committee
NCTU	Nottingham Clinical Trials Unit
NIHR	National Institute for Health Research
PMG	Platform Management Group
PSC	Platform Steering Committee

Table 1 - Potential competing interests for independent members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Ongoing advisory role to a company providing drugs to the trial
- Frequent speaking engagements on behalf of the intervention
- Career tied up in a product or technique assessed by trial
- Hands-on participation in the trial
- Involvement in the running of the trial
- Emotional involvement in the trial
- Intellectual conflict e.g. strong prior belief in the trial's experimental arm
- Involvement in regulatory issues relevant to the trial procedures
- Involvement in the writing up of the main trial results in the form of authorship

The definition of independent is as follows:

- Not part of the same institution as any of the applicants or members of the project team
- Not part of the same institution that is acting as a recruitment or investigative centre
- Not related to any of the applicants or members of the project team
- For the Chair only – not an applicant on a rival proposal

Table 2 - Potential competing interests for non-independent members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Ongoing advisory role to a company providing drugs to the trial
- Frequent speaking engagements on behalf of the intervention
- Intellectual conflict e.g. strong prior belief in the trial's experimental arm
- Involvement in regulatory issues relevant to the trial procedures

Annexe 3 - Agreement and competing interests form for PSC members

(please initial box)

I have read and understood the PROTECT PSC Charter Version 1.0 08-Jun-2021 ☐

I agree to join the PSC for this trial ☐

I agree to treat all sensitive trial data and discussions confidentially ☐

The avoidance of any perception that independent members of a PSC may be biased in some fashion is important for the credibility of the decisions made by the PSC and for the integrity of the trial.

Potential competing interests should be disclosed via the NCTU. In many cases simple disclosure up front should be enough. Otherwise, the (potential) independent PSC member should remove the conflict or stop participating in the PSC. **Table 1** lists potential competing interests for independent members. **Table 2** lists potential competing interests for non-independent members.

(please initial box)

No, I have no potential competing interests to declare ☐

Yes, I have potential competing interests to declare (please detail below) ☐

Please provide details of any potential competing interests:

_____

_____

_____

Name:_____

Signed:_____ Date:_____

Annexe 4 - Agreement and confidentiality agreement for observers

	(please initial box)
I have read and understood the PROTECT PSC Charter Version 1.0 dated 08-Jun-2021	
I agree to attend the Platform Steering Committee meeting as an observer	
I agree to treat as confidential any sensitive information gained during this meeting unless explicitly permitted	

Name:_____

Signed:_____ Date:_____

Annexe 5 - Summary of changes from previous version of PSC Charter

Version Number	Details/reason for change	Authorised by (print name)	Role	Signature	Date
1.0	This is version 1.0 of the PSC charter for this platform. There are no changes to be reported.				