



Centre for Tropical Medicine and Global Health

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Cambridge East REC
E-submission

15 October 2021

Dear Dr Lamont

Trial: Randomised evaluation of Covid-19 therapy (RECOVERY)
EudraCT: 2020-001113-21
IRAS: 281712
REC ref: 20/EE/0101

Please find enclosed an application for authorisation of a substantial amendment for the above trial. We are applying for this amendment following the critical finding during our recent MHRA inspection around informed consent. As you know, it was identified that participants whose consent was given by a legal representative were not always asked for their permission if they regained capacity. As part of our response to this finding we wish to:

- i. Amend the protocol so that such participants do not have to provide personal consent when they gain capacity, but instead the site must inform them of their participation and their rights and how to exercise them. We also wish to clarify in the protocol who can act as an independent legal representative.
- ii. We wish to write to all surviving participants to inform them about trial progress and results, and also provide information about their rights and how to exercise them for any participants who did not give personal consent. We therefore submit a newsletter that we intend to send. We have submitted the main text, which will be amended slightly if participants have received an earlier newsletter and depending on whether it is being sent via NHS Digital or Scotland's Health Informatics Centre in Dundee.
- iii. Update the PIS/ICF so that the legal representative section includes a statement to confirm their independence from the trial.

We also enclose the minutes of our public advisory group meeting which discussed whether we should contact relatives of deceased participants. As you will see, the group was not supportive of this.

We are planning to review a sample of consent forms at all our sites. We will select a 10% random sample across all sites. We will adjust the selection so that sites with very large (>400) numbers of participants do not get overburdened, and smaller sites (with 21-200 participants) do a higher proportion to compensate, so that it remains a random 10% sample of the entire trial cohort to date. (Sites with fewer than 21 participants would review all their consent forms and sites with 201-400 consent forms will review 10%.)

We also wish to re-order the outcomes for the early phase assessment of dimethyl fumarate. Since the trial began the duration of admission has shortened considerably, such that an

assessment of S/F₉₄ on day 5 is not possible for a substantial proportion of participants as they have been discharged before. This makes this an unsuitable primary outcome so we wish to use the WHO ordinal score instead (which is not affected in the same way). This will require an increase in sample size to 700 participants.

We would like to request that this amendment is **category A**, as per the amendment tool.

I believe all the necessary documentation required for this submission is attached and look forward to hearing the outcome.

Please let us know if you require any further information.

Yours faithfully



Professor Sir Peter W. Horby

BSc MSc MBBS FRCP FFPH PhD

Chief Investigator, RECOVERY Trial

Professor of Emerging Infectious Diseases and Global Health

Attached files:

1. RECOVERY Protocol V18.0 2021-10-14 (tracked and clean)
2. RECOVERY PIS/ICF (adult) V16.0 2021-10-14 (tracked and clean)
3. RECOVERY PIS/ICF (child) V10.0 2021-10-14
4. RECOVERY second participant newsletter V1.0 2021-10-14
5. Minutes of RECOVERY PAG 2021-09-30
6. Letter confirming sponsor approval
7. Amendment Tool for SA20