



Centre for Tropical Medicine and Global Health

Nuffield Department of Medicine
Nuffield Department of Medicine Research Building
University of Oxford
Old Road Campus, Roosevelt Drive
Headington
OXFORD
OX3 7FZ

Cambridge East REC
E-submission

14 April 2020

Dear Sir or Madam

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 an expedited authorisation of a substantial amendment for the above trial. The reasons for the substantial amendment are details in the Notice of Substantial Amendment, but in summary include adding a second randomization for participants who deteriorate after the main randomization and fulfil physiological (require oxygen or have oxygen saturations $<92\%$ on air) and inflammatory (CRP ≥ 75 mg/L) criteria. This randomization is between tocilizumab (IL6 receptor antagonist) and control.

We have not proposed exclusion criteria around pregnancy because there is no evidence that tocilizumab is associated with an excess of adverse pregnancy outcomes. We have added text to the Participant Information Sheet to recommend that participants do not attempt to get pregnant within 3 months of their COVID-19 admission, as discussed with MHRA.

We have also not proposed exclusion criteria around abnormal liver function tests or low platelet counts, but have included advice in the protocol that such tests are monitoring according to clinical need.

The protocol and Legal Representative Information Sheet also include the text that was requested after the committee's review of our previous substantial amendment.

We would like to request that this amendment is a **category C** amendment as we do not have 35 days to wait for trusts to respond before we implement it. As we will be able to ensure the supply of tocilizumab we do not think there are any local requirements that would need to be considered.

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.





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Yours faithfully

A handwritten signature in blue ink, appearing to read 'P. Horby', with a long horizontal flourish underneath.

Professor Peter W. Horby

BSc MSc MBBS FRCP FFPH PhD

Chief Investigator, RECOVERY Trial

Professor of Emerging Infectious Diseases and Global Health

Attached files:

1. Cover letter
2. Notification of Amendment form
3. RECOVERY Protocol V4.0 2020-04-14 (clean and tracked)
4. RECOVERY PIS+ICF V4.0 2020-04-14 (clean and tracked)
5. Tocilizumab Summary of Product Characteristics
6. Updated Legal Representative Information Leaflet V1.1 2020-04-08 (clean and tracked)
7. Sponsor Approval of Amendment

