NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES
Primary Care Clinical Trials Unit

PRINCIPLE: Platform Randomised trIal of treatmeNts in the Community for epIdemic and Pandemic iLlnEsses

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Date: 08 March 2022
REC Substantial Amendment 21
IRAS ID: 281958

Dear REC members,

Subject: Substantial Amendment 21 for the PRINCIPLE Trial in relation to COVID-19

Please find attached the amendment submission package for the trial entitled: Platform Randomised trIal of treatmeNts in the Community for epIdemic and Pandemic iLlnEsses (PRINCIPLE). The main amendments are described and justified below.

Certain documents have been updated or created for the trial.

Summary of key proposed changes to the PRINCIPLE Trial: Amendment 21:

The dose regimen and tablet strength of Favipiravir has been changed with the second batch of IMP, which has been provided free of charge by IPS Pharma, in exchange for access to data specific to this arm of the trial before publication. Therefore a new Investigator Brochure has been provided and corresponding documents have been modified to reflect this – the length of the treatment course is unchanged, however the number of tablets to be taken is reduced by half overall. Patient facing documents have been updated accordingly in line with this change.

The study end date has also been extended to September 2023 to allow sufficient time to complete the study, where optional twelve month follow-up is carried out for some participants, after the initial 28 day participation in the trial (LPLV). Updates to the current protocol to include COVID-19 vaccination status including number of vaccinations the participant has received. All reference to Public Health England has now been amended to UK Health Security Agency (UKHSA) in line with the change of name of body. The chair of the Trial Steering Committee (TSC) has also been changed and a new member join, and a replacement member has joined the Data Safety & Monitoring Committee (DMSC).

An IMP return letter has also been created to provide instructions on how participants should return their unused IMP if they decide to withdraw from taking the study medication. This will be enclosed when sending pre-paid delivery envelopes to participants whom we become aware have withdrawn.

Please contact us if you have any questions.

Yours sincerely,

Jared Robinson
On behalf of Professor Christopher Butler

Table 1: List of documentation submitted to REC (new documents highlighted in blue)

Document	Version	Date
Protocol (clean and tracked versions)	13.0	14-Jan-2022
PIS (clean and tracked versions)	8.0	17-Jan-2022
PIS Appendices (clean and tracked version)	4.0	17-Jan-2022
IMP Return Letter	1.0	16-Dec-2021
Favipiravir Participant Card (clean and tracked changes)	2.0	24-Jan-2022
Favipiravir IMP Label (clean and tracked changes)	2.0	02-Feb-2022
Favipiravir Investigator Brochure	3.0	03-Feb-2022
Privacy Notice (clean and tracked changes)	2.0	03-Feb-2022
Amendment Tool	1.6	06-Dec-2021