SECTION 1: REMAP-CAP ANTIVIRAL DOMAIN INTERVENTIONS

This domain aims to determine the effectiveness of different antiviral strategies for patients with severe CAP who have suspected or confirmed influenza virus infection. In this domain, patients are randomised to receive:

- No antiviral agents, including Oseltamivir (no placebo)
- 5 days of Oseltamivir
- 10 days of Oseltamivir

Your site may be participating in all three interventions in this domain or only two, depending on local practice. The allocated intervention should be commenced immediately following allocation reveal at the time of randomisation.

SECTION 2: DOSING GUIDE

Dosing of Oseltamivir is determined by the treating clinician and the following is provided only as a guide.

- The standard dose of Oseltamivir for adult patients is 75 mg enterally, twice per day.
- No dosage adjustment is suggested for body mass index, pregnancy, or for extracorporeal membrane oxygenation
- Dose adjustment for renal dysfunction will be as per local guidelines. If no local guideline exists, recommendations for dosing based on estimated Glomerular Filtration Rate (eGFR) are outlined in the Antiviral Domain-Specific Appendix.

NO ANTIVIRAL AGENTS INTERVENTION

Patients allocated to the No antiviral agents intervention should not receive any Oseltamivir or other antiviral agents active against influenza, while the patient remains in hospital up until study day 28. If Oseltamivir has been administered or prescribed prior to randomisation, it should be discontinued immediately.

Administration of antiviral agents after ICU discharge will not be considered to be a protocol deviation.

5-DAY OSELTAMIVIR INTERVENTION

Patients allocated to the 5-day course of Oseltamivir are to be prescribed a five-day course commencing immediately after randomisation (do not include a dose administered before randomisation). This course will be continued until at least the end of study day 5, and no longer than the end of study day 6 (i.e. 10 doses with BD administration).

It will be considered a protocol deviation if during the 5-day course two or more doses of Oseltamivir are missed.

Administration of Oseltamivir after the end of study day 6 or another antiviral agent that is active against influenza at any time is not permitted and will be considered a protocol deviation.

For patients who are discharged from ICU before the end of the five-day course of Oseltamivir, it is the responsibility of ICU staff to prescribe Oseltamivir to complete the five-day course. However, it is not the responsibility of ICU medical or research staff to ensure continuation of the Oseltamivir after discharge from ICU. It is not a protocol deviation if the course of Oseltamivir is not completed after ICU discharge.

Oseltamivir is not required to be prescribed if discharged from hospital before the end of study day 5.
10-DAY OSELTAMIVIR INTERVENTION

Patients allocated to the 10-day course of Oseltamivir are to be prescribed a ten-day course commencing immediately after randomisation (do not include a dose administered before randomisation). This course will be continued until at least the end of study day 10, and no longer than the end of study day 11 (i.e. 20 doses with BD administration).

It will be considered a protocol deviation if during the 10-day course two or more doses of Oseltamivir are missed.

Administration of Oseltamivir after the end of study day 11 or another antiviral agent that is active against influenza at any time is not permitted and will be considered a protocol deviation.

For patients who are discharged from ICU before the end of the ten-day course of Oseltamivir, it is the responsibility of ICU staff to prescribe Oseltamivir to complete the ten-day course. However, it is not the responsibility of ICU medical or research staff to ensure continuation of the Oseltamivir after discharge from ICU. It is not a protocol deviation if the course of Oseltamivir is not completed after ICU discharge.

Oseltamivir is not required to be prescribed if discharged from hospital before the end of study day 10.

SECTION 3: DISCONTINUATION OF INTERVENTION

In patients with suspected influenza who are allocated to the 5- or 10-day course of Oseltamivir, but who subsequently test negative for influenza, treatment with Oseltamivir can be ceased. If the treating clinician believes that continued administration of Oseltamivir is clinically appropriate they should comply with the allocated course.

SECTION 4: CONCOMITANT CARE

No additional antiviral agents that are active against influenza should be administered to patients randomised into the Antiviral Domain while the patient remains in hospital up until study day 28.