

21 August 2020

Dear participating organisations,

Study title: STRESS-L - Study into the Reversal of Septic Shock with Landiolol (Beta Blockade)

REC reference: 17/EE/0368

IRAS Project ID: 213669

RE: STRESS-L restart recruitment

As of 18 March 2020, recruitment to STRESS-L has been halted in response to the ongoing COVID-19 pandemic. We are delighted to announce STRESS-L has now received sponsor approval to restart recruitment as of 21 August 2020. The STRESS-L trial team will contact each site individually to provide the greenlight to locally restart recruitment. Please **do not** restart screening or recruitment until you have received this greenlight.

As per HRA guidance (<https://www.hra.nhs.uk/covid-19-research/covid-19-guidance-sponsors-sites-and-researchers/#reopening>), an amendment to HRA and REC is not required to restart the trial, as a formal amendment was not required to halt recruitment to the trial. Further to this, the HRA have confirmed changes to documents as a result of COVID-19 are classified as non-substantial, category C amendments and **do not require HRA or MHRA approval**. These documents can be implemented at sites immediately.

These changes include updates to processes to allow for recruitment and monitoring to continue in a practical and safe way. **Blood samples will not be taken for suspected or confirmed COVID-19 patients** and **consent can be sought verbally** from patients or personal legal representatives if there are concerns of viral transmission due to COVID-19. Further to this, **monitoring will take place remotely** due to restrictions with on-site monitoring in hospitals currently. The next page provides a summary of all updated documented due to the ongoing COVID-19 pandemic. Please note, the following documents have also been changed in response to the previous protocol amendment (v5.0) and updated IMP temperature reporting procedure: IMP manual, Screening Log, CRF and CRF completion guidelines.

If you have any further questions please do not hesitate to get in touch.

Kind regards,



Dr Tony Whitehouse
Chief Investigator



Emma Skilton
Trial Manager

Name	Version number	Document Date	Submission Date	REC Approval Date	Reason for change	Summary of changes made
Protocol	6.0	26/06/2020	N/A	N/A	Updates to processes in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> Verbal consent can be sought from a relative or patient due to visitation restrictions and risk of infection transmission. A witness must be present for discussion and countersign consent form. Blood samples will not be taken for suspected or confirmed COVID-19 patients. Monitoring will take place remotely during this time.
Patient Information Sheet	5.0	06/08/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> Verbal consent may be sought if there are concerns regarding risk of infection transmission due to the COVID-19 pandemic. If patient has suspected or confirmed COVID-19, blood samples will not be taken to minimise risk of viral transmission.
Short Patient Information Sheet	4.0	20/08/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> If patient has suspected or confirmed COVID-19, blood samples will not be taken to minimise risk of viral transmission.
Legal Representative Information Sheet	5.0	06/08/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> Verbal consent can be sought from a relative if there are concerns regarding risk of infection transmission due to the COVID-19 pandemic. If patient has suspected or confirmed COVID-19, blood samples will not be taken to minimise risk of viral transmission.
Consent Form	5.0	06/07/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> Addition of witness signature for verbal consent if there are concerns regarding risk

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						of infection transmission due to the COVID-19 pandemic.
Legal Representative Consent Form	5.0	26/06/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> • Addition of witness signature for verbal consent if there are concerns regarding risk of infection transmission due to the COVID-19 pandemic.
IMP Management Manual	5.0	17/08/2020	N/A	N/A	Additional stability data to support temperature excursions up to 25 degrees for a maximum of 1 week	<ul style="list-style-type: none"> • Updated information regarding identifying and reporting temperature excursions with new flow chart.
Lab Manual	3.0	06/07/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> • If patient has suspected or confirmed COVID-19, blood samples will not be taken to minimise risk of viral transmission.
Blood Sample Schedule Information	2.0	06/07/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> • Blood samples should not be taken for suspected or confirmed positive COVID-19 patients.
Screening Log	8.0	30/07/2020	N/A	N/A	Protocol amendment	<ul style="list-style-type: none"> • Changes to eligibility criteria
CRF Booklet	6.0	06/07/2020	N/A	N/A	Protocol amendment	<ul style="list-style-type: none"> • Inclusion and exclusion criteria updated on eligibility form in line with protocol amendment (v5.0, 17 December 2019).
Eligibility Form	4.0	06/07/2020	N/A	N/A	Protocol amendment	<ul style="list-style-type: none"> • Inclusion and exclusion criteria updated on eligibility form in line with protocol amendment (v5.0, 17 December 2019).
CRF Completion Guidelines	3.0	06/07/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> • Document positive COVID-19 infections in Microbiology Specimens CRF
Frequently Asked Questions	4.0	06/07/2020	N/A	N/A	Amended following v5.0 Protocol Amendment and in	<ul style="list-style-type: none"> • Clarification regarding protocol v5.0 eligibility criteria

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					response to COVID-19 pandemic	<ul style="list-style-type: none"> Blood samples will not be taken for suspected or confirmed COVID-19 patients.
Trial Participant Completion Checklist	3.0	06/07/2020	N/A	N/A	Updated in response to the ongoing COVID-19 pandemic	<ul style="list-style-type: none"> Blood samples will not be taken for suspected or confirmed COVID-19 patients.