TRIAL OFFICE USE: | *Received Date:* | *Initial:* | *Checked Date:* | *Initial:* | *SAE Reference Number:*

Serious Adverse Event Form— Initial

STRESS-L

Participant Trial Number: ☐☐☐☐☐ **Participant Initials:** ☐☐☐ **Date of Birth:** d d – m o n – y y y y **Gender:** F M

Site Number: ☐☐ **Site Name:**

Please email immediately to the STRESS-L Coordinating Centre at wctuqa@warwick.ac.uk

A. EVENT TYPE: *(please confirm 'Yes' or 'No' for each category)*

	No	Yes
1. Death	☐	☐
2. Life-threatening	☐	☐
3. Hospitalisation or prolongation of existing hospitalisation	☐	☐
4. Persistent or significant disability/incapacity	☐	☐
5. Congenital anomaly/birth defect	☐	☐
6. Other reason *(please specify below)*	☐	☐

B. EVENT DETAILS:

1. Date event deemed serious: d d – m o n – y y y y

2. Time event deemed serious: ☐☐ : ☐☐ *24 hour clock*

3. Date site aware of this event: d d – m o n – y y y y

4. Details of Event:

I. Please include all **relevant** details of the event including associated symptoms, any tests performed and associated results:

(Please continue on SAE Continuation Form as necessary)

II. Please add details of any **relevant** medical history, concomitant medication and associated dates of administration:

(Please continue on SAE Continuation Form as necessary)

C. SEVERITY / TOXICITY ASSESSMENT:

1. Please refer to pages 3 & 5 of this form for guidance on completion of this section:

System Organ Class (SOC)	**Adverse event** (CTCAE term v.4.0) *(Exactly as stated in the CTCAE document)*	**CTCAE Grade:**

2. Severity Assessment: ☐ Mild ☐ Moderate ☐ Severe ☐ Fatal/Life threatening

TRIAL OFFICE USE:

Received Date:	*Initial:*	*Checked Date:*	*Initial:*	*SAE Reference Number:*

D. TRIAL TREATMENT & CAUSALITY ASSESSMENT:

1. Treatment Allocation:
(please select one)

Landiolol Plus Standard Treatment: ☐

Standard Treatment Only: ☐

2. Causal Relationship:
Could this event have been caused by the trial medication? Causal Relationship **must** be assessed by a delegated medically qualified an investigator

☐ **Definitely** ☐ **Probably** ☐ **Possibly** ☐ **Unlikely** ☐ **Unrelated**

3. Causality: detail below all possible and suspected causes

E. IMP DETAILS:

Landiolol Hydrochloride 300mg →

1. Start date and time of IMP administration: → d d - m o n - y y y y : *24 hour clock*

2. Dose: ☐ *mcg/kg/min* →

3. Total Duration of IMP administration: ☐☐☐ *hours*

(For Trial Office use only)

4. Unexpected:
According to the info in the RSI/SmPC

☐ **No** ☐ **Yes**

F. ACTION TAKEN:

☐ **None** ☐ **Dose adjusted/ interrupted** ☐ **Trial treatment permanently discontinued** ☐ **Patient withdrawn** ☐ **Other**- please provide details →

(For Trial Office use only)

G. EVENT CLASSIFICATION:

1. Is the Event:

☐ **SAE -** Serious, not related to IMP

☐ **SAR -** Serious, and at least possibly related to IMP

☐ **SUSAR -** A SAR which is unexpected in nature, severity or frequency

H. OUTCOME OF EVENT:

1. Outcome of Event: Select one and provide details below.

☐ **Resolved** ☐ **Resolved with sequelae** ☐ **Ongoing-** Complete SAE Follow-up Form ☐ **Death-** Complete Notification of Death ☐ **Other-** please provide details

Details: If resolved, resolved with sequelae or death, provide a date and time

Reporting/ treating Clinician (print name): _____

(Please note: your name must be on the trial delegation log)

Signature: _____ **Date signed:** d d - m o n - y y y y

(By signing this you are confirming you have assessed causality)

Form completed by (print name): _____

Signature: _____ **Date signed:** d d - m o n - y y y y

TRIAL OFFICE USE:	*Received Date:*	*Initial:*	*Checked Date:*	*Initial:*	*SAE Reference Number:*

NOTES FOR GRADING OVERALL SEVERITY & TOXICITY

NCI Common Toxicity Criteria for Adverse Events (V4.0)

Symptoms in section 3 of this SAE form should be described and graded in accordance with the NCI Common Toxicity Criteria for Adverse Events v.4.0 (NCI CTCAE). The NCI CTCAE v4.0 can be found here http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf.
Symptoms should be recorded using the numbers linked to the System Organ Class (as listed below), the adverse event term within that class, and the accompanying grade (as listed in CTCAE v4.0).

System Organ Class (SOC)					
1.	Blood and lymphatic system disorders	10.	Immune System Disorders	19.	Psychiatric disorders
2.	Cardiac disorders	11.	Infections and infestations	20.	Renal and urinary disorders
3.	Congenital, familial and genetic disorders	12.	Injury, poisoning and procedural complications	21.	Reproductive system and breast disorders
4.	Ear and labyrinth disorders	13.	Investigations	22.	Respiratory, thoracic and mediastinal disorders
5.	Endocrine disorders	14.	Metabolism and nutrition disorders	23.	Skin and subcutaneous tissue disorders
6.	Eye disorders	15.	Musculoskeletal and connective tissue disorders	24.	Social circumstances
7.	Gastrointestinal disorders	16.	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	25.	Surgical and medical procedures
8.	General disorders and administration site conditions	17.	Nervous system disorders	26.	Vascular disorders
9.	Hepatobiliary disorders	18.	Pregnancy, puerperium and perinatal conditions		

Overall Severity

Mild: Does not interfere with patient's usual functioning

Moderate: Interferes to some extent with patient's usual functioning

Severe: Interferes significantly with patient's usual functioning

Fatal/Life threatening: Causes death or risk of death, organ damage or disability

NOTES FOR GRADING CAUSALITY

Unrelated: There is no evidence of any causal relationship

Unlikely: There is little evidence to suggest a causal relationship (e.g. because the event did not occur within a reasonable time after administration of the trial treatment). There is another reasonable explanation of the event (e.g. the patient's clinical condition, other concomitant medications).

Possibly: There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial treatment). However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant medications).

Probably: There is evidence to suggest a causal relationship and the influence of other factors is unlikely.

Definitely: There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.

TRIAL OFFICE USE:

Received Date:	*Initial:*	*Checked Date:*	*Initial:*	*SAE Reference Number:*

SAE EVALUATION FORM *(for Trial Office use only)*

Date adverse event information was passed to CI: d d – m o n – y y y y

Were further investigations requested by CI? **No** ☐ **Yes** ☐ → **Date further investigations carried out:** d d – m o n – y y y y

Details of investigations:

Date findings of further investigations passed to CI: d d – m o n – y y y y

Is the event related to the IMP? **No** ☐

Yes ☐

Is it Unexpected? **No** ☐

Yes ☐

Is it Fatal or Life Threatening? **No** ☐

Date report sent to MREC/MHRA/sponsor (within 15 days of sponsor first aware of event): d d – m o n – y y y y

Yes ☐

Date report sent to MREC/MHRA/sponsor (within 7 days of sponsor first aware of event): d d – m o n – y y y y

Chief Investigator to complete:

Confirm categorisation? **No** ☐ **Yes** ☐

If No state the reason and re-categorise:

Chief Investigators signature: _____ d d – m o n – y y y y

TRIAL OFFICE USE:	*Received Date:*	*Initial:*	*Checked Date:*	*Initial:*	*SAE Reference Number:*

Completion Guidelines for CRF STRESS-L Serious Adverse Event Form

The SAE Continuation Sheet must be signed and dated by both the person who has responsibility for completing the SAE Form and the

Date of Birth:	Please use the following formats for dates: 06/Jun/1956.
Severity / toxicity assessment:	Use the CTCAE booklet version 4.0 and guidance on page 3 to complete this section. The main diagnosis for the event/ serious classification should be entered here. Details of associated symptoms should be entered in section 4.
Date and time event deemed Serious:	This is the date and time when an adverse event is considered to be serious i.e. date and time the AE fitted one of the event types in box A to become categorised as a SAE
Date site became aware of the event:	Please enter the date the investigator team at site first became aware of this event—this may be different from the date the event was deemed to be serious. N.B. GCP requires that investigators report all SAEs to the trial sponsor 'immediately' or at least within 24 hours of their first knowledge of the event.
Causal relationship	The causal relationship must be assessed and initialled by a clinician on the delegation log. See notes on page 3 for grading causality.
Causality	The 'causality' section will be used to detail all possible and suspected causes of the event including causes not related to IMP.
Start date and time of IMP Administration:	This should be entered as the date and time the first dose of IMP is administered following randomisation.
Dose:	Write the current dose of landiolol hydrochloride (mcg/kg/min) or the dose in the last administration if IMP has been interrupted or discontinued
Unexpected:	This section will be completed by the Trial Office to assess whether or not this event is unexpected i.e. is not listed as an undesirable side effect in section 4.8 of the SmPC (summary of product characteristics) .
Action taken:	Please provide information with regards to action taken pertaining to this SAE. If the patient has been withdrawn please complete the withdrawal eCRF.

Clinician responsible for SAE attribution; the signatures must appear on your Site Signature and Delegation Log.