Form number: 6

Daily Data Collection—Follow-up

sepsis adapt
Biomarker-guided antibiotic duration for sepsis

Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

A. Date of Evaluation

1) Day: ☐☐ Date: d d - m o n - y y y y

B. Patient status

1) Is the patient a hospital inpatient? No ☐ Yes ☐

If no, please ensure a discharge form has been completed. Do not complete the remaining questions on this form and complete the 28-day follow up form when applicable

i) If yes are they a critical care inpatient?
- ☐ No
- ☐ Yes—Level 3 unit (ICU)
- ☐ Yes—Level 2 unit (HDU)

ii) Deemed fit for hospital discharge by treating clinical team? No ☐ Yes ☐

If yes, please complete date and time as documented in the medical notes.

Date: d d - m o n - y y y y

Time: h h : m m

C. Antibiotic use

1) Have systemic* antibiotics been changed / restarted within the past 24 hour period?

No ☐ Yes ☐ *If yes, ensure that the antibiotics—follow up form is updated.*

Completion Guidelines for CRF 6: Daily Data—Follow-Up

This form should be completed once the patient has stopped receiving antibiotics for suspected sepsis and should be completed each calendar day that they are a hospital inpatient. Once the patient is discharged, complete the discharge form and then the 28 day follow-up form as soon as possible after the patient reaches 28 days from randomisation.

If the patient is readmitted after they have been discharged, or their care escalation increases whilst in hospital and this is not related to an infection please complete the hospital care escalation / readmission form.

Participant Initials: Write the initials of the participant's first/given name and surname/family name only. For double barrelled surnames/ family names use the initial from the first part of the surname/family name.

Dates: Please use the following formats for dates: 06-Jun-1956.

Times: Please record all times in the 24-hour format.

Antibiotic Use Guidance:

- *Systemic = Intravenous/oral/rectal

Form number: 6

Daily Data Collection: Follow-up

Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

C. SOFA Score

1) Please complete the following table for SOFA:

SOFA Score		
Organ system	**Test**	**Day 3 value**
Respiration	Lowest PaO_2 / FiO_2 Ratio (kPa) (see reverse for conversion from mmHg to kPa#)	☐☐.☐☐
	Assisted Ventilation?	No ☐ Yes ☐ If yes was this: Invasive ☐ Non-invasive ☐
Coagulation	Lowest platelets (x 10^9/L)	☐☐☐.☐☐
Liver	Highest bilirubin (µmol/L)	☐☐☐.☐☐
Cardiovascular	Lowest Mean Arterial Pressure (MAP) (mmHg)	☐☐☐
	Inotrope (µg/kg/min)	Dopamine: No ☐ Yes ☐ Dose: ☐☐☐.☐☐ Dobutamine: No ☐ Yes ☐ Adrenaline (Epinephrine): No ☐ Yes ☐ Dose: ☐☐☐.☐☐ Noradrenaline (Norepinephrine): No ☐ Yes ☐ Dose: ☐☐☐.☐☐ Vasopressin: No ☐ Yes ☐ Milrinone: No ☐ Yes ☐ Levosimendan: No ☐ Yes ☐

Daily Data Collection: Follow-up

Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

C. SOFA Score continued

1) Please complete the following table for SOFA:

SOFA Score		
Organ system	Test	Day **3** value
Renal	Highest creatinine (µmol/L)	☐☐☐.☐☐
	Urine Output (mL/24 hours)	☐☐☐☐
Neurological	Glasgow Coma Score (GCS)	☐☐ *If not possible to complete GCS complete the following questions:* *A) Is patient sedated?* No ☐ Yes ☐ *B) Does patient have an endotracheal tube for ventilation?* No ☐ Yes ☐
Is the patient receiving systemic steroid treatment?		No ☐ Yes ☐
Is the patient on renal replacement therapy?		No ☐ Yes ☐

Daily Data Collection: Follow-up

Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

C. SOFA Score

1) Please complete the following table for SOFA:

SOFA Score		
Organ system	**Test**	**Day 7 value**
Respiration	Lowest PaO_2 / FiO_2 Ratio (kPa) (see reverse for conversion from mmHg to kPa#)	☐☐.☐☐
	Assisted Ventilation?	No ☐ Yes ☐ If yes was this: Invasive ☐ Non-invasive ☐
Coagulation	Lowest platelets (x 10^9/L)	☐☐☐.☐☐
Liver	Highest bilirubin (µmol/L)	☐☐☐.☐☐
Cardiovascular	Lowest Mean Arterial Pressure (MAP) (mmHg)	☐☐☐
	Inotrope (µg/kg/min)	Dopamine: No ☐ Yes ☐ Dose: ☐☐☐.☐☐ Dobutamine: No ☐ Yes ☐ Adrenaline (Epinephrine): No ☐ Yes ☐ Dose: ☐☐☐.☐☐ Noradrenaline (Norepinephrine): No ☐ Yes ☐ Dose: ☐☐☐.☐☐ Vasopressin: No ☐ Yes ☐ Milrinone: No ☐ Yes ☐ Levosimendan: No ☐ Yes ☐

Daily Data Collection: Follow-up

Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

C. SOFA Score continued

1) Please complete the following table for SOFA:

SOFA Score		
Organ system	Test	Day **7** value
Renal	Highest creatinine (µmol/L)	☐☐☐.☐☐
	Urine Output (mL/24 hours)	☐☐☐☐
Neurological	Glasgow Coma Score (GCS)	☐☐ *If not possible to complete GCS complete the following questions:* *A) Is patient sedated?* No ☐ Yes ☐ *B) Does patient have an endotracheal tube for ventilation?* No ☐ Yes ☐
Is the patient receiving systemic steroid treatment?		No ☐ Yes ☐
Is the patient on renal replacement therapy?		No ☐ Yes ☐

Completion Guidelines for CRF 6: Daily Data—Follow-Up

SOFA Score Guidance:

- Details from the SOFA score should be documented on days 3 and 7 post-randomisation.
- For the purposes of the ADAPT-Sepsis trial the following SOFA assessments will be calculated:

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

- Please note, the international name for Adrenaline is Epinephrine. The international name for Noradrenaline is Norepinephrine.
- Tick 'Yes' or 'No' to indicate whether the participant was receiving each inotrope. If 'Yes' is ticked for Noradrenaline, Adrenaline or Dopamine, provide the highest dose of that inotrope over the 24 hour period.

***Conversion of mmHg to kPa** = mmHg × 0.13332

Form number: 6

Daily Data Collection: Follow-up

sepsis adapt
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Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

E. Protocol Adherence *- to complete on first calendar day after stopping intervention only*

1) Have antibiotics been stopped during the last 24 hours? No ☐ Yes ☐

If yes, ensure that the antibiotics—follow up form is updated.

2) Was advice from **previous** 24 hour blood sample received by treating clinician:

No ☐ Yes ☐ *If no, complete a protocol deviation form.*

i) If yes, what was the advice provided:

Protocol STRONGLY supports stopping antibiotics — No ☐ Yes ☐
Protocol suggests stopping antibiotics — No ☐ Yes ☐
Protocol supports usual care — No ☐ Yes ☐

ii) If usual care advice was given for the previous 24 hour blood sample using our research protocol and the treating clinician stopped antibiotics, what influenced this decision?

N/A ☐

If antibiotics were not stopped, check N/A and move onto Section E question 2iii.

Choose all options that apply:

☐ Participant's clinical condition improved
☐ Participant's fever has resolved
☐ Fixed duration antibiotic course is completed
☐ Routine laboratory inflammatory markers suggest infection resolution, specify:_____
☐ Other:_____

iii) If stop advice was given from our research protocol for the previous 24 hour blood sample and the treating clinician stopped antibiotic treatment for the sepsis episode, did the protocol stop advice contribute at all to the decision to stop antibiotics?

N/A ☐ No ☐ Yes ☐ *If stoppage advice was not received, check N/A and move onto Section E question 3.*

3) Was there any evidence for protocol unblinding during the trial intervention (including of the treating clinical team)? No ☐ Yes ☐ *If yes, ensure that a protocol deviation form is completed.*

Form completed by (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

Completion Guidelines for CRF 6: Daily Data—Follow-Up

Protocol Adherence Guidance:

- Protocol adherence should only be completed on the first day of follow-up: the calendar day following stopping systemic antibiotics for suspected sepsis.
- Question E2 collects retrospective information regarding the previous 24 hour blood sample.
- Question E2iii: stoppage advice includes either '*Protocol STRONGLY supports stopping antibiotics*' or '*Protocol suggests stopping antibiotics'*. If this advice was received and contributed at all to the decision to stop antibiotics, tick 'Yes'.
- If any members of the blinded research team or treating clinical team responsible for antibiotic treatment decisions during the trial intervention period were unblinded to the participant's treatment allocation, tick 'Yes' and document in a protocol deviation form. E.g. if the research team were accidently unblinded following discussion with the biochemistry team.

Form number: 6

Daily Data Collection: Follow-up

sepsis adapt
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Participant Trial Number: ☐☐☐☐ **Participant Initials:** ☐☐

Randomising Site:

F. Suspected Clinically Relevant Antibiotic Related Events

1) Has the patient experienced any of the following suspected clinically relevant antibiotic related events in the past 24 hours? No ☐ Yes ☐

If yes, check all that apply

No ☐ Yes ☐ Anaphylaxis

No ☐ Yes ☐ Gastrointestinal

No ☐ Yes ☐ Haematological

No ☐ Yes ☐ Hepatobiliary

No ☐ Yes ☐ Renal

No ☐ Yes ☐ Neurological

No ☐ Yes ☐ Dermatological

No ☐ Yes ☐ Cardiac

No ☐ Yes ☐ Muscular

No ☐ Yes ☐ Other, please specify_____

2) Has the patient experienced proven new Clostridia Difficile diarrhoeal infection during the last 24 hour period? No ☐ Yes ☐

3) Has the patient experienced a proven new infection with a multi-drug resistant organism? No ☐ Yes ☐

If yes, specify_____

Form completed by (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

Completion Guidelines for CRF 6: Daily Data—Follow-Up

Center for Disease Classification for Multi-Drug Resistant (MDR) bacteria:

Phenotype Name	Phenotype Code	Phenotype Definition
Methicillin-resistant *Staphylococcus aureus*	MRSA_HAI	*Staphylococcus aureus* that has tested Resistant (R) to at least 1 of the following: methicillin, oxacillin, or cefoxitin
Carbapenem-resistant Enterobacteriaceae	CREall_HAI	Any *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, or Enterobacter* spp. that has tested Resistant (R) to at least 1 of the following: imipenem, meropenem, doripenem, or ertapenem
Carbapenem-resistant *E.coli*	CREecoli_HAI	Any *Escherichia coli* that has tested Resistant (R) to at least 1 of the following: imipenem, meropenem, doripenem, or ertapenem
Carbapenem-resistant *Enterobacter* spp.	CREenterobacter_HAI	Any *Enterobacter* spp. that has tested Resistant (R) to at least 1 of the following: imipenem, meropenem, doripenem, or ertapenem
Carbapenem-resistant *Klebsiella pneumoniae/oxytoca*	CREklebsiella_HAI	Any *Klebsiella oxytoca* or *Klebsiella pneumoniae* that has tested Resistant (R) to at least 1 of the following: imipenem, meropenem, doripenem, or ertapenem
Carbapenem-non-susceptible *Pseudomonas aeruginosa*	carbNS_PA_HAI	*Pseudomonas aeruginosa* that has tested either Intermediate (I) or Resistant (R) to at least 1 of the following: imipenem, meropenem, or doripenem
Extended-spectrum cephalosporin-resistant *E.coli*	ESCecoli_HAI	Any *Escherichia coli* that has tested Resistant (R) to at least 1 of the following: cefepime, ceftriaxone, cefotaxime, or ceftazidime.
Extended-spectrum cephalosporin-resistant *Klebsiella pneumoniae/oxytoca*	ESCklebsiella_HAI	Any *Klebsiella oxytoca* or *Klebsiella pneumoniae* that has tested Resistant (R) to at least 1 of the following: cefepime, ceftriaxone, cefotaxime, or ceftazidime.
Multidrug-resistant *Pseudomonas aeruginosa*	MDR_PA_HAI	*Pseudomonas aeruginosa* that has tested either Intermediate (I) or Resistant (R) to at least 1 drug in at least 3 of the following 5 categories: 1. Extended-spectrum cephalosporin (cefepime, ceftazidime) 2. Fluoroquinolones (ciprofloxacin, levofloxacin) 3. Aminoglycosides (amikacin, gentamicin, tobramycin) 4. Carbapenems (imipenem, meropenem, doripenem) 5. PIP/PIPTAZ (piperacillin, piperacillin/tazobactam)
Carbapenem-non-susceptible *Acinetobacter* spp.	carbNS_Acine_HAI	Any *Acinetobacter* spp. that has tested either Intermediate (I) or Resistant (R) to at least 1 of the following: imipenem, meropenem, or doripenem
Multidrug-resistant *Acinetobacter* spp.	MDR_Acine_HAI	Any *Acinetobacter* spp. that has tested either Intermediate (I) or Resistant (R) to at least 1 drug in at least 3 of the following 6 categories: 1. Extended-spectrum cephalosporin (cefepime, ceftazidime, ceftriaxone, cefotaxime) 2. Fluoroquinolones (ciprofloxacin, levofloxacin) 3. Aminoglycosides (amikacin, gentamicin, tobramycin) 4. Carbapenems (imipenem, meropenem, doripenem) 5. PIP/PIPTAZ (piperacillin, piperacillin/tazobactam) 6. Ampicillin/sulbactam
Vancomycin-resistant *Enterococcus faecalis*	VREfaecalis_HAI	*Enterococcus faecalis* that has tested Resistant (R) to vancomycin
Vancomycin-resistant *Enterococcus faecium*	VREfaecium_HAI	*Enterococcus faecium* that has tested Resistant (R) to vancomycin