Form number: 4

Daily Data Collection: Intervention

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 participant a hospital inpatient? No ☐ Yes ☐

If no, please ensure a discharge form has been completed. Move ahead to question D3.

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 the 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

Completion Guidelines for CRF 4: Daily Data Collection—Intervention

This CRF should first be completed the following calendar day from baseline, a new form should be completed each calendar day whilst the participant is receiving antibiotics for suspected sepsis. Once the participant has stopped receiving antibiotics for suspected sepsis, please continue completing daily data follow-up form each calendar day that they are a hospital inpatient. Once the participant is discharged, complete the discharge form and then the 28 day follow up form as soon as possible after the participant reaches 28 days from randomisation.

If the participant 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.

Daily Data Collection: Intervention

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

Randomising Site:

C. qSOFA, SOFA and APACHE II Scores

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: Intervention

sepsis adapt
Biomarker-guided antibiotic duration for sepsis

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

Randomising Site:

C. qSOFA, SOFA and APACHE II Scores 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: Intervention

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

Randomising Site:

C. qSOFA, SOFA and APACHE II Scores

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: Intervention

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Biomarker-guided antibiotic duration for sepsis

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

Randomising Site:

C. qSOFA, SOFA and APACHE II Scores 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 4: Daily Data Collection—Intervention

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: 4

Daily Data Collection: Intervention

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

Randomising Site:

D. Protocol Adherence

1) Was today's blood sample taken? No ☐ Yes ☐

i) If yes, date and time? d d – m o n – y y y y h h : m m

2) ii) If no, specify reason why? _____

2) Was today's research blood sample sent to the laboratory? No ☐ Yes ☐

i) If yes, date and time? d d – m o n – y y y y h h : m m

ii) If no, specify reason why? _____

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

No ☐ Yes ☐ *If no, complete 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 antibiotic stop advice was given for the previous 24 hour blood sample using our research protocol and the treating clinician did not follow this advice, what influenced this decision?

Choose all options that apply:

☐ Participant considered too sick/clinically unstable

☐ Participant has a fever

☐ Would not normally stop antibiotics so early

☐ Microbiology advice for fixed duration antibiotics

☐ Routine laboratory inflammatory markers raised, specify markers: _____

☐ Other:_____

If advice was followed, check N/A and move onto Section D question 4. N/A ☐

4)Have antibiotics been changed during the last 24 hours? No ☐ Yes ☐

If yes, ensure that the antibiotics form is updated.
If no, skip the next question and move on to Section F.

E. Antibiotic Focus Review - *to be completed at 72 hours only*

1) Has a documented review, of the clinical diagnosis and the continuing need for antibiotics, been performed by 72 hours (after the first antibiotics for sepsis)? No ☐ Yes ☐

i) If yes, does this include a clear plan of action? No ☐ Yes ☐

Completion Guidelines for CRF 4: Daily Data Collection—Intervention

Protocol Adherence Guidance:

- Record the date and time the blood sample for that day was sent to the lab.
- Question D3 collects retrospective information regarding the previous 24 hour blood sample.

Antibiotic Focus Review Guidance:

- Documented plan of action may include any of the following:

1. Stop antibiotics if there is no evidence of infection
2. Switch antibiotics from intravenous to oral
3. Change antibiotics—ideally to a narrower spectrum- or broader if required
4. Continue and document next review date or stop date
5. Outpatient Parenteral Antibiotic Therapy (OPAT)

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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 Clostridium Difficile diarrhoeal infection during this 24 hour period? No ☐ Yes ☐

3) Has the patient experienced a proven new infection with a multi-drug resistant organism within the last 24 hours? 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 4: Daily Data Collection—Intervention

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