

Study Reference Number: 2018/00354

Version Number: 1

Specific descriptions for each section can be found here

Please select the appropriate form for submission to the DSRB. Please refer to the explanatory notes below if you need more information.

- DSRB Application Form 1 - Non Exempt Category
- DSRB Application Form 2 - Exempt Category

Research activities in which the only involvement of human subjects will be in one or more of the following categories may be able to qualify for the Exempt category.

Please click on the DSRB Application Form 2 - Exempt Category option above to view the categories.

DSRB Application Form 1 - Non Exempt Category

Principal Investigators should use Application Form 1 if their research activity does not qualify under the Exempt Category. Application Form 1 should be used for submissions for the Full Board Review and Expedited Review.

DSRB Application Form 2 - Exempt Category

Research activities in which the only involvement of human subjects will be in one or more of the following categories may be able to qualify for the Exempt category.

IMPORTANT: The criteria for the Exempt category do not apply when the research activity:

(i) involves prisoners

(ii) involves children, when the research involves survey or interview procedures or observations of public behavior, except when the investigator(s) do not participate in the activities being observed

(iii) is a US FDA-regulated research activity.

A1 Please enter the full study title.

Prevalence, causes, management, and outcomes of sepsis in Asia's intensive care units

A2 (Optional) Please assign Study Administrators below.

B1 Study Sites & Study Team Members

All investigators who have a responsibility for the consent process and/or direct data collection for this study should be listed below.

Study Team Members with registered user account with us will be notified of their participation in this study when the Application is submitted.

For a Multi-centre study, please appoint a Site PI for each site (Mandatory).

The Principal Investigator will be the Site PI for their own Institution, and will also be the primary contact person for the DSRB.

(i) Overall Principal Investigator' (Main contact for DSRB): Andrew Yunkai Li

(ii) Study Sites under the oversight of NHG DSRB [Click here for help](#)

No.	Study Site	Name	Study Role	Institution	Department	Min Training
1	National University Hospital	Dr Andrew Yunkai Li	PI	National University Hospital	Respiratory & Critical Care Medicine	Completed
2	National University Hospital	Dr Jason Phua	Co-Investigator	National University Hospital	Respiratory & Critical Care Medicine	Completed
3	National University Hospital	Dr TAN YONG HUI ADDY	Collaborator	National University Hospital	Anaesthesia	Completed
4	National University Hospital	Dr Yip Hwee Seng	Collaborator	National University Hospital	Advanced Internal Medicine	Completed
5	Changi General Hospital (CGH)	Dr Siew Hua Noelle Louise Lim	Site PI	Changi General Hospital (CGH)	Anaesthesia	Completed
6	Tan Tock Seng Hospital	Dr Jit Ern Jonathan Tan	Site PI	Tan Tock Seng Hospital	Anesthesiology, Intensive Care and Pain Medicine	Completed
7	Tan Tock Seng Hospital	Dr Jin Wen Senen Lew	Collaborator	Tan Tock Seng Hospital	Respiratory Medicine	Completed
8	Khoo Teck Puat Hospital - Alexandra Health Pte Ltd	Dr naville chia	Site PI	Khoo Teck Puat Hospital - Alexandra Health Pte Ltd	Anesthesia	Completed
9	Khoo Teck Puat Hospital - A	Dr KUMARESH VENKATESAN	Collaborator	Khoo Teck Puat Hospital - A	Anesthesia	Completed

No.	Study Site	Name	Study Role	Institution	Department	Min Training
	alexandra Health Pte Ltd			alexandra Health Pte Ltd		
10	Ng Teng Fong General Hospital	Dr Chee Keat Tan	Site PI	Ng Teng Fong General Hospital	Intensive Care Medicine	Completed
11	Singapore General Hospital (SGH)	Dr Chee Kiang Melvin Tay	Site PI	Singapore General Hospital (SGH)	Respiratory & Critical Care Medicine	Completed
12	Singapore General Hospital (SGH)	Dr Ng Shin Yi	Collaborator	Singapore General Hospital (SGH)	Anaesthesiology	-
13	Singapore General Hospital (SGH)	Dr Vui Kian Ho	Collaborator	Singapore General Hospital (SGH)	Anaesthesiology	Not completed

(iii) External Study Sites under the supervision of the 'Overall Principal Investigator' (eg. Nursing Home, Community Hospitals, Community Centres etc).

B2 Research Specialty

Please select the Primary Specialty, and then choose the relevant Sub specialty that has been matched according to the Primary Specialty selected. If the Primary Specialty and/or Sub specialty cannot be found from the list, please choose 'Others' and specify.

No.	Primary Specialty	Primary Sub Specialty	Others
1	Respiratory & Critical Care Medicine	Others	

Please indicate/add Secondary Specialties.

No.	Primary Specialty	Primary Sub Specialty
1		

B3 Which Domain Specific Review Board (DSRB) is this application being submitted to? DSRB Domain B

B4 Has the application been previously rejected by any IRB? (Including NHG-DSRB)

- No
 Yes

With effect from 1 January 2015, all study team members involved in the design, conduct or reporting of the research are required to complete and endorse on an annual basis, a Conflict of Interest Declaration Form. This declaration includes any conflicts of interest of their immediate family members (includes parents, siblings, spouse and each dependent child).

The annual Conflict of Interest declaration cycle will be from 1 January to 31 January of each year and the validity will be from the date of Conflict of Interest declaration form submitted till until 31 December of the same year.

If any Conflict of Interest Declaration Forms were not previously submitted during the annual declaration cycle, it should be submitted to the DSRB FCOI secretariat (Email: DSRB_FCOI@nhg.com.sg) or must be attached with this DSRB Application Form under "Attachments" tab (see top of this page), Section/Question to select as "Others", to be submitted to DSRB for review, if not previously submitted during the annual declaration cycle.

The Conflict of Interest Declaration Form can be downloaded from <https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/hssp/financial+conflict+of+interest/fcoi+policy>

An updated Conflict of Interest Declaration Form must be submitted to the DSRB via a study amendment as soon as possible but no later than 30 days if any of the circumstances relevant described herein change during the conduct of the research.

Dr Andrew Yunkai Li (Principal Investigator)

- Yes
 No

Dr Jason Phua (Co-Investigator)

- Yes
 No

Dr TAN YONG HUI ADDY (Collaborator)

- Yes
 No

Dr Yip Hwee Seng (Collaborator)

- Yes
 No

Dr Siew Hua Noelle Louise Lim (Site Principal Investigator)

- Yes
 No

Dr Chee Kiang Melvin Tay (Site Principal Investigator)

- Yes
 No

Dr Jit Ern Jonathan Tan (Site Principal Investigator)

- Yes
 No

Dr Jin Wen Sennen Lew (Collaborator)

- Yes
 No

Dr naville chia (Site Principal Investigator)

- Yes
 No

Dr KUMARESH VENKATESAN (Collaborator)

- Yes

No

Dr Ng Shin Yi (Collaborator)

Yes

No

Dr Vui Kian Ho (Collaborator)

Yes

No

Dr CheeKeat Tan (Site Principal Investigator)

Yes

No

Please be reminded to attach the completed Conflict of Interest Declaration Form for all study team members involved in the design, conduct or reporting of the research. They may include study coordinators, biostatisticians etc. who may not be listed in Section B and C of the DSRB Application Form.

D1 Please select one category that best describes your research activities.

- Clinical Trials (which includes Drug, Device and Surgical-Procedure Trials)
- Questionnaire/ Survey/ Interviews
- Medical Records Review
- Clinical Research

Note: Clinical Trial Certificate from Health Sciences Authority might be required if you are testing the safety and efficacy of the medicinal product. You should check with HSA if you are unsure.

D2 Is this a US FDA IND/IDE study or data is intended to be reported to FDA in support of a IND/IDE application?

- Yes
- No

Note: US FDA-regulated (IND) research activities cannot qualify for Exemption from DSRB Review and Waiver of Informed Consent. The application must be submitted using the DSRB Application Form 1 - Non Exempt Category.

D3 Is this study subjected to any of the following regulations:

- No
- Yes
- US Code of Federal Regulations 45 CFR 46
- US Code of Federal Regulations 21 CFR 50
- US Code of Federal Regulations 21 CFR 56
- US Code of Federal Regulations 21 CFR 312
- US Code of Federal Regulations 21 CFR 812
- Others

E1 Who will be responsible for the payment and compensation of injury or illness arising from participation of research participants in the study?*

- National Clinical Trial (CT) Insurance Policy (Contact your institution research office for more information)
- Sponsor
- Others

E2 Please give information regarding the study's Funding source or Sponsor information.

- No funding is required for this study to be carried out
- Pharmaceutical / Industry Sponsored
- Grant

E3 Will the funding cover all subject study-related drugs, devices, procedures, tests and visits? * Click here for help

- Yes
- No
- Not Applicable (No subject study-related costs)

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J TAN+COI+Declaration+Form.doc

Dr Naville Chia.pdf

Informed consent v3 CGH.doc

Informed consent v3 TTSH.doc

Informed consent v3 SGH.doc

Informed consent v3 KTPH.doc

Informed consent v3 NTFGH.doc

Informed consent v3 NUH.doc

Aims**Methodology****Importance of proposed research to science or medicine****Potential benefits & risks****F1 What are the Specific Aims of this study?**

Primary objective of the main study To determine the prevalence of sepsis defined by the Sepsis-3 guidelines as a reason for ICU admission in Asia, as well as its causes and outcomes. Secondary objectives of the main study a. To evaluate the time to management of sepsis with a focus on recommendations by the Surviving Sepsis Campaign guidelines: blood cultures, antibiotics, lactate measurement, and fluid resuscitation. b. To compare the prevalence, causes, outcomes, and management of sepsis in Asian ICUs in high, middle, and low-income countries and regions, defined according to the World Bank classification. c. To specifically study the prevalence and outcomes of sepsis as a result of malaria, dengue, tuberculosis, cholera, and Salmonella infections, as well as culture-negative sepsis.

F2 What is the Hypothesis of this study? For qualitative studies, please provide the research question instead.

To determine the prevalence of sepsis defined by the Sepsis-3 guidelines as a reason for ICU admission in Asia, as well as its causes and outcomes.

F3 Please state concisely the importance of the research described in this application by relating the specific aims to the long term objectives.

To determine the prevalence of sepsis in Asia as well as the adherence rates to current sepsis bundles

F4 Please describe the background to the current study proposal. Critically evaluate the existing knowledge and specifically identify the gaps that the proposed study is intended to fill.

The latest definition of sepsis, Sepsis-3, requires patients to have life-threatening organ dysfunction (an increase of Sequential Organ Failure Assessment Score [SOFA] score > 2 from baseline) caused by a dysregulated host response to infection.¹ This definition was derived from and validated through databases in the United States (except for one hospital in Germany).² Compared with other well-established definitions such as the systemic inflammatory response syndrome (SIRS), SOFA was shown to be a better predictor of mortality. In addition, the abbreviated quick SOFA (qSOFA) score emerged as a new measure for the prediction of poor outcomes among patients with infection. Whether this is generalizable to the rest of the world remains unclear. Meanwhile, Fleischmann and colleagues, on behalf of the International Forum of Acute Care Trialists (InFACT), performed a systematic review to estimate the worldwide incidence and mortality of sepsis. Strikingly, only 13% of the world's countries were represented in the review, as population-level epidemiologic data for sepsis were close to non-existent for low and middle-income countries.³ Yet, the Global Burden of Disease Study 2015 found that while they did not feature significantly in high-income countries, diarrheal diseases such as cholera and Salmonella infections, human immunodeficiency virus (HIV) infections, and tropical diseases such as malaria and dengue fever were among the main causes of death in low-income countries.⁴ There thus exists a current disconnect between the way sepsis is perceived and defined in high-income countries and in low and middle-income countries.⁵ To illustrate, in the Extended Prevalence of Infection in Intensive Care (EPIC II) study, 51% of patients in the participating 1265 intensive care units (ICUs) from 75 countries were considered infected on the day of the study in the year 2007.⁶ Surprisingly, parasites accounted for only 0.7% of all defined infections (0% in Africa and 0.6% in Asia), and there was no specific mention of cholera, Salmonella infections, and viral infections. Asia is the world's largest continent and is home to approximately 60% of the world's population. Estimates – based predominantly on extrapolations from the West – that Asia accounts for at least half of the cases of sepsis in the world are thus not unexpected.⁷ Asia has a mix of high, middle, and low-income countries, and it is likely that the causes and outcomes of sepsis in these countries will vary significantly.⁸ The management of sepsis also varies across Asia. The Management Of Severe sepsis in Asia's Intensive Care unitS (MOSAICS) study showed compliance rates to the Surviving Sepsis Campaign's resuscitation bundles of only 2.3%, 6.9%, and 10.0% in low-income, middle-income, and high-income countries and regions respectively (compared to 19% in Europe and North America).⁹ Meanwhile, the management of sepsis has evolved over the last decade. Rather than early goal-

directed therapy guided by central venous pressure and central venous oxygen saturation¹⁰, the Surviving Sepsis Campaign's 3-hour bundle now focuses on blood cultures, early antibiotics, lactate measurement, and adequate fluid resuscitation.¹¹⁻¹⁵ Given the significant changes in the recommended definitions and management of sepsis despite the paucity of data on this life-threatening condition in much of the world, a re-examination of sepsis in this era of Sepsis-3 is timely. The Asian Critical Care Clinical Trials (ACCCT) Group has a good track record of multinational and multi-centre research in Asia and is well poised to do this.

F5 Please provide a list of relevant references.

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016;315:801-810. 2. Seymour CW, Liu V, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: For the Third International Consensus Definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016;315:762-774. 3. Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P, et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *Am J Respir Crit Care Med* 2016;193:259-272. 4. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016;388:1459-1544. 5. Schultz MJ, Dunser MW, Dondorp AM, Adhikari NKJ, Iyer S, Kwizera A, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. *Intensive Care Med* 2017;43:612-624. 6. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA* 2009;302:2323-2329. 7. Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. *Lancet* 2010;376:1339-1346. 8. Thwaites CL, Lundeg G, Dondorp AM, sepsis in resource-limited settings-expert consensus recommendations group of the European Society of Intensive Care Medicine, the Mahidol-Oxford Research Unit in Bangkok, Thailand. Recommendations for infection management in patients with sepsis and septic shock in resource-limited settings. *Intensive Care Med* 2016;42:2040-2042. 9. Rhodes A, Phillips G, Beale R, Cecconi M, Chiche JD, De Backer D, et al. The surviving sepsis campaign bundles and outcome: results from the international multicentre prevalence study on sepsis (the IMPreSS study). *Intensive Care Med* 2015;41:1620-1628. 10. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345:1368-1377. 11. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. *Intensive Care Med* 2017;43:304-377. 12. ProCESS investigators, Yealy DM, Kellum JA, Huang DT, Barnato AE, Weissfeld LA, Pike F, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med* 2014;370:1683-1693. 13. 11. ARISE investigators, ANZICS clinical trial group, Peake SL, Delaney A, Bailey M, Bellomo S, et al. Goal-directed resuscitation for patients with septic shock. *N Engl J Med* 2014;371:1496-1506. 14. 12. Mouncey PR, Osborn TM, Power GS, Harrison DA, Sadique MZ, Grieve RD, et al. Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med* 2015;372:1301-1311. 15. 13. The PRISM investigators. Early, goal-directed therapy for septic shock – a patient-level meta-analysis. *N Engl J Med* 2017;376:2223-2234. 16. Arabi Y, Phua J, Koh Y, Du B, Faruq MO, Nishimura M, et al. Structure, organization, and delivery of critical care in Asian ICUs. *Crit Care Med* 2016;44:e940-e948. 17. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818-829. 18. Beasley R, Chien J, Douglas, J, Eastlake L, Farah C, King G, et al. Thoracic society of Australia and New Zealand oxygen guidelines for acute oxygen use in adults: 'swimming between the flags'. *Respirology* 2015;20:1182-1191. 19. Freund Y, Lemachatti N, Krastinova E, Van Laer M, Claessens YE, Avondo A, et al. Prognostic accuracy of sepsis-3 criteria for in-hospital mortality among patients with suspected infection presenting to the emergency department. *JAMA* 2017;317:301-308. 20. Phua J, Wang JN, See KC, Tay CK, Kiong T, Lim HF, et al. Characteristics and outcomes of culture-negative versus culture-positive severe sepsis. *Crit Care* 2013;17:R20221. 21. Mermel LA, Allon M, Bouze E, Craven DE, Flynn P, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 updated by the Infectious Diseases Society of America. *Clin Infect Dis* 2009;49:1-45. 22. Ling ML, Apisarnthanarak A, Jaggi N, Harrington G, Morikane K, Thu LTA, et al. APSIC guide for prevention of central line associated blood stream infections (CLABSI). *Antimicrob Resist Infect Control* 2016;5:16. 23. Kauffman CA. Fungal infections. *Proc Am Thorac Soc* 2006;3:35-40. 24. Prasad N, Murdoch DR, Reyburn H, Crump JA. Etiology of severe febrile illness in low- and middle-income countries: a systematic review. *PLOS* 2015;10:e0127962. 25. Thwaites CL. Tetanus. *Current Anaesthesia and Critical Care* 2005;16:50-57. 26. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official

American thoracic society/Infectious diseases society of America/Centers for disease control and prevention clinical practice guidelines: diagnosis of tuberculosis in adults and children. Clin Infect Dis. 2016;00:1-33.

27. Meersseman W, Lagrou K, Maertens J, Wilmer A, Hermans G, Vanderschueren S, et al. Galactomannan in bronchoalveolar lavage fluid. A tool for diagnosis Aspergillosis in ICU patients. Am J Respir Crit Care Med 2008;177:27-34.

28. Patterson TF, Thomsson III GR, Denning DW, Fishman JA, Hadley S, Herbrecht R, et al. Practice guidelines for the diagnosis and management of Aspergillosis: 2016 updated by the Infectious Diseases Society of America. Clin Infect Dis 2016 ;63:e1-e60.

29. WHO Guidelines for the treatment of malaria 2015.

30. Economopoulou A, Dominguez M, Helynick B, Sissoko D, Wichman O, Quenel P, et al. Atypical Chikungunya virus infections: clinical manifestations, mortality and risk factors for severe disease during the 2005-2006 outbreak on Reunion. Epidemiol Infect 2009;137:534-541.

31. WHO Dengue guidelines for diagnosis, treatment, prevention and control 2009.

32. Harper SA, Bradley JS, Englund JA, File TM, Gravenstein S, Hayden FG, et al. Seasonal influenza in adults and children – diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the infectious diseases society of America. CID 2009;48:1003-1032.

33. Nichols WG, Peck Campbell AJ, Boeckh M. Respiratory viruses other than influenza virus: impact and therapeutic advances. Clin Microbiol Rev 2008;21:274-290.

34. WHO expert consultation on rabies. First Report. WHO technical report series 2004;931:1-121.

35. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever and other spotted fever group Rickettsioses, Ehrlichioses, and Anaplasmosis – United States. MMWR 2016;65:1-44.

36. Rahi M, Gupte MD, Bhargava A, Varghese GM, Arora R. DHR-ICMR guidelines for diagnosis and management of Rickettsial diseases in India. Indian J Med Res 2015;141:417-422.

37. Mark NM, Rayner SG, Lee NJ, Curtis JR. Global variability in withholding and withdrawal of life-sustaining treatment in the intensive care unit: a systematic review. Intensive Care Med 2015;41:1572-1585.

38. Phua J, Joynt GM, Nishimura M, Deng Y, Myatra SN, Chan YH, et al. Withholding and withdrawal of life-sustaining treatment in intensive care units in Asia. JAMA Intern Med 2015;175:363-371.

39. Laurantette A, Garrouste-Orgeas M, Bertrand PM, Goldgran-Toledano D, Jamali S, Laurent V, et al. Respective impact of no escalation of treatment, withholding and withdrawal of life-sustaining treatment on ICU patients' prognosis: a multicentre study of the Outcomerea Research Group. Intensive Care Med 2015;41:1763-1772.

F6 Please submit a copy of at least two relevant papers.

Consensus for Sepsis-3.pdf

Study - MOSAICS - BMJ 2011.pdf

F7 Discuss in detail the experimental design and procedures to be used to accomplish the specific aims of the study. (If this study involves a retrospective medical record review, please specify the period of data collection and the database to be accessed. (Note: NEHR cannot be accessed for research))* Note: W.e.f. 1 July 2014, all research studies submitted from National University Hospital (NUH), involving the use of radioactive materials and/or radiation-emitting equipment will need to obtain approval from the NUH Radiation Safety Committee (RSC) prior to the commencement of the study. For more information and to receive a copy of the 'Guidelines to undertake Research which involves the use of Ionizing and/or Non-Ionizing Radiation', please contact the NUH Radiation Safety Officer (michael_tong@nuhs.edu.sg) or the NUHS Research Office (clinical_research@nuhs.edu.sg).

This is a cross-sectional, point prevalence observational, multi-centre study where patients are enrolled on 4 separate days to represent the different seasons of the year. These days will be decided at a later date before the study commences. The study will be conducted over a year (2018/2019). On the study days, data collection will commence for all study patients in the participating ICUs via online case report forms. Details of the forms are provided in the next sections. First, data will be collected for all patients admitted with sepsis. There will also be a focus on time to blood cultures, antibiotics, lactate measurement, and fluid resuscitation. Second, each participating ICU will complete another online questionnaire detailing the type, capacity, and capabilities of the ICU prior to the commencement of the study. Management of the patients will be left completely to the managing physicians. The study protocol does not dictate the performance of specific investigations. Thus, only variables as part of usual care will be recorded.

F8 Please provide details on (i) sample size and power calculation and (ii) the means by which data will be analyzed and interpreted. If this is a pilot study/qualitative study and no sample size calculation is performed, please provide a rationale on how the recruitment target is determined.*

Nil sample size calculation performed. There is no recruitment target. Sample population is as mentioned above, based on the number of patients with sepsis in ICU on the days of collection

Mainly data collection of usual care.

F10 Please list all activities that are performed for routine diagnostic or standard medical treatment as part of the research participant's standard care. Research-related activities stated in F9 should be excluded from this section.

All aspects of regular ICU care for these patients

F11 Please describe the subject's visits (frequency and procedures involved). Please attach study schedule if available.

NA

F12 Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims.

Limitations would be the need to record down the data in an online portal. This online portal will be password-protected and only site collaborators and PIs will be allowed to assess the portal.

F13 What are the Potential Risks to research participants?

There is a risk from a breach of confidentiality as patient identifiers are being collected.

F14 What are the Potential Benefits (direct as well as indirect) to research participants?

This will enable us to be aware of adherence to sepsis bundles in Asia as well as what is the actual prevalence of sepsis in Asia based on the latest new guidelines.

F15 Preliminary Studies / Progress Reports. Please provide an account of the Principal Investigator's preliminary studies (if any) pertinent to this application.

Management of severe sepsis in patients admitted to Asian intensive care units: prospective cohort study. BMJ 2011;342:d3245

F16 What is the estimated time needed to conduct this study?*

No. of Years 1

No. of Months 0

F17 Does this study have a Study Protocol? Note: For Clinical Trials, investigators are required to submit a Study Protocol for review.

Yes

Please submit a copy of the Study Protocol.

MOSAICS II Study.docx

No

F18 The PI is responsible for ensuring that all Study research participants give informed consent before enrolling into the study.

Please select all the applicable consent scenarios.

- Informed Consent will be taken for all study subjects.
- Waiver of Informed Consent is requested for all study subjects.
- A combination of both Informed Consent and Waiver of Consent is required for different study populations.

H1 How will potential research participants be identified?

- Referral by attending healthcare professional
- Persons with dependent relationship with study team (e.g. doctor-patient, employee-employer, head-subordinate, student-teacher, departmental staff relationship)
- Databases
- Other methods of identifying potential subjects

Please elaborate on your method(s) of subject identification (e.g. Advertisement, word of mouth etc).

Members of the study team will approach the patient/legal representatives to obtain consent to participate in the study. All patients admitted to ICU for some form of sepsis will be part of the study

H2 Who will make the first contact with the research participant?* Click here for help

Members of the study team will approach the patient/legal representatives to obtain consent to participate in the study.

Site collaborators and PI. These patients may be critically ill and intubated. Family members' permission will be sought in the patient is unable to provide consent. If not, patient's consent will be obtained when he is able to do so after his period of treatment. Data collected is part of usual care and there will be no intervention involved.

- Yes
- No

H5 Will any other recruitment strategies be used? (Eg. Talks in public places, societies etc.)

- Yes
- No

H6 Please indicate the length of time of the participant's direct involvement in the study. E.g. For clinical visits, examinations etc. (If applicable)

NA

I1 Please state the target number of research participants to be recruited for each study site in Singapore. If the exact numbers are not available, please give an approximate number range in the Recruitment Target Minimum and Maximum columns.*

Please note that recruiting subjects beyond the Max. No. without DSRB's approval would constitute a Non-Compliance. If you intend to recruit beyond the Max. No., please submit a study amendment to increase the recruitment target.

For the distribution of Males, Females and Children to be recruited into the study, please use the Recruitment Target Max. No. to provide an approximate distribution ratio.

(Go back to Section B1 to add additional study site)

No.	Study Site	Recruitment Target Min	Recruitment Target Max	Males	Females	Children
1	National University Hospital	10	100	50	50	0
2	Changi General Hospital (CGH)	10	100	50	50	0
3	Singapore General Hospital (SGH)	10	100	50	50	0
4	Tan Tock Seng Hospital	10	100	50	50	0
5	Khoo Teck Puat Hospital - Alexandra Health Pte Ltd	10	100	50	50	0
6	Ng Teng Fong General Hospital	10	100	50	50	0

I2 Is this study part of an international study?

Yes

If yes, please state the total approximate number of worldwide research participants targeted for enrollment into this study. 2000

No

P1 Describe when the consent process will take place with the potential research participant, including the time provided for him/her to consider his/her participation in the study. Click here for help*

Consent will be requested from the patient/legal representative if the patient is unable to do so/died

P2 Where will consent be taken (e.g. room, ward, outpatient clinic etc)? How will privacy, freedom from intrusion and comfort be ensured? Click here for help*

In the intensive care unit in a consultation room

P3 Who will take consent from potential research participants (e.g. PI, Co-Investigators etc)? Click here for help*

PIs, Co-investigators and study administrators

P4 Besides the Informed Consent Form, will any other materials or documents be used to explain the study to potential Research Participants? (eg. scripts, handouts, brochures, videos, logs, etc).

- No
 Yes

P5 Will research participants receive any monetary payments (including transportation allowances) or gifts for their participation in the study? Click here for help*

- No
 Yes

P6 Will consent be documented in the form of a written and signed Informed Consent Form?

- Yes, all Research Participants will be given a copy of the Informed Consent Form.

Please attach a copy of the Informed Consent Form.

- No, Consent will not be documented. (E.g. verbal consent).

P7 Consent Language

Will the study enrol non-English speaking research participants?

- No
 Yes

a. What are the languages that will be used to communicate with the prospective participant or the legally acceptable representative?

- Chinese
 Malay
 Tamil
 Others (state the language)

b. How will the Non-English consent be documented?

- Informed Consent Form (Full) translated to the language understood by the prospective participant or the legally acceptable representative.
 Informed Consent Form (English) with DSRB Short Consent Form Template (Translated).

Please download the template from NHG Research Website.

The Short Consent Form is required to be appended to the Main English Language Informed Consent Form (ICF) as a single set of document. A document footer (mentioning the document version number and version date) and page number (i.e. Page X of Y) must be provided to link the English language ICF to each translated Short Consent Form.

Informed Consent Form (English) with Other Short Consent Form (Translated).

P8 Will the study be recruiting research participants under emergency situations, when prior consent of the research participant is not possible?

- Yes
- No

P9 Do you have any additional comments regarding the Informed Consent process?

- No
- Yes

R In general, to protect the Research Participant's confidentiality, research data should be coded, and the links between the Participant's identifiers and the codes should be stored separately from the research data.

R1 Will coded / anonymous research data be sent to the pharmaceutical sponsor?

- No, the study team would store all research data within the institution

R1(i) Please state how the research data will be protected to ensure confidentiality and security.

- For hardcopy data, they will be stored in designated locked cabinet(s) or room(s) that are accessible to authorized study personnel only.
- For electronic data, they will be stored on in a secured computer that is password-protected. The databases will not contain subject identifiers and the data linking subject identifiers and the subject identification codes will be stored separately. When portable media (e.g. CD, USB drives etc.) are used to store the data, subject identifiers are stored separately.

ii. Describe who will have access to the research data. (Please state the personnel who will have access to the study data eg. PI, Co-investigator, study coordinator.)

Only PIs and collaborators will have access to the research data

iii. Will research data be released and shared with individuals or entities outside the institution?

- No
- Yes, please ensure that there is an agreement in place to protect data confidentiality

iv. Will the research data be used for future research after the study is completed?

- No, the research data will be destroyed after it has been stored for 6 years or minimum duration of retention period as specific by your institutional policy, whichever that is longer.
- Yes, the research data will be used for future research. Please register a standing database with DSRB.

- Yes, the study team would send research data to the study sponsor

R2 Will any part of the study procedures be recorded on audiotape, film/video, or other electronic medium (excluding non-identifiable images such as MRI/ X-Ray/ CT)?

- No
- Yes

Please ensure that the Curriculum Vitae is accurate and up to date.

If the PI or Study Team Member Curriculum Vitae does not appear on the list, they will need to update and upload it through their ROAM profile.

The DSRB will use the information contained here to assess the qualifications of the Principal Investigator and Study team members to carry out the Study as described in this Application.

No.	Study Site	Name	Study Role	CV
1	National University Hospital	Dr Andrew Yunkai Li	PI	Abridged CV.doc 21-Feb-201
2	National University Hospital	Dr Jason Phua	Co-Investigator	JP Curriculum Vitae 2011.doc 09-Nov-201
3	National University Hospital	Dr TAN YONG HUI ADDY	Collaborator	Addy CV May 2012.doc 29-Jul-201
4	National University Hospital	Dr Yip Hwee Seng	Collaborator	CV 050318.doc 05-Mar-201
5	Changi General Hospital (CGH)	Dr Siew Hua Noelle Louise Lim	Site PI	CVFormat_NL_Apr 13 to Mar 14.doc 12-Jul-201
6	Tan Tock Seng Hospital	Dr Jit Ern Jonathan Tan	Site PI	Dr Jonathan Tan cv.doc 22-Nov-201
7	Tan Tock Seng Hospital	Dr Jin Wen Sennen Lew	Collaborator	CV2014.doc 20-Jul-201
8	Khoo Teck Puat Hospital - Alexandra Health Pte Ltd	Dr naville chia	Site PI	CV for NHG Roam.doc 08-Dec-201
9	Khoo Teck Puat Hospital - Alexandra Health Pte Ltd	Dr KUMARESH VENKATESAN	Collaborator	KV CV Apr 2015.doc 27-Apr-201
10	Ng Teng Fong General Hospital	Dr CheeKeat Tan	Site PI	CVtck%25202010[1][1].rtf 19-Nov-201
11	Singapore General Hospital (SGH)	Dr Chee Kiang Melvin Tay	Site PI	CV.doc 24-Jul-201
12	Singapore General Hospital (SGH)	Dr Ng Shin Yi	Collaborator	CV NgSY.doc 07-Feb-201
13	Singapore General Hospital (SGH)	Dr Vui Kian Ho	Collaborator	Ho VK_CV SGH.doc 13-Oct-201

Your DSRB Application is now complete and ready for submission.

Principal Investigator's Declaration

I will not initiate this study until I have received approval notification from the DSRB and all applicable regulatory authorities.

I will not initiate any change in the study protocol without prior written approval from the DSRB, except when it is necessary to reduce or eliminate any immediate risks to the Research Participants. Thereafter, I will submit the proposed amendment to the DSRB and all applicable regulatory authorities for approval.

I will promptly report any unexpected or serious adverse events, unanticipated problems or incidents that may occur in the course of this study.

I will maintain all relevant documents and recognise that the DSRB staff and applicable regulatory authorities may inspect these records.

I understand that failure to comply with all applicable regulations, institutional and DSRB policies and requirements may result in the suspension or termination of this study.

I declare that there are no existing or potential conflicts of interest for any of the investigators participating in this study and their immediate family members. If there are, I have declared them in the relevant section of this application form.

By checking the "I agree" box, you confirm that you have read, understood and accept the Principal Investigator's Declaration

I have read and agree to the above declaration.

Principal Investigator: Andrew Yunkai Li