ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease

Institutional Review Board (IRB) / Ethical Application Master Guide

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1. Document Purpose

This document has been created to help reduce the amount of time sites spend on compiling an Ethics/IRB application for local IRB/Ethics approval. It is intended as a guide only, all local IRB/Ethics rules and requirements must be taken into account when writing your application. If you have any questions or need more information please contact ECMOCARD Chief Investigator (email g.libassi@uq.edu.au) or ECMOCARD Research Coordinator (Amanda.Corley@health.qld.gov.au).

2. General Information

2.1. Title

ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease. The ECMOCARD Study.

2.2. Investigator/supervisor, collaborator names

Investigators involved in this project at your site should be named on your IRB/Ethical application. The site lead investigator assumes primary responsibility for the execution of the research at all locations this IRB/Ethical application is covering. The site lead investigator is also responsible for ensuring that the research is conducted in accordance with all local ethical and regulatory requirements.

2.3. Type of research

This is an observational study, using data collected routinely as a part of clinical care. This research will add valuable knowledge and data to the study and management of patients admitted to the intensive care unit with acute respiratory disease caused by the novel coronavirus (COVID-19).

2.4. IRB/Ethical level of project

Waiver of Consent / low / negligible or minimal risk will be sought.

Due to the importance of complete case ascertainment, that only de-identified data are submitted, and the potential benefits of the research to the wider community we are seeking to streamline data collection and ask that consent be waived. Waiver of consent is requested because this study is a population-based, epidemiology study. This research involves no intervention and all clinical information will have been collected as part of routine clinical care by health care workers who normally have access to health care records. We believe this research carries negligible risk to participants. The major potential risk is breach of privacy and this is minimised by mandatory submission of de-identified data. It is unlikely to be feasible for sites to participate if consent is required. Some documents have been created in the APPENDIX A, in English, Korean, Chinese and Japanese to help reduce the amount of time sites spend on compiling. If consent is required by your
IRB/ Ethics board please contact your Regional lead or the ECMOCARD Research Coordinator (Amanda.Corley@health.qld.gov.au) to discuss how to progress.

This study involves the collection of protected health information (PHI) only by the participating site who have legitimate access to this data. The collection and retention of PHI by sites is necessary to ensure data integrity. Identifiers collected are name, date of birth, and medical record number. The data will be stored in a restricted access folder and will only be accessible to the research team at the site. NO PHI data will be disclosed to another institution or submitted centrally for analysis. PHI data will be de-identified before entering data into the central study database. The information collected does not include information that may be damaging to the individual should it be wrongfully disclosed. Of note, all data submitted centrally for analysis will be identified for country, but not for specific institution where data have been collected.

2.5. Purpose and/or rationale for the proposed project

This is a multi-centre study in patients with COVID-2019 who require admission to the intensive care unit, mechanical ventilation and ECMO to characterize the following features:

1. Incidence of ICU admission, use of mechanical ventilation and ECMO
2. Risk factors
3. Clinical features
4. Severity of respiratory failure
5. Need for non-invasive and invasive mechanical ventilation and ECMO
6. Settings of invasive mechanical ventilation
7. ECMO technical characteristics
8. Duration of ECMO
9. Complications
10. ICU survival
11. Hospital survival.
12. Requirements and the time frame for approvals in each participating network region

2.6. Plain language description

In late December, 2019, in Wuhan, Hubei Region, China, a new respiratory syndrome emerged with clinical signs resembling viral pneumonia and person-to-person transmission\(^1\). Samples from lower respiratory tract, corroborated emergence of a novel coronavirus, namely the 2019 novel coronavirus (2019-nCoV). In particular, several patients with pneumonia of unknown cause were in Wuhan on December 21, 2019 or later, and who had been present at the Huanan Seafood Market. Thus far, more than 111,000 confirmed cases, including health-care workers, have been identified...
worldwide, and several exported cases have been confirmed in other provinces in China, Thailand\(^2\), Japan\(^3\), South Korea\(^4\), Germany, Italy\(^5\), France, Iran\(^6\), USA\(^7\) and many other countries. An early case report in 41 patients with laboratory-confirmed COVID-19 infection in Wuhan has been reported\(^9\). The median age of the patients was 49 years and mostly men (73%). Among those, 32% were admitted to the intensive care unit. In a later retrospective report by Wang and collaborators\(^10\), clinical characteristics of 138 patients with COVID-19 infection were described. Those patients were admitted at Zhongnan Hospital of Wuhan University in Wuhan, China, from January 1 to January 28, 2020. The median age was 56 years and admission to the intensive care unit was required in 26.1% and 47.2% required mechanical ventilation.

Unfortunately, these initial clinical reports provide marginal characterization of patients who are admitted to the intensive care unit and require mechanical ventilation or other highly invasive procedures such as extracorporeal membrane oxygenation (ECMO) to support the failing lungs.

**Reference List:**


2.7. Administering Institution

The global management of this project is led by the 1) **Asian-Pacific Extracorporeal Life Support Organisation (APELSO)**, 2) The Critical Care Research Group (CCRG), The Prince Charles Hospital, Chermside, Australia and 3) University of Queensland, St Lucia, Australia in collaboration with The Alfred Hospital and Monash University, Melbourne, Australia, the SPRINT-SARI Study Group and International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) Coordination Centre based at the University of Oxford, Oxford, England. This study will also be coordinated regionally and /or at a Network.

2.8. Study dates/ length of time

We are seeking approval to conduct this research for the maximum number of months the IRB or Ethical board is able to approve, with the intention that IRB/ethical board renewals are maintained on an ongoing basis. We request the ability to activate this study as per the current study protocol as soon as possible due to the ongoing COVID-19 epidemic. We intend to collect data using the study documents for the length of time the outbreak is considered active. The decision on the outbreak study period will be made by the local lead investigator.

2.9. Project funding

Site may receive funding to potentially support a research nurse who will collect data in the collaborating Institution. The study has some central funding from the Asian-Pacific Extracorporeal Life Support Organisation.

2.10. Conflict of interest

No researchers or investigators have a conflict of interest in the outcome of the study’s results.

2.11. Time-critical aspects

To commence this study within the critical phase of the COVID-19 epidemics, we must have approval from IRB/Ethical boards within one week to commence participant screening/recruitment in the relevant peak of the outbreak.

2.12. Study Design

ECMOCARD is an observational study enrolling all participants newly admitted to the site who meet the COVID-19 case-definition and who are admitted to the intensive care unit. Patients will be studied from time of ICU admission up to 28 days or until hospital discharge, whichever occurs later. Data will be collected either prospectively or retrospectively. Wherever possible, data should be collected prospectively and entered as soon as possible. All clinical information and data recorded
will be from routine clinical practice, available from existing medical records. **Fully anonymised and de-identified data will be entered into an online eCRF database.** The central database, built on the CliRes Data Management System software is hosted in the United Kingdom (UK), for information on problems with the database or login details, email ncov@isaric.org. In Australia, re-identifiable data will be entered into a central REDCap database hosted by Monash University and harmonised with the SPRINT-SARI study. In countries unable to upload data on a centralised database the right to retain a local database on a national server is available with aggregated completely anonymised data exported centrally for analysis.

### 2.13. Data Analysis

The global analysis of ECMOCARD categorical variables will be described as proportions and will be compared using chi-square or Fisher’s exact test. Continuous variables will be described as mean and standard deviation if normally distributed or median and inter-quartile range if not normally distributed. Comparisons of continuous variables will be performed using one-way ANOVA or Mann-Whitney test, as appropriate. A logistic regression model will be performed to assess independent association between prognostic factors and outcomes, taking into account the hierarchical nature of the data. Significance will be set at p<0.05.

### 3. Participant enrolment

It is anticipated that between 0-40 participants will be enrolled at each site but there is no lower or upper limit on participant numbers. This study will require site staff review all enrolled participants’ site medical records/chart admitted to the unit of interest during the study period. Consent at the participant or surrogate decision maker level will not be sought, unless specifically required by the local IRB (APPENDIX A).

### 4. Benefits of the project

#### 4.1. Participant Benefits

Participants in this study will not directly benefit by participating in this study. It is hoped that by undertaking this study we will enhance the knowledge of COVID-19 which may help to improve future management of patients who are admitted to the intensive care unit and require mechanical ventilation and extracorporeal membrane oxygenation for the wider community.

#### 4.2. Institution Benefits

The potential benefits of the research to the general community, our local region and worldwide are substantial. This research is critical to acquiring an early understanding of COVID-19 of major public health significance. This study allows a globally coordinated research response to collecting

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Version 1.2.6 – March 10, 2020
information about the novel COVID-19 infection. The ECMOCARD will provide national and global estimates of intensive care utilisation (based upon common definitions), and will characterize presentations, progression, treatments, with specific focus on mechanical ventilation and extracorporeal membrane oxygenation and outcomes, to provide the basis for planning of future syndromic and infection-specific observational and interventional research.

4.3. Country /Network Benefits

The project will inform public health authorities of the burden of COVID-19 in intensive care units worldwide and on a local level, allows public health authorities to rapidly respond to escalation of either number or severity of disease. This study will potentially provide future logistic planning during epidemics and/or pandemics of infections similar to the COVID-19 epidemic.

5. Risks of the project

- This research has the potential to be conducted on vulnerable participants (e.g. children, those dependent on care, psychological/psychiatric conditions, elderly and pregnancy);
  - Data will be accessed/used without an individual’s informed prior consent
  - Data will be accessed/used without specific identification of the specific research institution in which data were collected

There are no additional risks to participants or investigators. No biological specimens will be collected for research purposes. All measures will be taken to prevent inappropriate release of any personal health information which will be harmful or embarrassing to any of the stakeholder.

6. Anonymity and confidentiality

6.1. How is privacy protected

Enrolled participants will be given a unique study ID on paper/electronic case report form (CRF). A master file linking unique ID with participants’ name, medical record number and date of birth will be created on paper/server used by research staff at each site. Only designated person(s) at the site will be allowed to access the master file. All CRFs will be kept on paper/password protected encrypted computer in a locked cabinet by the research team/lead Investigator. Completed CRFs will not be shared with anyone.

Electronic data files with the unique study ID will be stored on a secure password protected server that will have access granted to the site research staff and lead investigator only. Any information leaving the site (e.g. aggregate data for pooled analysis) will be anonymized and identified with a unique study ID, according to data sharing plans. Data will be completely de-identified with participants recognized by unique study identifier only.
6.2. Data storage at central centre after analysis
Data will be retained indefinitely by the Asian Pacific Extracorporeal Life Support Organisation (APELSO) but data will be destroyed or removed if requested at any time by participating sites/Network. Paper records will be held at site for a period of time as defined by local ethical guidelines.

Only the data management institution and the participating site investigator(s) will have access to the data. If others would like to use the data for analysis or publication an agreement must be reached with the coordinating centre, the site and the ECMOCARD steering committee. All ethical, legal and regulatory requirements in that location must be adhered with.

Data will be retained to provide a time-series over subsequent years that allows comparison of SARI activity with previous years.

6.3. Data confidentiality
Only de-identified data will be entered in the study database, to ensure participants cannot be identified. Data will be stored securely on the database in the University of Oxford, United Kingdom and backed up on a secure server. Only aggregate data will be reported in any publication or presentation, as such no individual participant will be able to be identified from the results.

7. Data

7.1. Data access after study completion
At the end of study, data will only be accessible to the research team (lead investigator, project manager, study statistician) and study sponsor on appropriate request in accordance with data sharing agreements.

7.2. Future use of data
The data collected during this project will only be used for the purposes described above. Any additional use of data will be subject to separate ethical/IRB approval applications. Ancillary studies must submit a formal proposal to the Management Committee and include one ECMOCARD Management Committee member as an investigator on the ancillary study.

8. International Collaboration
ECMOCARD will be conducted in conjunction with SPRINT-SARI and the World Health Organisation (WHO), the Australian and New Zealand Intensive Care Research Centre (ANZIC RC) International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), The International Forum of Acute Care Trialists (InFACT), the Platform for European Preparedness Against (re)-emerging
Epidemics (PREPARE). 20-30 hospital/ICU based formal and informal Networks are participating supporting and/or identifying approximately 100 hospitals/ICUs worldwide.

9. Publication policy

Publications using data collected by the ECMOCARD Investigators will be published on behalf of the ECMOCARD Investigators with a writing committee taking responsibility for all manuscripts. All members will be given the opportunity to contribute to the work of writing and all members of the writing committee who make a contribution to the writing will be recognised with authorship. Site lead investigators who are not on the writing committee will be recognised as ECMOCARD Investigator and noted in all manuscripts. ECMOCARD adheres to the ISARIC Publication Policy, Version 2, 21 July 2014 (https://isaric.tghn.org/).
Appendix A

Retrospective patient Information Sheet English

Centre No. ______________
City, Country ______________

PATIENT INFORMATION SHEET

Version 1.2.6 – March 10, 2020

Title of project: ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease

Local Investigator: [name and telephone number]: __________________________

While you were admitted to the intensive care unit, we asked your relatives permission to collect your clinical data for an observational research study. Before you decide to allow us to use these data, it is important for you to understand why the research is being done and what it is involving. Please read the following information carefully and, if you wish, to discuss it with your relatives or friends. Ask us if there is anything that is unclear or if you would like more information. Thank you for reading this.

1) What is the purpose of the study?

In late December 2019, a new virus causing severe respiratory infection has been discovered. The infection originated from Wuhan, Hubei, China, and spread worldwide. The infection is caused by a coronavirus named 2019-nCOv. Patients with COVID-19 often need respiratory support and, in case of severe respiratory failure, an advanced and invasive support named extracorporeal membrane oxygenation (ECMO). During ECMO, blood is oxygenated through an artificial lung in order to buy time until the infected lungs recover. To date, little is known regarding patients on ECMO for COVID-19 infection. The main purpose of this study is to collect data of patients with COVID-19 infection admitted to the intensive care unit and on ECMO to describe clinical features and improve treatment of future patients with this severe infection. This study has been designed by highly specialized doctors in the field of Intensive Care Medicine, Respiratory

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Medicine and ECMO, and with great experience in clinical studies. This is an international study, which comprises many hospitals in Asia and Australia, involving patients admitted into the intensive care units. This study has been reviewed and approved by the Research Ethics Committee of your hospital.

2) Why have I been chosen?
You have been chosen because you have been infected by the COVID-19 virus and during the course of the infection you were admitted to the intensive care unit and you have required mechanical ventilation and ECMO. Hence, the clinical data of your stay in the intensive care unit are essential to understand this disease.

3) Do I have to take part?
Data related to your intensive care unit stay have been already collected, but it is up to you to decide whether to allow the investigators to use these data. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive in the future from any hospital. If you do decide to take part you will be given this information sheet to keep and be asked to sign a retrospective consent form, a copy of the consent form will be also given to you.

4) What will happen to me if I take part?
As part of the study, routine information on your treatment collected, during your stay in the intensive care unit will be used for analysis. After you are discharged by the intensive care unit, we will contact you to see how you are doing. If you decide not to allow us to follow up your health status after the intensive care discharge, then we will abide by your wishes and not collect follow up data on you. You do not have to give a reason, and the standard of care you receive will not be affected.

5) What do I have to do?
You do not have to do anything yourself. The doctors and nurses on the Intensive Care Unit will keep you informed at all times.

6) What are the possible risks and benefits of taking part?
This study is only observational, which means only clinical data have been collected and no interventions have been carried out during your stay in the intensive care unit. Hence, no risks are associated with this study.

7) Will my taking part be kept confidential?
All information that has been collected about you during the course of the research study will be kept strictly confidential. Your identifying details will be held in a secure environment and only accessed by the research team for the purposes of follow up.

8) What will happen to the results of the research study?
The study is estimated to take around six months; it started in January 2020. It is hoped to be finished by June 2020. If you would like a copy of the published results, please contact the Principal Local Investigator.

**Contact for further information**

If you would like further information, please feel free to contact ____________________________________________, the leading investigator of the study on this unit.
Title of project: ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease

Local Investigator: [name and telephone number]:______________________________

We would like your relative to take part in a research study while he/she is here as a patient in the intensive care unit. Before you decide to give us permission to include your relative into this study, it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and, if you wish, to discuss it with your relatives or friends. Ask us if there is anything that is unclear or if you would like more information. Thank you for reading this.

1) What is the purpose of the study?

In late December 2019, a new virus causing respiratory infection has been discovered. The infection originated from Wuhan, Hubei, China, and spread worldwide. The infection is caused by a coronavirus named 2019-nCOv. Patients with COVID-19 often need respiratory support and, in case of severe respiratory failure, an advanced and invasive support named extracorporeal membrane oxygenation (ECMO). During ECMO, blood is oxygenated through an artificial lung in order to buy time until the infected lungs recover. To date, little is known regarding the patients on ECMO for COVID-19 infection. The main purpose of this study is to collect data of patients with COVID-19 infection on ECMO to describe clinical features and improve treatment of future patients with this severe infection. No novel treatments will be administered to your relative. This study has been designed by highly specialized doctors in the field of Intensive Care Medicine, Respiratory Medicine and ECMO, and with great experience in clinical studies. This is an international study, which comprises many university-hospitals in Asia and Australia, involving patients admitted into the intensive care units. This study has been reviewed and approved by the Research Ethics Committee of your hospital.
2) Why your relative has been chosen?
Your relative has been chosen because he/she has been infected by the COVID-19 virus and during the course of the infection he/she has required mechanical ventilation and ECMO. Hence, the clinical data of his/her stay in the intensive care unit are essential to understand this disease.

3) Does your relative have to take part?
It is up to you to decide whether your relative could take part to this observational study. If you decide for him/her to take part, you are still free to withdraw his/her participation at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your relative will receive in the future from any hospital. If you do decide that your relative can take part you will be given this information sheet to keep and be asked to sign a consent form, a copy of the consent form will be also given to you.

4) What will happen to your relative if he/she takes part?
As part of the study, routine information on your relative treatment will be collected, during his/her stay in the intensive care unit. These data will be used for analysis. After he/she will be discharged by the intensive care we will contact you to see how he/she is doing. If you decide not to allow us to follow up his/her health status after the intensive care discharge, then we will abide by your wishes and not collect follow up data on you. You do not have to give a reason, and the standard of care he/she receives will not be affected.

5) What do I have to do?
You do not have to do anything yourself. The doctors and nurses on the Intensive Care Unit will keep you informed at all times.

6) What are the possible risks and benefits of taking part?
This study is only observational, which means only clinical data will be collected and no interventions will be carried out during your relative stay in the intensive care unit. Hence, no risks are associated with this study.

7) Will your relative taking part be kept confidential?
All information that will be collected about your relative during the course of the research study will be kept strictly confidential. His/Her identifying details will be held in a secure environment and only accessed by the research team for the purposes of follow up.

8) What will happen to the results of the research study?
The study is estimated to take around six months; it started in January 2020. It is hoped to be finished by June 2020. If you would like a copy of the published results, please contact the Principal Local Investigator.

Contact for further information
If you would like further information, please feel free to contact ________________________________, the leading investigator of the study on this unit.
Next of Kin Consent Form English

Centre No. ______________________
City, Country ________________

NEXT OF KIN CONSENT FORM

Version 1.2.6 – March 10, 2020

Title of project: ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease

Local Investigator: [name and telephone number]: __________________________

I…………………………………………..(Full Name and Surname),………………………………………(Family Relation to the Patient) of……………………………… (Full Name and Surname of the Patient) acknowledge and certify that:

1. I confirm that I have read and understand the information sheet dated ________________ for the above study and have had the opportunity to ask questions
2. I understand that participation of my relative is voluntary and that I am free to withdraw the patient at any time, without giving any reason and without my medical care or legal rights being affected
3. I understand that sections of any of my relative’s medical notes may be looked at by responsible individuals involved with the study. I give permission for these individuals to have access to my relative’s records
4. I give permission for my relative’s personal identifying information to be collected, stored and used by the study office to enable follow up my relative’s health status. This is on the understanding that any information will be treated with the strictest security and confidentiality
5. I give permission for my local investigator to be contacted about my relative’s health status
6. I agree that my relative takes part in the above study

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Name of person taking consent
(if not Principal Local Investigator)

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Name of Principal
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I copy for patient, 1 for Principal Local Investigator, 1 to be kept with hospital notes