Date: 6 April 2020

To: Dr. Tarek Loubani

Project ID: 115775

Study Title: Reduced-aerosolizing BiPAP for patients in environment at risk of COVID-19

Application Type: HSREB Initial Application

Review Type: Delegated *PRELIMINARY REVIEW FOR COMPLETENESS*

Dear Dr. Tarek Loubani,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed the application for the study named above and determined that it may be reviewed at a Full Board meeting on receipt of satisfactory responses to the items outlined below.Please note that the HSREB is expediting reviews for COVID-19 related studies. As such, if there is not a HSREB meeting scheduled within ~7days of your response, we will do our best to convene an Ad-hoc meeting such that our regular deadlines do not apply an you are encouraged to respond ASAP.

List of requests and recommendations:

Review Form Comments
The HSREB acknowledges the critical healthcare problem this study is aiming to address. However, overall there are significant details lacking that require clarification (prior to full review). 1. Q1.4 Please explain how this study team will be able to implement this study. As per Lawson M. Columbus is located in Alberta and MT and AM are not in the LHSC directory. Further, there is no UH physician identified on the team. Please also ensure that if you will list Co-Is on the LOI, that all are listed on the LOI. a. Also, Lawson has pointed out that Dr. Loubani has not completed all of the mandatory training including GCP. Will this be able to be completed in a timely fashion such that this study is still relevant? 2. Q1.10 Protocol. Missing from the protocol and WREM is a sense of who has manufactured the experimental device and what testing has been done to date. The HSREB recognizes the long-standing relationship of the PI with his company Glia and simple searches reveal that funding has been received (Bassel Khartabil Fellowship) for the development of open-source 3D printed equipment for COVID-19 however none of this is explained in the application. Without some background it is very difficult to assess the safety implications of what you propose. Please provide the context for the device's development and if this is done by Glia, with other (Italian?) collaborators, or by the PI in his academic role. 3. Q2.10 There are most certainly procedures to be carried out that are not usual care as this is a RCT with an experimental device. Randomization, how will efficacy of ventilation support be measured (only chart review data?), how will aerosolization be measured (Q2.24 mentions more frequent assessment of the seal)? Are participants enrolled in the study for the entirety of their BiPap usage or for how long? Please ensure an explanation of everything the patient participant will experience is included. 4. Q2.15 Please enter a version date in the footer of the document. 5. Q2.16 The LibreOffice database would be a technology to acknowledge here. Although, it is unclear how this technology will be used as Section 13 discusses only the LHSC P: drive and paper documents. 6. Q3.7 The NCT number will be required prior to approval. 7. Q3.8 The background and rationale in Q2.6 do not explain any previous trials of this device or similar devices. Please explain this response. 8. Q6.9 Please explain whether or not you will pursue and ITA and if not, what the exemption is as per Health Canada. Q13.14 indicates a 25 year data retention which suggests that this is a Health Canada regulated study. 9. Q11.1 Please also acknowledge here and in the LOI/C that participants may also not benefit since it would seem that the device has not been proven efficacious. 10. Q11.3 What if the new device does not reduce aerosolization? If the patient has a large leak volume, there are risks to both health care providers as well as the patient (less Vt; hence less Ve). It would seem that there is significant risk to health care providers and patients not only potentially from the new device but from those randomized to control if the practice of using non-invasive support is currently controversial or discouraged due to risk of leaks and infection spread. Is there a risk the new device components will not work and the participant will need invasive support anyway? Please discuss these risks and how they will be mitigated Q11.5. a. Please also acknowledge risk of privacy breach. 11. Q11.9 Please discuss any conflict of interest of the PI serving on the DSMB? Are Dr. Mashari and/or Mr. Rhiger involved in device development? 12. Q12.1 It is unclear how PRE screening could be under participant authorization since it would occur prior to consent. Please explain or revise. 13. Q12.11 Can patients who are being considered for this kind of support be given "as much time as needed"? Or, is this not a much more emergent situation? Please speak to the condition of these patients and the actual timeline from determining

that support is needed to needing to actually implement this support. Q12.16 touches on this but seems at odds with the consent process outlined here. It is unclear if most of your participants would require an SDM or delayed consent? Please also discuss the appropriateness of SDM or defered consent given that standard of care is "in flux".

14. Q12.12/12.14 Please further justify why it is acceptable for the PI, who may be in circle of care, and is presumably involved with the development of the device being tested needs to obtain informed consent?
15. Q12.20 Would there not potentially be communication difficulties given that your exclusion criteria do not exclude those with communication difficulties?
16. Q12.21 Does this include other studies for COVID-19? Might there be mitigating circumstances that would impact the integrity of this trial?
17. Q13.3
a. You will also need hospital PIN for the master list and chart data collection.
b. Name. This will also have to be on your master list, it cannot be only on your LOI/Cs.
18. Q13.7 and Q13.8 are at odds with respect to memory stick use. Please clarify and provide name of encryption if they will be used.
19. Section 14. Please clarify source of funding more specifically than “self” and indicate where the funds are held if not at Lawson or Western. Please also attach a budget.
20. Q16.7 Will Dr. Loubani participate in data analysis?

21. Q2.20 Please clarify this statement. B-A analysis is used when comparing two measurements within a participant (i.e. flow using two different spirometers; blood tests purporting to measure "the same thing"). Our understanding in this study is that only one of the two masks are being applied. So, the relevant of the B-A method is not clear

22. Q2.24 One of the hypotheses of this study is that the novel mask will permit safe NIV due to a good seal. Specifically, "To validate that an easy-to-produce, specifically-engineered mask and circuit has the ability to maintain non-invasive ventilatory support while reducing aerosolization of viral particles."

Measuring leak volumes at four-hourly intervals says nothing about the possible contamination of said mask in the intervening period. Also, droplets/virions can escape in just a few mL of leak volume, contaminating the area around the patient (and at positive pressure). Therefore, I fail to see how measuring leak volumes equates to safety in a potentially covid +ve patient (who has not yet received a negative test).

Also, the statement above states a novel mask and CIRCUIT will be tested. So, does the experimental intervention include the mask and circuit or just the mask?

23. Q12.13 The statement "The data that is taken from you will be used validate the effectiveness of a non-aerosolizing mask in providing ventilatory support without aerosolizing viral particles, putting health care professionals and other patients at risk." is misleading. Nothing in this protocol measures anything about aerosolizing viral particles. At best, this protocol uses the surrogate outcome of leak volume, and then, only in a very non-granular way (i.e. only a few times, hours apart).

The LOI needs to be updated to express only what is actually being done in the study, and not surmise anything beyond that. The LOI will be reviewed "as new" when the application is complete and ready for Full Board review.

IMPORTANT RESUBMISSION NOTES:

- Ensure that you change Q1.1 from "Initial Submission" to "Response to REB Recommendations". Consult the "Help" tab in WREM for a guidance document on submitting responses.

- In a separate document, include each REB question/recommendation and your specific response to each. DO NOT refer to other documents.
- Submit all revised documents (e.g. instruments, LOI etc.) in TRACKED and CLEAN copies. The TRACKED copies must only be uploaded when prompted (i.e., in the section called “Resubmission Information”).
- When uploading the revised CLEAN copies, you MUST delete the old versions. Deleting the old versions will archive them and NOT permanently delete them.
- Ensure there is a version date (dd/mm/yyyy) in the footer of each revised document. This version date must be consistent with the version date entered when uploading the document.
- Please note that if a response is not received within 1 year of recommendations, this application will be considered stalled and be withdrawn.

If the above instructions are not followed, the file will be sent back until this is done. Please note that once we receive your response, further questions generated by your response may be asked.

DO NOT begin any study related activities until you receive final notification of approval from the Office of Research Ethics (ORE). If this study involves Lawson, you must also ensure you have received Lawson’s Institutional Approval (IA).

Please submit your response through WREM at your earliest convenience.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Nicola Geoghegan-Morphet, Ethics Officer on behalf of Dr. Philip Jones, HSREB Vice-Chair