Participant Information and Consent Form
Version 2.1, 23rd July 2020

Title of study	**Reducing acute severe respiratory events in health care workers during the Covid-19 pandemic with OM85**
Short title	COVID RASP
Study number	BV-2020/19
Protocol number	Version 2.1, 23 July 2020
Sponsor	The University of Queensland - Child Health Research Centre
Principal investigator	Professor Peter Sly
Institution	Child Health Research Centre
Phone number	(07) 3069 7002

You are being asked to participate in this research study because you are a "front line" Health Care Worker assessing or caring for patient with suspected or proven Covid-19 infection.

- This information sheet explains this research study and your participation in the study.
- Please read it carefully and take as much time as you need.
- Ask questions about anything that you do not understand now, or when you think of them later.
- Your participation is voluntary. If you enrol in the study and change your mind later, you may withdraw at any time without fear or loss of benefits.
- Whilst you are in the study, the study team will keep you informed of any new information that could affect your decision to remain in the study.
- Once all of your questions have been answered and you understand the research study, and you agree to take part, you will be asked to sign the consent form when you meet with the study team for your screening visit. You will be given a copy of the signed consent form for your records at that time.

Why are we doing the study?
You are being given this information sheet because you are a "front-line" health care worker assessing or caring for patient with suspected or proven Covid-19 infection, working at one of the hospitals that are participating in the study during the Covid-19 pandemic.

The purpose of this study is to see if we can prevent you developing an acute respiratory infection (ARI) that necessitates your removal from the workforce.

In theory, personal protective equipment (PPE) can protect health care workers from infection. However, adequate PPE is in short supply and commonly used surgical masks are unlikely to protect health care workers from virus-containing aerosols generated by infectious patients. These masks are not designed to form a seal around the nose and mouth nor to protect the wearer from submicronic particulate matter, including viruses such as COV.

OM85 is an immunostimulant. This means the drug works by priming the immune system so that the body can respond quickly to infections. Evidence from numerous trials has demonstrated that OM85 treatment during periods of high infection risk can reduce the frequency of symptomatic ARI. The mechanism-of-action appears to involve reduction in susceptibility to upper respiratory infection and attenuation of the intensity of inflammation-associated symptoms that accompany infection spread to the lower airways.

How is the study designed?
This is a phase three, randomized, parallel group, wait list design study.

Phase three means that the medicine has been tested in humans before and has been found to be safe, however the study will determine is efficacy in the circumstance and population intended.
Randomised means that whether you will be allocated participation in Group 1 (waitlist control, delayed treatment group) or Group 2 (initial treatment group) will be assigned by a computer. Your will have a 50:50 chance of allocation to the initial treatment group
Parallel group means that there are two distinct groups of treatment, in this case, Group 1 (waitlist control, delayed treatment group) or Group 1 (initial treatment group)
Wait list means that one group is randomised onto a "waitlist" for three months prior to commencing active treatment

Who is carrying out the study?
The study is being conducted at hospitals in Brisbane, Australia, A total of 1000 participants will be taking part in the study in Brisbane (at the Queensland Children's Hospital, the Princess Alexandra Hospital and the Prince Charles Hospital). A parallel study will be undertaken in London, Manchester, and Liverpool hospitals to recruit another 1000 health care workers.

This study is funded by the Medical Research Future Fund. The drug company, OM-Pharma, is supplying the OM85, free of charge.

The Child Health Research Centre at The University of Queensland is the sponsor of the study.

Do I have to take part?
No. You can say no to the study and this will not affect your employment or any care you require by doctors or other staff at the hospital.

What will you be asked to do if you decide to take part in this study?
This study runs for 12 months and will require either 4 or 5 visits, over either 6 or 9 months (dependant on the group you are enrolled in) at the hospital you are currently employed in. We may also call, SMS or email you during the study.

The first visit is a screening visit at which we will see if you are eligible to be in the study. We will complete the randomisation process at this time which will determine which treatment group you are allocated to (Group 1 [waitlist control, delayed treatment group] or Group 2 [initial treatment group]). At this time you can ask the study team any questions you may have.

If you are eligible and you wish to be a part of the study, you will be treated with study medication (OM85) as a participant of either group 1([waitlist control, delayed treatment group] - treatment commences at three months, visit 2) or group 2 ([initial treatment group] - treatment commences at visit 1). There will be a 50:50 chance of allocation to either group.

There will be an interim analysis of the study results to date at month, and if it is discovered that the treatment of OM85 is effective in preventing/reducing lower respiratory infections the Data Safety and Monitoring Board may recommend the study be stopped and all participants be treated with OM85.

What do I need to do to be in the study?
If you are eligible for the study, you will be required to attend either 4 or 5 visits (depending on whether you are randomized to study group 1 or 2) at the hospital you are currently employed in:-
Group 1 - (waitlist control, delayed treatment group) for 5 visits in 9 months
Group 2 - (initial treatment group) 4 visits in 6 months.
We will try to find appointment times that suit you

Below is a table showing you what procedures will be done at each study visit and when they occur.

Group =1 (Wait List Control, delayed treatment)

	Recruitment and Randomisation	Treatment initiation	Treatment Cessation	Follow-up Cessation	Unscheduled visit
Visit	1	2	3	4	5
Day	0	90	180	270	
Visit Window		±5 days	±5 days	±5 days	
Informed consent	x				
Eligibility criteria	x				
Randomisation	x				
Medical history	x	x			
Demographic history	x				
Vital signs	x	x	x	x	x
Nasal swab		x	x	x	x
Study bloods		x	x	x	x
Drug delivery		x			
Drug distribution		x			
Drug collection			x		
Daily symptom data explained & first day completed	x				
Diary Daily symptom data reviewed		x	x	x	x
Adverse events		x	x	x	x

Group 2 (Initial Treatment)

	Recruitment Randomisation and Treatment	Treatment Cessation	Follow-up Cessation	Unscheduled visit
Visit	1	2	3	4
Day	0	90	120	
Visit Window		±5 days	±5 days	
Informed consent	x			
Eligibility criteria	x			
Randomisation	x			
Medical history	x			
Demographic history	x			
Vital signs	x	x	x	x
Nasal swab	x	x	x	x
Study bloods	x	x	x	x
Drug delivery	x			
Drug distribution	x			
Drug collection		x		
Daily symptom data explained & first day completed	x			
Diary Daily symptom data reviewed		x	x	x
Adverse events		x	x	x

The study procedures and assessments are described below:

Demographic and medical history
We will need to ask you some questions such as about your date of birth, ethnicity, sex, smoking history and any medical conditions that may increase your risk of developing a lower respiratory illness necessitating workforce removal.

Vital signs
The study nurse will take some vital signs like temperature, heart and respiratory rate, at study visits, to monitor your health during the trial.

Collection of blood
We would like to take approximately 20ml of blood at each study at visit. We will take blood by venepuncture. We will only attempt to do this once, so the maximum number of venepunctures at each visit is one. If we cannot get blood, or enough blood we will not try again at that visit, unless you specifically provide verbal consent for us to do so at that time,

however you do not need to agree to this. Sometimes taking blood may leave a small bruise but this is not harmful.

The blood will be used to test for Covid-19 seroconversion and to develop an immune cell profile. As these tests will be done in batches in Perth, we will not be in a position to give you immediate feedback on your results. You will be given a report at the end of the study that shows what influence OM85 had on immune profiles.

Nasal swabs
We would like you to collect a swab from your nose during each visit. We will show you how to do this. We will ask you to insert the swab a short distance into each nostril, gently rubbing the nasal mucosa. The one swab will be used for both nostrils. The study nurse will collect the swab from you at the visits. This is not a painful or unpleasant experience for you. The nasal swab will be used for viral identification, including Covid-19.

SMS/ Respiratory symptom diary
Following randomisation, we will be explaining to you how to document/respond to a daily SMS regarding any respiratory symptoms. We ask that you complete these every day during the study. These symptoms and/or condition related to the symptoms will be recorded as adverse events.

Adverse event review
During the study these are collected from your response to the daily SMS (see above). Staff will check these responses and any unclear or missing entries will be clarified with you.

How is the study drug given?
OM85 comes in a hard capsule and is given orally. The study dose is one capsule (7.0 mg) daily for three months.

Are there alternative treatments?
There are currently no approved treatments for preventing Covid-19. Viral infections may be treated with retroviral therapy, however we think OM85 may help prevent or reduce the number and severity of acute severe respiratory events should you contract Covid-19. This is a research study and the treatment is experimental.

Is there likely to be a benefit to you?
There may be no direct benefit to you. We anticipate treatment with OM85 will reduce the number and severity of acute severe respiratory events should you contract Covid-19, however we cannot guarantee this.

Is there likely to be a benefit to other people in the future?
If this study shows that OM85 can reduce acute severe respiratory events in health care workers during the current Covid-19 pandemic, then other people may benefit in the near future.

What are the possible risks and/or side effects?
Participation in this study may also involve some risks and/or discomforts. These are described in detail below:

Study Medication
OM85 is currently not approved by the Therapeutics Goods Administration. OM85 (as Broncho Vaxom) has been used in 65 countries for the last 30 years in children and in adults and has an excellent safety profile.

It is possible for any medication to cause unwanted side effects. If they occur, most are likely to be minor and temporary. However, some may be serious. Check with your doctor as soon as possible if you think you are experiencing any side effects from this medicine, even if the problem is not listed below.

Published clinical trials have reported OM85 to be well tolerated in children and adults. Most side effects previously reported using OM85 were mild and related to underlying disease and/or age. In adults, the most common reported adverse events were gastrointestinal, including nausea and diarrhoea.

Other risks
The treatment and procedures involved in this research study may involve unexpected risks that are impossible to predict. These unforeseen risks may affect you during your participation in the study and/or some point in the future.

Blood test: You may experience discomfort and/or bruising as a result of the blood test.

What happens if I am injured as a result of participating in this research project?
You will be compensated if you suffer an injury as a result of your participation in this research project. Compensation will be provided in accordance with the Medicines Australia (formerly known as APMA) Guidelines for compensation for injury resulting from participation in a company-sponsored clinical trial subject to the scope of the conditions "No-Fault Compensation Insurance for Clinical Trials". A copy of the Medicines Australia Guidelines is available to you from the research staff on request.

Can I voluntary withdraw from the study?
Yes. You may decide to not to take part or you may withdraw from this study at any time. If you decide to withdraw from this study, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you would otherwise be entitled to receive. The decision to withdraw from the study will not prejudice future relations with the any of the hospital's participating in this study, including any you may work in, or with any people treating you or working with you. If you withdraw from the study, you will be provided with results of the overall study and with your own results from the time you participated.

What are the reasons that I may be withdrawn from the study?
You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- The doctor determines that it is in your best interest not to continue;
- You are unable to complete required study treatments and examinations;
- The study is stopped by the Institution, the Sponsor(s), or the Therapeutic Goods Administration (TGA) or other health authorities in Australia;
- The study is cancelled due to adverse events or in circumstances where the trial is halted because of safety concerns.

Will I receive payment or have expenses for being involved in the study?
You will not receive payment for taking part in this study. There will be no cost to you as a result of taking part in this study.

Where is my information kept?
Electronic and paper copies of data will be stored by the relevant site investigator for the appropriate period of time as determined by local regulations and ICH-GCP (International conference on harmonization- Good clinical practice).

Some of the tests we are doing on the samples we collect are very specialized and not available everywhere. This means that we want to be able to share the samples with members of our research team and other scientists elsewhere in Australia and overseas. At all times your confidentiality will be protected and the samples we share will not be labelled with your name.

We are also asking your consent to keep any samples not used in the study analyses. This is because new tests may become available and your samples may provide valuable data in the future. Any future use of your samples will need to be approved by the ethics committee and will be consistent with the purpose you consented to in this study, namely to investigate host responses to viral infections, including Covid-19.

What about my privacy?
We hope to able to publish the results of this research study so that other doctors will be able to benefit from this research. Your medical and research records will be confidential to the extent permitted by law. Every possible effort will be made to keep your personal information confidential. However, we cannot guarantee complete confidentiality.

You will be identified by a code. This is called de-identification. Results may be discussed at conferences or may be published, but you will not be identified.

Your medical and research records will be reviewed by the Sponsor (including its representatives, agents, and contractors that assist in conducting, monitoring or analysing the study). These records may also be reviewed for regulatory purposes by the Australian Therapeutic Goods Administration (TGA) and/or other relevant health authorities.

Who has approved the study?
This study has been approved by the Children's Health Queensland Human Research Ethics Committee.

Will I be informed of the results when the research study is finished?
The study staff will send you a letter with the results when the study is finished. Because of the length of the study, it may be some time before we are able to do this.

Who should I contact for more information?

If you would like more information about the project or if you need to speak to a member of the research team in an emergency please contact:

Name:	<insert name>
Contact telephone:	<insert contact phone number>
Email:	<insert email>

HREC Information:

The Children's Health Queensland Hospital and Health Service Human Research Ethics Committee (HREC) has approved this study. If you have any concerns and/or complaints about the project, the way it is being conducted or your child's rights as a research participant, and would like to speak to someone independent of the project, please contact the HREC Co-ordinator on:
3069 7002 or email CHQETHICS@health.qld.gov.au

Local Governance Contact Information

Name:	Research Governance Officer
Contact telephone:	<insert contact phone number>
Email:	<insert email> - must be generic address

Form of Consent

Please note that participation in research studies is voluntary and subjects can withdraw at any time with no impact on current or future care.

I have read the information sheet explaining the study entitled "**Reducing acute severe respiratory events in health care workers during the Covid-19 pandemic with OM85**"

I have read and understood the information given to me. Any questions I have asked have been answered to my satisfaction.

I agree to participate. I understand I may withdraw from the study at any stage and withdrawal will not interfere with routine care or my employment.

I agree that research data gathered from the results of this study may be published, provided that names are not used.

Participant name: _____

Participant signature: _____ Date: _ _ / _ _ _ / _ _ _ _

I have explained the above study to the signatories who stated that he/she understood the same.

Name of person obtaining consent:_____

Signature: _____Date: _ _ / _ _ _ / _ _ _ _

Revocation of Consent

Please note that participation in research studies is voluntary and subjects can withdraw at any time with no impact on current or future care.

I hereby wish to WITHDRAW my consent for my participation in the study entitled "**Reducing acute severe respiratory events in health care workers during the Covid-19 pandemic with OM85**"

I understand that such withdrawal WILL NOT jeopardize any treatment I may require or my relationship with Queensland Health and/or my employing hospital

I acknowledge that my health information and samples collected up to the time of withdrawal may continue to be used and shared in accordance with the Participant Information and Consent Form.

Participant name: _____

Participant signature: _____Date: _ _ / _ _ _ / _ _ _ _

I have discussed revocation of consent to the signatories who stated that he/she understood the same.

Name of person consenting the participant:_____

Signature: _____ Date: _ _ / _ _ _ / _ _ _ _