PARTICIPANT INFORMATION SHEET/ CONSENT FORM

Title	Investigation of nasal deposition a nasal mesh nebuliser
Short title	Nasal deposition by NMN
Protocol number	RT16-NMN-V01/ AFT-MD-1
Project Sponsor	Woolcock Institute of Medical Research
Coordinating Principal Investigator/ Principal Investigator	A/Prof. Gregory King
Associate Investigator(s)	Prof. Paul Young, Prof. Dale Bailey, A/Prof. Daniela Traini, Dr. Hui Xin Ong, Dr. Yang Chen
Location	Royal North Shore Hospital

Part 1 What does my participation involve?

1. Introduction

You are invited to take part in this research project because you are a healthy individual with no history of smoking or any nose and lung disease. This study will involve testing a new nasal delivery device called Nasal Mesh Nebuliser (NMN) to target the sinus regions of the nose. We want to see if this device is more efficient in targeting the sinuses.

This Participant Information Sheet/Consent Form tells you about the research project, and tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend, or your local doctor. We have specialists available to answer any questions.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the nasal delivery?

Nasal delivery is used to administer topical treatment for local diseases in the nose and paranasal sinuses, such as rhinitis (swelling of the inside of the nose) and sinusitis (inflammation of the sinuses). Researches have been trying to develop new technologies and devices to specifically target the nasal sinuses to better treat sinusitis (inflammation of the sinuses) caused by bacteria infections. Currently, there is no efficient device capable of specifically targeting the sinus cavity in the nose. A device that could target the sinus cavity will particularly be useful for the treatment of chronic sinus infection where patients have excessive mucus, abnormal sinus structure and bacteria infection resulting in severe pain and discomfort. This disease is difficult to treat with current therapy and in many cases, requires surgical intervention.

Figure A: Nasal Mesh Nebuliser device (NMN).

The Nasal Mesh Nebuliser (NMN, Figure A) is a device designed to deliver medicines to the nose which could potentially be used for the treatment of chronic sinus infection in the future. Understanding where the aerosols produced by this nasal delivery device land in the nose regions will help fine tune the NMN device parameters to maximise delivery of drugs into the sinuses.

3. What is the purpose of this research

The purpose of the research project is to see where the aerosols generated from the NMN device will land in the nasal regions by varying the aerosol flow (continuous vs. pulsative flow). To do this, we will perform a series of nasal radio-aerosol scans. We want to determine the optimum device settings to efficiently target the sinus cavities in the nose. This will provide the platform for future treatments that targets this region.

This research has been initiated by the study doctor, Associate Professor Gregory King and has been funded by the NH&MRC Development Grant and in partnership with the device manufacturer AFT Pharmaceuticals.

4. What does participation in this research involve?

If you are interested in being part of this study we will ask you to come to Royal North Shore Hospital at St Leonards for the following visits:

- **Visit 1** – you will sign a written informed consent and undergo a screening test with includes lung function, urinary cotinine and skin prick tests. You will also be asked to complete 2 standard and validated clinical questionnaires: Woolcock's Clinical questionnaire and SinoNasal Outcome Test (SNOT) 22. We will then do baseline high-resolution CT scan and a Nasal Radio-Aerosol Scan measurements using NMN device at a set setting.
- **Visit 2-4** –three separate Nasal Radio-Aerosol Scans with the new NMN device of different settings.

The total duration of the study for each participant is less than 60 days.

As much as possible, we will schedule the timing of the test to your convenience. We will provide you with details of how to reach the department and contact numbers in case of any problems.

Before each visit

We will also ask you to refrain from taking any products that contain caffeine such as coffee and chocolate for 6 hours before each of the visits as this too may have a small effect on the results.

Visit 1: Initial screening visit
(45 minutes - 1 hour)

After you have read what this study is about, please ask questions to clarify things you are unsure about. Once you are fully informed you can sign a consent form, which states that you agree to participate in the study, take part in the testing and perform the Nasal Radio-Aerosol Scans.

To see if you are in fact eligible to participate in this study we will do the following:

- Check if you have any nasal or lung disease with a Woolcock respiratory, sinus and medical questionnaire.
- Your height and weight will be measured.
- Check your medical history
- Check if you have any common allergies by performing a skin prick test.
- Check your lung function by performing a simple breathing test called spirometry: This will determine how quickly your lungs can breathe air in and squeeze air out. You will need to suck and blow air as fast as you can and as forcefully as you can.
- You will be asked to provide a urine sample to confirm your smoking status.

If you are eligible, you will be enrolled into the study. Once you are enrolled in this study it is **important** that you attend **all** visits on the scheduled dates. But you have the right to withdraw from the study at anytime. Research staff will schedule these dates with you once you are enrolled in the study and will remind you of upcoming appointments.

Visit 1-4: Nasal Radio-Aerosol Scans.
These visits are very similar. All visits take place at the Royal North Shore Hospital. Each 'Visit' will take about 1 hour AND there will be follow-up via telephone at the 24-hour time point and to re-schedule the next visit.

Before the start of the study (Visit 2-4) you will do the following:

- You will be asked to provide a urine sample for evidence of smoking.
- Refrain from taking any products that contain caffeine, such as coffee and chocolate for 6 hours before each of the visits as this too may have a small effect on the results. You will be asked to continue refraining from caffeinated products during the visit.
- Check your lung function by performing the spirometry-breathing test.

The ***Nasal Radio-Aerosol Scan*** itself involves receiving into your nose a small amount of a radioactive marker called technetium in saline solution. This marker is used for many medical imaging protocols such as those used for bone and kidney scans and has been in use for over 20 years. It will be administered as a fine mist that you deliver into each side of your nose via the device (nasal mesh nebulizer) that we have provided you with
We will give you detailed instructions on how to use the device and help on the day. You should not feel anything unusual while receiving the saline solution as no drugs are involved in this trial.

After you have received the technetium solution, your head will be imaged using gamma camera (a device used to carry out functional scans of your head) at different time points over an initial period

of 1 hour. This allows us to see where the aerosols have landed in the different areas of your nose and also how this is being cleared from your nose.

During the imaging scan, you will be asked to:

1) Sit down in front of the gamma camera (a device used to carry out functional scans of your head) head to receive a head and upper respiratory tract imaging.
2) This is followed by lying down in a comfortable position on a table and the two cameras will be positioned in front and behind you.
3) You will be scanned continuously for 20 minutes after receiving the technetium. A final scan at 1 hour time point will be taken.
4) Breathe as normal but you will be asked to keep still during these scans. These scans do not involve an enclosed space. You will be able to listen to music during the imaging, please bring your own portable music device. The cameras will move around you to get a detailed view of the deposition of the inhaled technetium in your nose.

All tests that are part of the research project will be provided to you free of charge. Participants will be reimbursed for expenses related to their participation in this study (e.g. time, parking, taxi and/or other travel expenses). This reimbursement will be up to $250 when completing all the four visits.

5. Who to contact in case of side-effects?

If you have any medical problems which may be related to your involvement in this project (any side effects), you can contact the principal medical clinician for this project, Associate Professor Gregory King on (02) 94632935 or (04) 25255916 who will assist you in arranging appropriate medical treatment. Alternatively you can report any side-effects experiences to the study investigators [Dr. Hui Xin Ong (02) 9114 0473 or Dr. Yang Chen (02) 9114 0370] during the follow-up phone call or during your next visit at RNSH. In case of emergency outside of office hours, you can contact Associate Professor Gregory King (02) 94632935/(04) 25255916, Dr. Hui Xin Ong (02) 9114 0473/(04) 33381575 or Dr. Yang Chen (02) 9114 0370/(04) 33569006.

6. Other relevant information about the research project

This research study is going to be taking place at the Royal North Shore Hospital (NSW). We will be recruiting 11 people into this study.

7. Do I have to take part in this research project?

Participation in this study is entirely voluntary. You do not have to take part in it. You can withdraw at any time without having to give a reason.
Whatever your decision, please be assured that it will not affect your future medical treatment or your relationship with the staff who are caring for you.

8 What are the possible benefits of taking part?

You will not directly benefit from taking part in this study but information we get from this study will help improve future treatment for patients with chronic sinus infection.

9 What are the possible risks and disadvantages of taking part?

This research study involves exposure to a small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2

millisieverts (mSv) each year. The effective dose from this study is about 2.86 mSv. The dose from this study is comparable to that received from any diagnostic medical x-ray and nuclear medicine procedures. At this dose level, no harmful effects of radiation have been demonstrated as any effect is too small to measure. The risk is believed to be low and theoretically is approximately equivalent to 1 in 7000.

The risks associated with inhalation of a radioactive marker are minimal, that of discomfort in performing the breathing tests, which require blowing forcefully and maximally into a mouthpiece, or slight nasal irritation or “tickling” during the nasal administration using the device. The effective dose contained in the radioactive marker for inhalation is very low (0.96 mSv in total for all the four visits) and it is compliant with the practicing code of Exposure of Humans to Ionizing Radiation for Research Purpose. The radioactive marker inhaled will be cleared by your body within a couple of hours and we will monitor the clearance rate at certain time points.

You may experience discomfort from having the skin prick test. In some people the skin prick may result in local redness and inflammation
However, all medical procedures carry some risk of injury but all precautions will be taken to minimise these risks. The biggest problem might be the inconvenience of the study visits and as mentioned we will try, as much as possible, to schedule visits at your convenience.

If you experience any side effects from the procedures described above we will provide you with appropriate medical care or withdraw you from the study, if keeping you in the study is not in your best interest.

10. What will happen to information about me?

This study requires you to come to the Royal North Shore Hospital (RNSH) multiple times and also receive reminder phone calls from our research staff. The phone calls require re-identifying you from your unique numerical code so we can get your contact details and also enter any data from these calls into the correct file. Data will be stored under a study number, in a separate file so that on study completion, data cannot be identified during data analyses.

Your test results will have all identifiers (e.g. name and personal details) removed and replaced with a unique numerical code. It will be possible to re-identify the results as yours using the code. Only authorised personnel on the research team will have access to password-protected databases containing your identifiable information. Your data will not be released for any use without your prior consent, unless required by law.

In accordance with relevant NSW privacy and other relevant laws, you have the right to request access to your information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

11 Banking of Health Information

Banking is storing health information for future research studies. A bank represents a database where the health information is stored.

The data will be stored for 15 years regardless of whether the project ceases or whether any researchers cease employment at the current organisations. After 15 years the data will be destroyed. Paper copies will be placed into a locked bin allocated for sensitive material. The contents of this box are regularly and securely disposed of. Computer files will be permanently deleted from computers, hard-drives, and any other locations with assistance from the Information Technology department.

We would like to store your lung function results, questionnaires and scan images for future use in research studies that are an extension of this study or closely related to this study.

Your personal information and identifiers (name, date of birth) will be replaced with a unique numerical code and your results will no longer be tracked to your identity.

The health information that we would like to bank for use in future research studies includes:

1) All the imaging data such as head CT and Nasal Radio-Aerosol Scans.
2) Results from the lung function, skin prick and urine tests.
3) Responses to questionnaires.

It is possible that this data would be useful in future research, audit and teaching projects, helping us to continually improve health outcomes and develop new treatment. Your data would be anonymised prior to being used for this work. If you do not wish your data to be used in any future research, after this study, it will not affect your participation in any way. Consenting your data to be used in future research is optional – it is your choice, you don't have to agree with it. You will be asked to sign an additional form to indicate your consent for the banking of your data. You are also free to withdraw consent of banked data at anytime and it will not affect your future medical care.

We will not use your personal health information for a different research project without the permission of a Human Research Ethics Committee. Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the research project may be presented in public talks or written articles but information will not be presented that identifies the participant.

12 What will happen to my test results?

Upon request we can provide you with your lung function measurements and skin prick test throughout the study. Although unlikely, making incidental findings on medical imaging and during screening can occur and may warrant further investigation. In the event of any finding, the study investigators will inform both you and, with your permission, your primary care physician.

The results of this research will be shared with the device manufacturer.

Upon request, we can provide you a summary of the results of this research.

Part 2 How is the research project being conducted?

13 Complaints and compensation

If you suffer any injuries or complications as a result of this study, you should contact the study doctor (A/Prof Greg King on (02) 9114 0413) as soon as possible, who will assist you in arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). You do not give up any legal rights to compensation by participating in this study.

14 Who is organising and funding the research?

This research project is being conducted by Associate Professor Gregory King and funded by Woolcock Institute of Medical Research and NH&MRC development grant. The device manufacturer (AFT Pharmaceuticals PTY Ltd.) does not provide any funding for this research, but providing the devices (funding in-kind) and technical support. .

There are no financial benefits to you, the research staff, clinicians, the Royal North Shore Hospital, Woolcock Institute of Medical Research, or the NH&MRC Centre of Excellence (project from your participation in this research study.

15 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the Northern Sydney Local Health District (NSLHD) (HREC Reference: HREC/16/HAWKE/256).

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

16 Further information and who to contact

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (any side effects), you can contact the principal medical clinician for this project, Associate Professor Gregory King on (02) 94632935 or Professor Dale Bailey on (02) 9926 8375.

For more information on the study please contact: Dr. Hui Xin Ong (02) 9114 0473, Associate Professor Daniela Traini (02) 9114 0352, or Professor Paul Young (02) 9114 0350.

For emergency medical care outside of office hours contact emergency on 000.

Clinical contact person

Name	Associate Professor Gregory King
Position	Head of the department of Respiratory Medicine
Telephone	(02) 9463 2935
Email	gregory.king@sydney.edu.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Woolcock Institute of Medical Research:

Name	Professor Paul Young
Position	Head of Respiratory Technology
Telephone	(02) 9114 0350
Email	paul.young@sydney.edu.au

Royal North Shore Hospital:

Name	Associate Professor Gregory King
Position	Staff specialist, Department of Respiratory Medicine
Telephone	(02) 9463 2935
Email	gregory.king@sydney.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Contact	Research Ethics Manager
Telephone	(02) 9926 4590
Email	NSLHD-research@health.nsw.gov.au

CONSENT FORM

Title	Investigation of nasal deposition using a nasal mesh nebuliser
Short title	Nasal deposition by NMN
Protocol number	RT16-NMN-V01/AFT-MD-1
Project Sponsor	Woolcock Institute of Medical Research
Coordinating Principal Investigator/ Principal Investigator	A/Prof. Gregory King
Associate Investigator(s)	Prof. Paul Young, Prof. Dale Bailey, A/Prof. Daniela Traini, Dr. Hui Xin Ong, Dr. Yang Chen
Location	Royal North Shore Hospital

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Study Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

CONSENT FORM

DATABASE STORAGE

WIMR Data Bank

I consent to the banking of information collected about me as described in Section 11 of this document (lung function results, skin prick and urine test results, responses to questionnaires and scan images) for use in future research studies that are an extension of this study or closely related to this study.

Signature of Participant	Please PRINT name	Date

Signature of Investigator	Please PRINT name	Date