Participant Information Sheet/Consent Form

Health
Western Sydney
Local Health District

Interventional Study - *Adult providing own consent*

Westmead Hospital

Title	A randomized, double-blind crossover controlled study of botulinum toxin treatment in upper limb tremor
Short Title	The role of botulinum toxin treatment in upper limb tremor
Coordinating Principal Investigator/ Principal Investigator	Associate Professor Victor Fung
Associate Investigator(s)	
Location	Westmead Hospital

Part 1 What does my participation involve?

Introduction
You are invited to take part in this research project. This is because you have upper limbs tremor. The research project is testing a new treatment for upper limbs tremor. The new treatment is called botulinum toxin injection.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the 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.

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 purpose of this research?

The purpose of the study is to evaluate clinical, functional, and quality of life outcomes in patients with upper limbs tremor following treatment with botulinum toxin injections. Botulinum toxin type A (BoNTA) has been widely used in treatment of various movement disorders. There have been studies suggesting the effectiveness of BoNTA in treating upper limb tremor related to multiple sclerosis and essential tremor. It is hoped that the study will provide more information about the functional outcome of BoNTA in treating upper limb tremor, regardless of its aetiology.

Botox and Xeomin both brands of BoNTA, are approved in Australia to treat excessive muscle contractions arising from abnormal brain activity following stroke (spasticity of the upper limb), dystonia (spasms of the neck or eyelids - cervical dystonia and blepharospasm), legs (dynamic foot deformity due to spasticity or paediatric cerebral palsy), face (hemifacial spasms), and frown lines (glabellar lines - vertical lines between the eyebrows and above the nose visible when a person frowns). However it is not approved to treat upper limb tremor. Therefore, it is an experimental treatment for upper limb tremor. This means that it must be tested to see if it is an effective treatment for upper limb tremor.

This research has been initiated by the study doctor, Associate Professor Victor Fung and funded by Neurology Department..

3 What does participation in this research involve?

If you decide to participate in this study, you will be asked to sign the Participant Information and Consent Form.

You have been asked to participate in this study because you have upper limb tremor. This is a randomized, double-blind, controlled study.

For your first treatment, you will be assigned completely at random to receive one of the two possible study treatments- Xeomin or placebo (a placebo is a dummy treatment that looks like the real thing but is not and contains no active ingredient). You will have 50% chance of receiving placebo but the same chance of receiving Xeomin as your first treatment. Your doctor will assess your tremor to determine the affected muscles and the dosage of the study treatment. The doctor will then inject the assigned study treatment (Xeomin or placebo) into the affected muscles of your arms.

Definitions
‘Randomised trial’: Sometimes doctors don’t know the best way of treating patients with a particular condition so comparisons need to be made between different treatments. To do this, study participants are put into groups and given different treatments, and the results are compared to see whether one treatment is better. To ensure the groups are similar to start with, a computer allocates each study participant into a group randomly, like the flip of a coin. Neither the doctor nor the study participant can decide which treatment the participant receives.

‘Blind trial’: In a ‘blind trial’ the study participants do not know which treatment group they are in. If the trial is “double blind”, neither the doctor nor the study participant knows which treatment the participant is receiving (although, if the doctor needs to find out, he/she can do so).

‘Placebo’: A placebo is a dummy treatment that looks like the genuine medicine but contains no active ingredient.]

‘Crossover’: Rather than participants remaining on a single treatment path in a parallel trial, patients in a crossover study will "crossover" or move to another treatment arm during the course of the trial. This means that even if they are initially put into a placebo arm, they will also eventually receive the study drug or standard of care during the trial. This mean that you can

start the trial receiving Xeomin and then placebo have treatment after the second period of the trial.

If you agree to participate in this study, you will then be asked to undergo an initial assessment prior to starting the therapy, with repeat assessments at 4, 8, 12, 16, 20, 24 weeks .

At the initial assessment, data will be collected from you. This includes details about your general medical condition and your tremor, including your current medications. The goal of the treatment will be discussed and set. Your tremor pattern will be videotaped and also recorded by surface electromyography (tremor study), which is a device that records your muscle activities using surface electrodes. You will also be asked to complete several questionnaires. The questionnaires include questions about your activities of your daily livings and the quality of life. The initial assessments are estimated to take 2 hours to complete. At follow-up assessments, you and your study partner will be asked to complete the same assessments as you did in the initial assessment.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge. It is desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that you inform them of your participation in this research project.

4 What do I have to do?

As part of the study, there are no lifestyle or dietary restrictions and you can take your regular medications. However, if the regular medications contain active ingredient that might affect your tremor, which your doctor will tell you, you should not make changes to the dosing during the study period.
All changes in the state of your health during the study must be reported to your doctor or a member of the hospital personnel, regardless of whether or not you think that these changes are related to the study. During the whole study you will be monitored in regard to new symptoms, new diseases, side effects, other medications and compliance with the appointment schedule.
In certain cases you might need to be prescribed new medications that you need by other doctors. In such cases you must inform the doctor who would like to prescribe new medications that you are taking part in a clinical study and that you have received a Botulinum toxin type A product.
You must not take or receive any of the following medications while participating in the study: Botulinum toxin of any type into any other site of the body, Aminoglycoside, penicillamine, procainamide, spectoinomycin, polymixin, tetracycline, lincomycin or other agents interfering with neuromuscular transmission or any investigational new drug or device.
Blood donation is not allowed during the study period.

5 Other relevant information about the research project

There will be a total of 30 patients taking part in this project in Westmead hospital. You will be randomly divided into two groups, the treatment group and the placebo group.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.
If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Westmead hospital

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Other options are available; these include many kinds of oral medications. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefit is improvement of your tremor, which hopefully will result in improvement of your hand function.

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

All medical procedures involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown or unforeseeable. In spite of all reasonable precautions, you might develop medical complications from participating in this study. The known risks of this study are:

In clinical trials in patients suffering from illnesses including cervical dystonia approximately 30% of patients treated with Xeomin experienced an adverse event. These were:

- Generalised weakness 1-10%
- Fatigue (exhaustion, lethargy, tiredness, and/or asthenia) 1-10%
- Flu-like syndrome 1-10%
- Pain / bruising /swelling / reddening at injection site 1-10%
- Itching 0.1- to 1%
- Muscle weakness 0.01 - 0.1%
- Skin rashes including rashes at the injection site 0.01 -.1 %

In 21 clinical trials involving approximately 4100 patients with cervical dystonia only the following adverse effects were reported:

- Dysphagia (difficulty swallowing) more than 10%
- Neck muscle weakness 1-10%
- Dysphonia (voice changes) 1-10%
- Headache 0.1-1%
- Neck pain 0.1-1%
- Jaw weakness 0.1-1%
- Dry mouth / throat 0.1-1%
- Vertigo / dizziness 0.1-1%
- Diplopia (double vision) 0.1-1%
- Blurred vision / visual difficulty 0.1-1%
- Respiratory disorders 0.01 – 0.1%
- Aspiration (drawing foreign bodies such as food into the lungs) 0.01-0.1%
- Pharyngitis (sore throat) 0.0.1-0.1%

Having a drug injected may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Pregnancy and contraception
It is important that women participating in this study are not breast-feeding, pregnant and do not become pregnant during the study as the study drugs may damage a born/unborn baby. The effect of the study drugs on an unborn baby is unknown. If you are a woman of childbearing age and there is any possibility that you are pregnant, the researchers will need to perform a urine pregnancy test before you start in the study.

If necessary, you should use reliable contraception (such as oral or implanted contraception, an IUD or have had a tubal ligation if you are female, or condoms if you are male) during the course of the study. If at any time you think you may be pregnant, it is important to let the researchers know immediately.

It is important that you understand that if you are capable of becoming pregnant or fathering a child you must agree, **prior** to the first injection of Xeomin for the duration of study participation and within 90 days after your last dose of test medication or completion of the study to use adequate contraception (hormonal or barrier method). Your doctor may discuss acceptable forms of birth control with you.

10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.
Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The drug/treatment/device being shown not to be effective
- The drug/treatment/device being shown to work and not need further testing
- Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

15 What happens when the research project ends?

You may be able to continue with a similar drug at your own cost following completion of this study if it found to be of benefit to you. This decision will be made in consultation between you and your treating doctor about the most appropriate treatment for you at that time.

After the research project is completed, a summary of the result will be completed within 6 months and you will be informed by the study doctor about the success of the project.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

If you give us your permission by signing the consent document, we plan to discuss/publish the results.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Information (data) collected from you and all other participants taking part in this study will be saved indefinitely and processed using validated computerised means. This will include assigning appropriate coding to some of your data to help with the analysis (e.g. medical conditions will be given a reference code from a recognised coding manual, and this code will be added to the database created). Access to the data shall at all times be restricted to authorised personnel only, who will respect the confidentiality of such information. These data will remain the property of Westmead Hospital.

The results of this research study may be submitted to regulatory authorities, published, or presented at scientific meetings and may be used for further research, but your data will be anonymous and you will not be identifiable. For this, the data may be transferred within or to countries outside Australia e.g. Europe/US, and including to other countries not covered by data protection legislation.

In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you, if you wish. Information about your participation in this research project may be recorded in your health records.

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

Any information obtained for the purpose of this research that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. 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). If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensations monies. You do not give up any legal rights to compensation by participating in this study.

If you are no eligible for compensation for your injury or complication under the law, but 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.

18 Who is organising and funding the research?

This research project is being conducted by Dr. Victor Fung and being sponsored in Australia either by Merz Pty Ltd or the Neurology budget in Westmead Hospital. Participants don't need to pay.

Merz Pty Ltd may benefit from this research project if they sponsor their product and results show the effectiveness of the medication for treating upper limbs tremor.

If knowledge acquired through this research leads to discoveries that are of commercial value to Merz Pty Ltd, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 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 Westmead Hospital.

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.

20 Further information and who to contact

When you have read this information, the researcher Associate Professor Victor Fung will discuss it with you and any queries you may have. 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 (for example, any side effects), please do not hesitate to contact him 98456793.

Clinical contact person

Name	Associate Professor Victor Fung
Position	Principle researcher
Telephone	Working hours Telephone no 98456793 After hours Telephone no 98455555 (via switchboard)

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

Name	Westmead Hospital Patient Representative
Telephone	98457014

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:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Western Sydney Local Health District
HREC Executive Officer	Kellie Hansen
Telephone	98459171
Email	wslhd-researchoffice@health.nsw.gov.au

Local HREC Office contact (Single Site -Research Governance Officer)

Name	Maggie Piper
Position	Research governance officer
Telephone	98459634
Email	Wslhd-rgo@health.nsw.gov.au

Thank you for taking time to consider this study.

If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

Consent Form - *Adult providing own consent*

Title	A randomized, double-blind controlled study of botulinum toxin treatment in upper limb tremor
Short Title	The role of botulinum toxin treatment in upper limb tremor
Coordinating Principal Investigator/ Principal Investigator	Associate Professor Victor Fung
Associate Investigator(s)	
Location	Westmead 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 give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Westmead hospital concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

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 study 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 _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior 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.

I understand that, if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to
Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

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.

Form for Withdrawal of Participation - *Adult providing own consent*

It is recommended that this form NOT be included as part of the PICF itself, but that it be developed at the same time and made available to researchers for later use, if necessary. Note that a participant's decision to withdraw their separate consent to the use and storage of tissue will need to be documented separately and linked to the PICF used for that purpose.

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Short Title	The role of botulinum toxin treatment in upper limb tremor
Coordinating Principal Investigator/ Principal Investigator	Associate Professor Victor Fung
Associate Investigator(s)	
Location	Westmead Hospital

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Westmead Hospital.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project 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 withdrawal from the research project.

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