Request for participation in a clinical trial

"Does botulinumtoxin A (botox) make walking easier in children and adolescents with cerebral palsy?"

To parents and guardians of children and adolescents with cerebral palsy (CP);

The medical doctor in charge of your child's treatment thinks that your child will benefit from injections with botox in the calf muscles (your child has probably been treated with Botox earlier as well). We would like to ask you as parents if you are willing to let your child take part in a research project.

Background and purpose
This project aims to explore if treatment with botox in the calf muscles makes walking easier. The study is a co-operation between five hospitals in Norway (St. Olavs Hospital in Trondheim, Vestfold Hospital Trust, Oslo University Hospital, University Hospital of North Norway and Haukeland University Hospital) and the Norwegian University of Science and Technology (NTNU).

Injections with botox are widely used in the treatment of children and adolescents with CP. The goal is to reduce the spasticity («tension») in the muscles to ease walking. The treatment does, in short term, reduce the spasticity. This effect lasts for 3-4 months. In some clinics, the treatment is therefore administered up to four times per year, while in other clinics just one time annually. Botox-treatment is considered to be a safe treatment with little side effects, and is offered to approximately two out of three children with CP.

Despite the common use of botox, we do not know enough about the functional effects related to walking, and especially if such effects last longer than 3-4 months. The main purpose of the treatment is to get a more lasting effect. Since the treatment (the injections) can be painful and sometimes require general anesthesia, we think it is important to determine if botox has a longer effect.

Therefore, we want to conduct a research project that examines if treatment with botox actually makes walking easier in children and adolescents with CP during a timeframe of 6 months. In addition we want to determine why the effect varies from person to person, and from treatment to treatment.

To answer these questions we have designed a randomized controlled trial. A draw will be made to divide the participants into two equally sized groups. For one group, botox will be injected in the calf muscles, and for the other group sodium chloride will be injected instead. Neither you (parents of the child), the treating physician (medical doctor), nor the study team performing the testing of the child afterwards, will know if botox or sodium chloride was injected. This information will be released when all study participants have been treated and tested. Thus, it may take 3-4 years before you know which injection your child received. The child will continue the regular treatment after 6 months when the individual study participation has ended.

What does study participation involve?
Study participation involves that your child will be tested four times during a six months period. The first testing will be done before treatment is given, and the following three tests 1, 3 and 6 months after treatment. At testing we will examine spasticity in the calf muscles and see how much energy your child uses when walking (for five minutes). In addition, both child and parents will be asked questions

regarding the child's gait function, and we will ask you to fill out two questionnaires. This will take approximately 1-1.5 hour. The child will carry a small computer chip for a week after the four testing points. The chip is registering how much the child is moving and what type of movements it is making, but not what it is doing or where. For study participants in Trondheim and Vestfold, an ankle strength test and a gait analysis will also be done. Participants in Haukeland will also have the gait analysis, but not the ankle strength test. Each test in these locations will be about one hour longer (in total 2-2.5 hours). Participation also involves that information about the child's CP diagnosis and earlier treatment will be collected from the child's medical journal.

Selected study participants and their parents will be interviewed about treatment expectations and perceived effect. The interviews will be conducted before treatment and four weeks after treatment.

Unfortunately, we are not able to cover income losses, but travel expenses (of the least expensive way of transport) are covered.

Potential advantages and disadvantages
Study participation will, in connection with the testing, involve child and parent to spend time at the hospital. None of the tests are connected with discomfort or pain. The injection can be painful but the child will be offered local anesthesia to prevent pain. Both botox and sodium chloride can cause transient pain or soreness in the muscle after injection. In rare cases, localized swelling, tenderness, erythema and infection can occur after the injection. If your child has any of these symptoms after the injection point, you should contact the child's medical doctor. Botox can cause transient muscle weakness in the treated muscle. Rash and pain in the legs have also been reported. Other adverse reactions, such as trouble with breathing, are very rare and have never, to our knowledge, been reported in Norwegian children with mild CP after injections with botox in the calf muscles.

If your child is randomized to the control group receiving sodium chloride instead of botox, this means that treatment with botox will be postponed by six months. This will not have lasting effects on the spasticity or function of the muscles. Eventually, study participation can lead to a confirmation of the Botox effect in your child, or indicate that treatment frequency for your child can be extended.

What will happen with the information regarding your child?
The data that are registered about your child will only be used in accordance with the purpose of the study as described above. All the data will be processed without name, personal identification number or other directly recognisable type of information. A code number links the child to the data through a list of names. The list that can link the child's name to the code number will be stored at the clinic/hospital only, and only the authorised study staff will have access to this list. The data and the code number list will be stored until 2033 to ensure thorough analyzation and enable control of the results. Then the code list will be shredded.

It will not be possible to identify your child in the results of the study when these are published.

Follow-up studies to gain more knowledge of the long term effects of the treatment may be applied. If so, there will be a new request.

Voluntary participation
Participation in the study is voluntary. You can withdraw your consent at any time and without stating any particular reason. This will not have any consequences for your child's further treatment. If you wish to participate, sign the declaration of consent on the final page. If you have questions concerning the study, you may contact:

- Anne Elisabeth Ross Raftemo, Vestfold Hospital Trust
  Tel.: 920 64 296
- Siri Merete Brændvik, St. Olavs Hospital
  Tel.: 72573830 / 934 26 016

Check out the study's homepage on https://stolav.no/WE-studien.

Further information on the study can be found in Chapter A – *Elaboration of what the study involves.*

Further information about biobank, data privacy, finance and insurance can be found in Chapter B – *Data privacy, biobank, funding and insurance.*

The declaration of consent follows Chapter B.

Chapter A – Further explanation of what the study involves

Criteria for participation
Children and adolescents from 4 to 18 years diagnosed with spastic CP in the calf muscles will be asked to participate. We wish to recruit 96 participants for this study. Because this is a clinical study involving a pharmaceutical substance, pregnancy prevents participation.

Chapter B – Data privacy, biobank, funding and insurance

Data privacy
Information that is registered about your child is

- Gender, height, weight, CP diagnosis and gross motor function
- Information about previous treatment with botulinum toxin A and surgery in the legs related to the CP diagnosis will be collected from the medical journal and registered
- Information about activity and energy cost and –capacity, movement pattern and muscle activity during walking, and measurement of spasticity and strength
- Gait analysis involves video taping

St. Olavs Hospital, represented by the head of clinic, is the study data controller.

Releasing material and data to other parties
If you agree to participate in the study, you also consent to non-identifiable data from this project being compared to data from a similar project in the Netherlands.

Right to access and material storage
If you agree to participate in the study, you are entitled to have access to the information registered about your child. You are further entitled to correct any mistakes in the information we have registered. If you withdraw from the study, you are entitled to demand that the collected data are deleted, unless the data have already been incorporated in analyses or used in scientific publications.

Funding
The study is funded by the four Regional Health Authorities in Norway, the Liaison Committee between the Central Norway Regional Health Authority (RHA) and the Norwegian University of Science and Technology (NTNU), Joint Research Committee between St. Olavs Hospital and Faculty of Medicine, NTNU, the Norwegian Fund for Postgraduate Training in Physiotherapy and Medicines for Children Network, Norway. There are no economic benefits or conflict of interest.

Insurance
The study participants are insured through the Norwegian patient injury compensation system, and in accordance with the Product Liability Act in the Drug Insurance.

Information about the outcome of the study
The results from the study will be submitted to international journals. The individual results will be described in the child's medical journal.

Consent for participation in the study

I hereby confirm that I have received both oral and written information about the study and that I am willing to let my child participate

Name:_____ Born:_____
(In block letters)

Date: _____ Signature:_____
Parent (1)

Date: _____ Signature:_____
Parent (2)

I hereby confirm that I have given information about the study

Date: _____ Signature:_____
(Name, study role)