***Title*: Effect of Single Event Multi Level Chemoneurolysis with AbobotulinumtoxinA (Dysport®) on Energy Expenditure and Walking Efficiency in Children with Cerebral Palsy**

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INFORMED CONSENT FORM

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1. INTRODUCTION

Cerebral palsy (CP) is a movement and postural disorder due to lesion to immature brain. Spasticity is the most common movement disorder in children with cerebral palsy (CDC) and causes difficulty with walking, musculoskeletal complications such as hip dislocation, scoliosis and joint contracture, pain and balance issues (Balaban et al., 2012). Spastic muscles are stiff and weak (Campbell & Ball, 1978). A combination of spasticity and weakness in children with CP makes them walk difficult and less efficient. Spasticity management has been very important for children with CP for activity of daily living including walking (Massin & Allington, n.d.) Using botulinum toxin A (BoNT-A) injections to control spastic lower limbs became almost first line treatment for children with CP to improve gait, range of motion and quality of life. (Ade-Hall & Moore, 2000). Several studies reported that children with CP showed higher energy expenditure during walking compared to typically developing peers. (Balaban 2007 & Rose et al 1990 Steele K et al 2017) This increase is due to combination of the mechanical inefficiencies during ambulation caused by spasticity (Reddihough et al., 2002), muscle co-contraction ((Balaban et al., 2012), limited range of motion, muscle weakness and loss of balance (Norman, 2004). Perhaps, improving coordination of walking by reducing in spasticity with BoNT-A may improve energy expenditure by improving coordination of muscle activity which is related to peak power output (Wakeling et al, 2010). Energy expenditure is an objective measure of evaluating the energy cost required for movement (Rose et al., n.d.) Generally, the oxygen consumption (VO2) is used to measure energy expenditure and one of the most significant markers of aerobic fitness and endurance (*ACSM's Advanced Exercise Physiology*, 2006). The rate of oxygen consumption (mL/kg/min) was significantly higher in the children with diplegia than in those with hemiplegia or with spina bifida or the healthy children (Rose et al., n.d.). Oxygen cost (mL/kg/m) was significantly higher, and velocity was significantly slower in all the groups with disability than in the healthy children (Duffy and Graham 2014). Balaban et al showed that botulinum toxin A injections to spastic gastric muscles decreased VO2 and gait parameters at 2-month post injections. We hypothesized that BoNT-A injections to spastic lower limbs of ambulant spastic CP decrease energy expenditure during walking. The aim of this study is to investigate the effect of spasticity management using Dysport® (AbobotulinumtoxinA) on the walking efficiency, oxygen consumption and gross motor function and gait parameters of children with CP.

2.DESIGN

This study is a single center, open label study.

We seek to recruit 15 children diagnosed with Cerebral Palsy (CP) in order to determine the efficacy of single event multi level chemoneurolysis (SEMLC) with Dysport® on energy expenditure as measured by oxygen consumption (VO2) during the 6 minute walk test.

Subject Visits:

- **Baseline**: Consent, Modified Ashworth Scale, modified Tardieu Scale, CP Quality of Life Questionnaire for Children/Adolescents, 6 minute walk with VO2 and gait analysis
- **Treatment:** SEMLC treatment

- **4 week follow-up:** Modified Ashworth Scale, modified Tardieu Scale, CP Quality of Life Questionnaire for Children/Adolescents, 6 minute walk with VO2 and gait analysis
- **12 week follow-up:** Modified Ashworth Scale, modified Tardieu Scale, CP Quality of Life Questionnaire for Children/Adolescents, 6 minute walk with VO2 and gait analysis

2.1 Participants

All subjects will be recruited from Dr. Kim's Pediatric Physical Medicine & Rehabilitation clinic. Dr. Kim will approach eligible patients and their parents in order to explain the study and to determine interest. A researcher of the study team will email and/or telephone call eligible participants on behalf of Dr. Kim and with her permission to inform the parents of the eligible participant of the study.

Inclusion Criteria:

- Age: 5-17 years. *Must be <18 prior to injection.*
- >10 kilograms at screening and injection visits
- Diagnosis of spastic diplegia OR mild- to moderate spastic quadriplegia Cerebral Palsy
- Gross Motor Function Classification System level: I, II, III
- Ability to ambulate independently without aid, equinus gait
- Absent of joint or bone deformities
- Eligible to receive SEMLC
- Cooperative and tolerant to testing procedures during clinic screening
- Presence of spasticity in one or both legs
- Be on a stable dose and regimen if on any prescribed medication/s
- Parent must have signed written informed consent and the Patient Authorization for Use and Release of Health and Research Study Information

Exclusion Criteria:

- Ankle contractures no more than -10 degrees with the knee extended
- Hemiplegia
- Wheelchair dependent
- Received Botulinum toxin within previous 4 months
- Uncontrolled epilepsy or certain types of seizures
- Fracture in the study limb within previous 12 months
- Infection or skin disorder at planned injection site
- Shortness of breath or other respiratory issues
- Uncontrolled clinically significant medical condition
- Received phenol or alcohol block in the study limb within previous 6 months
- Surgery in the study limb within previous 12 months
- Serial casting within previous 12 months
- New physiotherapy and/or orthotic regimen <1 month before study start. (physiotherapy and/or orthotic regimen will be permitted if it began >1 month before study start and maintained throughout study)

2.2 Outcome Measures

Primary Question: Does single event multi level chemoneurolysis (SEMLC) have an effect on energy expenditure and walking efficiency as measured by oxygen consumption (VO2) and gait parameters during the 6 minute walk test in 15 children diagnosed with cerebral palsy (CP)?
Hypothesis: If 15 children receive SEMLC, then energy expenditure (VO2) will decrease due to increased walking efficiency and gait parameters during the 6 minute walk test.

Secondary Question: Does SEMLC have an effect on 6 minute walking distance in 15 children diagnosed with CP?
Hypothesis: SEMLC will increase the distance walked during the 6 minute walk test.

Secondary Question: Does SEMLC have an effect on the Gross Motor Functional Classification System (GMFCS) classification in 15 children diagnosed with CP?
Hypothesis: SEMLC will decrease a child's GMFCS classification due to increased physical function.

Secondary Question: Does SEMLC have an effect on ankle muscle spasticity as measured by the Modified Ashworth Scale (MAS) and the modified Tardieu Scale?
Hypothesis: SEMLC will decrease ankle muscle spasticity and in turn improve MAS and modified Tardieu Scale scores.

Secondary Question: Does SEMLC have an effect on dynamic balance during walking in 15 children diagnosed with CP?
Hypothesis: SEMLC will increase dynamic balance during walking.

2.3 Procedures

Baseline (within 1 week prior to Dysport® treatment):

Before initiating any study procedures the informed consent will be discussed and signed with the parent(s) of the participants and the researcher will answer any questions. If capable of providing assent (>7 years old), the participant will sign the assent form. Once the consent and assent forms are discussed and signed the following assessments will be performed: demographics, height, weight, calculated body mass index (BMI), Modified Ashworth Scale (MAS), modified Tardieu Scale, range of motion of major joints (i.e., hip, knee, ankle), the Cerebral Palsy Quality of Life Questionnaire (CP QOL) for Children (9-12 years) or Adolescents (13-18 years), and the CP QOL for caregivers, 6 minute walk test (with mobile oxygen consumption), and gait analysis.

Degree of spasticity/tone in the lower limbs will be measured by the Modified Ashworth scale while the participant is relaxed and in the supine position (1). If testing a muscle that primarily flexes the hip, knee, or ankle joint the investigator will place the joint in a maximally flexed position and move the joint to a position of maximal extension over one second. If testing a muscle that primarily extends the hip, knee, or ankle joint the investigator will place the

joint in a maximally extended position and move the joint to a position of maximal flexion over one second.

The Modified Tardieu Scale will be used to assess spasticity by measuring different angles of muscle reaction in response to a passive force (2). Two angles will be measured from each major joint (i.e., hip, knee, ankle): R1, the angle in which clonus was felt during a quick passive stretch of the muscle; R2, the angle of full passive range of motion. The difference between the two angles (R2 – R1) will be recorded for each muscle group. The participant will be lying supine for all angle measurements.

Range of motion of the lower limbs (hip, knee, ankle) will be measured by passively moving the patient's joint to a point of resistance where then the joint angle will be measured by a goniometer. Hip flexion will be measured with the patient lying supine. Knee flexion and extension will be measured with the patient lying supine. Ankle dorsiflexion will be measured with the knee extended in the supine position. The Thomas Test will also be used to assess hip flexion with the patient lying in supine (3).

The CP QOL for children, adolescents, and caregivers will be used to assess quality of life and wellbeing across multiple domains of life (4). For children 4-12 years, we will give the primary caregiver version to their parent or guardian. For children 9-12 years, we will give the child self-report version. For adolescents 13-18 years, we will give the teen self-report version as well as the primary caregiver version to their parents or guardian. The sum for each domain will be calculated as well as the total sum.

Gait analysis and the 6 Minute Walk Test (6MWT) with oxygen consumption measurement (energy expenditure) will be performed in the Department of Rehab by an exercise physiologist. Children will be given at least a ten minute rest between measures.

Gait analysis will be measured with the GAITRite® mat, a commercially available instrumented mat for collection of gait data. The GAITRite system is an electronic walkway that connects to a computer, and automates the measurement of temporal (timing) and spatial (distance) gait parameters, such as cadence, step length and velocity. The standard GAITRite walkway is (5m long) and contains 13824 sensors encapsulated in a roll up mat to produce an active area 0.6 m wide and 4.25 m long. The walkway is portable, can be laid over any flat surface and requires no placement of any devices on the patient. GAITRite uses no radiation, electricity or ultrasound to measure these parameters and is therefore a safe method for evaluating walking function, even during pregnancy. The system has been validated for use in healthy children and children with movement disorders (such as cerebral palsy, and spinal muscular atrophy) (5, 6). The laboratory consists of a 10-meter walkway. The GAITRite mat is placed in the middle of the 10 meter walkway to collect data on steady state gait without the influence of gait initiation and termination. Subjects will be asked to wear the same shoes and orthoses throughout the study. A gait aid can be used during the test if the child cannot walk without it. Subjects will be asked to begin walking at a starting position located 1.5 meters from the mat and walk at their preferred typical speed until a termination position marked on the floor (1.5m from the end of the mat). Each subject will perform five trials of walking at their preferred speed. We will compute gait

velocity, step length, cadence, percent time spent in double support, foot angle, and base of support.

After at least a ten minute rest, oxygen consumption via the breath-by-breath method using a portable spirometric device (Cosmed K5; COSMED USA Inc, Concord, CA) will be determined while the participant performs the 6MWT (7). After instruction the participant will don the face mask and a 12 lead ECG will be applied. In order for the child to become comfortable with the face mask, a three minute rest period will be given while resting heart rate (HR) and oxygen consumption (VO2) is measured. After the three minute rest, the participant will begin the 6MWT while the K5 mobile device collects gas exchange variables [VO2, VCO2, respiratory exchange ratio (RER)] and HR will be monitored via the 12-lead ECG as well as cardiac rhythm. Participants will be instructed to walk at their normal walking pace as far as they can for six minutes. They will be allowed to walk with any orthoses and/or assistive devices however the same orthoses and/or devices will be used throughout the study. The participant can stop at any time if they feel dizzy or fatigued to the point of increased risk of falling. The total distance walked (meters) will be recorded at six minutes.

(Dysport® Injection/Treatment)
The procedures for Single Event Multi Level Chemoneurolysis (SEMLC) with Dysport® will mimic those currently used by Dr. Kim in the pediatric rehab clinic (8). The study drug, Dysport, will be provided by the funding source IPSEN and will be the sole abobotulinumtoxinA used in the SEMLC injection. Dysport® is currently FDA-approved for pediatric patients 2 years and older to treat lower limb spasticity (gastrocnemius and soleus). Selected dose of medication will be determined by affected muscle(s), severity of spasticity, and the patient's body weight. We will follow the recommended total Dysport dose of 10-15 units/kg per limb, not to exceed 15 units/kg for unilateral lower limb, 30 units/kg for bilateral lower limb, or a total of 1000 units, whichever is lower in a given session. The research pharmacy will be responsible for housing and preparing all Dysport® vials according to manufacturer (prescribing information sheet attached). The research pharmacy will also be responsible for study drug disposal at end of study. Electrical stimulation and/or ultrasound will be used for guidance of injection point. General anesthesia will be used to prevent pain and anxiety in adolescents if extensive multi-level injections are planned. All injection procedures will take place in the pediatric Endoscopy Suite (CHONY), and will be led by Dr. Kim (PI).

(4 Weeks Post Treatment)
All procedures during the 4 weeks post treatment will mimic those conducted during the baseline visit (i.e., Modified Ashworth Scale, Modified Tardieu Scale, range of motion, CP QOL, gait analysis, 6MWT with oxygen consumption).

(12 Weeks Post Treatment)
All procedures during the 12 weeks post treatment day 1 will mimic those conducted during the baseline day 1 visit (i.e., Modified Ashworth Scale, Modified Tardieu Scale, range of motion, CP QOL, gait analysis, 6MWT with oxygen consumption).

(1) Smith, M. B. (2000). Interrater Reliability of a Modified Ashworth Scale of Muscle Spasticity, 1986–1987.

Columbia University Consent Form

Protocol Information

Attached to Protocol: IRB-AAAR1322
Principal Investigator: Heakyung Kim (hk2641)
IRB Protocol Title: Effect of Single Event Multi Level Chemoneurolysis with AbobotulinumtoxinA (Dysport) on Energy Expenditure and Walking Efficiency in Children with Cerebral Palsy

General Information

Consent Number: CF-AAAU4163
Participation Duration: 4 months
Anticipated Number of Subjects: 15
Research Purpose: The purpose of this study is to investigate the efficacy of single event multi level chemoneurolysis with Dysport® on energy expenditure and walking efficiency in children with Cerebral Palsy.

Information on Research

Introduction

Your child has been invited to participate in a research study, involving patients with spastic (abnormal muscle stiffness or rigidness) Cerebral Palsy of the lower limbs (legs). This consent form describes the study and your child's role in it should they wish to participate. Dr. Heakyung Kim has reviewed the study and is the investigator (study doctor). The study doctor will answer any questions you or your child may have about this study or this consent form. Please read this form carefully and ask any questions you have regarding the information it contains.

Study Procedures

This study will consist of approximately 4 clinic visits over a period of 4 months. The study will occur as follows:

-Screening visit (within 1 week of day 1)
-Treatment visit with Dysport® (day 1)
-Follow-up visits (4 weeks & 3 months post injection)

Screening Visit

At this visit:
-After being provided time to consider the study and all your questions have been answered you will sign this informed consent and HIPAA form.
-If your child is aged between 7 and 17 years and 11 months of age (prior to 18th birth date), they will be provided with

an assent form; this form explains what will happen to your child during the study and gives them the right to decide to take part or not
-You and your child will be asked questions about your childs medical history and use of any medications and the study doctor will confirm whether your child is suitable for the study.
-Your child will have their vital signs taken (blood pressure, pulse rate, breathing rate, temperature)
-Your child will be weighed and their height recorded
-Your childs affected leg(s) will be evaluated for spasticity (muscle stiffness)
-You and your child (age > 8) will complete the Cerebral Palsy Quality of Life questionnaire
-Your child will then walk up and down the hallway for 6 minutes while wearing a tight fitting mask which measures their oxygen consumption (walking energy expenditure).
-Lastly your child will walk on a 10 meter mat 5 times which measures parameters of their gait.

Treatment visit

At this visit:
-The study doctor will check if your child is still eligible to take part in the study
-Your child will be asked about the pain in his or her limbs
-The study doctor will ask about the health of your child since your last visit and check what medications your child is taking and if there have been any change since their last visit this includes whether your child has taken any medication bought from the pharmacy or supermarket including medicines such as aspirin, cold remedies, herbal supplements (it is useful to write these down at the time and take this information with you)
-Your child's vital signs will be recorded (blood pressure, pulse rate, breathing rate, temperature)
-Your child will be weighed
-Assessments will be made of the function of your childs affected limbs
-Your child will receive single event multi level chemoneurolysis with the study drug, Dysport® medication. This will be administered through a number of injections in your childs affected limb(s). Your child may receive injections in one or both of their affected legs, depending on the study doctors assessment. The study doctor will determine which of your childs muscles are eligible for treatment. The number of injections may vary.
-The study doctor will most likely use ultrasound, but in some cases may be required to use electromyography with electrical stimulation (machines to aid in locating the muscles that will be injected) to assist him/her in the injection of the study medication
-Your child may receive medicine prior to the injections to reduce injection-related pain. You should discuss this with the study doctor as he/she will be able to explain what the normal method is at their clinic

Follow-up visits (4 weeks post and 3 months post)

At these visits:
-Your child will be asked about the pain in his or her limbs
-The study doctor will ask about the health of your child since your last visit and check what medications your child is taking and if there has been any change since their last visit. It is very important that you inform the study doctor about any change no matter how small
-Assessments will be made of the function of your child's affected limb
-The study doctor will assess the overall change in your childs condition since the beginning of the study
-You and your child (age > 8) will complete the Cerebral Palsy Quality of Life questionnaire (only at 3 months post)
-Your child will then walk up and down the hallway for 6 minutes while wearing a tight fitting mask which measures their oxygen consumption (walking energy expenditure).

-Lastly your child will walk on a 10 meter mat 6 times which measures parameters of their gait.

You and your child can also contact the study doctor directly at any time during the study.
Your child should not enter this study if they are unable to attend all the study visits.

It is important that you share any information about medical problems your child may have with the study doctor.

If your child is currently using any medications or receiving other therapies (e.g., physical therapy or occupational therapy, exercise program, etc.) you should tell the study doctor about them. During the study your child will be allowed to continue taking their routine medications. However, you should immediately report any changes in your childs medications or doses (including any new dietary supplements, herbal medications, and overthe- counter medication).

We ask that your child not start certain medications while the study is underway including antispastic medications, muscle relaxants, anti-epileptic medications and Botulinum toxin therapy of any serotype except for study medication. If your child does start one of these new medications during the study protocol, s/he will not continue to be part of this research study.

Subject Responsibilities

As your child is a study subject, you are responsible for ensuring that your child follows the study directions and those of the study doctor. This includes returning promptly to the study doctors office for all necessary study follow-up visits, reporting any changes in your childs medications (over-the counter and prescription), and reporting any changes in how your child feels to the study doctor.

If your child experiences any illness or discomfort during the study, you should notify the study doctor. The study doctor will then evaluate your child to determine if they should continue the study.

Risks

What are the risks of the study?

What side effects can be expected?

The following frequency descriptors are being used in this section to describe how often side effects occurs: Very common (more frequent than 1 in 10 patients/children); common (between 1 in 10 to 1 in 100 patients/children); uncommon (between 1 in 100 to 1 in 1000 patients/children); rare (between 1 in 1000 to 1 in 10,000 patients/children) and very rare (in less than 1 in 10,000 patients).

Along with benefits of Dysport® treatment, there are also some side effects which your child may experience. As expected for any injection procedure, Dysport® injections when given in arm or leg may commonly cause injection site reactions (such as pain, bruising, erythema and swelling). In addition your child may also experience skin rash (common) and itching (uncommon). Another common effect that your child may feel is weakness in the injected leg(s) or may be unable to use his/her leg(s) as usual; however this effect does wear off with time. Other possible side effect that your child may also experience is difficulty swallowing (uncommon). If your child develops any difficulty in swallowing, you must report it to the study doctor immediately. Occasional reports of some breathing difficulties were reported in adult spasticity conditions.

The commonly reported side effects observed in a clinical study in which children were treated with Dysport® for upper limb spasticity were muscular weakness, drowsiness and injection site reactions. In addition, uncommon events of constipation, difficulty in swallowing (dysphagia), fatigue, influenza-like illness, drooping eyelid, speech disorder and urinary incontinence were also reported.

Additional side effects seen in children with cerebral palsy treated with Dysport® for lower limb spasticity were myalgia (common), gait disturbance (common), fall (common) and generalised weakness (uncommon).

The possibility exists that repeated treatment with Dysport® may result in the production of antibodies (proteins that normally help to get rid of bacteria and viruses etc.) which may reduce the effectiveness of the treatment.

These are not all of the side effects that might be experienced when Dysport® is given and there may be new side effects that have not yet been seen. Please tell the study doctor about any side effects your child has experienced or concerns that you have during this study.

Excessive doses of BTX-A may produce distant and profound neuromuscular paralysis (very rare). Overdose may lead to an increased risk of the neurotoxin entering the bloodstream and may cause complications associated with the effects of oral BTX poisoning (e.g. deglutition disorder and dysphonia). Respiratory support may be required where excessive doses cause paralysis of the respiratory muscles. There is no specific antidote (antitoxin should not be expected to be beneficial) so general supportive care is advised. In the event of overdose, the subject should be medically monitored for any signs and/or symptoms of excessive muscle weakness and/or muscle paralysis. Symptomatic treatment should be instigated if necessary. The signs and/or symptoms of overdose may not present immediately following treatment. Should accidental treatment or oral ingestion occur, the person should be medically supervised for several weeks for any signs and symptoms of excessive muscle weakness or muscle paralysis.

Additional discomforts associated with the study procedures that your child could experience include:
-discomfort with the mouthpiece worn while walking
-if the child becomes fatigued or tired during the self-paced six-minute walk test, they will be allowed to slow down, stop, and rest as necessary. They should resume walking as soon as they are able.

Loss of confidentiality
A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your child's personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your child's privacy. Their plans for keeping your child's information private are described in the Confidentiality section of this consent form.

Benefits

Will your child benefit from being in this study?

Your child will be given study treatment and will receive the study doctor's care during the full study. The study treatment (i.e. Dysport®) may or may not help your child. It is hoped that the information gained from the study will help in the future treatment of children with Cerebral Palsy.

Alternative Procedures

What other options are there?

The alternative is to not participate in the study. Your child will still receive all necessary standard of care under Dr. Kim not associated with this study.

Confidentiality

What about confidentiality

Any information collected during this study that can identify your child by name will be kept confidential. We will do everything we can to keep your child's data secure, however, complete confidentiality cannot be promised. Despite all of our efforts, unanticipated problems, such as a stolen computer may occur, although it is highly unlikely.

Any research information that is shared with people outside of Columbia University Medical Center and New YorkPresbyterian
Hospital will not include your child's name, address, telephone number or any other direct identifier unless disclosure of the information is required by law or you have authorized the disclosure.

All material will be kept under lock and key in the Principal Investigator's office in Harkness Pavilion. Only study personnel will have access to the study information. All study forms will be de-identified for confidentiality.

The following individuals and/or agencies will be able to look at and copy your research records:
- The investigator, study staff and other medical professionals who may be evaluating the study
- Authorities from Columbia University and New York Presbyterian Hospital, including the Institutional Review Board (IRB)
- The United States Food and Drug Administration (FDA) and/or the Office of Human Research (OHRP)

Your authorization to use and share your child's health information will expire when the research is completed. Once your child's health information has been disclosed to a third party federal privacy laws may no longer protect it from further disclosure; however we do not anticipate sharing any collected health information. You and/or child may

change your mind and revoke (take back) this consent and authorization at any time and for any reason. To revoke this consent and authorization, you must contact the Principal Investigator, Dr. Heakyung Kim at 212-342-1395. However, if you and/or child revoke your child's consent and authorization, they will not be allowed to continue taking part in the Research. Also, even if you revoke this consent and authorization, the Researchers may continue to use and disclose the information they have already collected. The study team will have access to your child's data for future use of research. Only members of the research team will have access to your child's de-identified data which will remain in a password-protected encrypted database. Your child's data will be kept indefinitely as define by law.

Compensation

Will we be compensated?

Your child and your family will receive $75 per visit which adds up to a total of $300. You will be given a prepaid debit card at the end of the study for each visit attended for a maximum of $300.

Research Related Injuries

Costs / compensation for illness or injury

Dysport® will be supplied to you free of charge. You will not incur any costs by your child's participation in this study. Columbia University Medical Center will receive a payment from IPSEN Innovation for performing this study, which is intended to cover the costs of all the procedures and facilities used, as well as the researchers performing this study. Your doctor will make every effort to prevent physical injury that could result from this research. If your child sustains an injury or illness determined by your doctor as a direct result of participating in this study, you will be reimbursed by IPSEN for reasonable medical expenses necessary for the treatment of the injury or illness that are not covered by your health insurance, provided that the study medication administered and the study procedures performed were according to the study protocol. IPSEN will not compensate your child for any unrelated or preexisting medical conditions or any complications not directly caused by participating in this study. This study will be performed under the International Conference on Harmonisation guidelines on good clinical practice. If however, your child should suffer harm as a result of receiving 'Dysport®' or any other procedure performed in accordance with the protocol, the pharmaceutical company will compensate you, as described hereafter. The pharmaceutical company has taken out appropriate insurance for the duration of the study.

Voluntary Participation

Does my child have to be in the study?

Participation in this study is completely voluntary. Whether your child decides to partake in the study or not will in no way impact your child's medical care.

Additional Information

Use of Data/Specimens
We would like to store the data that you agreed to provide as part of this study and possibly use them for future research and/or publications. They will be stored in a locked filing cabinet in the researcher's office only accessible to this research team. Your child's data will be labeled with a code number that only the researchers on this study will be able to link to your child.

If you have any further questions, please contact the study Doctor, Heakyung Kim at (212)305-5337.

If you have any questions about your rights as a subject, you may contact:
Institutional Review Board
Columbia University Medical Center
722 West 168th Street, 4th Floor
New York, NY 10032
Telephone: (212) 305-5883

An Institutional Review Board is a committee organized to protect the rights and welfare of human subjects involved in research.

Statement of Consent

Statement of consent and HIPAA authorization

I have read the consent and HIPAA authorization form and talked about this research study, including the purpose, procedures, risks, benefits and alternatives with the researcher. Any questions I had were answered to my satisfaction. I am aware that by signing below, I am agreeing for my child to take part in this research study and that we can stop being in the study at any time. My child is not waiving (giving up) any of their legal rights by signing this consent form. I will be given a copy of this consent and HIPAA authorization form to keep for my records.

Signatures

Participant Signature Lines

Parent/Guardian

Print Name _____ Signature _____

Date _____

Research Signature Lines

Person Obtaining Consent

Print Name _____ Signature _____

Date _____