### STATEMENT OF JANET HIESHETTER EXECUTIVE DIRECTOR DYSTONIA MEDICAL RESEARCH FOUNDATION ONE EAST WACKER DRIVE, SUITE 2810 CHICAGO, IL 60601

#### REGARDING FISCAL YEAR 2011 APPROPRIATIONS FOR THE NATIONAL INSTITUTES OF HEALTH AND THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

#### SUBMITTED TO THE SENATE COMMITTEE ON APPROPRIATIONS; SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES

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Dystonia is a neurological movement disorder characterized by involuntary muscle spasms that cause the body to twist, repetitively jerk, and sustain postural deformities. Dystonia can affect movement in several different ways; focal dystonias affect specific parts of the body, while generalized dystonia affects multiple parts of the body at the same time. Some forms of dystonia are genetic, but can also be caused by injury or illness. Although dystonia is a chronic and progressive disease, it does not impact cognition, intelligence, or shorten a person's life span. Conservative estimates indicate that between 300,000 and 500,000 individuals suffer from some form of dystonia in North America alone. Dystonia does not discriminate, affecting all demographic groups. There is no known cure for dystonia and treatment options remain limited.

Although little is known regarding the causes and onset of dystonia, two therapies have been developed and proved particularly useful to control patients' symptoms. Botulinum toxin (Botox/Myobloc) injections and deep brain stimulation have shown varying degrees of success alleviating dystonia symptoms. More research is needed to fully understand the onset and progression of the disease, in order to better treat patients. Until a cure is discovered, the development of management therapies remains vital.

#### **DEEP BRAIN STIMULATION (DBS)**

Deep brain stimulation (DBS) is a surgical procedure originally developed to treat Parkinson's

disease, but is now being applied to severe cases of dystonia. A neurostimulator, or "brain pacemaker", is surgically implanted to deliver electrical stimulation to the areas that control movement. While the exact reasons for effectiveness are unknown, the electrical stimulation blocks abnormal nerve signals that cause debilitating muscle spasms and contractions.

DBS was approved for use by dystonia patients in 2003 and has since drastically improved the lives of many individuals. Results have ranged from quickly regaining the ability to walk and speak, to regaining complete control over one's body and returning to an independent life as an able-bodied person. DBS is currently used to treat severe cases of generalized dystonia, but with increased research may also be a promising treatment for those suffering from focal dystonias. Surgical interventions are a crucial and active area of dystonia research, and must be pursued in the development of new treatment options.

## **BOTULINUM TOXIN INJECTIONS (BOTOX/MYOBLOC)**

The introduction of botulinum toxin as a therapeutic tool in the late 1980s revolutionized the treatment of dystonia by offering a new, localized method to significantly relieve symptoms for many people. Botulinum toxin, a biologic, is injected into specific muscles where it acts to relax the muscles and reduce excessive muscle contractions.

Botulinum toxin is derived from the bacterium *Clostridium botulinum*. It is a nerve "blocker" that binds to the nerves that lead to the muscle and prevents the release of acetylcholine, a neurotransmitter that activates muscle contractions. If the message is blocked, muscle spasms are significantly reduced or eliminated, providing considerable relief from the patient's symptoms.

Injections of botulinum toxin should only be performed by a physician who is trained to administer this treatment. The physician administering treatment may palpate the muscles carefully, trying to ascertain which muscles are over-contracting and which muscles may be compensating. In some instances, such as in the treatment of laryngeal dystonia, a team approach including other specialists may be required.

For selected areas of the body, and particularly when injecting muscles that are difficult or impossible to palpate, guidance using an electromyograph (EMG) may be necessary. For instance, when injecting the deep muscles of the jaw, neck, or vocal cords, an EMG-guided injection may improve precision since these muscles cannot be readily palpated. An EMG measures and records muscle activity and may help the physician locate overactive muscles.

Injections into the overactive muscle are done with a small needle, with one to three injections per muscle. Discomfort at the site of injections is usually temporary, and a local anesthetic is sometimes used to minimize any discomfort associated with the injection. Many dystonia patients frequently rely on botulinum toxins injections to maintain their improved standard of living due to the fact that the benefits of the treatment peak in approximately four weeks and lasts just three or four months. Currently, FDA approved forms of botulinum toxin include Botox and Myobloc.

DMRF supports the recent "follow-on" biologics or biosimilars provisions included in the

*Patient Protection and Affordable Care Act.* This creates a regulatory pathway for biosimilars at the Food and Drug Administration (FDA). This will help remove significant cost barriers to treatment for dystonia patients and maintain strong patient protections, while providing incentive for the development of new biologic treatments.

# DYSTONIA AND THE NATIONAL INSTITUTES OF HEALTH (NIH)

Currently, dystonia research at NIH is conducted through the National Institutes on Neurological Disorders and Stroke (NINDS), the National Institute on Deafness and Other Communication Disorders (NIDCD), the National Eye Institute (NEI), and the Office of the Director.

## NATIONAL INSTITUTE ON NEUROLOGICAL DISORDERS AND STROKE (NINDS)

The majority of dystonia research at NIH is conducted through NINDS. NINDS has utilized a number of funding mechanisms in recent years to study the causes and mechanisms of dystonia. These grants cover a wide range of research included gene discovery, the genetics and genomics of dystonia, the development of animal models of primary and secondary dystonia, molecular and cellular studies inherited forms of dystonia, epidemiology studies, and brain imaging. DMRF works to support NINDS in conducting critical research and advancing understating of dystonia.

# NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)

NIDCD has funded many studies on brainstem systems and their role in spasmodic dysphonia. Spasmodic dysphonia is a form of focal dystonia, and involves involuntary spasms of the vocal cords causing interruptions of speech and affecting voice quality. Our understanding of spasmodic dysphonia has been greatly enhanced by research initiatives at NIDCD, like the brainstem systems studies. DMRF encourages partnerships between NINDS and NIDCD to further dystonia research.

# NATIONAL EYE INSTITUTE (NEI)

NEI focuses some of its resources on the study of blepharospasm. Blepharospasm is an abnormal, involuntary blinking of the eyelids from an unknown cause that is associated with abnormal function of the basal ganglion. The condition can progress to the point where facial spasms develop. While myectomy surgery, botulinum toxin injections, and oral medication can help manage some of the symptoms of blepharospasm, further study by NEI is needed to develop more predictable treatment options.

### Rare Diseases Clinical Research Network (RDCRN)

The second phase of the RDCRN at NIH provided funding for an additional 19 grants aimed at studying the natural history, epidemiology, diagnosis, and treatment of rare diseases. This includes the Dystonia Coalition, which will facilitate collaboration between researchers, patients, and patient advocacy groups to advance the pace of clinical research on cervical dystonia, blepharospasm, spasmodic dysphonia, craniofacial dystonia, and limb dystonia. Working

primarily through NINDS and the Office of Rare Disease Research in the Office of the Director, the RDCRN holds great hope for advancing understanding and treatment of primary focal dystonias.

After years of near-level funding for NIH, the \$10.4 billion provided in the American Recovery and Reinvestment Act (ARRA) helped reinvigorate biomedical research efforts. However, as those funds come to an end, DMRF joins the greater biomedical research community in its concern that research funding will "fall off the cliff." In order to prevent the loss of research spearheaded under ARRA, continued support for initiatives like the Cures Acceleration Network (CAN) included in the recent healthcare reform legislation are vital as we push for rapid translation of basic science into clinical treatments.

For FY 2011, DMRF recommends a funding increase of at least 12% for NIH and its Institutes and Centers.

For FY 2011, DMRF recommends that the NIH expand dystonia research through the National Institute on Neurological Disorders and Stroke, the National Institute on Deafness and Other Communication Disorders, the National Eye Institute, and the National Institute on Child Health and Human Development.

For FY 2011, DMRF recommends continued partnerships on dystonia research between the Office of Rare Disease Research, the Rare Diseases Clinical Research Network, and the dystonia patient community.

For FY 2011, DMRF recommends appropriating \$500 million for the Cures Acceleration Network, as authorized in the Patient Protection and Affordable Care Act.

# THE DYSTONIA MEDICAL RESEARCH FOUNDATION (DMRF)

The Dystonia Medical Research Foundation was founded over 30 years ago and has been a membership-driven organization since 1993. Since our inception, the goals of DMRF have remained: to advance research for more effective treatments of dystonia and ultimately find a cure; to promote awareness and education; and support the needs and well being of affected individuals and their families.

Thank you for the opportunity to present the views of the dystonia community, we look forward to providing any additional information.