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Rup Tandan, MD, FRCP
Professor Emeritus

Senator Virginia Lyons
Chair, Health and Welfare Committee
State of Vermont Legislature

February 21, 2022

Re: Summary of Testimony for a Mandatory ALS Registry in Vermont
Testimony given via Zoom on February 16, 2022

Dear Senator Lyons:

This is a summary of my testimony given to the Vermont Legislature Committee on Wednesday, February 16th 2022, for consideration of a mandatory amyotrophic lateral sclerosis (ALS) (also known in as Luo Gehrig's disease after the famous NY Yankees baseball player) Registry for the State of Vermont. The incidence (new cases with the disease) of ALS is about 2 per 100,000 population/year (almost at par with other diseases such as multiple sclerosis), and the prevalence (total number of cases with the disease at any given time point) is 7-8/100,000. With this epidemiological statistic, there are about 45-50 cases of ALS in the State of Vermont at any given time.

I am a trained Neurologist and Neuromuscular Specialist at the University of Vermont (UVM) and the UVM Medical Center, where I direct the National ALS Association Center of Excellence. I serve on the National ALS Association Medical Advisory Board, and have over 36 years' experience caring for patients with ALS. I am a Clinician Scientist, having been involved in novel research into finding new medications and clinical therapies for ALS. ALS is a neurodegenerative disease associated with a monumental physical burden on patients; and a psychological effect on caregivers that can be far greater than for patients. The life span of ALS patients after diagnosis is an average of a short 3 years, which is due to the rapid progression of symptoms, and which limits the time period for action to provide help and support. There are currently 2 FDA approved drugs for ALS, which only slow the disease course but do not cure the disease. Our ALS Center clinic follows about 80 patients with ALS from the northern New England region. Between our ALS Center, and the National ALS Center of Excellence at Dartmouth-Hitchcock Medical Center in Lebanon, NH, directed by Dr. Elijah Stommel) we follow about 80% of ALS cases in Vermont; thus, about 20% of ALS patients in Vermont that are unascertained are unreported, unaccounted for and are unable to seek the benefits of being evaluated in our specialized centers of excellence. Thus, lack of complete ascertainment of ALS is an ever-present issue.

Nationally, there are 41 ALS Association Chapters that support patients and family members with psychological, emotional, physical, and end-of-life help and guidance at home and through Support Groups. Data from the National ALS Association's regional ALS Chapters suggests that there is under-reporting of ALS cases among 19 of the 41 (29%) of the chapter regions; 42% of the chapters in the country are from rural parts of the US. Data from the Northern New England ALS Chapter, which is comprised of the predominantly rural states of Vermont, New Hampshire and Maine, indicated about 20% underreporting of ALS cases; in Vermont, there was 14% under-reporting of ALS cases between January 2020 and January 2021. There are, therefore, many ALS patients that do not participate in ALS Centers of Excellence clinics that exist both at UVM and at Dartmouth. ALS patients that are not ascertained are denied specialty care and expertise, support and counseling, genetic testing, symptomatic treatment,

opportunities to participate in clinical trials of new therapies, and the advantage of attending support and bereavement groups organized by chapter personnel. A mandatory ALS registry in the State of Vermont would help identify ALL patients living with the disease to provide them the care that they deserve. Further, ascertainment of ALL ALS patients in the State of Vermont will also promote research endeavors such as the opportunity to participate in the development of new therapies; identification of risk factors for the disease; clarification of the epidemiology of the disease, including trends in the incidence and prevalence; and overall be very helpful to patients, their families, health care planners, economists in establishing resource needs, and the ALS community in general.

Patients not recognized as having ALS, due to incomplete or incorrect ascertainment, are at vastly increased risk of not having their emotional and physical well-being identified, discussed, and appropriately managed with appropriate therapies. Support and bereavement groups run by the Northern New England ALS Chapter in Vermont and across northern New England are helpful not only for patients, but also for family members and children in families with ALS.

The elements sought in any registry would depend on the objectives. A mandatory ALS Registry in the State of Vermont would not only have demographic data, but also information on regions of domicile, environmental exposures, dietary habits, genetics and genealogy. The existing National ALS Registry and Biorepository is funded by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Centers for Disease Control (CDC); however, reporting of ALS cases to this registry is not mandatory. In view of the higher proportion of cases throughout northern New England, as revealed by our collaborative epidemiological research with Dr. Elijah Stommel of the Dartmouth-Hitchcock Medical Center, the National ALS Registry has encouraged the identification of ALL ALS cases in regions of the country and agreed to collaborate with ALS clinicians and researchers. The National ALS Registry will accept data from the Vermont Registry at no cost, and it is understood by Dr. Paul Mehta, Director of the National ALS Registry (who also testified at the hearing on February 16th) that this will strengthen the conclusions from its research. The National ALS Registry is encouraging states in the country to set up mandatory registries to promote ALS case ascertainment, such that appropriate services can reach all patients and families with the disease, and temporal trends can be examined. The National ALS Registry is currently collaborating with the ALS Registry in the Commonwealth of Massachusetts (the only state in the US that currently has an ALS Registry) to further this objective.

We envision the UVM ALS Center being the central location for the ALS Registry and Dartmouth being the main satellite location for running the Vermont ALS Registry. As previously noted, the majority of ALS patients in Vermont are shared by these two tertiary care academic medical centers that house ALS Centers of Excellence. De-identified data from confirmed cases of ALS can be entered by primary care doctors' office staff, or be emailed or faxed to the UVM or Dartmouth ALS Centers to be entered into the registry. If most of the ALS cases will be attending the ALS Center clinics at UVM or Dartmouth, the issue of breach of confidentiality will be moot. If necessary, and in appropriate cases, Drs. Stommel and Tandan will review the diagnostic workup data of patients to confirm the diagnosis of ALS, so as to avoid false positive diagnoses relating to ALS-mimic disorders.

The ALS teams assembled by the Directors of the two ALS Centers of Excellence where patients from Vermont are evaluated (Dr. Rup Tandan and Dr. Elijah Stommel) have the experience and capacity to cover the management of ALS patients, and also the shared infrastructure and personnel expenses related to the registry. Data collected from patients can be inputted into RedCap and shared with the National ALS Registry. Data stored within the National ALS Registry will be invaluable to correctly identify ALL ALS cases, and understand the epidemiology of the disease in Vermont. If other states, especially large states, were to participate in this initiative, it would be a gigantic step forward in identifying and offering care to ALL patients with ALS, and allowing better understanding of the risk factors associated with the disease.

The confidentiality of patients' information in any registry is of paramount importance. Having a mandatory registry represents no danger of potential identification of patients if the proper steps are taken through de-identification. We have the support of the National ALS Registry which has a highly

functional infrastructure for collecting data and keeping it uncompromised. Appropriate referral of ALL ALS cases in Vermont, either to the UVM or Dartmouth Center, for expert ongoing care will ensure that these cases are then reported to the Registry. The ALS teams assembled by the Directors of these two ALS Centers of Excellence have the majority of the infrastructure and personnel expenses related to the registry; the experience and capacity for the management of ALS patients; and the expertise to report cases seen in the ALS clinics in a de-identified manner. Data collected from these patients can then be entered into the secure RedCap system, which is available at UVM and Dartmouth, and shared with the National ALS Registry. As noted by Dr. Paul Mehta in his testimony on February 16th, there should be no concern for loss of confidentiality of ALS patients as secure systems are available at the institutional and federal levels to make this very unlikely.

Identification of ALL ALS patients in Vermont will also permit the ascertainment of all Veterans with the disease. ALS cases within the VA system have the advantage of being classified as having service-related disease, which then entitles them to the multitude of VA benefits given to these patients. This will undoubtedly lift a remarkable amount of stress off the shoulders of these patients, who will not have to negotiate the often tedious and lengthy process of insurance approval of prescribed medications or equipment that they need and deserve. Once ascertained, these Veteran ALS patients can be referred to the White River Junction, VT VA hospital to fulfill these needs.

In general, about 85-90% of ALS cases are non-familial (sporadic) and about 10-15% are genetic and inherited. There are now multiple genes recognized as being associated with familial ALS, most of which are responsible for manufacturing abnormal proteins that are toxic to nerve cells, causing their death. There are ongoing studies with a research technique, called antisense oligonucleotides (ASO), which is being used to try and suppress these genes from making toxic proteins. Interestingly, in the last decade, research has shown that several of these genes may also be implicated in non-familial ALS, thus making it possible for identified ALS patients with mutations in these genes to be eligible for these state-of-the-art treatments.

Vermont has a history of ALS care and research and is poised to continue this tradition by becoming a pioneer in ALS clinical care and research. The first family found to have a genetic form of ALS with the superoxide dismutase 1 (SOD1) gene mutation (the Farr family) was described from the St. Johnsbury area. Mutations in this gene results in accumulated oxidative damage in the nervous system; on the basis of this data, one of the two FDA approved medications for ALS was developed (a drug called edaravone). Both the UVM and Dartmouth ALS Center clinics follow patients from families where several members have come down with the disease. Additionally, a good proportion of ALS cases with non-familial disease have in the last decade been found to have mutations in the SOD1 and other genes. Relatedly, ALL ALS patients seen in the UVM and Dartmouth Centers undergo testing for a battery of ALS-related genes, in an attempt to identify any mutations. Such testing would not typically be available otherwise, except in academic institutions with expertise. It would be very helpful to identify ALL cases of ALS in Vermont so as to be able to offer them new and exciting contemporary gene therapies (such as ASO therapy and other gene therapies) that are now being studied in clinical trials.

Currently, there is only one reportable/mandatory registry for ALS in the US, in Massachusetts. It would be rousing for Vermont to become the second state in the country to have a reportable ALS registry, and help familial and non-familial cases of the disease. It will reflect well on Vermont's desire to better understand neurodegenerative diseases in general, and ALS in particular, that afflict so many of its residents. For example, a Registry will be able to answer some, and other, questions. Are all the residents in the state with the disease receiving expert care? Is the incidence of ALS increasing? Are there identifiable risk factors and clusters of ALS cases in Vermont? Are people getting ALS at an earlier age? Can Vermont identify genetic cases of ALS?

Vermont is a small state and the cost of a registry should be minimal. Both Dr. Tandan and Dr. Stommel are certain of providing some resources for the registry. Both the UVM and Dartmouth ALS Centers have a workforce of residents, fellows, research team members and attending neuromuscular specialists to review the records of all patients reported to such a registry to ensure a correct diagnosis, and to avoid

false-positive cases being entered into the registry. Such verification and re-verification will also ensure that ALS cases are not recorded twice in the registry

There is a real need for states to come together to help create a mandatory, nation-wide ALS National Registry. Setting a precedence on the state level will likely make this happen. If larger states such as California, Michigan and Florida follow suit, we would be on our way to a mandatory National ALS Registry. There are several other states interested in this goal. In mandating a reportable ALS registry in Vermont, the Legislature has a great opportunity to help set forth a vision.

Senator Lyons, thank you very much for giving me the opportunity to testify on behalf of our ALS patients, families, and the community at large. Please let me know if you have any questions.

Sincerely,

A handwritten signature in cursive script that reads "Rup Tandan". The signature is written in black ink and is positioned above the typed name and title.

Rup Tandan, MD, FRCP, FAAN
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