

Testimony of the National Sleep Foundation

**Presented to the
Peripheral and Central Nervous System Drugs Advisory Committee
Of the
U.S. Food and Drug Administration**

June 6, 2001

By

**Richard L. Gelula, MSW
Executive Director
National Sleep Foundation**

Disclosure

The speaker, Richard L. Gelula, is a full-time employee of the National Sleep Foundation (NSF), an independent non-profit organization recognized under the U.S. Tax Code as qualifying for charitable donations under section 501(c)3. The Foundation was established in 1990 by the American Academy of Sleep Medicine (formerly known as the American Sleep Disorders Association) and was made a separate organization at that time. It is governed by a Board of Directors with 21 non-paid members who, historically and currently, have been drawn from the leading ranks of sleep science and sleep medicine and lay persons with an interest in sleep disorders. A current roster of NSF Directors is attached. As Executive Director, Mr. Gelula is salaried by NSF and receives no compensation or benefits from Orphan Medical or any other organization.

NSF is dedicated to improving public health and safety by achieving understanding of sleep and sleep disorders, and by supporting public education, sleep-related research and sleep advocacy. Its total revenue for its most recently completed year (fy 2000) was \$2,500,222. Primary sources of Foundation revenue are sponsorships and contributions to broadly supported special events. NSF is also supported by organizational, professional and individual memberships; project grants from government agencies, corporations, foundations, and private sources; individual subscriptions and contributions; federated giving through United Way and the Combined Federal Campaign; interest income; sales of educational materials; and advertising. The Foundation has enjoyed the support of many sleep professionals through a membership program called the Pickwick Club, which holds an annual fund raising dinner to benefit two-year basic research fellowships.

Orphan Medical has made contributions to NSF totaling \$160,000. These funds supported special event and public education projects, two of which combine support from many donors: co-sponsorship (one of eight paying sponsors) of *National Sleep Awareness Week*, one table (of 40) at our *Night of a Thousand Dreams* fundraising gala and two publications, an update of our previously published public education brochure, "Living with Narcolepsy," and a single issue of our professional newsletter, "Sleep Medicine Alert;" both of these publications were only supported in part by Orphan's contributions, the remainder being provided through NSF's general operating fund. It is important to note that such grants are unrestricted and that the Foundation and the experts it recruits independently write and review them. Given recent breakthroughs in our understanding of the pathophysiology of narcolepsy, the failure of government agencies or other organizations to publish consumer and professional materials reflecting these new developments, and the limited resources available by patient organizations, receipt of these unrestricted grants was timely and helpful for professionals and patients alike.

Finally, from a financial perspective, the Foundation has operated conservatively and has had budget surpluses for each of the past five years. Support from Orphan Medical did not contribute materially to NSF's maintenance or development. The absence of their contributions would not have differentially affected the Foundation's programs or its functioning.

Qualifications

The National Sleep Foundation has been an advocate for people with narcolepsy for some time. In 1998, upon recommendation of its Research Committee, then chaired by Thomas Roth, Ph.D., editor of the journal *Sleep*, the NSF Board approved a comprehensive program titled, "Toward the Cause of Narcolepsy." This program has provided grant funding that supported the breakthrough research at Stanford University, which in 2000 led to the discovery of the canine narcolepsy gene and the subsequent finding that the recently discovered hypocretin peptide is almost or entirely missing in people with narcolepsy. Since 1996, NSF has also invested in another approach to the discovery of the pathophysiology of narcolepsy, the establishment of the National Narcolepsy Registry, a serum DNA and family history registry for narcoleptics and their family members. The National Narcolepsy Registry is housed at and managed by the Montefiore Medical Center in New York City and currently has registered nearly 700 patients and family members. The NNR has been a research resource in seven narcolepsy studies. This initiative was funded by private (non-corporate) donations and by NSF's general operating fund.

Through our Pickwick Post-doctoral Research Fellowship program, NSF is also now funding a two-year study at UCLA on the neurochemical control of muscle tone in sleep and cataplexy.

Additionally, NSF has also provided a significant number of resources to professional and public education about narcolepsy and cataplexy. Given the small number of people directly affected by narcolepsy and the debilitating character of the disease, these contributions to education have been important. We publish brochures about the disease and distribute them at public, patient and medical meetings, through sleep centers across the U.S., upon written request, and we also place them on our Web site, www.sleepfoundation.org. We provide a lot of coverage about narcolepsy in our quarterly news magazine, *sleepmatters*. And over the years, we have devoted a significant number of issues of *Sleep Medicine Alert* to issues related to narcolepsy and cataplexy. Our professional outreach includes attendance and exhibits at such meetings as those held by the Associated Professional Sleep Societies, American College of Physicians/American College of Internal Medicine, American Academy of Neurology, American Psychiatric Association, Academy of Family Practice, and others.

Finally, based on a perspective grounded in patient interests, NSF, under the leadership of its Government Affairs Chair, Dr. William C. Dement, took an active role in advocating against legislation that would have assigned Gamma Hydroxybutyrate (GHB) a Schedule I classification under the Controlled Substances Act, which would have jeopardized further investigation of its therapeutic benefits; and NSF supported the final bill authorizing bifurcated scheduling for this medication. Our advocacy activity was primarily carried out through NSF volunteers and its Advocacy Network, and to a limited degree by NSF's general operating fund.

Summary of NSF's Position on Sodium Oxybate

The National Sleep Foundation calls upon the Peripheral and Central Nervous System Drugs Advisory Committee to fully consider the safety and efficacy of sodium oxybate for the treatment of narcolepsy and cataplexy, and to do so in a comprehensive context that fully recognizes the extreme psychological, emotional, economic, social and health toll that this AFFLICTION exacts from people who suffer from it. The National Sleep Foundation does not presume to second-guess the evidence that has been submitted about the safety and efficacy of this drug, but goes on record to say that such considerations should only pertain to affected patients and not other societal considerations: if safe and effective for people with narcolepsy, sodium oxybate should be made readily available to them; any concern for illicit use should be addressed through other channels such as law enforcement and professional licensing. The fact that narcolepsy is an "orphan" disease, for which only one medication is currently indicated, should be weighed as a factor in favor of approval of sodium oxybate because it is likely that availability of an approved drug will foster faster diagnosis and more appropriate treatment, and will also stabilize patients who usually first experience the dreadful effects of narcolepsy and cataplexy during their developmental years before the completion of education and development of a career.

Background and Key Issues

Narcolepsy and all of its primary characteristics, including cataplexy, are truly life-altering AFFLICTIONS, a term that best connotes the life-diminishing and debilitating aspects of this disabling disease.

Untreated, narcolepsy not only causes vivid nightmares and undermines the safe and secure feeling that most people get when they go to sleep, but it makes daily existence both objectively and subjectively frightening and strange, even alienating to the self and others. It makes the well-controlled process that routinely governs existence for almost all other humans – the alternating cycle of sleep and alertness – into something entirely different, an uncontrolled and uncontrollable process where the maintenance of conscious attention becomes random and cannot be sustained or relied upon. Both the phenomenon of overwhelming sleep attacks and the muscular weakness and collapse that occur with cataplectic attacks undermine the sense of predictability and confidence required to fully develop and function in our contemporary world.

But a true understanding of narcolepsy goes beyond physiology. The cumulative effects of the distinctive daytime and nighttime characteristics of this disease are truly traumatic. They not only disrupt, they undermine and frighten and change the core experience of the individual, exacting a toll that ranges from difficulty coping and functioning to total disability.

Just imagine what it would be like to have a life where the predictability of alertness cannot be counted on, where you felt such overwhelming sleepiness during the day that you could not stay awake to read texts, listen to lectures, or have the simple pleasure of

going out with a friend or watching a movie, where the experience of extreme emotion, the most human of attributes, such as laughter, anger or surprise, must be guarded against to prevent the loss of control, collapse and embarrassment that comes with a cataplectic attack, where despite all of the sleepiness, you do not even get a good night's sleep and awaken unrefreshed, and where available treatments often are inappropriate and leave you jittery or with other adverse side-effects. And these are only some of the effects of untreated or inadequately treated narcolepsy.

My guess is that if this disease occurred to me or during the development of any person who is here today in a professional capacity, that the AFFLICTION of narcolepsy would have proved to be a sufficient barrier that none of us would have been able to compete at a level necessary to keep up with our unaffected peers or to complete educational and career development at a professional level -- such that, in fact, none of us would be here today.

With this AFFLICTION we are not just talking about "sleepiness," an annoyance, but a condition where no amount of sleep or behavioral intervention provides sustained relief.

And the debilitating characteristics of narcolepsy are compounded by the fact that it is a low prevalence, orphan disease and that its onset most often occurs in the second decade of life when psychological and emotional development is unfinished and when people have not yet completed their education or established a career. It should also be recognized that:

Narcolepsy is not well understood or accepted – this applies to individuals suffering from this affliction as well as their families, schools and universities, employers and including personnel such as teachers, counselors and physicians, as well as peers, classmates and co-workers – in other words, the patient's entire world!

People suffer a double blow because it is thought their sleepiness is volitional and a sign of laziness – a stigma that has a troubling personal effect.

Primary care physicians are not familiar with its signs or symptoms and are unlikely to ask the kinds of questions or order tests that would speed an accurate diagnosis. One report states that it takes narcoleptics 15 years and visits to five different physicians to obtain an accurate diagnosis and in his text on Sleep Medicine, the late neurologist Michael Aldrich states that in his practice, he saw five narcoleptic patients in their 70's who had never been accurately diagnosed with the disease.

People who suffer from narcolepsy usually suffer alone, without support and are confused about their own symptoms. Their numbers are insufficient to ensure the availability of support groups in most locations.

Most people with narcolepsy do NOT have a relative with the disease, thus, even within their family context, the disease is strange and unfamiliar.

Thus, it should come as no surprise that people with narcolepsy suffer from a high rate of depression (Aldrich, 1999; Daniels, E., et.al, 2001) and research has shown that people with narcolepsy have a health-related quality of life rating as bad or worse than persons with Parkinson's disease, epilepsy or suffering from chronic migraine headache (Beusterien, et.al, 1999). Worse is that a rating by health professionals found that they desired greater social distance from narcoleptics than a number of conditions that one might expect a higher ranking such as epileptics and colostomy patients (Cohen & Mudro, 1992).

But the good news is that one study on health-related quality of life found that appropriate medical treatment does improve the HQL for people with narcolepsy (Beusterien, et.al, 1999). At this time, there are no pharmacological treatments indicated for cataplexy and those used off-label such as tricyclic antidepressants have significant quality of life side-effects including suppression of libido.

The National Sleep Foundation believe that narcolepsy exacts an unusual and cruel toll on those who suffer from this AFFLICTION and that this is a patient population greatly in need of medications that would control their symptoms. Such medications would foster more timely and appropriate diagnosis and treatment and would restore a good measure of the confidence and capability otherwise impaired by this cruel disease. I think of my own teenage child and I know that if she developed narcolepsy, I would want her to have access to any medication that might control her symptoms regardless of its effects on other members of society. We ask this panel to do all that it can to help people with narcolepsy and to consider the safety and efficacy of this drug as it applies to patients suffering from this disease.

#