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For the FDA Arthritis Advisory Committee Meeting of December 20, 2012
NDA 22151

The announcement by the Food and Drug Administration that its Arthritis Advisory Committee is meeting on December 20, 2012 to discuss the new drug application for Ampligen, for the treatment of patients with Chronic Fatigue Syndrome, sends the wrong message to those ignorant of Chronic Fatigue Syndrome (CFS) and raises the eyebrows of those with even glancing knowledge of the illness. Those ignorant of Chronic Fatigue Syndrome might assume that the illness must be related to arthritis. Why else would the Arthritis Advisory Committee be considering the application of a drug dealing with CFS? While CFS is a multisystem illness, and there are at least four current case definitions by which to diagnose the illness, not one of those case definitions lists arthritis, or arthritis-like symptoms, as one of the features of this illness. The decision to place the fate of Ampligen and CFS patients, some of whom have been successfully treated with Ampligen, in the hands of the Arthritis Advisory Committee must have alternative reasoning.

Those of us who have even a glancing knowledge of CFS, know that CFS has been treated like the plague-ridden buttocks of chronic diseases. Neither the National Institutes of Health or the Centers for Disease Control and Prevention (CDC) will conduct a proper epidemiological study to estimate or confirm actual number of patients who have CFS in the United States. Indeed, the CDC, who changes case definitions of the illness apparently on whim, has varied the number of patients from 800,000 to 4 million – a more than fourfold difference – without any concern for the accuracy of its numbers. But upon the assumption that there are 1 million CFS patients in the United States, you would think that the National Institutes of Health (NIH) would have a program dedicated to researching the illness within the walls of at least one of its institutes. Not so. There is not one, research laboratory within the entire NIH studying CFS. And as for the CDC, despite its having a laboratory devoted to CFS research in its Chronic Viral Diseases Branch, there are no recent studies emanating from it dealing with the etiology or pathophysiology of the illness. Hence, our concern is that the FDA is following the lead of its sister agencies of choosing to ignore, or worse, undermine, its responsibilities to CFS patients and those who attempt to assist them.

While the FDA announcement speaks of this application as being "new," in fact, it is not. The manufacturer of Ampligen, a small pharmaceutical company named Hemispherx, has appeared before the FDA before, only to be turned away and ordered to perform more clinical studies. Without the resources of a large pharmaceutical company, it has conducted clinical trials to the best of its ability in a patient-cost-recovery program. If the object of clinical trials is to prove drug efficacy, the trials have done so: some CFS patients when given Ampligen, improve dramatically. Take their Ampligen away, they relapse. Reinstitute the Ampligen, they improve again. Not all CFS patients improve, but if the CDC can vary its estimate of the number of CFS patients by varying its CFS case definition, the fact that not all patients improve suggests that the case definition of CFS needs to be improved, or that subsets of CFS patients exist, and that Ampligen works on a specific subset or, perhaps, even several subsets.

The second consideration of the FDA in determining whether or not to award approval of Ampligen use for CFS patients is the drug's safety when administered. To our knowledge, CFS patients either improve on Ampligen or they do not. We have not heard of any patient dying as a consequence of Ampligen administration. We have not heard of any severe or life-threatening reaction to the administration of Ampligen. If there are adverse reactions to Ampligen, we must presume them to be minor. Given the risk-benefit ratio of Ampligen administration, the patients have spoken: Many have moved themselves and their families to geographically disparate regions of the country in order to gain access to treatment. Without the treatment, they languish in bed; unable to care for themselves much less interact with their families.

So why then is the Ampligen application before the Arthritis Advisory Committee? Two possible reasons come to mind: (1) The FDA does not have an advisory committee better equipped to deal with this application, or (2) The prejudice against CFS, its research and its treatment is so large, that the FDA feels that the application would have a less prejudicial review before an irrelevant advisory committee rather than a committee more familiar with CFS. Perhaps, the FDA, like the NIH, does not have an existing advisory committee with the appropriate expertise to competently process CFS applications and considers the formation of such an advisory committee too costly. The National Institutes of Health has been notorious for having inappropriate reviewers sit in judgment of extramural, CFS research applications only to reject those applications for specious reasons generated by ignorance. Institutional and peer prejudice against CFS, CFS research, and the brave investigators who attempt to investigate this illness have been called to this nation's attention at the NIH, Chronic Fatigue Syndrome State of Knowledge Workshop (http://www.vtcfids.org/images/Elephants%20in%20the%20Room%20As%20Delivered.pdf). The failure of the federal government to act on the deliberate closure of CFS laboratories at universities and the termination of CFS researchers has led to yet another closure of a university research and clinical laboratory dedicated to CFS within recent months - proving the pervasive, poisoned environment for CFS treatment and research within the United States. How could the attitudes and culture which cause and permit universities, literally from coast-to-coast, to close CFS laboratories and prevent their faculties from engaging in CFS-related scholarly activity not infiltrate federal advisory committees?

Quite possibly, the timidity of the FDA to approve the use of Ampligen for CFS patients, as well as its timidity in the approval of a variety of other applications under its consideration, is a response to lessons learned in the past. When the FDA received the application to market thalidomide in the United States, after it had been marketed by 14 pharmaceutical companies in 46 different countries, it was considered to be a rather straightforward application. However, little was known about its side effects, and the drug affected experimental animals differently than humans. The FDA delayed approval. Subsequently, reports from Australia and West Germany indicated that thalidomide was associated with cases of human limb deformities and other congenital abnormalities. The drug was removed from all world markets and the application for approval in the United States was withdrawn. A national health crisis had been averted by stringent and slow adherence to FDA, drug approval rules.

However, subsequent to its initial removal from the market, thalidomide has been shown to be an effective therapeutic agent in leprosy, tuberculosis, sepsis, and cancer. Thalidomide may be useful in

the treatment of macular degeneration, in combating lesions in the mouths and esophagi of AIDS patients, and in the treatment of multiple myeloma. Consequently, in 1998, the FDA approved the use of thalidomide for the treatment of leprosy under a program (System for Thalidomide Education and Prescribing Safety [STEPS]) with severe restrictions and limitations. The message: Even for thalidomide, the FDA has weighed the risks vs. the benefits, and has decided to cautiously approve thalidomide.[1]

There is no evidence to suggest that Ampligen is a thalidomide. There is no evidence to suggest that are as severe, potential side effects to the use of Ampligen as there are to thalidomide. Yet, for some CFS patients, the consequences of being denied Ampligen therapy are as severe and possibly worse than living with the side effects of thalidomide.[2] Some CFS patients without Ampligen have no lives whereas with Ampligen they do. If the FDA can approve thalidomide for patient use in the United States, can there be any reason not to approve Ampligen?

[1] http://www.nyu.edu/classes/jaeger/thalidomide.htm

[2] http://ffdn.se/web/england-1/