LDA Remarks Before Vaccines & Related Biological Products Advisory Committee

REMARKS OF PAT SMITH, PRESIDENT, LYME DISEASE ASSOCIATION, INC. BEFORE THE VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE, MAY 21, 2002. Why more adverse events were seen after the vaccine reached the market:

People receiving Lymerix after product launch lived in Lyme-endemic areas.

REMARKS OF PAT SMITH, PRESIDENT, LYME DISEASE ASSOCIATION, INC. BEFORE THE VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE, MAY 21, 2002

DISCLOSURE: No money from SKB.

The Lyme Disease Association, LDA, an all-volunteer organization with five nationwide affiliates, consists of patients and families of patients. The LDA has provded funding for research coast to coast, some published in peer review journals including *JAMA*. Along with our Greenwich affiliate, we were recently honored at a luncheon by Columbia University for partnering with them in the establishment of an endowed chronic Lyme disease research center at Columbia, and we also co-sponsored a fully accredited medical conference for physicians with Columbia. Working with legislators, we developed a bill in Congress, HR 1254, which will provide $125 million for Lyme disease research, prevention, and physician education.

The Lyme Disease Association provided testimony to this committee in January 2001, seeking a moratorium on the vaccine, but felt no action was taken by the FDA, and to that end, in January 2002, the LDA had a private meeting with the FDA’s Center for Biologics Evaluation and Research (CBER) and brought several experts to discuss the vaccine issue with FDA officials including Karen Midthun, Susan Ellenberg, Peter Beckerman,

Norman Baylor, Miles Braun, and Robert Ball.

Donald H. Marks, MD, PhD, former lab director for Cannaught, fourteen years of clinical research and regulatory affairs experience in the pharmaceutical industry including Director of Clinical Research, in charge of the Lyme disease vaccine program at Aventis Pasteur, presented to the FDA. Dr. Marks was the leader of the competttitive effort to manufacturer a virtually identical vaccine.

Currently, his focus is diagnosis of adverse events from medications, vaccines, biologicals, and medical devices. Lymerix associated cases he reviewed included athralgias and arthritis as well as complicated neurological problems and include adverse events that are long-lasting. A summary of Dr. Mark's power point presentation follows.

WHY MORE ADVERSE EVENTS WERE SEEN AFTER THE VACCINE REACHED THE MARKET:

- People receiving Lymerix after product launch lived in Lyme-endemic areas.
- Many people may have had prior exposure and clinical or subclinical infection. In these cases, Lymerix could be triggering or reactivating the damage caused by old and presumably cured Lyme disease.
- Pattern of symptoms experienced after Lymerix mimicked pattern of prior infections in many individuals. In these patients, Lymerix-related symptoms seemed to respond to antibiotics, as did the initial infection, bolstering the theory of disease reactivation.

ISSUES WHICH CONFUSED THE VACCINE PICTURE

- As proof of safety, the company inoculated arthritis-prone mice with Osp-A. But since the mice did not possess the HLA marker known to interact with Osp-A in humans, rendering the experiment meaningless.
- The company masked serious causally-related adverse events behind qualifiers, such as "…and which may have no causal relationship with the vaccine" and "…cannot be distinguished from the natural history of the underlying disease."
- The company says that "the possibility of a severe rheumatologic,

neurologic, autoimmune adverse event is inherent in Lyme disease," attempting to shift the blame onto the patient and their illness, and does not inform physicians that the same adverse events can be separately caused by the vaccine, in addition to the symptoms of an underlying disease

- As a result of these actions, GPs in the US were kept in the dark about the life-threatening side effects of Lymerix, severe rheumatologic, neurologic, autoimmune adverse events.

SOME BASIC PROBLEMS.

- Non-specific hyper-activation of the immune system, often evidenced through swollen hands or arthritis, is an adverse event associated with Lymerix. This may be due to the presence of adjuvant.
- This hyper-activation creates "dirty" Western blots in which multiple Lyme disease bands appear, whether the individual has Lyme disease or not.
- The dirty banding makes it impossible for physicians to differentiate between Lymerix vaccination, new infection with Borrelia burgdorferi, or reactivation of infection.
- The net result is that cases of Lyme disease will go undiagnosed and untreated. Adverse reactions to Lymerix will be misdiagnosed as Lyme disease and people will be unnecessarily treated with antibiotics.
- The vaccine manufacture provides no warnings as to these possibilities.
- Physicians unaware of the spectrum of problems cannot appropriately treat these patients.
- The intention of FDA regulations is to provide a vaccine that is safe and effective. The intention of prescribing regulations is to provide sufficient information to prescribing physicians to enable safe and effective use of the vaccine. In both regards, SKB's actions appear to be contrary to FDA regulations and intentions, and contrary to accepted standards within the vaccine industry.

Dr. Marks provided some case assessments based on stringent parameters and his extensive experience in the field. "The adverse events I have examine from Lymerix are similar to those I am familiar with from another

vaccine." In the cases Marks examined –in his opinion, the adverse events were not anecdotal but a medical certainty.

- 4 of 4 neurological adverse events were related to Lymerix with presentations including transverse myelitis, inflammatory polyneuropathy, radiculopathy and cervical throacic myelopathy with multiple neurologic, including CNS, symptoms, memory loss and difficulty concentrating with immune-related complex of joint pain and fatigue.
- 15 of 17 rheumatologic adverse events were related, including inflammatory seronegative spondyloarthropathy, polyarthropathy, arthralgias, and arthritis.
- 2 of 2 miscellaneous reports were unrelated. These included chest pain and myofacial pain.

Based on his research, Marks said, "SKB should have devised and conducted clinical trials, epidemiological studies, or after-the-fact investigations to study the causal relationship between severe rheumatologic, neurologic, autoimmune and other adverse events and the use of Lymerix….there is sufficient evidence that Lymerix is causally related to severe rheumatologic, neurologic, autoimmune, and other adverse events in some individuals. This evidence is such as to warrant a significantly heightened degree of warnings and possible limitations or removal from marketing of Lymerix."

Andrea Gaito, MD, a rheumatologist seeing 35 patients with vaccine problems described three categories (**bold)** of problems to FDA. The first case, no history of Lyme, presented with acute synovitis, tests showed negative rheumatoid factor, Western Blot suggestive of active Lyme disease, with eight IgM and three IgG bands. Patient had minimal response to doxycycline, was prescribed and continues on anti-inflammatory medication. Conclusion: **autoimmune disease.**

The second case, **asymptomatic at time of innoculation, with a history of IV treated Lyme** meningitis. After Lymerix, patient experienced the onset of Obsessive Compulsive Disorder, headache, and fatigue. Upon testing, he had a positive ELISA and a Western Blot with every band positive. Retreatment with IV was not effective. Patient remains sick.
The third case, three shots of Lymerix, then bitten by a tick. S**he went on to develop symptoms of Lyme disease**, including night sweats and

fatigue. Tests showed: a Western Blot with every band positive; positive for the HLA markers that have been associated with Lyme-related autoimmune disease. Two courses of antibiotics produced no response. This patient now has Lyme disease but does not respond to treatment.

Dr Gaito is concerned about the efficacy of this vaccine and boosters. Will vaccinated individuals with prior Lyme who ultimately present with symptoms respond to retreatment? Is the vaccine itself retriggering an autoimmune response? She felt it is possible that the difference between the pre- and post-marketing results of Lymerix relates to the fact that those using it post-marketing lived in endemic areas for Lyme disease.

The LDA is concerned that despite presentations to the contrary by individuals at both the Vaccine Advisory Committee hearing in January 2001, the private meeting above, VAERS data, and other communications from the public, the FDA has not seemed to find any problems with this vaccine. LDA’s concern stems from the fact that although the approved vaccine is not on the market currently, since it was a unilateral decision by the company to remove the product, this same or a similar product may be remarketed without the full implications of the safety and efficacy of the current vaccine having been fully assessed or integrated into the Lyme vaccine picture. The LDA asks this committee to advise the FDA that significant arguments have been raised about safety and efficacy of this vaccine and that objective studies should continue on safety and efficacy of this vaccine or any other future vaccine that may seek FDA approval. Thank you for your time.