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Diane Griffin MD PhD
 Chair,
 Vaccine and Related Biological Products
 Advisory Committee
 Federal and Drug Administration
 FAX# 301-827-0294

Dear Dr Griffin:

We were made aware that the Advisory committee was scheduled to meet on January 31, 2001 to review Lymrix™ safety data. We wish to make sure the members are aware of our data, which were presented at the American College of Rheumatology annual Meeting in Philadelphia, PA in November 2000. In that presentation we reported arthritic manifestations in 4 individuals in who documented arthritis was observed following vaccination with OspA. Two of the individuals were from a controlled IRB approved. In-house vaccine study that we conducted. The other two were children from a Phase III study sponsored by SKB in which our Center participated.

Please find enclosed a copy of the abstract.

With our best regards

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REMOTE AND IMMEDIATE RHEUMATOLOGIC MANIFESTATIONS OF r-OspA VACCINE RECIPIENTS FOR PREVENTION OF LYME BORRELIOSIS. Carlos D Rose, Paul T Fawcett, Kathleen M Gibney, DuPont Children's Hospital, Wilmington, Delaware, 19899, USA.

The potential arthritogenic effects of OspA vaccination were the concern of some investigators once AA homology between OspA and LFA-1 was demonstrated. Commercialization went forward after extensive field trials failed to show increased frequency of arthritis among vaccine recipients. We suggested that the combination of a less than universal level of protection combined with intense "seropositivity" among recipients would complicate the interpretation of serologic data among vaccinees who present with rheumatic symptoms. We suggest the following scenarios as potentially challenging for the clinician: A-Vaccine induced arthritis; B-Lyme arthritis in a vaccinee and C-arthritis of other origin in a "seropositive" vaccine recipient. We report herein 4 cases in whom rheumatic symptoms presented among vaccine recipients. Cases 1 and 2 were identified among 20 adult volunteers participating in a prospective vaccine trial set out to investigate the natural course of the immune response to OspA. Cases 3 and 4 are children who consulted for arthritis who were participants of a Phase III clinical trial sponsored by the vaccine manufacturer. Cases 1 and 2 were adult males who developed acute disabling small and large joint symmetrical synovitis and myalgia within 48 hrs of the 2nd dose of *Lymerix*TM. In both cases the disease was self-limited required moderate doses of NSAID therapy and resolved without sequela within 7 days. Case 3 is a 16 year-old male who presented with monoarticular knee synovitis 4 months after the 3rd dose of OspA. His serology at the time revealed antibodies to 93, 66, 41, 31, 30, 28 and 21 Kd on IgG and 93 and 41 on IgM. Because of difficulties differentiating scenario A from B he received a full course of doxycycline therapy. Four months later he was asymptomatic. Case 4 is a 10 year-old male who developed bilateral knee synovitis a months after dose 3. Over the ensuing 5 months he developed intermittent asymmetrical olygoarthritis of knees, ankles, elbows and PIP joints at roughly monthly intervals. His serum 5 months post-vaccination revealed: antibodies to 93, 69, 66, 64, 54, 53, 41, 39, 31, 30, 28, 26, 25, 22, and 21 Kd on IgG. He had no reactivity on IgM. He was also noted to carry HLA DR4. Again because of the possibility of scenario A vs B, a full course of antibiotics was prescribed. Two months later he was asymptomatic. All four refused any further OspA inoculation. **COMMENTS:** Cases 1 and 2 confirm the arthritogenic, albeit transient, effects of OspA vaccination. Cases 2 and 3 are likely delayed vaccine induced arthritis, although in Case 4 the extent of the immune response suggests either current or previous contact with wild *B burgdorferi* with disease re-activation induced by the vaccine. In addition both cases illustrate the difficulties in interpreting Western blots in vaccine recipients. The atypical clinical manifestations, the presence of DR4 and the extent of the immune response make Case 4 highly intriguing.