September 20, 2011

Dr. Jerome Rosenberg
Research Integrity Officer
University of Pittsburgh

Dear Dr. Rosenberg,

Regarding our meeting of September 20, 2011 and my discussion with Dr. Juhl on September 8, 2011, I am requesting an inquiry into possible research misconduct by Dr. Jay Kolls, Professor of Pediatrics, University of Pittsburgh and Chief Scientific Officer of Minivax Corporation.

The principal concerns are:

1) The use of data generated in my laboratory, the use of my name as a collaborator without my knowledge, and the claim that data generated in my laboratory was produced in collaboration with Dr. Kolls in an NIH grant (Small Business Technology Transfer (STTR), R41AI097069-01, entitled, DEVELOPMENT OF A NOVEL PCP VACCINE FOR AIDS PATIENTS) which was awarded in July 2011 to Dr. Kolls and Dr. Ray Chaudhuri, through their company, Minivax Corp.

2) The use of data generated in my laboratory, the use of my name as a collaborator without my knowledge, and the claim that data generated in my laboratory was produced in collaboration with Dr. Kolls in an NIH P01 grant (P01 HL076100-07) in which Dr. Kolls was the principal investigator (PI) of the Project in question (Project 2). I have attached a portion that grant. I became aware of the P01 grant application after its original submission was not funded, and Dr. Kolls and the PI of the PO1, Dr. Judd Shellito, of LSU, asked me to participate in the revision and resubmission of the P01 as PI of a Project and PI of the Non-human Primate Core. In June 2010, I had agreed to participate in the resubmission of the P01 for September 2010 NIH submission date. After several requests for the
original grant so that I would have an overall view of the Projects, Dr. Kolls sent me a portion of the grant containing the research plan section of his Project. It is his Project 2 of this P01 that contained my data and stated that he had generated the data in collaboration with me while he was a faculty member of the University of Pittsburgh. These statements are false and Dr. Kolls and I did not have a collaborative arrangement regarding the research in question. The statements in Dr. Koll’s research plan of the P01 HL076100-07 that are the basis for this inquiry request are as follows:

a. **Page 2, Line 7**: “Preliminary studies suggest that Pneumocystis colonization occurs in up to 80% of SIV infected macaques compared to none in non SIV infected monkeys”.

b. **P4, L26**: “Lastly in collaboration with Karen Norris’s lab at the University of Pittsburgh we have examined anti-Kex1 titers in SIV-infected macaques and rate of PC lung infection as determined by nested PCR in BAL fluid. In a cohort of 12 macaques, 75% (9 of 12) became PCP positive within 3 months of SIV infection. The three animals that remained PCP negative in BAL had mean serum anti-Kex1 Ab levels that were a minimum of 10 fold greater (as measured by end point dilution at 1:64) compared to PCP positive monkeys (see preliminary studies). These data support the concept of anti-Kex1 antibodies as a protective response to prevent PCP and supports the further evaluation of our vaccine in SIV-infected macaques”.

c. **P6, L3**: “In collaboration with Karen Norris’s lab at the University of Pittsburgh who supplied us with both overlapping peptides in this region of Kex1 as well as this conserved region as recombinant protein expressed in E. coli we demonstrated that antibodies recognizing epitopes in this region account for a significant amount of the opsonic killing of PC (Figure 2)”.

d. **P9, L39**: “In collaboration with the Norris lab at the University of Pittsburgh we have assessed spontaneous PC infection macaques infected with SIV/Delta B670. Kling et al. have recently shown that CD4 counts below 500 cells/uL are strongly associated with an increase in PC colonization in the lung as assessed by nested PCR for PC in BAL fluid (58). Five of five monkeys developed detectable PC colonization by nested PCR. Interestingly several monkeys had an initial increase followed by a fall in anti-Kexin antibody titers prior to the development of a positive PCR for PC. In a second cohort of animals preliminary studies suggest that monkeys that have high baseline anti-Kex1 titers are protected against PC positivity by PCR in BAL after SIV infection. It is important to note that these data are from the Pittsburgh animal facility”
and may not reflect what occurs at the Tulane Regional Primate Center. As part of the animal core, in this renewal, we will determine the rate of PC infection at necropsy in 25 SIV and 25 non-SIV infected macaques. For these studies we will assess PC colonization by nested PCR, real-time PCR on lung tissue and BAL. These data will also be compared to standard histological detection of PC by GMS staining of lung tissue. Based on our preliminary studies, we clearly have the technology to assess anti-Kexin antibody repose in monkeys as well as assess the rate of PC colonization in BAL and at necropsy”.

3) Dr. Kolls became aware of the details of our work while serving as an advisor on the thesis committee of my doctoral student, Heather Kling from 2006 until the completion of her dissertation in April 2010 and I believe he used this information in both the P01 and the STTR grant applications. The work that Heather Kling generated as part of her thesis project was presented to her committee at approximately 6-month intervals and in her dissertation. It is portions of this work that are presented in Dr. Kolls’ grant proposals regarding the transmission rates of Pneumocystis in SIV-infected macaques and the protective role of anti-kexin antibodies in SIV-infected macaques (points a, b, and d, above).

4.) As indicated in the abstract of the Small Business Technology Transfer (STTR) R41 grant to Drs. Kolls and Chaudhuri, a patent was filed based on the Pneumocystis Kexin gene and protein as a vaccine. This patent, WIPO Patent Application WO/2011/087934, and possibly a US provisional patent application, contain data generated in my laboratory and states that I will be providing recombinant kexin protein for use in immunological assays described in the patent. I had previously provided Dr. Kolls with the macaque-derived Pneumocystis KEX1 gene fragment (Kexin 1 gene, GenBank accession no. EU918304, submitted in 2008 by Norris et al.) and the recombinant protein (which are referred to as “mini-kexin” in the patent application). I am requesting an inquiry to determine if this gene sequence, the recombinant protein or sequences derived from this gene were used to generate a portion of the data described in this patent application. I had no knowledge of this patent application, its contents prior to its submission, the use of my data, nor did I agree to provide Dr. Kolls with Kex-related materials or preliminary data as stated in sections [0082 and 0171] of the patent WO/2011/087934, indicated below:

“[0082] Example 3. CD4IND pathogen-specific immune responses against Pneumocystis kexin are generated in an SIV model of immunodeficiency in macaques. We expect that the mini-kexin constructs will produce vaccine-induced immune responses in SIV-infected, CD4 deficient macaques… Preliminary studies suggest that Pneumocystis colonization occurs in up to 80% of SIV infected macaques, compared to 0% in non-SIV infected monkeys”.

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To determine anti-PC or Kex1 IgG titers, ELISA plates (Corning, NY) are coated with 100 ng of PC antigen or Kex 1 antigen (provided by Dr. Karen Norris, University of Pittsburgh)...

This patent application was filed through Louisiana State University and I further request that an inquiry be made into the claim that the work was performed at LSU rather that University of Pittsburgh and the claim of Dr. Kolls is the inventor of the kexin construct referred to as mini-kexin in the patent.

Thank you for you assistance in this matter.

Sincerely yours,

Karen A. Norris, Ph.D.
Professor of Immunology