January 16, 2003

Immunization Safety Review Committee
c/o: Amy Grossman
Institute of Medicine
Keck Center w/833
500 Fifth Street, NW
Washington, DC 20001

Dear Immunization Safety Review Committee:

I am writing to share with you concerns related to the topic of vaccines and autism, the subject of your February 9, 2004 meeting.

I initially shared many of these concerns with the FDA/CBER division in December 2002. In a response I received in May 2003 from Karen Midthune, Director of the Office of Vaccines Research and Review, it was noted that the previous IOM review of the potential association between MMR vaccines and subsequent autism did not consider the specific scenario I envisioned – one that focuses on the mothers of children with autism and a long-term side effect of rubella containing vaccines.

As you know, many of the vaccine-related autism concerns that are debated and studied today are focused on short-term side effects in immunized children. My vaccine safety concern is long-term in nature and is directed specifically at the mothers of children with autism. In summary, my concerns are:

Are Some Cases of Autism the Result of a Persistent, Attenuated Rubella Infection in the Mother?

Are Some Cases of Autism Actually Congenital, Subclinical Attenuated Rubella Syndrome?

I have provided for IOM information and data points with this letter which are the basis of these concerns. No formal autism studies have focused on mothers of autistic children, their rubella vaccination histories and their susceptibility to rubella in pregnancy. No studies have focused on the possibility that persistent attenuated, vaccine-strain rubella infection might play a role. Several scientists who have reviewed these ideas agree that such investigations are warranted.

In addition to having IOM review the data related to my questions above, I would also like to request that future vaccine safety investigations be focused on **why** persistent vaccine-strain virus infections might occur. Instead of trying to prove or disprove a link between persistent vaccine-strain measles virions, inflammatory bowel problems and autism as is being done today, and instead of trying to prove or disprove an association between persistent vaccine-strain rubella viremia and chronic arthralgias as was done in the 1980's, I would like IOM to conduct a thorough investigation on **why** vaccine viruses might persist in some vaccine recipients. Such an investigation should include not only looking at potential defects in vaccine recipients but also potential defects in vaccine design and development methods that are more than 40 years old.

Please see the 1991 IOM Report excerpt below and the comments that follow for insights into this request.

***From the 1991 IOM report Adverse Side Effects of Pertussis and Rubella Vaccines:**

"In any event, it is not clear at this time whether patients who develop arthritis, acute or persistent, after rubella vaccination have a specific immune system defect that prevents their systems from clearing the virus normally." (p. 195)

The quote above was in reference to studies from the 1980's that found persistent vaccine strain rubella virus in synovial fluid and joints of arthritic patients as long as several years after vaccination. No consideration appears to have been given to potential design flaws in the vaccine, no consideration was given to the potential long-term side effects that a persistent rubella infection may have on females' reproductive health, and no consideration appears to have been given to possible injuries that could be sustained to future offspring if reactivation of the persistent rubella virus occurred during pregnancy causing intrauterine infection.

Vaccines are not supposed to leave behind persistent viruses; they are supposed to trigger an immune response and the viruses are supposed to be cleared from the body. An investigation into why this does not always occur and why vaccine-strain measles virus and vaccine-strain rubella virus can persist in individuals is urgently needed. A layperson's questions on this subject would include:

1) Measles, rubella and MMR vaccine package inserts state that 1-5% of vaccinees fail to seroconvert and develop antibodies to the virus. What does this mean in terms of clearing virus? If an immune response is not triggered in an individual, what happens to the vaccine virus? Does it persist undetected in some of those individuals who fail to seroconvert?
2) Can live viruses in vaccines "perform" molecular mimicry and mimic human cell epitopes post-vaccination so that the viruses adapt themselves to survive and remain undetected causing subclinical infection in some vaccinees?
3) Could molecular mimicry have occurred in the original human hosts from whom the vaccine strain viruses were derived? Are there genetic similarities, similar haplotypes, etc., among those in whom vaccine viruses persist and the original human hosts from whom vaccine viruses were derived?
4) Could the attenuation process that was used in the 1960's whereby live viruses were passaged many times in human fetal tissue and amniotic cell cultures increase the opportunity for molecular mimicry of human cell epitopes and decoding of cellular pathways to occur? Subsequently, is it possible that what has appeared to be a weakened vaccine virus since 1960 actually is a potentially more dangerous virus given an enhanced ability to go undetected by the host immune system?
5) Is a "genetic predisposition" to tolerate and serve as host to a vaccine-strain virus simply a matter of having genetic similarities to the source host of the vaccine virus and/or the human source of the cell cultures used in manufacturing?
6) Are persistent vaccine-strain virus infections responsible for producing high measles and high rubella titers that are common in children with autism?

As today's knowledge about microbes, molecular biology, genetics and subcellular processes has advanced significantly since the 1960's, I think most people would agree that the safety of 40-year-old vaccine development methods should be reviewed and any concerns related to molecular mimicry, decoding of human cellular pathways and persistent vaccine strain virus infections be thoroughly and adequately addressed.

Thank you for your consideration,
E.H. Granai