

Public Comment
Use of Insect Cells for Influenza Vaccine Production
Barbara Loe Fisher
Co-Founder & President
National Vaccine Information Center
Vaccines & Related Biological Products Advisory Committee
Food and Drug Administration
November 19, 2009

My name is Barbara Loe Fisher. I am co-founder and president of the National Vaccine Information Center. I have no financial conflicts of interest.

It is understandable why both industry and public health agencies want to develop influenza vaccines that do not depend upon chicken eggs for production. Expedited delivery and higher antigen yields, as well as avoidance of egg allergy issues and eliminating the need for preservatives or adjuvants are all worthy goals. And I would like to commend Protein Sciences on the excellent methodology used in these small clinical trials that included a head to head comparison with a true placebo and, then, with another influenza vaccine with no potential co-founding variables in terms of other vaccines being given simultaneously.

I remember in 1995 when Swiss scientists found reverse transcriptase, which copies RNA into DNA, in the live measles and mumps vaccines as well as some influenza vaccines prepared in chicken embryo cells. Reverse transcriptase activity has been associated with the presence of retroviruses which can permanently alter the genes of the cells they infect. I recall the CDC's explanation, which was that an avian retrovirus integrated itself into the ancestors of the chickens which laid the eggs that were used to produce the chick embryo fibroblasts used for vaccine production.

In the current effort to fast track the use of a new technology which clones hemagglutinin genes from three influenza viruses – which may be of human as well as mammal and bird origin – and splice them into baculoviruses, which are then used to infect caterpillar cells to produce the hemagglutinin contained in the new recombinant protein based influenza vaccine, there is always the possibility that adventitious agents contaminating insect cells could end up in the vaccines. In fact, a 2005 World Health Organization document on regulation of candidate human vaccines states that “Most insect cells may have viruses in them and infection can be hard to detect and difficult to eliminate...steps should be taken to eliminate them.”

The inadvertent contamination of polio vaccines with SV40 serves as a cautionary tale and the public will clearly want reassurance that sufficient adventitious agent contamination screening is in place with this vaccine using an

insect virus and insect cells for production, guaranteeing that no future unusual adverse effects will be seen as more people receive the vaccine.

In addition, FluBlok contains three times as much protein as other influenza vaccines. There is always the potential for increased cross-reactive autoimmune responses in individuals who are genetically predisposed to autoimmunity and immune mediated neurological dysfunction. I am thinking of the Bell's Palsy case in these trials that may or may not have been triggered or exacerbated by FluBlok vaccination. The relatively small numbers of individuals in these clinical trials may not reveal the rarer but very serious complications involving demyelination of the brain and autoimmune disorders that have been reported following receipt of recombinant protein vaccines such as hepatitis B and HPV vaccines, including GBS, CNS vasculitis, rheumatoid arthritis, lupus and multiple sclerosis.

This new cell based technology is promising but there are many unknowns. A larger pre-licensure clinical trial may answer outstanding questions about safety and efficacy and, hopefully, will include adults with chronic brain and immune system dysfunction, particularly those with autoimmune disorders, with a minimum one year follow-up period to determine if this vaccine exacerbates pre-existing chronic disease.