The Flu Fix: Short-Term and Long-Term Changes Are Needed

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Hospital pharmacies spent a considerable amount of time this past fall and winter wondering where their next batch of influenza vaccine would be coming from or whether it would be coming at all. And when the vaccine finally arrived, there were troubling questions about its price and even its authenticity. Allegations of price gouging, for example, led Tommy Thompson, outgoing Secretary of the Department of Health and Human Services (DHHS), to write to U.S. governors, encouraging them to investigate unscrupulous distributors and to prosecute them when necessary.

I guess we shouldn’t be surprised at incidents of criminal behavior penetrating the flu vaccine distribution chain. After all, drug counterfeiting has been with us for a while. So what ought to be done to ensure an adequate flu vaccine supply for both the near and distant future?

For the near term, we are stuck with the current manufacturing method: using chicken eggs to grow a virus that is then killed and injected into people. It is a dirty process that uses old technology, and it is subject to bacterial contamination at every turn. This problem of possible contamination is what prevented the U.S. from receiving the expected 48 million doses of Fluvirin® from Chiron Corporation’s United Kingdom plant. Over the long term, this manufacturing process cannot continue.

Given that we are stuck with this outdated chicken egg method for the time being, the U.S. Food and Drug Administration (FDA) needs to be more forgiving in its inspections. I still don’t understand why we lost all 50 million doses of Fluvirin®. Chiron found bacterial contamination in eight of its lots at the end of August 2004, then rechecked all the lots. At the end of September, the company declared that the rest of the vaccine was fine and that the U.S. would be getting 46 to 48 million doses instead of 50 million. A week later, British regulatory officials suspended shipments of the vaccine for three months. The FDA sent inspectors over to the U.K. immediately. In the end, the FDA differed with Chiron; it did not think that the company was accurate in its determination that 46 to 48 million doses were perfectly safe.

Maybe the FDA had good cause, but it has been very “quick on the trigger” in the past. What drove many vaccine manufacturers out of the business and what makes other companies think twice about getting into it is the difficulty of complying with the FDA’s ever-stricter current Good Manufacturing Practices (CGMPs). Wyeth stopped manufacturing injectable influenza vaccine, diphtheria, tetanus, and acellular pertussis (DTaP) vaccine, and tetanus–diphtheria (toxoid) (Td) vaccine after the FDA assessed a $30 million fine to the company in 2000.

Current CGMP violations had been found at two plants in Marietta, Pennsylvania, and in Pearl River, New Jersey. Despite the steep fine and strict terms, the FDA admitted that it “never actually found contaminated Wyeth products and is aware of no illnesses” resulting from the CGMP violations at the plants in question.

For the long term, we must move to a new, less precarious method for manufacturing flu vaccine. One technique is already on the cusp of commercialization; it involves growing the virus in cell cultures. The federal government needs to give this method a big push, and now.

Protein Sciences Corporation in Meriden, Connecticut, has a product called FluBlok™. This influenza vaccine consists of three recombinant hemagglutinin (rHA) proteins that are produced in serum-free insect cells.

“We’ve been through seven clinical trials, all of which were sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), and if the FDA wanted to approve our investigational new vaccine under its expedited authority it could,” says Dan Adams, President and Chief Executive Officer of Protein Sciences.

This is the biggest imperative at the moment: getting cell culture manufacturing up and running. A number of major and smaller drug companies are investigating making flu vaccine this way, including Baxter Healthcare and ID Biomedical, which supplies 75% of Canada’s flu vaccine, albeit via chicken egg manufacturing. But the FDA has been slow to respond, and the NIAID has awarded three meagre grants, the latest to ID Biomedical for $7.5 million. It is a drop in the bucket.

Congress hasn’t been much help either. Lester Crawford, the acting FDA commissioner, noted that when he appeared before House and Senate committees in November, the FDA had asked Congress for $100 million for unspecified cell culture manufacturing activities for fiscal year 2004, which ended on September 30. Congress gave him $50 million.

Since the hearing on October 8, 2004, regarding the nation’s shortage of flu vaccine, both Aventis Pasteur and MedImmune have been able to produce additional doses. The FDA has also identified and negotiated for approximately five million doses of vaccine from foreign manufacturers. In addition, the nation has a supply of enough antiviral medications to treat about 40 million people. These antiviral drugs can be used to prevent or treat influenza if symptoms are identified early.

So maybe eventually the manufacturing and distribution of flu vaccine will no longer be a “chicken and egg” proposition.