

<http://denverpost.com/Stories/0,1413,36%257E23827%257E2479289,00.html>

## **Flu-vaccine process gets a shot in the arm**

By [Marsha Austin](#)  
[Denver Post Staff Writer](#)

As the U.S. embarks on a flu season that could leave many people unprotected against the potentially deadly virus, public health experts are making inroads toward replacing the flu shot's outdated - and unreliable - manufacturing process.

At issue is how to entice a pharmaceutical industry that's fixated on discovering the next billion-dollar blockbuster drug to instead spend time and money on more reliable and effective vaccines.

Granted, it will take years of expensive laboratory research and then the the testing of new vaccines on human patients - with no guarantee of success.

But despite financial and regulatory obstacles, several drug companies are making considerable headway, creating fast- growing and super-potent flu vaccine in cells from humans, monkeys and caterpillars.

The first of these next-generation flu vaccines could be available to the U.S. public within three years, health experts said.

300 million chicken eggs

Currently, it takes nine months and nearly 300 million chicken eggs to grow enough flu vaccine to supply the United States each year.

When British regulators shut down the U.S.-owned Chiron Corp. plant last month because of safety violations that could have contaminated flu vaccine, it left the U.S. with only half its expected 100 million doses.

Last year, millions of Americans were given shots that offered no protection against the virulent Fujian flu strain because scientists couldn't grow the strain in an egg-based culture in time to have shots ready that fall.

"The problem with eggs is, if some glitch occurs, you can't go back to square one because you've run out of time," said Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, a division of the National Institutes of Health.

Fauci and other health officials want to jump-start flu vaccine research with federal funds. Last year, Congress allocated \$50 million for flu-outbreak readiness, including research into new vaccines. Fauci said he plans to ask lawmakers for \$100 million more this year.

"It costs money, and the vaccine industry is already extraordinarily fragile," Fauci said. "It's very difficult to get pharmaceutical companies to go into a field where the margins are thin at best, the risk is high ... and the market is small."

But federal interest in developing vaccines against bioterror agents, such as smallpox and anthrax, is at an all-time high. And because of the nature of vaccine development, that research can be applied to the development of flu shots, health experts said.

For example, scientists at Illinois-based Baxter Corp. are working to bolster government smallpox vaccine stockpiles by growing doses in a line of African green monkey kidney cells used to make polio vaccine. That same cell line is the foundation of a flu vaccine project that Baxter researchers say could yield market-ready flu shots as soon as 2007.

Growing vaccine in cells instead of eggs shaves months off production time and allows researchers to more specifically target vaccine to flu virus strains circulating in humans during any given year.

It takes Baxter eight to nine weeks to make a batch of flu vaccine using the cell-based method, said Deborah Spak, spokeswoman for Baxter.

Meanwhile, Baxter is building a manufacturing plant in the Czech Republic for its monkey-cell-based flu vaccine and will test the shots in Europe this flu season, Spak said.

If the vaccine proves safe and effective, Baxter will test it in the U.S. next year, she added.

Using human stem cells

Aventis Pasteur, the world's largest producer of egg-based flu vaccine, began work this year on a vaccine derived from embryonic stem cells. The cell line belongs to Dutch biotech company Crucell.

Growing flu vaccine in human cells is safer than working with monkey or other mammalian cells because there is no risk of animal viruses slipping undetected into the shots, said Michel DeWilde, an Aventis research and development executive.

"It's not worth the risk," said DeWilde.

A third major player in the race to produce a next-generation flu vaccine is Connecticut-based Protein Sciences Corp., best known for its work on a vaccine for HIV/AIDS.

The biotech company uses ovarian cells from caterpillars to grow vaccines for many viruses and has had early success with a flu vaccine.

Last year in a clinical trial, healthy elderly adults who were given Protein Sciences FluBlok vaccine, derived from flu virus DNA injected into the insect cells, were

protected at least as well against the flu as those who got egg-based shots, said Penny Post, the company's director of quality and regulatory affairs.

And participants were able to tolerate stronger doses of the vaccine - indicating that the new shots may house the potential for better, longer-lasting immunity, Post added.

Protein Sciences received federal funding for its clinical trial and plans another during this year's flu season if it gets the go-ahead from the Food and Drug Administration.

Unlike egg-based flu shots, cell-based vaccines can be stored year-round and production ramped up quickly to meet unexpected demand, health experts said.

"It has greater flexibility and dependability," said Fauci.

Despite all of the optimism surrounding cell-based flu vaccine, many regulatory hurdles remain, cautioned Dr. Ted Eickhoff, professor emeritus at the University of Colorado Health Sciences Center's division of infectious disease.

Eickhoff, a member of an FDA vaccine advisory committee, said panel members are excited about the potential of new flu vaccines - but don't expect any to replace egg-based vaccines for at least five years.

"This is still a big 'if,'" he said.

"Will this year's experience bring things to a head and alert both Congress and the executive branch to the urgency that we need to do something about this?" Eickhoff asked. "If we have an epidemic year, will there will be a lot of screaming and crying to change things? Probably."

But if the flu season is relatively light: "There will be yawning," he predicted.

*Staff writer Marsha Austin can be reached at 303-820-1242 or [maustin@denverpost.com](mailto:maustin@denverpost.com).*