Pandemic fears hatch new methods in flu vaccine industry

Spurred by warnings of an impending worldwide influenza epidemic, biotechnology companies are racing to develop faster ways to make flu vaccines.

With current vaccine manufacturing methods, it would take six months to create a clinically tested vaccine if a pandemic started today, says Klaus Stöhr, head of the World Health Organization's (WHO) Global Influenza Program. "By that time, the virus could have circled the globe."

But because new technologies take so long to develop, license and test in the clinic, manufacturers and health agencies need to lay the groundwork now, before a pandemic hits, experts say.

Flu vaccines are currently grown in eggs, a lengthy process that requires large numbers of embryos. But many companies are developing methods that use cell culture, a technique that could potentially grow vaccines in several weeks, rather than the months necessary for egg-based production. In the cell-culture process, cells are infected with the virus and then grown in tanks, like those used for fermenting beer.

Dutch biotechnology company Crucell N.V. is partnering with Aventis Pasteur, one of the US flu suppliers, to develop large-scale cell-culture methods using healthy human cells. According to Crucell spokeswoman Elizabeth Goodwin, the company can make enough vaccine for all of the Netherlands and Germany in a 100-liter bioreactor. Crucell is working on preclinical versions of both a pandemic vaccine and the annual flu vaccine and expects to begin clinical trials in the summer of 2005.

Solvay Pharmaceuticals, also based in the Netherlands, is building a manufacturing plant dedicated to cell-culture flu vaccines. The facility, expected to be completed in 2005, will be the first of its kind in the world. The company is also planning to build a second plant near Moscow.

Most cell-based methods grow whole viruses to make vaccines, but Connecticut-based Protein Sciences Corporation uses insect cells to grow hemagglutinin, a protein abundant on the surface of the flu virus. Hemagglutinin is a component of current vaccines and is responsible for most of the immunogenic response, says Manon Cox, the company's chief operating officer. Because the vaccine doesn't use the whole virus, this method is safer and faster than traditional techniques, she says. Those vaccines aren't licensed in the US, but the company hopes to gain approval from the US Food and Drug Administration by 2007.

Itar-Tass/Grigory Sobcheko

Flu vaccine researchers are no longer placing all their eggs in one basket.

MedImmune, a Maryland-based company, is developing seed strains of several virulent influenza viruses, which could be used to create vaccines during a pandemic. The technique—called reverse genetics—allows scientists to hand-pick viral genes to create the vaccine. Texas-based DelSite Biotechnologies is working on a nasal powder vaccine against the H5N1 strain. The powder may eliminate the restrictive need for cold storage.

Progress in vaccine technology has been slow because the vaccines do not provide enough economic incentive for manufacturers. In November, the WHO convened an unprecedented closed-door meeting to encourage public-private partnerships and gather financial support. Several countries have agreed to support programs to develop pandemic vaccines.

Most schemes are geared toward the H5N1 bird flu virus—the strain experts have identified as the most likely cause of a pandemic. The US is developing test batches of H5N1 vaccine with two licensed manufacturers, Chiron and Aventis, the same companies that supply the country with annual lots of flu vaccine. Clinical trials are set to begin in early 2005.

The US also has a contract with Aventis to secure a year-round supply of eggs, enabling immediate vaccine production in the event of a pandemic. A limited egg supply was one of the reasons manufacturers couldn't ramp up flu vaccine production in October (*Nat. Med.* **10**, 1148; 2004) after problems at a Chiron manufacturing plant stripped the country of half its supply.

Emily Singer, Boston

Allegations fly over fate of UK medical research institute

Colin Blakemore, head of the UK's Medical Research Council (MRC), is to be investigated after a senior scientist at the prestigious National Institute for Medical Research (NIMR) claimed that Blakemore threatened him with dismissal if he continued to oppose relocation plans for the institute.

After many contentious discussions, an MRC task force said in July that the NIMR should be moved to London and partner with either King's College London or University College London to boost translational research (*Nat. Med.* 10, 762; 2004).

But NIMR scientists reacted angrily when they learned that there was no option to keep the institute at its current site in Mill Hill. "We are dismayed by this rejection," the institute's leaders said in a statement in August.

After receiving multiple complaints, the House of Commons Science and Technology Committee launched an inquiry. At a hearing on 1 December, the NIMR's Robin Lovell-Badge said that Blakemore, who led the task force, had tried to change Lovell-Badge's mind. "I was in receipt of various forms of attempts at coercion, such as phone calls late at night threatening me with my job," Lovell-Badge said.

Because of the serious nature of the allegations, Britain's Secretary of State for Trade and Industry has been urged to investigate. "I totally refute the accusations that I threatened Robin Lovell-Badge with dismissal, and that excessive pressure was put on any task force member to agree to statements contrary to their opinion," Blakemore told *Nature Medicine*.

Blakemore says Lovell-Badge telephoned him on 28 June, and not the other way around, and "criticized me aggressively." He adds that the alleged phrase—"Robin, I don't know how you can disagree with me. I am your employer"—is not a threat of dismissal. "But, in any case, I did not say it," Blakemore says.

Blakemore has sent a letter to the committee refuting the allegations. He says that during the task force's deliberations, he was at several times pressured by NIMR Director Sir John Skehel, and "was shouted at, laughed at and derided by Sir John on almost every occasion."

Stephen Tomlinson, deputy vice-chancellor of Cardiff University and a member of the task force, says he supports the view that the future of NIMR is not at Mill Hill. But if the task force recommendations are not acceptable to the MRC, he says, the council should explore other alternatives, "including the option of simply closing it and redeploying the £30 million annual funding across the UK."

Xavier Bosch, Barcelona