

## INFECTION CONTROL

## Countries ill-prepared for influenza pandemic

H5N1 is the best candidate flu strain for an expected influenza pandemic, but countries around the globe are ill prepared to manufacture it, the World Health Organization is warning.

“There is currently too little momentum in the development of influenza pandemic vaccine,” says Dr. Klaus Stöhr, coordinator of the WHO Global Influenza Programme. “There is a need to raise the profile of pandemic preparedness as a matter of national security planning.”

Countries have a narrow window of opportunity to prepare before a pandemic strikes, Stöhr says.

An influenza pandemic involves a novel strain of influenza that has not circulated among humans. Based on the historic emergence of influenza pandemics — on average every 25 years — the world is overdue for another one. The last one occurred in 1968–69.

WHO has been hosting meetings in Geneva to focus specifically on encouraging more manufacturing and clinical testing of potential vaccines. The organization is also urging governments to finance vaccine development and to plan the logistics of a vaccination ground war against whichever virus emerges as the pandemic strain.

Although no one knows for certain what strain of influenza will prevail, the WHO is keeping a close eye on emergent avian flu strains in Asia. “We have in Asia an H5N1 virus which is ready to cause a pandemic,” Stöhr said after the WHO meeting on vac-

cine development in November.

WHO wants governments to demonstrate their commitment to preparing for a pandemic by investing in the development and clinical trials of potential vaccines, particularly “mock” vaccines, or “seed” pandemic candidates, which can be tailored at the last minute to the specific pandemic strain. Most pharmaceutical companies won’t invest in these seed vaccines because they won’t get a return unless a pandemic occurs, Stöhr says.

“The single most important matter now is that clinical testing start. And that costs money,” he says.

At the moment, only the US and Japanese governments have agreed to finance clinical trials of potential vaccines.

Canada is one of only a few countries with a pandemic plan and a contract with a domestic supplier to produce enough vaccine for its entire population — but there are significant gaps in our preparedness, health officials acknowledge.

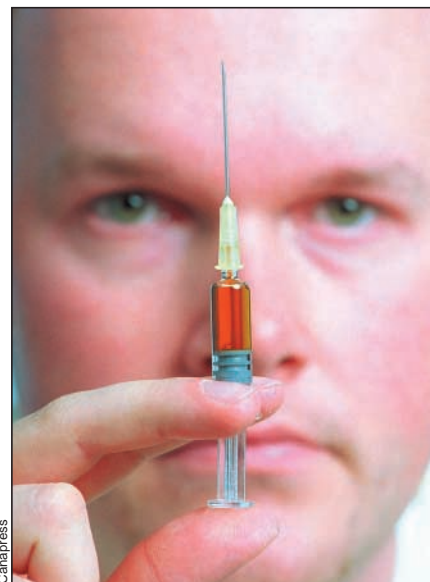
Cabinet has not yet seen or approved a proposal to invest in the development of a mock pandemic vaccine. “One of the key areas and key challenges is being able to make the case for doing that to government,” says Dr. Arlene King, the Public Health Agency’s director of immunization and respiratory infectious diseases division.

Dr. Carolyn Bennett, secretary of state for public health, would not discuss the cost of this development, but said her agency is working on a Memo-

randum to Cabinet.

Health Minister Ujjal Dosanjh supports the development of a seed vaccine. “Politicians should always be guided by science in these situations,” he said in a statement to *CMAJ*. “If the Public Health Agency recommends this approach I’m prepared to support it.”

Currently, Canada is committed to a \$325-million contract over 10 years with ID Biomedical in Vancouver to supply vaccine in the event of a pandemic. That contract requires the company to keep all the raw materials on hand in order to produce a pandemic vaccine once the critical influenza strain is identified, says Dean Linden, a spokesman for ID Biomedical. It would then take the company 7 months to produce a vaccine — not includ-



Canada has a pandemic plan, but needs more manufacturing capability.

ing regulatory approval or clinical trials. Even then, the vaccine would be produced in batches. The federal government also spends \$7 million annually to ensure a supply of fertilized eggs (for incubating a vaccine) and equipment, says King.

However, ID Biomedical cannot work on a mock vaccine because it doesn't have a manufacturing plant with the level of containment required to handle an active virus. In fact, no one in Canada does, says King. It would take several months to build such a facility, before even beginning to manufacture a vaccine.

Pandemic influenza could develop in one of 2 ways — by recombining or reassorting. In recombination, an influenza strain that occurs in nature mutates and recombines to infect humans. In reassortment, a strain of influenza that already infects humans encounters a strain that infects another species — such as birds or pigs. If the two viruses exchange genetic material, the novel strain can infect humans more easily, jumping the species barrier.

Dr. Frank Plummer, head of the National Microbiology Laboratory, says Canada needs more rapid vaccine development capacity. The issue of manufacturing capacity is critical. “We need to look at not only vaccines for the H5N1, but also strategies that might allow us to more rapidly develop a vaccine for any pandemic, whatever type it happens to be,” he told *CMAJ*.

Using current vaccine types and manufacturing facilities, it could take “about a year to get enough vaccine for the Canadian population,” Plummer says. “We need to do everything we

can to shorten this.”

King acknowledges that vaccines, “the cornerstone of our pandemic response ... will not be available at the beginning of a pandemic.”

“Consequently, we are going to have to rely on other measures to try to mitigate or to lessen the harm caused by the emergence of a pandemic virus,” she says.

One of those measures is the use of antiviral drugs, both to treat influenza and as a prophylactic for health care workers and others considered at high risk or deemed to provide essential services. But Canada does not have enough antiviral drugs stockpiled to meet that initial need.

“We do have a limited stockpile of antivirals in Canada, and this issue of having a larger stockpile of antivirals is something that is under active and urgent consideration by the Public Health Agency of Canada,” King says. — *Laura Eggertson, CMAJ*

## GLOBAL HEALTH

### Vaccinating the world: How likely?

The World Health Organization wants 6 billion people around the globe vaccinated in the event of an influenza pandemic — but it will be 6–7 years at best before we have the capacity to do that, says the physician who headed the successful smallpox eradication program.

“At this point in time, we don't have a chance of producing vaccine in the traditional manner and beginning to be able to cope with a global pandemic,” says Dr. D.A. Henderson, a professor of medicine and public health at the University of Pittsburgh. In 1974, Henderson helped start the WHO global vaccination program, and from 1966 to 1977 headed WHO's successful global smallpox eradication campaign.

An influenza pandemic could strike at any time (see previous page), and unless countries adopt and fast-track emerging vaccine technologies, they will run out of time.

Unlike smallpox, where the vaccine composition needed to be altered only every 5–10 years, influenza vaccines must be adapted yearly to the circulating strain. Middle-income and poorer countries do not have the resources to continually adapt and alter vaccine strains, Henderson says.

Countries also need substantial, dedicated manufacturing capacity on standby in order to accelerate vaccine production.

Possible solutions include producing more vaccine quickly with adjuvants that don't require as much antigen, and incubating vaccine in tissue cell culture rather than eggs. Russian researchers, for example, have developed a live vaccine that might be given as a spray or droplets and wouldn't require as much antigen. But these and similar technologies have not been adopted or developed widely.

Finding a modern method of producing vaccine is now a high priority, says Henderson.

Even with adequate supplies, distribution is problematic. Several countries have experience with mass vaccinations. In India, volunteers vaccinated more than 100 million people against polio in November 2004. In 2003, more than 35 countries in Latin America administered 45 million measles vaccinations in a week. But most countries do not yet have that capacity.

“We're looking at [up to] 7 years before you have a really effective solution — and that's being optimistic,” says Henderson.

Countries should prepare by planning to accommodate more patients in hospitals or alternative housing spaces, and stockpiling antibiotics to treat secondary infections, he says.

People have become complacent since the 1918 influenza pandemic, because resulting pandemics in 1957 and 1968 killed much fewer people, Henderson says. “It's hard to crank up.” — *Laura Eggertson, CMAJ*