Bush's Pandemic Plan Doesn't Add Up

by Christine Craig and Laurence Hecht

President Bush released his long-awaited National Strategy for Pandemic Influenza on Nov. 1, calling on Congress for $7.1 billion to fight the spread of a deadly strain of avian flu. Senate Minority leader Harry Reid said that he was "pleased to see that the President has finally followed our lead, and released his avian flu plan today," but pointed out that the amount was nearly $1 billion less than the $8-billion proposal which passed the Senate by a vote of 94 to 3 the previous week.

In truth, the amounts in both proposals are vastly out of touch with the reality of a threatened global pandemic, and the deteriorated hospital and public health infrastructure in the United States. The H5N1 influenza virus has stricken millions of poultry, and proved over 50% fatal in the 122 humans so far infected. A mutation or reassortment of the virus to a form easily transmissible from human to human could happen at any time, creating a global pandemic that could kill hundreds of millions of people in a matter of months.

Bush's plan cuts $1.2 billion from the Senate proposal of $3 billion for stockpiling and development of new antivirals, putting 75% of the burden for antiviral purchase on the states, and cuts $500 million from the Senate's proposed $600 million to aid state and local public health systems. It adds somewhat to the funding for vaccine development.

At the heart of the Administration pandemic plan is the development of the capacity to produce 300 million courses (two doses per person) of pandemic flu vaccine within six months of pandemic onset. To accomplish this, $4.7 billion of $6.7 billion of new funding requested for HHS in 2006 will be used for creating and increasing vaccine production capacity and stockpiles sufficient to achieve that goal. However, according to Secretary of Health and Human Services (HHS) Michael Leavitt, this capability will only begin to be phased in between 2008 and 2013. This leaves us very vulnerable for the next decade.

The first stage of vaccine production increase will focus on ramping up egg-based vaccine production, to give 20 million courses by 2009. This vaccine would be slated for first responders, medical personnel, and other workers critical to pandemic response. Eventually, 60 million courses of vaccine could be produced in six months by this technology.

The rest of our vaccine production is envisioned to come from the relatively new technology of cell culture-based production. This technology, which involves growing flu virus in mammalian cells rather than eggs, has been used for other

vaccines, but is new to influenza vaccine production. It has the capability of cutting the time for production by several weeks over egg-based systems. According to Leavitt, "While promising, success of cell-based influenza vaccine production and licensure is still years off, and not a guarantee." Industry, universities, and HHS would collaborate in developing cell-based capabilities, which would not come on line before 2010. This technology is expected to eventually provide the other 240 million courses of vaccine which would protect the general population in a pandemic.

So, according to HHS projections, and coherent with their strategy, *average citizens will not receive pandemic vaccines, should a pandemic occur, until at least 2010, if then.*

New Strategies To Flank the Time Factor

Of course, new technologies, such as DNA vaccines, and vaccine-stretching strategies, like the use of adjuvants to stimulate immune response to vaccines, could change that outlook. But major funding certainly is not flowing in that direction. Earlier this year the San Diego company Vical, was awarded a paltry $0.5 million by the Defense Advanced Research Projects Agency (DARPA) for research and development on its DNA vaccine technology.

DNA vaccines, using recombinant DNA technology and plasmid insertion systems, could change the face of vaccine production, potentially shaving months off the production process, and allowing huge flexibility in the choice of antigenic DNA. A DNA vaccine is basically a double-stranded circle of DNA (plasmid) consisting of an "instructions" and "tools" section, and a segment containing the code for the virus protein which will elicit the body's immune response. The "instructions" and "tools" are required for successful transcription of the antigenic section, so that it can be turned into protein by the body's cells. Because the cells keep making the protein, at least for a while, theoretically, smaller quantities of vaccine need to be given, relative to killed vaccines.

No amplification of effect is possible with traditional killed virus vaccines—unless adjuvants are used. Adjuvants are a diverse group of chemicals which, for diverse reasons, pump up the body's immune response to challenge by an antigen (vaccine). Their mode of action often is not known, but empirical evidence has shown the effectiveness of many simple substances, such as alum and oil/water emulsions, when given as part of the vaccine. European vaccines often contain adjuvants.

The World Health Organization has been looking hard at the use of adjuvants to boost the antigenicity of pandemic avian flu vaccines, which will be in critically short supply for the next few years, and may be only weakly antigenic on their own. If adjuvants could boost immune response by six times, for instance (not out of the question), the amount of vaccine necessary could be reduced by six times, allowing six times as many people to be vaccinated. Given the Administration timetable for getting up to speed on vaccine production, the use of adjuvants could prove critical for reducing mortality in the short run.

In the absence of adequate vaccine production, the only hope for the population if a pandemic strikes soon, is a sufficient supply of effective antiviral drugs. The Administration has requested $1.4 billion in funds to secure 81 million courses of antivirals—75 million to treat 25% of the population, and a six million reserve supply to help contain an initial outbreak. This funding would also be used for research into new antivirals.

Even if all of the $1.4 billion were used to stockpile antivirals, that leaves just $17.30 per course, which would be enough for one 5-day supply for one-quarter of the population. In a pandemic lasting perhaps a year, that won't keep death at bay for long. But there's more: HHS would fork up the money for 44 million courses, which would go to critical personnel. The states would be permitted to acquire the rest, up to 31 million courses by paying 75% of the costs. The remaining 25% would be paid by the Federal government. At a Senate Labor, Health, and Human Services, and Education sub-committee appropriations hearing on Nov. 2, Sen. Tom Harkin (D-Ia.) grilled Secretary Leavitt on the requirement for states to pay for antiviral stockpiles, commenting, "It almost seems, then, that they will be allocated based upon a state's ability to pay. How are you going to ask Louisiana right now to come up with money for that?. . . I don't think it's right to ask the states to come up with approximately $500 million to stockpile them."

Do the Infrastructure Math

The most grievous error in the Administration's pandemic planning arithmetic, though, lies not in technology lag, but in health-care infrastructure lack. At the recent Senate hearing, Senator Harkin mentioned that his father's most vivid impressions from youth were of the 1918 flu pandemic and the Great Depression. This led into a question to John Barry, author of *The Great Influenza: The Epic Story of the Deadliest Plague in History.* He was asked about hospital surge capacity, which Secretary Leavitt had not addressed. Barry replied: "Well, I think that's part of our increased vulnerability. Hospitals, like everything else, have become more efficient. There are no vacant, or much fewer vacant, beds than there used to be. . . . The health care system today, without any question, would be overwhelmed by a major pandemic."

The shortages in hospital and public health facilities and trained personnel derives from decades of government chiseling on health care and other infrastructural costs, and looting by medical insurance operators and providers. We must return to the Hill-Burton approach to health care, in which the government guarantees a high ratio of hospital beds to population in every community, with built-in surge capacity. With a "Manhattan Project" type mobilization (as some public health advocates have begun to call for), we can begin to rapidly remedy the shortfalls. The time to act is now.