



**Report to the President
on Reengineering the Influenza Vaccine Production Enterprise
to Meet the Challenges of Pandemic Influenza**

BACKGROUND

- Influenza vaccines in the U.S. are made using long-standing methods—including the growth of viruses in fertilized chicken eggs—that normally require at least twenty weeks, and often more, to provide initial doses of vaccine after declaration of a pandemic.
- Changes in methods of production have been slow to occur because the methods are generally adequate for annual (seasonal) influenza; the vaccine industry has little economic incentive to make expensive improvements in production of a commodity with a relatively small profit margin; and pandemics are uncommon. However, **in a serious pandemic, saving weeks can translate into saving tens of thousands of lives.**
- During the 2009-2010 H1N1 influenza pandemic, delays relating to the traditional methodology slowed production of a protective vaccine, leaving large numbers of Americans vulnerable to severe illness or death, and raising greater awareness of the limitations of the current system.
- In response, the President's Council of Advisors on Science and Technology (PCAST) undertook a review of current processes to identify ways the Federal Government could support improvements in the relevant technologies and reduce the time required to supply effective vaccine to the U.S. population when the next influenza pandemic occurs.
- Implementation of the report's recommendations, including the development of technical platforms with the potential to serve a variety of biomedical needs, could improve the Nation's response to a wide range of pandemic threats beyond influenza, whether naturally occurring or the result of a biological attack.
- The report identifies several steps in current practice that could be improved to achieve a faster overall response, and it specifies those agencies that should receive Federal support to accomplish the work:
 - **Surveillance:** Accelerate identification of newly emerging pandemic viruses, so vaccine production can start sooner (Centers for Disease Control and Prevention);

- **Seed viruses:** Develop a collection of stock viral “backbones” to allow faster production of specific vaccine strains (National Institute of Allergy and Infectious Diseases and the Biomedical Advanced Research and Development Authority (BARDA));
 - **Sterility tests:** Develop better and faster tests to ensure sterility during vaccines production (BARDA and the Food and Drug Administration (FDA));
 - **Potency-test reagents:** Develop faster and more reliable tests to document vaccine potency (BARDA and FDA);
 - **Fill-and-finish:** Enlarge capacity and modernize machinery used in final stages of vaccine production, including vial-filling (Federal agencies in collaboration with manufacturers).
- With proper support, the improvements outlined above can be achieved in as little as one year and in some cases in two to three years.
 - With the exception of improved sterility testing (which is estimated to have the potential to trim only one week from production times), each of the above options has the potential to accelerate delivery of final product by a few weeks or more.
 - The report also recommends that the Nation should invest in research and product development that promises even greater benefits in the longer term, including:
 - Moving away from the current practice of growing influenza viruses in eggs, which is inefficient, and using modern cell-culture systems instead;
 - Expanding the use of live, weakened (or “attenuated”) viruses instead of killed viruses in vaccine production to allow production of more doses of vaccine for a given amount of virus;
 - Developing recombinant vaccines using modern genetic engineering tools, to speed scaled-up production of vaccines;
 - Conducting research into the use of adjuvants, vaccine ingredients that can boost potency and thus increase the available number of doses of vaccine by reducing the amount of virus material needed in each dose.
 - PCAST also recommends that the Administration develop a new management structure that vests authority with the Assistant Secretary for Preparedness Response (ASPR) at the Department of Health and Human Services (HHS) to coordinate and direct agencies at HHS to support and implement the above recommendations. In addition, it recommends that HHS create a small advisory committee comprised of representatives from the biotechnology, pharmaceutical, and investment communities, to guide the Department’s engagement with industry

and to entrust a component of the Executive Office of the President, most obviously the National Security Council, with the responsibility to ensure that the jobs get done.

- Recognizing that Federal investments in influenza pandemic response would speed development of technical platforms and production facilities that would support medical countermeasures against a variety of dangerous pathogens, and not just influenza, with the potential to save many lives in the face of biological threats and pandemics, PCAST concludes that an investment of \$1 billion or more annually for several years can be justified on a cost-benefit basis.

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