Appendix A

Comments on Vaccine Production During a Flu Pandemic
COMMENTS ON VACCINE PRODUCTION DURING A FLU PANDEMIC

At present, the mainstay of vaccine production is an old method—growing influenza virus in fertilized chicken eggs, and then purifying the virus and converting it to vaccine. The method, devised in the mid-1940s, is dependable but slow. It can take four months or longer from the first step (large-scale production of eggs) to the finished vaccine. The speed with which eggs can be produced by the hundreds of millions—with roughly one egg needed per individual vaccine dose—imposes a limit on the amount of vaccine that can be made quickly.

In contrast, modern cell-based methods of growing viruses have a faster start-up, and they have a production capacity whose limits are set in part by the number and size of the vats in which the cells and virus are grown. At present, however, the maximum production capacity of both methods together, at top speed, is still far too low.

There are several ways to expand vaccine production. The standard influenza vaccine contains inactivated (killed) virus, but a few vaccines—some in development and some now in use—contain live attenuated (weakened) virus. The latter has several advantages: it creates immunity quickly, and a much smaller amount of material is needed per dose, perhaps as little as one-thirtieth or less, which means that many more people can be protected. Also, some experimental vaccines are composed of virus-related protein or DNA. Vaccines of this type are generally potent in smaller doses and are relatively easy to manufacture quickly on a large scale.

At present most vaccines for H5N1 virus also include added substances—“adjuvants”—that improve the effectiveness of small doses of the inactivated virus in the vaccine. Adjuvants could further enhance the total supply of vaccine.

Most of the new, quicker methods have yet to be approved by the Food and Drug Administration.

The immediate construction of many new manufacturing plants – plants held in readiness for the production of pandemic influenza vaccine – would increase the world’s capacity to make vaccine quickly when needed. However, this is costly and may not be the best use of limited resources. In contrast, some of the methods mentioned above lend themselves to rapid large-scale vaccine production in existing manufacturing facilities.

The leading candidate for the source of the next pandemic is the H5N1 avian influenza virus. For this reason, material to prepare H5N1 vaccines is now being manufactured and stockpiled under contracts with the U.S. Department of Health and Human Services. The efficacy of these “pre-pandemic vaccines” in a pandemic is uncertain. In any case, the amounts in the stockpile are sufficient to immunize only a few percent of the U.S. population.

Whether or not the stockpiled vaccines prove usable, the process of manufacturing them has important indirect benefits. Manufacturers are acquiring experience that will help them get a quicker start on vaccine production in a pandemic.
A universal vaccine

Of the many different vaccines under development, almost all are tailored to only a single strain of virus. A single-strain vaccine generally provides little or no protection against the dozens of influenza strains that differ from the single targeted strain.

In contrast, a “universal vaccine”—one that is effective against most or all influenza strains—could be manufactured in quantity long before the outbreak of a pandemic and would be ideal for protecting this country’s and the world’s population. However, a universal vaccine that serves as a replacement for single-strain vaccines may prove unattainable in the foreseeable future.

The multiplicity of approaches, and the importance of free access to materials and methods

Of the various approaches to vaccine development and manufacture, it is hard to predict which will prove best. It depends on the success of work still in progress, on the capacity of manufacturing facilities, and on how soon a pandemic begins.

The sheer multiplicity of approaches, combined with the urgent need for success in the vaccine program before the start of a pandemic, provides a strong reason for scientists, engineers, and industry executives to have unencumbered access to a full range of materials and methods that may be useful, whether patented or not. This kind of free access should begin now and should continue until the vaccine problem is solved or until the pandemic is behind us.

For more information

Further information about vaccine production can be found in the “Vaccine Development” section of CIDRAP’s (Center for Infectious Disease Research and Policy) “Pandemic Influenza” web page.¹

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¹ Center for Infectious Disease Research and Policy. “Pandemic Influenza.” (Updated February 20, 2008.) www.cidrap.umn.edu/cidrap/content/influenza/panflu/biofacts/panflu.html (Downloaded February 25, 2008).