A Coronavirus Vaccine October Surprise Could Become A November Nightmare

By Henry Miller — September 8, 2020

What happens when politics and science mix? Scary stuff. Dr. Henry Miller examines the considerable downside of releasing any COVID vaccine prior to the completion of Phase 3 trials. The founding director of the FDA’s Office of Biotechnology, Dr. Miller argues that precise science, not the date of an election, is critical at this time.

There is widespread anticipation of the availability of vaccines to prevent COVID-19 infections so that Americans can get their lives back to some semblance of normal. About four dozen, made with a variety of technology platforms, are now in clinical trials, nine in large-scale safety/efficacy testing.

It was hardly a secret that there would be intense pressure on the FDA from a White House desperate for good news to provide an "October Surprise" in the form of a vaccine approval before the November 3rd election, even if that approval was premature. Well, that pressure is having an effect, but it’s not what Trump administration officials wanted or expected.

First, some background. Ordinarily, the vaccine developers would amass a voluminous dossier of data from animal studies; documentation that they can produce batch after batch that meets
standards of purity, potency, and sterility; and finally, the guts of the application – the results of clinical trials involving tens of thousands of subjects, demonstrating that the vaccine is safe and effective at actually preventing COVID-19 infections. Then, the data would be organized and analyzed, first by the manufacturer and finally, by vaccine experts at the Food & Drug Administration. (The data are now submitted electronically, but when I was an FDA reviewer, the binders containing the tens of thousands of pages of the submission filled most of my office from floor to ceiling, and that was only the clinical trials portion.)

Historically, on average, bringing a new drug to market takes many years and costs about $2.5 billion, but the Trump administration has pumped huge amounts of money into speeding up the process. Several of the more promising development programs have been accelerated by a White House crash program, "Operation Warp Speed" [3], which was launched in May. It provided not only research and development support but funding to build bricks and mortar plants to produce huge amounts of certain vaccines even before it was known whether the products passed the testing for safety and efficacy.

So far, so good, but politics has begun to intrude, and, as with fast cars, in drug development, there is a point beyond which acceleration becomes dangerous.

Government officials have begun to drop more than hints that a vaccine will be available by the end of October. There are credible reports [4] that top administration officials told congressional leaders in July that they were likely to issue emergency authorization for a vaccine before the end of Phase 3 testing (the final, large-scale, clinical trials) in the United States, and UPS and other delivery partners are planning [5] to perform test runs this month, in preparation for actually beginning to ship a coronavirus vaccine by November 1st.

Another indication is that in a move that is unprecedented, several drug companies, including Johnson & Johnson, Pfizer, and Moderna, that are developing COVID-19 vaccines are about to issue a statement [6] describing their commitment not to seek government approval until their products have been proven to be safe and effective, and to adhere to the highest standards in clinical trials and manufacturing. The logic is so unassailable and obvious that one wonders why it even needs to be publicly articulated – unless the companies are being pressured to submit applications to FDA prematurely.

For months, FDA Commissioner Dr. Stephen Hahn has been emphasizing the agency’s independence, commitment to evidence-based approvals and unwillingness to cut corners, once coronavirus vaccine applications are received.

First came an FDA policy statement, "Development and Licensure of Vaccines to Prevent COVID-19: Guidance for Industry [7]," published on June 30th. It specifies in great detail the criteria for FDA approval of coronavirus vaccines, but the overarching principle is simple: “the goal of development programs should be to pursue traditional approval via direct evidence of vaccine efficacy” in protecting humans from COVID-19 — through clinical trials — and a vaccine must be at least 50% more effective than a placebo in preventing the disease. The clinical trials would also need to demonstrate that the vaccine is safe, of course.

On July 21st, Dr. Hahn emphasized the FDA's independence and integrity, tweeting [8], "Americans
should know that we are steadfast in maintaining our regulatory independence & ensuring our
decisions for treatments & vaccines for #COVID19 [9] are based on science & data. This is a
commitment that the American public can have confidence that I will continue to uphold."

And in a podcast interview [10] with the editor of JAMA, Dr. Hahn repeated that theme: "Americans' and the world's public trust in the FDA is really important ... People depend upon us every day of their lives, and we cannot do anything that would break that trust. That's a solemn promise." Part of that promise was that the Agency's vaccines advisory committee, which is comprised of outside experts, would review vaccine candidates prior to approval.

However, two recent actions by the FDA and its sister agency, the Centers for Disease Control and Prevention (CDC) have raised concerns among scientists and public health experts.

The first was the FDA’s issuance of an Emergency Use Authorization (EUA) for convalescent plasma, an antibody-rich blood product obtained from patients who have recovered from COVID-19. In theory, infusing a sick patient with the antibodies should neutralize the virus and spur recovery, but many in the medical community -- including senior NIH and FDA scientists -- felt the EUA was predicated on insufficient evidence [11] (and which has made the completion of rigorous clinical trials difficult or impossible). Notably, the EUA came a day after President Trump accused “deep state” bureaucrats at the FDA of trying to sabotage him by delaying approval of a COVID-19 vaccine.

The second was the CDC’s new guidance on testing [12] for the SARS-CoV-2 virus, released on August 24th. It amended the agency's guidance to recommend that people who have been exposed to the virus -- typically defined as being within six feet of an infected person for at least 15 minutes -- "do not necessarily need a test" if they do not have symptoms. This flies in the face of evidence [13] that the time of highest virus shedding and infectivity is in the days shortly before symptoms emerge and would seem to represent an abandonment of any attempt at contact tracing and isolation of infected persons. It has baffled the public health community.

The above two examples could presage a possible, far more damaging action – a premature Emergency Use Authorization for a COVID-19 vaccine not adequately tested for safety and efficacy. FDA Commissioner Hahn may be moving toward that: In an interview published by the Financial Times [14] on August 30, he said his agency was prepared to authorize a vaccine before Phase 3 clinical trials (the final, definitive stage of testing) were complete if regulators become convinced that the benefits outweigh the risks.

But once applications for vaccine approval are submitted by drug companies, Dr. Hahn’s superiors may intend to do an “end-around” the FDA entirely. That is possible because of the existence of a loophole in federal law [15] (U.S. Code, Title 21, Chapter 9) that could be exploited by Hahn’s boss, Secretary of Health and Human Services Alex Azar, a political appointee and lawyer who has hardly been a reassuring presence during the pandemic.

The relevant section of the law, “Authorization for medical products for use in emergencies,” specifies that:  

"The Secretary [16] may issue an authorization under this section with respect to the emergency use
of a product only if, after consultation with the Assistant Secretary for Preparedness and Response, the Director of the National Institutes of Health, and the Director of the Centers for Disease Control and Prevention... the Secretary concludes (1) that an agent referred to in a declaration under subsection (b) can cause a serious or life-threatening disease or condition; (2) that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that (A) the product may be effective in diagnosing, treating, or preventing (i) such disease or condition.”

Note that the Secretary is required only to consult with, but not obtain agreement from, the three subordinates specified in the law. It would surprise me not at all if Secretary Azar was already having and documenting conversations with them, and staffers in the White House and the Department of HHS were preparing the necessary decision documents for an emergency authorization for one or more of the COVID-19 vaccine candidates.

Hence, the pressure on drug companies to submit applications before adequate testing has been completed – and the extraordinary statement from the companies that they won’t do so.

For several reasons, circumventing the FDA would be unwise. The perception that the authorization was rushed and issued via an unorthodox pathway would fan the passions of the anti-vaccine movement and undermine public confidence in COVID-19 vaccines; but, more important, the short-circuiting of the usual evaluation mechanisms could endanger the vaccine recipients.

There is a reason that vaccines intended to be administered to hundreds of millions of healthy people are extensively tested and the results carefully evaluated. This is a time that science, meticulously applied, and experience with vaccine evaluation must prevail. Politics should not guide life or death medical decisions, lest an October Surprise becomes a November Nightmare.

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