Experts warn new HHS requirement for placebo-controlled vaccine trials undermines public health

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Andrew Nixon, spokesman for Department of Health and Human Services (HHS) Secretary Robert F. Kennedy Jr., announced on Thursday that moving forward, "all new vaccines will undergo safety testing in placebo-controlled trials prior to licensure—a radical departure from past practices."

This announcement signals a significant shift in the approach to vaccine regulation in the United States, prompting alarm among medical experts. The statement itself is another bald-faced lie in a slew of disinformation from the HHS. All vaccines for new pathogens are tested against a placebo, that is, with a randomized control group receiving no vaccine.

However, for previously well-researched pathogens like polio and measles, it would be unethical to leave groups of patients untreated when proven vaccines exist, and the disease carries significant potential for harm, including death.

Typically, such decisions are made by vaccine scientists at the FDA. The announcement by Nixon, as such, is considered an extraordinary abuse of Kennedy's position as secretary of HHS. That this move comes on his earlier statement to parents of newborns to do their "own research" is telling.

Fundamentally, the announcement functions to sow deep mistrust and divide in vaccines and the research behind them, which has been the primary stated goal of the unhinged health secretary. It will have untold consequences for the life and well-being of public health. The tragedy of the measles epidemic in Samoa in 2019, a byproduct of Kennedy's anti-vaccine propaganda, is instructive in the present circumstance.

Historically, placebo-controlled trials have indeed been a cornerstone of vaccine development for novel immunizations. Many groundbreaking vaccines were initially tested using this methodology. For example, the Salk polio vaccine field trial in the 1950s employed a randomized, placebo-controlled design. Measles vaccines underwent placebo-controlled testing in the 1960s, and the hepatitis B surface antigen vaccine was assessed through randomized placebo-controlled trials in the 1970s.

Dr. Peter Hotez, vaccine researcher at the Baylor College of Medicine in Houston, provided a comprehensive list of these studies in a recent social media post.

Importantly, the original COVID-19 vaccines that received Emergency Use Authorization (EUA) were also evaluated in large, well-designed placebo-controlled trials that demonstrated their safety and effectiveness. Participants in these trials received either the vaccine or an inert substance, such as saline, before results were compared.

Given this history, many vaccine experts contest Secretary Kennedy's characterization of the new policy as a "radical departure." Dr. Peter Marks, former FDA vaccine official who was essentially fired for not condoning Kennedy's prerogatives, clarified that the FDA has "mandated placebo-controlled trials for most vaccines, using either an inert placebo or sometimes an irrelevant vaccine." Dr. Jesse Goodman, a former FDA official, similarly stated, "The blanket statement that none of the routine vaccines were ever tested against placebo is incorrect. Placebo trials have been done."

The proposed policy raises significant ethical concerns among medical and public health experts. At the core of justifying the use of placebos in research is the principle of clinical equipoise. Clinical equipoise refers to a state of uncertainty within the scientific community about the merits of the interventions being assessed in a trial. Ethical randomized controlled trials must allocate participants to an intervention that is not known to be inferior to any available alternative.

Testing updated versions of established vaccines

The shift introduced by this policy to all "new" vaccines potentially includes updated versions of established vaccines, particularly those for COVID-19. Although the media has completely abandoned its reporting on the ongoing COVID-19 pandemic, COVID-19 continues to infect people at alarming numbers, with more than 44,000 people dying in 2024 and many more suffering long-term consequences to their health.

To force a placebo trial with new iterations of the vaccine would not only be cost-prohibitive and lengthy, but it would also place in peril the lives of the most frail and vulnerable. Historically, for minor modifications or updates to established vaccine platforms (like annual flu shots), regulatory agencies have recognized that the same level of testing as entirely new vaccines is not always necessary. This distinction is critical and lies at the heart of the controversy.

Experts argue that including a placebo group in trials for new vaccines or updates becomes ethically unacceptable when there is already a well-established standard of prevention in the form of an available, effective vaccine. In such situations, providing a placebo to a control group would mean withholding a proven effective intervention, thereby exposing them to avoidable harm and the risk of contracting a preventable disease, which the World Health Organization deems unethical when effective interventions exist.

For diseases like polio, experts warn this could mean "exposing children to a virus that can cause death, but also, in many cases, causes permanent, irreversible disability." Similarly, for COVID-19, it would be unethical to deprive even a small group of patients of effective vaccines against a potentially deadly pathogen.

The new HHS policy challenges the ethical framework that has guided vaccine development for decades. Paul Offitt, director of the Vaccine

Education Center at Children's Hospital of Philadelphia, stated that making people acquire a disease because they receive a placebo is not ethical. Experts also express dismay that the change could make studies costlier and potentially limit production and access to vaccines, leaving more Americans at risk of preventable diseases.

They suggest the policy could be interpreted as an effort to make vaccines costlier, scarcer and more distrusted. Furthermore, requiring placebo-controlled trials for updates could lead to difficulties in recruiting participants, as individuals may refuse enrollment if they know they might be assigned to a placebo without access to established vaccines.

WHO analysis of ethical issues in placebo testing

These issues have been addressed by the WHO in recent history. A 2013 WHO expert consultation specifically addressed the challenging ethical questions raised by using placebos in vaccine clinical trials, when an effective or partially effective vaccine already exists. While current ethics guidelines generally recommend against using placebos in such cases, the expert panel acknowledged that these guidelines do not always fully account for the specific nuances of vaccine research.

The report clarifies that the use of placebos is clearly unacceptable when an effective and safe vaccine exists, is currently accessible in the public health system of the trial country, and the risk to participants of not receiving the current vaccine cannot be adequately mitigated.

However, the panel identified five specific situations where the conduct of a placebo-controlled trial may be justified, even in the presence of an efficacious vaccine. These situations require that the risks of using placebos are mitigated and justified by the scientific and social value of the research, the research is responsive to local health needs, and general research ethics principles are respected.

The five situations are:

1. Resource Constraints: A new, potentially lower-cost vaccine is tested against a placebo in a setting where the existing vaccine is inaccessible to most of the population due to cost and is likely to remain so. (Researchers must provide evidence that these barriers are unlikely to be overcome, and that the new vaccine would not face the same barriers.)
2. Confirming Local Efficacy: An existing vaccine is tested against a placebo to confirm its efficacy in the specific trial country, as there may be insufficient information or consensus about its safety and efficacy in that particular setting.
3. Doubt About Existing Vaccine's Local Effectiveness: A new vaccine is tested against a placebo because there is a legitimate reason to doubt the efficacy or effectiveness of the existing vaccine in the local population. (Researchers should consult relevant experts for evidence supporting this doubt.)
4. Clearer Public Health Impact Data: Using a placebo yields clearer information on whether the introduction of the new vaccine would have a public health impact. (This is often linked to Situation 3.)
5. Existing Vaccine Unacceptable: The existing vaccine is unacceptable to potential study participants in the trial country (e.g., due to ingredient concerns or administration method).

The goal of the WHO recommendations is twofold: to assure that participants are protected from unjustifiable risks, and to facilitate the conduct of beneficial and urgently needed vaccine research. The proposed HHS policy, by broadly requiring placebo trials even for updates, appears to contradict the nuanced, risk-mitigating approach outlined by the WHO for situations where effective vaccines exist.

Scientific advances in vaccine testing and development

Vaccine trial design and statistical analysis methods have evolved significantly. While traditional designs were fixed, modern trials increasingly benefit from innovative approaches like adaptive designs, which allow for planned modifications based on accumulating data, offering ethical advantages and enabling early termination if indicated (e.g., due to overwhelming evidence of efficacy or futility).

These advancements are particularly important for vaccines requiring frequent updates, such as those for influenza or COVID-19, where circulating strains evolve rapidly. For well-understood diseases or updated vaccines, scientists can often assess effectiveness by looking for evidence that the vaccine induces a biological response (correlate of protection) that is scientifically known to protect against the disease, rather than waiting for participants to become ill. This allows for quicker assessment without compromising safety standards.

Experts warn that requiring large, time-consuming placebo-controlled trials for updated vaccines would significantly delay their availability. For rapidly evolving pathogens like SARS-CoV-2, by the time a large placebo-controlled trial for an updated vaccine targeting a specific strain is completed, the dominant strain might have already changed, rendering the study results less relevant and potentially leading to the use of less optimal vaccines for no reason, or even paralyzing the public health system entirely.

Secretary Kennedy has a long history of skepticism towards vaccines and particularly towards the mRNA vaccines used for COVID-19. He has publicly questioned their safety and efficacy, promoted discredited theories and has actively challenged their regulatory approval. He has claimed, contrary to scientific consensus and evidence, that mRNA vaccines "don't stop infection, don't block transmission, don't block mutants, don't last, don't work at all."

In May 2021, his organization, Children's Health Defense, petitioned the FDA to revoke the authorization for all COVID-19 vaccines, claiming risks outweighed benefits and citing ineffective alternative treatments.

While the new policy is framed as applying to "all new vaccines," statements from HHS indicate a specific focus on COVID-19 vaccine updates. Despite using the same mRNA platform since 2020, updates are seemingly being targeted by this new requirement. This suggests that, unlike annual flu vaccine updates which HHS stated would be exempt, COVID-19 booster shots could face new, extensive testing requirements.

The requirement for lengthy placebo-controlled trials, particularly for updated vaccines, could severely hamper the response to future infectious disease threats. This approach might impact preparedness for potential pandemics, such as bird flu, where the rapid development and deployment of vaccines would be urgent. Delays in evaluating and approving vaccines during an outbreak could cost lives and exacerbate the public health crisis.

Despite skepticism and misinformation, the COVID-19 vaccines have had a substantial positive impact. Estimates released in early 2024 found that COVID-19 vaccines and mitigation measures saved about 800,000 lives in the United States. Earlier estimates from May 2021 indicated that the rapid rollout of COVID-19 vaccines had already saved about 140,000 lives in the US by that time. A Commonwealth Fund study from December 2022 estimated vaccinations in the US averted over 3.2 million deaths, 18.6 million hospitalizations and 120 million infections.

While vaccines can have side effects, these are rare, and public health officials weigh the harms against the potential to save lives. Existing surveillance systems have proven capable of rapidly identifying side effects, such as myocarditis or rare blood clots.

Looking more broadly, the impact of vaccination on global health is immense. A modeling study assessing 50 years of the Expanded Programme on Immunization (EPI) between 1974 and 2024 provides the most comprehensive assessment of historical vaccine program impact. The study estimated that vaccines against 14 pathogens have saved 154 million lives since 1974, with 95 percent of these being children younger than 5 years. This equates to 9.0 billion life-years saved and, when accounting for reduced morbidity as well, 10.2 billion healthy years of life gained.

The measles vaccination has been the single greatest contributor to these gains, estimated to have averted 93.7 million deaths and saved 5.7 billion years of life. Other diseases for which vaccination has averted millions of deaths include tetanus (27.9 million), pertussis (13.2 million), and tuberculosis (10.9 million). Vaccination has accounted for close to half of the total global reduction in infant mortality. As a result of 50 years of vaccination, a child born today has a 40 percent increase in survival for each year of infancy and childhood.

The claims made by HHS that “none of the vaccines on the CDC’s childhood recommended schedule was tested against an inert placebo, meaning we know very little about the actual risk profiles of these products” is directly disputed by health experts and historical evidence. Secretary Kennedy has a documented history of making baseless claims about vaccine safety, including linking vaccines to autism despite overwhelming scientific consensus to the contrary, questioning the safety monitoring systems and making unfounded comments about race-based vaccine schedules.

Experts note that Kennedy tends to ignore or cherry-pick science, citing flawed or tangential research to support his views. As Dr. Hotez commented: “He appears to be on full-on attack mode when it comes to vaccines. And it’s so self-defeating for our country and globally as well. It’s absolutely dangerous.” Coming from the chief public health official in the United States, this irrational and anti-scientific approach has the potential to significantly damage public confidence in the entire immunization infrastructure.

The risks of declining vaccination coverage are well-documented. Another modeling study, looking at potential scenarios in the US under declining vaccination rates, estimated the increased risks of outbreaks, total cases, and the chance of re-establishing endemicity for vaccine-preventable infections. Recent data shows a decline in vaccination coverage among young children, and localized outbreaks of diseases like measles have been occurring, and not just in the US. Experts warn that damaged confidence could lead to a return of diseases that have been largely controlled, resulting in suffering and preventable deaths, particularly among children.

Kennedy’s stated policy requiring placebo-controlled trials for “all new vaccines” is framed by HHS as a radical departure aimed at increasing safety and transparency. However, this framing is misleading, as placebo or appropriate comparator trials have historically been standard for genuinely novel vaccines, including the initial COVID-19 shots. Experts widely dispute the claims that established childhood vaccines were not adequately tested.

Ultimately, this policy, coupled with the dissemination of misleading information about the testing of existing vaccines, appears to be a dangerous approach dressed as a concern for safety and transparency. By undermining public trust in proven, life-saving interventions and hindering the efficient development and deployment of new and updated vaccines, it carries the potential for tremendous damage to public health, both domestically and globally, risking a resurgence of preventable diseases and leaving populations vulnerable to future outbreaks.