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VIA ELECTRONIC SUBMISSION

December 18, 2023

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2023-D-2318
Formal Comment on Draft Guidance: "Demonstrating Substantial Evidence of Effectiveness with One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence; Draft Guidance for Industry"

Dear Sir or Madam:

On behalf of Informed Consent Action Network ("**ICAN**"), we submit this formal comment to FDA's Draft Guidance titled, "Demonstrating Substantial Evidence of Effectiveness with One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence," published on September 19, 2023 in the Federal Register.[1]

On September 11, 2023, FDA licensed a booster vaccine for COVID-19 that was tested for efficacy in a single trial involving mice.[2] Coincidentally, on the same day, FDA penned this Draft Guidance and posted it on its website.[3] When finalized, this Guidance indicates that FDA's official position will be that, under certain circumstances, a drug sponsor can show evidence of effectiveness for a biological product with a *single* clinical investigation conducted in *animals*.[4] The example provided was "[w]hen the product is a preventive vaccine, and there is a well-established model of infection for a relevant infectious disease, and use of the vaccine in the animal model demonstrates prevention of disease."[5]

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[1] https://www.federalregister.gov/documents/2023/09/19/2023-20228/demonstrating-substantial-evidence-of-effectiveness-based-on-one-adequate-and-well-controlled.

[2] https://www.fda.gov/news-events/press-announcements/fda-takes-action-updated-mrna-covid-19-vaccines-better-protect-against-currently-circulating.

[3] https://www.fda.gov/media/172166/download.

[4] As the Draft Guidance points out, although FDA has generally required two clinical investigations to establish substantial evidence of a drug's effectiveness, guidance issued by FDA in 1998, in accordance with the Food and Drug Administration Modernization Act of 1997, dictated that that data from a single adequate and well controlled trial, along with confirmatory evidence, could suffice. https://www.fda.gov/media/172166/download at 5.

[5] https://www.fda.gov/media/172166/download at 16.

The FDA's lowering of a drug sponsor's burden for demonstrating efficacy is incredibly troubling, as it effectively permits the fox to guard the henhouse.

Despite urging by ICAN in 2020, the FDA failed to amend the Phase III trials of the currently licensed COVID-19 vaccines to ensure they met the required standard of "substantial evidence" of effectiveness. ICAN demanded, among other things, that the trials test and determine (1) whether these vaccines will prevent severe cases of COVID-19; and (2) whether they would stop the spread of the virus. The FDA did not amend its endpoint protocols and, instead, licensed these products based on the mere speculation that they were effective. It is now widely known that these vaccines did not have the efficacy initially claimed. Nonetheless, the FDA permitted COVID-19 boosters based on even more questionable basis: testing on rodents.

In summary, FDA is drafting guidance that permits vaccine manufacturers to obtain licenses for products based on a single animal study, even without a "well-established model of infection," while *simultaneously* licensing these products. In short, it is apparent that FDA is tailoring guidance based on the vaccine manufacturers' clinical trials instead of requiring that these trials comply with what any reasonable licensing agency should and would require. FDA has seemingly forgotten that its function is to regulate the pharmaceutical industry, not rubber stamp it. The Draft Guidance does not provide oversight, and even worse lends illegitimacy to the FDA when there is clearly insufficient evidence to support authorization or licensure. This is especially troubling for products that will be injected into healthy humans—including babies, children, and pregnant women.

On behalf of ICAN, we strongly encourage withdrawal of the Draft Guidance and require drug sponsors to conduct long-term, high-powered, double-blind, ethical clinical trials before FDA considers authorizing or approving any drug or biologic.

Yours truly,

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