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VIA ELECTRONIC FILING

March 3, 2021

Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
Commissioner Stephen M. Hahn, M.D.
5630 Fishers Lane
Rm. 1061
Rockville, MD 20852

Re: *Citizen Petition and Petition for Administrative Stay of Action (Docket Number: FDA-2020-P-2180)*

Dear Commissioner Hahn,

Attached is a reply to the FDA's December 11, 2020 response to ICAN's Citizen Petition and petition for administrative stay of action regarding Phase 3 trials of certain vaccines to prevent the novel coronavirus SARS-CoV-2 (COVID-19).

This demands your careful attention and ICAN looks forward to receiving a timely response. ICAN is available to answer questions and provide any relevant additional information.

Very truly yours,

/s/ Aaron Siri
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Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
Commissioner Stephen M. Hahn, M.D.
5630 Fishers Lane
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Dear Commissioner Hahn,

We write on behalf of our client Informed Consent Action Network ("ICAN"), in reply to your December 11, 2020 response to ICAN's Amended Citizen Petition and Petitions for Administrative Stay of Action (Docket Number FDA-2020-P-2180) regarding Phase 3 trials of COVID-19 vaccines.

Reduction in severe COVID-19 as a primary endpoint

The Petitioner requested that reduction in severe COVID-19 be a primary endpoint in the vaccine trials. The FDA responded that it does not agree that it "must limit the primary efficacy analysis to" such an assessment. However, Petitioner is not asking that this be the only analysis, simply that it be a part of the analysis. To be clear, Petitioner is not asking the FDA to limit any endpoints. Petitioner agrees with the FDA that "severe cases of COVID-19 occur less frequently than mild-to-moderate cases." However, Petitioner does not agree that because this analysis "would require a higher number of study participants and take a longer time to conduct," it should be foreclosed. These "practical concerns" are not reason to accept lower efficacy standards. Given that the public health emergency touted by the FDA is not caused by mild or moderate cases of COVID-19 but by severe cases, those cases should be the primary focus of the trials and of the FDA's decision making.

You also assert that "[w]e are not aware of an example of any vaccine that is effective against mild disease that is not also effective against severe disease." This statement ignores the fact that SARS-CoV-2 is unlike other viruses and has produced symptoms and pathology not seen with other viruses. Compounding this novelty is the fact that mRNA technology is being used for the first time in an authorized vaccine for COVID-19. Analogizing to other viruses and other vaccines ignores these important distinctions. Moreover, most licensed vaccines were licensed

based on endpoints that did not involve the reduction of disease, but rather a measure of some correlate of protection. In practice, there are many individuals that have been vaccinated but yet can suffer serious disease from the virus for which they were vaccinated, as seen, for example, in the recent cases of measles during the last three years.

PCR tests used to qualify an event of COVID-19 for a trials' endpoint use a maximum of 24 amplification cycles

The Petitioner further requested that the PCR tests used to qualify an event of COVID-19 for a trial's endpoint use a maximum of 24 amplification cycles. It is well-known that PCR tests have a very high rate of false positives. Petitioner appreciates the FDA's acknowledgements that "accurate testing is an important part of ensuring the reliability of the vaccine trial outcomes" and that "generally the fewer number of amplification cycles on a sample that shows a positive indicates a higher viral load." However, Petitioner does not agree that making it "the sponsors' obligation to ensure reliable testing" is a satisfactory solution. The sponsors should not be the sole party responsible for ensuring the reliability of the tests used in their trials. The FDA should determine any amplification cycle cut-offs necessary for any PCR tests used in the trials and demand accuracy so that the trials' outcomes are reliable.

Interruption of transmission be a primary endpoint

Because a vaccine may lessen the severity of symptoms in a recipient does not mean that it is able to prevent infection and transmission. For this reason, and others, Petitioner requested that interruption of transmission be a primary endpoint. The FDA has acknowledged that it "has not required that COVID-19 vaccine trials assess person-to-person transmission" and justifies this by stating that "the applicable statutory standards for licensure or authorization" do not require this. Simply because it may not be required does not mean the FDA should not and cannot require such an important analysis. The fact that the vaccines are limited to "protecting vaccinated individuals from symptomatic COVID-19" severely limits their ability to end a pandemic.

Also, since COVID-19 vaccines have been granted emergency use authorization, and are being widely used, there appears little reason to rush licensure. It appears more prudent to assure their safety and efficacy profile, including preventing infection and transmission, are robust.

* * *

In conclusion, Petitioner reiterates its reasonable requests: that reduction in severe COVID-19 and interruption of transmission be primary endpoints in the vaccine trials before licensure and that the PCR tests used within the trials are reliable and accurate with amplification

cycles that ensure little to no false positive results. These are necessary in order to demonstrate that the vaccines are effective and to build vaccine confidence.

Very truly yours,

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