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VIA EMAIL

Members, Vaccines and Related Biological Products Advisory Committee
Food and Drug Administration

Re: *Emergency Use Authorization for* Pfizer/BioNTech's vaccine (BNT162b2)

Dear Sir or Madam:

Our client, Informed Consent Action Network ("**ICAN**"), has asked us to bring to your attention critical and noteworthy issues regarding the current COVID-19 vaccines in development, prior to your meeting tomorrow and future meetings regarding same. ICAN's mission is to raise public awareness about public health safety and to provide the public with information to give informed consent regarding related health interventions.

ICAN has received numerous questions from its supporters regarding the potential Emergency Use Authorization of the Pfizer/BioNTech COVID-19 vaccine as well as the other COVID-19 vaccines in development. It is ICAN's understanding that Emergency Use Authorization for Pfizer/BioNTech's vaccine (BNT162b2) will be discussed at the December 10, 2020 meeting.

On behalf of its constituents, and in order to provide a more complete understanding of the ramifications of authorizing this vaccine, ICAN herein details the following serious concerns regarding the Pfizer/BioNTech COVID-19 vaccine and its clinical trials, each equally deserving of your attention:

(i) the potential for anti-body dependent enhancement;

(ii) the potential loss of any placebo comparator group after, at most, 6 months post-vaccination;

(iii) the risk of serious allergic reactions to the vaccine; and

(iv) the lack of knowledge regarding impairment of fertility post-vaccination.

ICAN respectfully requests that you devote the time and attention needed to understand and resolve these concerns before voting on whether to authorize the widespread use of this vaccine.

I. Antibody-dependent Enhancement

Antibody-dependent enhancement ("**ADE**") has been identified in over 40 kinds of viruses, and in some cases, has been shown to increase the susceptibility of those who are vaccinated. ADE of disease is a general concern for the development of vaccines because the mechanisms that underlie antibody protection against any virus have a theoretical potential to amplify the infection or trigger harmful immunopathology.[1] Data from the study of SARS-CoV and other respiratory viruses suggest that anti-SARS-CoV-2 antibodies could exacerbate COVID-19 through ADE.[2] Although the mechanism behind ADE is not fully understood, secondary infection via ADE remains a serious question and concern still unanswered from the available data of COVID-19 vaccine candidates, including Pfizer/BioNTech's vaccine. As a result, ADE of disease cannot be reliably predicted after vaccination regardless of what virus is the causative agent. Therefore, it will be essential to depend on careful analysis of safety in humans as use of the COVID-19 vaccine candidates move forward.[3]

Early phase 1 data from Moderna's mRNA vaccine (mRNA-1273) against novel coronavirus showed a high affinity for trial subjects to develop binding antibodies vs. neutralizing antibodies.[4] Interim results from their phase 1 study states, "Seroconversion was rapid for binding antibodies, occurring within 2 weeks after the first vaccination, but pseudovirus neutralizing activity was low before the second vaccination, which supports the need for a two-dose vaccination schedule."[5] It remains to be seen what Pfizer/BioNTech's vaccine candidate's elicited binding and neutralizing antibodies translate to when a vaccinated individual is faced with the wild virus.

Of utmost concern is the following data from the FDA's Briefing document, released on December 8, 2020, regarding Pfizer/BioNTech's vaccine:

> Among 3410 total cases of suspected but unconfirmed COVID-19 in the overall study population, 1594 occurred in the vaccine group vs. 1816 in the placebo group. **Suspected COVID-19 cases that occurred within 7 days after any vaccination were 409 in the vaccine group vs. 287 in the placebo group**.[6]

The stark difference in COVID-19 infections within a week between the vaccinated and unvaccinated groups raises concerns regarding ADE. Moreover, the potential window for ADE between the first and second doses of COVID-19 vaccines leads ICAN to urge that concrete actions be taken to document vaccine safety especially regarding vaccine-induced ADE. A close analysis should be conducted of COVID-19 cases, including between the first day of the trial and up

[1] https://pubmed.ncbi.nlm.nih.gov/32659783/.

[2] https://pubmed.ncbi.nlm.nih.gov/32908214/.

[3] https://pubmed.ncbi.nlm.nih.gov/32659783/.

[4] https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-interim-phase-1-data-its-mrna-vaccine.

[5] https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-publication-new-england-journal-medicine.

[6] https://www.fda.gov/media/144245/download at 42 (emphasis added).

through 7 days post-second dose. A comparison of those cases in the vaccine group to those in the placebo group must be made.

Given the magnitude of scientific data surrounding the potential for vaccine-induced ADE with novel viral vaccines, we also urge that careful consideration be taken *before* allowing expedited, emergency authorization of novel coronavirus vaccines for what may eventually be the entirety of the American population.

II. Loss of Placebo Comparator Group

The FDA's June 2020 guidance document called for a placebo-controlled trial for COVID-19 vaccine candidates.[7] Nevertheless, Pfizer and BioNTech have announced that they plan to unblind the placebo recipients no later than 6 months following the second dose of the vaccine:

> The Sponsor plans to offer vaccination to participants ≥16 years of age who originally received placebo and who become eligible for receipt of BNT162b2 according to local or national recommendations. The Sponsor proposes that these participants will be unblinded upon request and will have the opportunity to receive BNT162b2 as part of the study. The Sponsor also proposes that all placebo recipients ≥16 years of age will be offered BNT162b2 after completing 6 months of follow-up after Dose 2, if they did not request and receive vaccine previously. The participants will provide consent to receive vaccination and to continue follow-up. For these participants, the Sponsor plans a total follow up period of 18 months, with one visit 1-month postvaccination and subsequent phone contacts at 1, 6, and 18 months postvaccination. Safety and efficacy monitoring during this period will include collection of AEs, SAEs, and screening and diagnosing COVID-19 cases.[8]

Offering the vaccine to those in the placebo group effectively removes any chance of an existing placebo comparator group any time beyond 6 months post-second dose. In practical terms, this means that any differences between these groups – concerning both efficacy and safety – will not be able to be observed for long-term effects. In light of the fact that this vaccine (and other potential vaccine candidates) are novel vaccine platforms that have never been used in humans and are therefore experimental, this is unacceptable. If there is a rise in cancer or infertility or any other host of medical signals or concerns at any point beyond 6 months (at most) following the groups' second doses, there will be no clear way to determine causality. At that point, an ethical obligation will prevent a true placebo-controlled study as an approved vaccine will be available and withholding such a vaccine from a placebo group will be said to be unethical. Thus,

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[7] FDA. Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19. June 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19.

[8] https://www.fda.gov/media/144245/download at 44.

the existing placebo group represents the one and only chance to ensure that a comparator group exists so that all signals can be fully examined and all causal relationships established.

III. Serious Allergic Reactions to the Vaccine

The United Kingdom authorized use of the Pfizer/BioNTech vaccine and, as of December 8, 2020, the UK has begun to administer it to thousands of individuals. Yesterday, the first day of vaccine administration in the UK outside of the trials, the Medicines and Healthcare products Regulatory Agency ("**MHRA**") sent a guidance document to healthcare professionals after allergic reactions occurred in at least 2 vaccine recipients. The guidance reads: "Any person with a history of a significant allergic reaction to a vaccine, medicine or food (such as previous history of anaphylactoid reaction or those who have been advised to carry an adrenaline autoinjector) should not receive the Pfizer/BioNTech vaccine."[9]

Notably, aside from a troubling report that there was "a slight numerical **imbalance of adverse events potentially representing allergic reactions**, with **more participants reporting hypersensitivity-related adverse events in the vaccine group** (137 [0.63%]) compared with the placebo group (111 [0.51%])," the FDA Briefing document regarding the Pfizer/BioNTech vaccine was silent on allergic reactions or potential anaphylactic or anaphylactoid reactions.[10]

This potential for an adverse event must be addressed and analyzed in the clinical trials by the manufacturers. In addition, a contraindication matching the MHRA's guidance must be included with the Pfizer/BioNTech (and potentially other) vaccine(s). Until this issue can be fully understood, no person with a history of an allergic reaction to a vaccine, medicine, or food should be administered this vaccine and such individuals should certainly not be mandated or required to receive it (as some states and private entities have stated they intend to do).

IV. Impairment of Fertility

The Pfizer/BioNTech vaccine is expected to induce the formation of humoral antibodies against spike proteins of SARS-Cov-2. Syncytin-1 [11] is derived from human endogenous retroviruses and is an essential prerequisite for a successful pregnancy as it is responsible for the development of a placenta in humans. This protein is also found in homologous form in the spike proteins of SARS viruses. There is a dearth of data regarding whether antibodies against the spike proteins of SARS viruses will also act as antibodies to Syncytin-1. If this were the case, formulation of a human placenta may be prevented, leaving those who were vaccinated unable to carry a successful pregnancy and, essentially, infertile.

The information regarding Pfizer/BioNTech's vaccine for healthcare professionals in the UK states: "It is unknown whether COVID-19 mRNA Vaccine BNT162b2 has an impact on

[9] https://www.cnbc.com/2020/12/09/pfizer-jab-warning-for-people-with-history-of-significant-allergic-reactions.html.

[10] https://www.fda.gov/media/144245/download at 40 (emphasis added).

[11] *See* Gallaher, B., "Response to nCoV2019 Against Backdrop of Endogenous Retroviruses" - https://virological.org/t/response-to-ncov2019-against-backdrop-of-endogenous-retroviruses/396.

fertility."[12] This must become a known before this vaccine is approved, authorized, or licensed for use in females in the United States.

The Pfizer/BioNTech vaccine has not been tested in pregnant women, and the documents released by Pfizer/BioNTech do not address the Syncytin-1 antibody issue. Given the potential widespread damage that could occur, more careful analysis is needed before this vaccine can be safely given to any female who wishes to have the option of carrying a pregnancy.

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If a COVID-19 vaccine is authorized and/or approved based on substandard or incomplete clinical trials and data, there could be potentially catastrophic repercussions affecting both American's health and their confidence, or lack thereof, in the country's vaccine programs at large for years to come. Thus, it is critical that the approval process not be rushed and that all relevant issues are addressed and resolved prior to the vaccine's authorization.

ICAN remains dedicated to ensuring that the public has accurate, up-to-date, unbiased information regarding the COVID-19 vaccines. Each of the above concerns, individually and together, warrants your further review **prior to any authorization** so that you can act accordingly, thereby ensuring the safety of all American citizens, including those who are likely to be mandated to receive one or more of the COVID-19 vaccines that the FDA approves and/or licenses. We would welcome providing any additional information or meeting with you to discuss any of the foregoing information.

Very truly yours,

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[12] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/941452/Information_for_healthcare_professionals.pdf.