July 18, 2023

Aaron Siri
Siri & Glimstad LLP
200 Park Avenue
17th Floor
New York, NY 10166

Sent via email to: aaron@sirillp.com

RE: Citizen Petition (Docket Number: FDA-2020-P-1768)

Dear Mr. Siri:

This letter responds to the following citizen petitions and petition for administrative stay of action that you submitted to the Food and Drug Administration (FDA, the Agency, we) on behalf of Del Bigtree and the Informed Consent Action Network (ICAN) (Petitioner) relating to the clinical trial of ChAdOx1 nCoV-19, an investigational name for a vaccine to prevent Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2):

- The citizen petition dated August 17, 2020 (the CP);
- The petition for administrative stay of action dated August 19, 2020 (the PSA); and
- The amended citizen petition dated October 16, 2020 (the Amended CP)[1] (collectively, the Petitions).

While ChAdOx1 nCoV-19 and ChAdOx1-S [recombinant] are names used for the vaccine while it was under clinical investigation in various countries, it was referred to as the COVID-19 Vaccine AstraZeneca while under emergency use in some countries and has been referred to as Vaxzevria while under approval status.[2] AstraZeneca has publicly stated that the clinical

[1] This submission is entitled "Amended Citizen Petition" and references the CP. Amended CP at 1. However, it also states that "[t]his amended petition for administrative action is submitted…pursuant to 21 C.F.R. § 10.35" (Petitions for administrative stay of action). *Id.* at 2. For purposes of this response, we are treating this as a citizen petition submitted under 21 CFR § 10.30. The requested actions and formatting of the submission are consistent with citizen petitions submitted under 21 CFR § 10.30.

[2] *See* Press Release, Astra Zeneca, Vaxzevria receives full Marketing Authorisation in the EU for the prevention of COVID-19 (Nov. 1, 2022), https://www.astrazeneca.com/media-centre/press-releases/2022/vaxzevria-receives-full-marketing-authorisation-in-the-eu-for-the-prevention-of-covid-19.html; *Vaxzeria (previously COVID-10 Vaccine AstraZeneca)*, ema.europa.eu, https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria (last visited July 11, 2023).

development of the vaccine was initiated by the University of Oxford.[3] On the World Health Organization's website, AstraZeneca is listed as the sponsor for the vaccine.[4] In the United States, the vaccine has never been authorized for emergency use or licensed (approved).

In the CP, Petitioner requests that "before licensure" of the vaccine, FDA require the following changes to "the study design for the Phase III trial":

"the study design for the Phase III trial of ChAdOx1 nCoV-19 (NCT04400838) […] be amended to provide that:

a. the control group will receive a placebo (saline injection);

b. any and all adverse events and reactions […] will be documented for the entire duration of the trial;

c. such documenting of adverse events and reactions shall last at least twelve months for adults, thirty-six months for children, and sixty months for infants and toddlers;

d. it uses an adequate sample size, appropriately powered, in order to (i) detect an increase in rare adverse events or any untoward medical occurrence, whether or not considered vaccine related, and (ii) determine that the rate of adverse events from the vaccine will not exceed the rate of adverse events known to occur from SARS-CoV-2 in the group under review […];

e. participants are tested for T-cell reactivity to SARS-CoV-2 pre-vaccination and post-vaccination; and

f. germline transmission tests are conducted for male participants."

The petitioner also states that they "will suffer irreparable harm if the action requested herein is not granted because once the FDA licenses this COVID-19 vaccine, states are expected to make this product mandatory"[5] and "if the vaccine is licensed without a placebo control group and an

[3] *See* Astra Zeneca AB, *A Phase III Randomized, Double-blind, Placebo-controlled Multicenter Study in Adults to Determine the Safety, Efficacy, and Immunogenicity of AZD122, a Non-replicating ChAdOx1 Vector Vaccine, for the Prevention of COVID-19*, (September 17, 2020), https://s3.amazonaws.com/ctr-med-7111/D8110C00001/52bec400-80f6-4c1b-8791-0483923d0867/c8070a4e-6a9d-46f9-8c32-cece903592b9/D8110C00001_CSP-v2.pdf (the clinical investigation information publicly released by AstraZeneca); *Investigating a Vaccine Against COVID-19*, clinicaltrials.gov, https://www.clinicaltrials.gov/ct2/show/NCT04400838, (January 21, 2022) (The information on clinicaltrials.gov about the NCT number cited in the petitions lists the University of Oxford as the sponsor).

[4] *COVID-19 Vaccines with WHO Emergency Use Listing*, extranet.who.int, https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued (last visited July 11, 2023); *RECOMMENDATION FOR AN EMERGENCY USE LISTING OF AZD122 SUBMITTED BY AstraZeneca AB and manufactured by SK Bioscience Co Ltd*., extranet.who.int, https://extranet.who.int/pqweb/key-resources/documents/who-recommendation-eul-azd1222-submitted-astrazeneca-ab-and-manufactured-sk (last visited July 11, 2023).

[5] Petition at 3

appropriate safety review, ethical considerations prevent a placebo-controlled study post-licensure, thereby preventing any such study from ever occurring."[6]

In the Amended CP, Petitioner states that "[i]n light of the clinical trial protocol dated September 17, 2020 and titled 'A Phase III Randomized, Double-blind, Placebo-controlled Multicenter Study in Adults to Determine the Safety, Efficacy, and Immunogenicity of AZD1222, a Non-replicating ChAdOx1 Vector Vaccine, for the Prevention of COVID-19' made public by Astra Zeneca following Petitioner's submission, it appears that some of Petitioner's conditions have been met and Petitioner therefore submits this amended petition to address the outstanding conditions."[7]

In the Amended CP, Petitioner requests that "before licensure" FDA require the following changes to "the study design for the Phase III trial":

a. any and all adverse events and reactions […] will be documented for the entire duration of the trial;

b. such documenting of adverse events and reactions shall last *at least* twenty-four months for adults, thirty-six months for children and sixty months for infants and toddlers or such longer duration as appropriate, and in no event end prior to the subject reaching eight years of age;

c. it uses an adequate sample size, appropriately powered, in order to (i) detect an increase in rare adverse events or any untoward medical occurrence, whether or not considered vaccine related, and (ii) determine that the rate of adverse events from the vaccine will not exceed the rate of adverse events known to occur from SARS-CoV-2 in the group under review […];

d. participants are tested for T-cell reactivity to SARS-CoV-2 pre-vaccination and post-vaccination;

e. germline transmission tests are conducted for male participants; and

f. HIV incidence will be "monitored at the end of the study and for an appropriate follow-up period" […] and the trial will "evaluate the levels and distribution of both vector and insert responses in target tissues where HIV acquisition is known to occur […]."

In the PSA, Petitioner describes the "Decision Involved" as "[a]ny and all incremental steps . . . toward approval of ChAdOx1 nCoV-19," and specifically requests FDA to:

[6] *Id.*
[7] Amended petition at 1

"Stay any and all FDA action or guidance, formal or informal, indicating any support in favor of licensing ChAdOx1 nCoV-19 (NCT04400838) until the study design for the Phase III trial of this vaccine is amended to provide that:

a. the control group will receive a placebo (saline injection);

b. any and all adverse events and reactions […] will be documented for the entire duration of the trial;

c. such documenting of adverse events and reactions shall last at least twelve months for adults, thirty-six months for children, and sixty months for infants and toddlers;

d. it uses an adequate sample size, appropriately powered, in order to (i) detect an increase in rare adverse events or any untoward medial occurrence, whether or not considered vaccine related and (ii) determine that the rate of adverse events from the vaccine will not exceed the rate of adverse events known to occur from SARS-CoV-2 in the group under review […];

e. participants are tested for T-cell reactivity to SARS-CoV-2 pre-vaccination and post-vaccination; and

f. germline transmission tests are conducted for male participants."[8]

Since the submission of the CP, Amended CP, and PSA, AstraZeneca made the following public statement: "As the primary vaccination needs of the US are being met already, AstraZeneca has decided that it will not submit a Biologics Licence (sic) Application for Vaxzevria in the US." The statement appears in the quarterly earnings report to investors posted on AstraZeneca.com dated November 10, 2022.[9]

Given that AstraZeneca has stated that it will not submit a Biologics License Application (BLA), we conclude that the circumstances since the date you submitted your Petitions have rendered your Petitions moot.[10] The CP, Amended CP, and PSA all request that FDA take certain actions related to clinical study design of the investigational vaccine developed by AstraZeneca and University of Oxford before FDA's licensure/approval of the vaccine, and AstraZeneca has now announced that it has no plans to seek FDA licensure. Accordingly, we are dismissing them in accordance with 21 CFR 10.30(e) and 21 CFR 10.35(e).

[8] PSA at 2

[9] *Astra Zeneca PLC YTD and Q3 2022 results,* AstraZeneca.com (Nov.10, 2022), https://www.astrazeneca.com/content/dam/az/PDF/2022/Q3/Year-to-date_and_Q3_2022_results_announcement.pdf.

[10] We acknowledge that there are differences in the requests between the CP and the Amended CP. For example, the CP includes a request that FDA require that "the control group will receive a placebo (saline injection)," while the Amended CP omits this request. Irrespective of which petition is controlling, the issues identified in the Petitions are moot because there are no regulatory issues to resolve.

Sincerely yours,

Peter Marks

Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research

cc: Dockets Management Staff