Center for Biologics
Evaluation and Research

CENTER DIRECTOR DECISIONAL MEMO

August 26, 2025

sBLA:	STN125817/6
Product Name:	NUVAXOVID
Indication:	Indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in adults 65 years of age and older and individuals 12 through 64 years who have at least one underlying condition that puts them at high risk for severe outcomes from COVID-19
Applicant:	Novavax
Author:	Vinayak Prasad, MD, MPH, Director, Center for Biologics Evaluation and Research (CBER), FDA

This memorandum seeks to explain CBER Office of the Director's (CBER OCD's) decision to require 2 additional 506B Postmarketing Commitment (PMC) studies for the Applicant's efficacy prior approval supplement (PAS) submission. In addition to the Applicant-agreed upon 506B PMC randomized, saline placebo-controlled, safety and clinical efficacy study [referred to as PMC (2) study], the 2 two new 506B PMC studies are: 506B PMC (1) study – a safety and immunogenicity study in the indicated population; and 506B PMC (3) study – an analysis of circulating spike protein paired with a long-covid questionnaire in a subset of individuals in a PMC randomized trial at several time points. I will consider these in turn.

CBER OCD's decision to require the 506B PMC (1) study is based on several considerations. First, the prior standard in CBER was acceptance of small immunogenicity studies using human sera, largely aimed at demonstrating numerical improvements in antibody formation against prevailing strains. These studies lacked formal statistical prespecification and power to test a clear scientific hypothesis. These studies were largely conducted, in CBER OCD's opinion, to provide nominal justification for a strain change, even while there has been substantial uncertainty in whether such changes were necessary and/or beneficial. Moreover, these studies were not confined to the population of the current COVID-19 regulatory scheme, namely persons with 1+ risk factors for severe disease younger than age of 65 years and all those older than the age of 65 years.

Now CBER will demand studies roughly 5 to 10 times larger than historically accepted. When paired with information derived from 506B PMC (2) study (i.e., randomized trials, specifically antibody titers and clinical efficacy data), CBER may at last be able to unlock a key scientific question in vaccine regulation: at what threshold of antibody production, if any, are COVID-19 vaccines protective against COVID-19 caused by SARS-CoV-2. CBER OCD can use this information to improve vaccine regulation. Is it possible that current COVID-19 vaccines actually fail those who need them the most—the immune compromised—because they generate insufficient antibodies in the groups who would most benefit? Or instead, is current COVID-19 vaccine policy doing justice for these Americans. CBER OCD acknowledges that PMC (1) study represents an improvement in evidence generation, and appropriately and justifiably raising the bar in the vaccine space. CBER OCD has reviewed and agrees with the Applicant's proposal for 506B PMC (1) study, including milestones.

CBER OCD's decision to require PMC (3) study is based on several factors. First, there is growing clinical evidence that spike protein which is generated as a result of or in the course of vaccination may persist for some time in a subset of individuals. Second, the symptoms of long covid or the post-acute covid syndrome are ill-defined but concern many Americans. Third, there is a fraction of people (Note: this does not include CBER OCD) who believe there is a link between these two. As such, CBER OCD believes it has an obligation to Americans to request the Applicant generate information which may link or exculpate any such relationship. If a real, positive association is present in randomized fashion, it would constitute a concerning finding. CBER OCD also notes that this substudy design may also be able to adjudicate if annual COVID-19 vaccines reduce long-covid symptoms, a claim that FDA has never permitted the applicant to make, depending on power. CBER OCD has reviewed and agrees with the Applicant's proposal for 506B PMC (1) study, including milestones.