1.9.2 Request for Deferral of Pediatric Studies

In December 2020, Moderna Tx, Inc. submitted an Agreed Initial Pediatric Study Plan (Section 1.9.6 Agreed iPSP). The agreement on the iPSP was received on 01 January 2021 (Section 1.9.6 Agreed iPSP Agreement).

Within the iPSP, the proposed plan was to request a deferral for pediatric studies based on the statutory rationale that *the drug or biological product will be ready for approval for use in adults before pediatric studies are complete* [Section 505B(a)(4)(i)(I) of FD&C Act].

An overview of the ongoing and planned clinical studies (in pediatric populations) for mRNA-1273 SARS-CoV-2 vaccine is provided in Table 1.

Table 1: Table of Ongoing/Planned Pediatric Clinical Study for mRNA-1273 SARS-CoV-2 vaccine

PLANNED PEDIATRIC CLINICAL STUDIES			
Pediatric Safety and Effectiveness Study			
Ongoing			
Age Group	**Type of Study**	**Comments**	**Deferral Request (Y/N)**
12 to <18 years of age	Phase 2/3 safety, reactogenicity, and effectiveness study	Randomized, observer-blind, placebo-controlled study to evaluate safety and effectiveness of the mRNA-1273 SARS-CoV-2 vaccine administered as two doses of 100 µg in healthy adolescents.	Y
6 months to <12 years of age	Phase 2/3 dose-finding, safety, reactogenicity, and effectiveness study	Randomized, observer-blind, placebo-controlled, dose finding, age de-escalation study to evaluate safety and effectiveness of the mRNA-1273 SARS-CoV-2 vaccine administered as two doses in healthy children. Dose escalation using mRNA-1273 at doses of 25, 50 and 100 µg.	Y
Planned			
0 to < 6 months	Safety and effectiveness study	Request deferral until reasonable safety and efficacy is demonstrated in older infants in the pediatric trial and/or data is available in pregnant women which may provide passive immunity to infants < 6 months of age.	Y

Pediatric studies have been initiated, but data supporting licensure in this population are not available at this time to include in the current BLA submission for an adult indication. Given this, a deferral for the submission of data supporting an indication in pediatric populations is formally requested in this BLA submission.

Hereafter is a description of the status of the ongoing studies within the pediatric development program.

Phase 2/3 Study mRNA-1273-P203 (NCT04649151) is an ongoing, Phase 2/3, randomized, observer-blind, placebo-controlled study being conducted to assess the safety and immunogenicity (to infer the effectiveness) of mRNA-1273 in an adolescent population aged 12 to < 18 years. The study includes 2 arms: 100 µg of mRNA-1273 and placebo. A total of 3,732 participants between 12 to < 18 years of age were randomly assigned in a 2:1 ratio to receive mRNA-1273 (n=2489) or placebo (n=1243). All participants are being monitored for 12 months following the second dose of vaccine or placebo to enable assessment of safety and immunogenicity.

Enrollment was completed in this study on 28FEB21.

An EUA amendment was submitted on 09 June 2021 based on the following: 1) safety and efficacy data, which included approximately 2-months follow-up after the second injection in the Phase 2/3 Study mRNA-1273-P203 (Study 203); and 2) immunogenicity data from Study P203 and from the ≥ 18 to < 25 years age group from Study mRNA-1273-P301 (Study P301) to infer vaccine effectiveness.

A database lock will be planned no earlier than when all subjects have reached 6 months of follow-up post-dose 2 to support a future sBLA. In addition, an end of study clinical study report will be prepared once all subjects have completed the protocol specified follow-up period.

Phase 2/3 Study mRNA-1273-P204 (NCT04796896) is an ongoing Phase 2/3 two-part study with an open-label, dose-escalation and age de-escalation (Part 1) and a randomized, observer-blind, placebo-controlled expansion (Part 2) to evaluate the safety, tolerability, reactogenicity, and immunogenicity (to infer the effectiveness) of mRNA-1273 in healthy children aged 6 months to < 12 years, divided into 3 age groups (6 to < 12 years, 2 to < 6 years, and 6 months to < 2 years).

Part 1 of the study is open label and consists of dose escalation and age de-escalation in approximately 1,275 participants to select the dose for each age group.

Part 2 of the study is a placebo-controlled observer-blind evaluation of the selected dose from Part 1 in up to 12,000 participants (up to 4,000 participants in each of the 6 to < 12 years, 2 to < 6 years, and the 6 months to < 2 years age groups). in up to 12,000 participants (up to 4,000 participants in each of the 6 to < 12 years, 2 to < 6 years, and the 6 months to < 2 years age groups).

Dose selection for each of the three age cohorts is informed by both the tolerability profile (reactogenicity profile) and the immunogenicity. Part 1 initiated with enrollment of the oldest age

cohort, children between 6 and <12 years of age, first receiving 50 µg (N= 380) and a subsequent group receiving 100 µg (N= 371). Immunogenicity results predict that the 50 ug dose has a very high likelihood of meeting the success criteria for immunobridging as described in the statistical analysis plan for study mRNA-1273-P204. Together with the tolerability profile of the 50 ug dose observed in the oldest age cohort, the favorable immunogenicity supported advancement of 50 ug to Part 2 for the oldest age cohort. Enrollment of Part 2 for 6 to < 12 years of age is ongoing (874/4000 participants enrolled in these arms as of mid-August).

For age groups 2 to < 6 years and 6 months to < 2 years, dose selection based on Part 1 data is projected to occur within September with Part 2 initiating no earlier than end September 2021.