MODERNATX, INC.

Pharmacovigilance Plan

Spikevax (COVID-19 Vaccine mRNA)

December 16, 2021

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1. INTRODUCTION

Following an outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December 2019 and the subsequent declaration by the World Health Organization (WHO) of a Public Health Emergency of International Concern (PHEIC) on March 11, 2020, ModernaTX, Inc. (Sponsor), leveraged its foundational understanding of mRNA vaccine approaches against coronavirus (CoV) to develop a rapid response investigational vaccine based upon its proprietary vaccine platform. mRNA-1273 is a novel, lipid nanoparticle (LNP) encapsulated, mRNA-based vaccine targeted against SARS-CoV-2. The proprietary LNPs encapsulating the mRNA increase its delivery efficiency and improve vaccine tolerability.

Since December 2020, mRNA-1273 and other COVID-19 vaccines have been available under emergency use authorization (EUA) in the US, and by conditional approvals in numerous countries worldwide. The product is currently authorized or approved in 45 countries, regions, and unions/areas for use in one or more of these indications: adults 18 years of age and older, adolescents 12 to 18 years of age; booster; and for use as a third dose in immunocompromised patients. As of November 30, 2021, a total of 673,259,720 doses of mRNA-1273 had been delivered to 63 countries and an estimated total of 371,566,228 doses of mRNA-1273 have been administered.

Apart from public health implementation challenges in vaccinating populations at risk, two major concerns have arisen in optimizing strategies to control the pandemic through vaccination. The duration of protection remains to be determined. Additionally, with the emergence of variant strains (e.g. Delta variant [B.1.617.2]), the level of protection provided by the vaccines currently in use in the United States (which were targeted against the Wuhan strain) against these variant strains is unclear. With the Delta variant [B.1.617.2] circulation, public health experts have observed cases of breakthrough infection, although most such cases have been mild to moderate.

In this Pharmacovigilance Plan, information related to the mRNA-1273 primary series originates from the EU Risk Management Plan for SPIKEVAX (COVID-19 mRNA vaccine) version 2.2, with a data lock point of 30 June 2021, and from BLA information requests.

1.1 BACKGROUND

1.1.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part I: Product Overview**

2. SAFETY SPECIFICATION

2.1 Elements of the Safety Specification

2.1.1 Nonclinical Specification

2.1.1.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SII – Nonclinical Part of the Safety Specification**

2.1.2 Clinical

2.1.2.1 Exposure in Clinical Trials

2.1.2.1.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SIII – Clinical Trial Exposure**

2.1.2.2 Limitations of the Human Safety Database

2.1.2.2.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SIV.2 Limitations to Detect Adverse Reactions in Clinical Trial Development Program**

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SIV.3 Limitations in Respect to Populations Typically Under-Represented in Clinical Trial Development Program**

2.1.2.3 Populations not studied in the clinical trials

2.1.2.3.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SIV – Populations Not Studied in Clinical Trials**

2.1.2.4 Adverse events (AEs)/adverse drug reactions (ADRs)

2.1.2.4.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part SVII.1.1 Risks Not Considered Important for Inclusion in the List of Safety Concerns in the RMP**

2.2 Summary of the Safety Specification

2.2.1 Identified and Potential Risks

2.2.1.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part SVII.1.2 Risks Considered Important for Inclusion in the List of Safety Concerns in the RMP**

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part SVII.3 Details of Important Identified Risks, Important Potential Risks, and Missing Information**

A summary of these safety concerns is included in Table 1.

2.2.2 Epidemiology

2.2.2.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SI – Epidemiology of the Indication and Target Population**

2.2.3 Summary of Safety Concerns

Table 1. mRNA-1273 Summary of Safety Concerns

Summary of Safety Concerns	
Important identified risks	Anaphylaxis Myocarditis Pericarditis
Important potential risks	Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)
Missing information	Use in pregnancy and while breast-feeding Long-term safety Use in immunocompromised subjects Interaction with other vaccines Use in frail subjects with unstable health conditions and co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders) Use in subjects with autoimmune or inflammatory disorders

3. PHARMACOVIGILANCE PLAN

3.1 Structure of the Pharmacovigilance Plan

3.1.1 Summary of Ongoing Issues

The pharmacovigilance plan addresses the important safety concerns and missing information in Table 1.

3.1.1.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II: Module SVII – Identified and Potential Risks**

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part SVII.3 Details of Important Identified Risks, Important Potential Risks, and Missing Information**

3.1.2 Routine Pharmacovigilance Activities

The Sponsor has an established signal management process including signal detection, validation and evaluation of spontaneous reports from all sources. During signal detection data sources are screened for new safety information related to mRNA-1273. Following initial review of the available data, a determination is made on the basis of the nature and the quality of the new information whether further investigation is warranted, at which point those topics referred for further investigation are considered "validated signals". Potential signal detection data sources include safety data from sponsored clinical trials, non-interventional studies, spontaneous AE reports, published literature, and communications from external sources (including regulatory agencies and if applicable business partners). Moderna's PV system relies primarily on AEs contained in its global safety database (Argus platform) that captures suspected AE reports and in addition, signal from regulatory databases (e.g., EudraVigilance, VAERS). Routine PV also includes a periodic review of the literature that involves targeted keyword searches in widely recognized databases (i.e., MEDLINE, EMBASE). Moderna performs a weekly aggregate quantitative signal detection review of the global safety database in order to identify possible adverse reactions. Moderna also conducts monthly safety reports that are shared with regulatory agencies worldwide.

3.1.2.1 Routine Pharmacovigilance Activities Beyond Adverse Reactions Reporting and Signal Detection

3.1.2.1.1 Specific Adverse Reaction Follow-Up Questionnaires for mRNA-1273

Anaphylaxis Questionnaire

The questionnaire is intended to collect structured information on severe cases of anaphylactic reaction including anaphylaxis. It is intended to assist with capturing information that can support case classification using the Brighton Collaboration case definition.

COVID-19/Vaccine Failure Questionnaire

The questionnaire is intended to better characterize the extent and severity of COVID-19 disease reported after vaccination by mRNA-1273. This questionnaire is for use following the reporting of vaccine failure and/or COVID-19 disease cases and/or AESI associated with COVID-19 disease after mRNA-1273.

Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD) is an Important Potential risk in the RMP. However, the broad spectrum of the COVID-19 disease manifestations in different populations and age groups makes it impossible, to determine how severe COVID-19 infection would have been in the absence of vaccination in the individual case. There is no uniformly accepted definition of vaccine-associated enhanced disease (VAED) or vaccine-associated enhanced respiratory disease (VAERD), and no single or combination of specific confirmatory tests to diagnose VAED. However, the case definition from the Brighton Collaboration will be used to the best possible extent for level of diagnostic certainty with respect to AE reports of potential VAED or VAERD (Munoz 2020).

Myocarditis Questionnaire

The questionnaire is intended to collect structured information on cases of myocarditis. It is intended to assist with capturing information that can support case classification using the Myocarditis Brighton Collaboration case definition (Brighton Collaboration 2021) as well as the CDC working case definition on Acute Myocarditis (Gargano 2021).

Pericarditis Questionnaire

The questionnaire is intended to collect structured information on cases of pericarditis. It is intended to assist with capturing information that can support case classification using the CDC working case definition on Acute Pericarditis (Gargano 2021).

Signal Detection

The Moderna signal management process for mRNA-1273 includes signal detection, validation, prioritization, evaluation, and recommendation for actions as well as documentation and tracking of signals. It follows the principles of the Good Pharmacovigilance Practices Module IX for Signal Management (refer to https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/good-pharmacovigilance-practices).

Moderna signal detection strategy for mRNA-1273 is described in the product safety strategy form. It describes the data sources, type and frequency of the signal detection analyses summarized in (Table 2).

As available, standard case definitions from the Brighton Collaboration will be used to classify AESIs by level of diagnostic certainty (Table 3.).

Table 2. mRNA-1273 Signal Data Sources and Periodicity of Assessment

Data Source	Frequency of Safety Evaluations
Company global safety database	Ongoing monitoring of Individual Cases Safety Reports (ICSRs) from all sources, safety concerns, and Adverse Events (AE) of Special Interest. Weekly aggregated review of ICSRs for trend analyses. Review of disproportionate reporting of preferred terms (PT) during a time interval as compared to all data prior to the RP for mRNA-1273. Review of endpoints of interest (i.e., case counts, demographics, country of origin, time to onset, seriousness, batch numbers, fatalities, AE from the product surveillance list of safety topics and based on MedDRA system organ class and high-level term, and identification of potential clusters of ICSRs.
Literature	Weekly literature review. Any literature abstract or article signal detection run will be reviewed.
EudraVigilance	Continuous monitoring. Biweekly critical review of the EudraVigilance data analysis system using available reports (ie, Electronic Reaction Monitoring Reports [e-RMRs] and active substance groupings, ICSR line listings and ICSR forms).
VAERS	Frequency of review will depend on public availability of redacted VAERS extracts. Current estimates based on public communication as well as processing time indicate this frequency will range between every two to four weeks. Generation of disproportionality scores using Empirical Bayesian Geometrical Mean and its 90% confidence intervals after new uploads of Vaccine Adverse Event Reporting System extracts in Empirica Signal.
Health Authorities websites	Ongoing review of data published on the Safety Web Portals of selected major regulatory agencies to identify required actions regarding the product and similar products.

Product surveillance to identify safety signals will occur for any reported AEs including reactogenicity. Safety surveillance prioritization is for the safety concerns of the RMP, AESIs, or those AEs that may be serious or known to be often medicine related.

If any cluster of events is detected which points towards an unexpected event/syndrome, Moderna will perform appropriate signal evaluation and will provide this information to the appropriate regulatory agencies.

Table 3. Product Surveillance List of mRNA-1273 Signaling Strategy By Category

Category	Safety Topics (Updates may be Needed if New Adverse Events Emerge)
Safety concerns	• Anaphylaxis • Myocarditis • Pericarditis • Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD) • Use in pregnancy and while breast-feeding • Long-term safety • Use in immunocompromised subjects • Interaction with other vaccines • Use in frail subjects with unstable health conditions and co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders) • Use in subjects with autoimmune or inflammatory disorders
Adverse events of special interest (AESI)	• List of AESI (AESIs will be updated at least quarterly and as new information arises and is based upon): • Brighton Collaboration (Safety Platform for Emergency vACcines) • ACCESS protocol • US Centers for Disease Control and Prevention (preliminary list of AESI for VAERS surveillance) • Medicines and Healthcare products Regulatory Agency (unpublished guideline).
Standard safety topics	• Off-label Use • Overdose • Vaccination Administration Errors • Product Quality Issues • Drug-Drug Interactions • Death • Pediatric Use • Geriatric Use • Designated Medical Events (EMA/326038/2020)

3.1.3 Action plan for Safety Issues

3.1.3.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part V: Risk Minimisation Measures (Including Evaluation of the Effectiveness of Risk Minimisation Activities)**

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part V.1 Routine Risk Minimisation Measures**

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part V.2 Additional Risk Minimisation Measures**

3.1.4 Summary of Actions to be completed, Including Milestones

3.1.4.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part V.3 Summary of Risk Minimisation Measures**.

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part VI: Summary of the Risk Management Plan - II.B Summary of Important Risks**

3.1.5 Continued Clinical Trials Follow-up

3.1.5.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II.C Post-Authorisation Development Plan**

The Pharmacovigilance Plan of the RMP for mRNA-1273 includes information on efforts from the Sponsor to address the general safety of mRNA-1273 including further characterization of identified and potential risks described in the RMP.

3.1.5.1.1 Clinical Studies

Additional information about these studies, including milestone dates, is provided in Table 4.

Ongoing Study P201 Part B, an open-label interventional phase of a Phase 2a, randomized, observer-blind, placebo-controlled, dose confirmation study to evaluate the safety, reactogenicity, and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine in adults aged 18 years and older, collects in the open-label phase AEs leading to discontinuation from study participation, MAAEs, and SAEs through Month 6 or withdrawal from the study.

Ongoing study P301 is offering a booster dose of 50 µg of mRNA-1273 to the remaining ~25,000 participants in accordance with the expected public health recommendations (starting 20 September 2021) to provide the opportunity to study the safety of the booster dose on a larger scale than the P201 Part B study. The study (P301 Part C) will assess safety, immunogenicity, and the impact of the booster on the incidence rates of COVID-19. This study will focus on unsolicited AEs, MAAEs, and SAEs. Any cases of suspected myocarditis and pericarditis will be evaluated by a Cardiac Endpoint Adjudication Committee, implemented uniformly across all clinical studies in the mRNA-1273 program in order to further evaluate the risk of myocarditis and pericarditis, in particular after the booster dose. Serum samples will be requested from all study participants who sign the consent for Part C to receive a booster dose. Samples will be collected within the first ~4 days after vaccination, from all participants who agree to provide the sample, and banked for potential cardiac biomarker testing. Ongoing study P203, is offering a booster dose of 50 µg of mRNA-1273 to all participants to provide the opportunity to study the safety of the booster dose in an adolescent population. The study (P203 Part C) will assess safety, immunogenicity, and the impact of the booster on the incidence rates of COVID-19. This study will focus on unsolicited AEs, MAAEs, and SAEs. Any cases of suspected myocarditis

and pericarditis will be evaluated by a Cardiac Endpoint Adjudication Committee, implemented uniformly across all clinical studies in the mRNA-1273 program in order to further evaluate the risk of myocarditis and pericarditis, in particular after the booster dose. Serum samples will be requested from all study participants who sign the consent for Part C to receive a booster dose. Samples will be collected within the first ~4 days after vaccination and banked for potential cardiac biomarker testing.

Ongoing study P204 is studying different doses of a 2-dose primary series of mRNA-1273 in children aged 6 months to < 12 years old. The study will evaluate the safety, reactogenicity, and effectiveness of mRNA-1273 primary series. Any cases of suspected myocarditis and pericarditis will be evaluated by a Cardiac Endpoint Adjudication Committee, implemented uniformly across all clinical studies in the mRNA-1273 program in order to further evaluate the risk of myocarditis and pericarditis. Samples will be requested from all participants in Cohort D Part 2 of the study. . Samples will be collected within the first ~4 days after Dose 2, from all participants who agree to provide the sample for ages 6-12 years, and all participants from 6 months to 6 years, and banked for potential cardiac biomarker testing.

Table 4. Ongoing Interventional Clinical Studies with mRNA-1273

Study Number, Title, and Categories Status	**Summary of Objectives**	**Safety Concerns Addressed**	**Milestones**	**Due Dates (MM/DD/YYYY)**
Study mRNA-1273-P301 Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older Study Status: Ongoing	Evaluate long-term safety data and durability of vaccine effectiveness (VE)	Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD) Anaphylaxis Myocarditis Pericarditis Long-term safety	Final Protocol Submission Date	09/14/2021
			Study Completion Date	12/31/2022
			Final CSR	06/30/2023
Study mRNA-1273-P203 A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the	Evaluate the safety, reactogenicity, and effectiveness	Anaphylaxis Myocarditis Pericarditis Long-term safety	Final Protocol Submission Date	01/31/2022

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates (MM/DD/YYYY)
Safety, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Adolescents 12 to < 18 years of age Study Status: Ongoing			Study Completion Date	04/30/2024
			Final CSR	07/31/2024
P204 A Phase 2/3, two-part, open-label, dose-escalation, age de-escalation and randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 SARS-CoV 2 vaccine in healthy children 6 months to less than 12 years of age.	Evaluate the safety, reactogenicity, and effectiveness	Anaphylaxis Myocarditis Pericarditis Long-term safety	Final Protocol Submission Date	02/28/2022
			Study Completion Date	12/31/2023
			Final CSR	03/31/2024

3.1.5.1.2 Non-interventional Studies

Additional information about these studies, including milestone dates, is provided in Table 5.

The following ongoing noninterventional studies will capture safety data after any dose, including a booster dose:

- P903, an ongoing post-marketing safety of SARS-CoV-2 mRNA-1273 vaccine in the US: Active surveillance, signal refinement and self-controlled risk interval signal evaluation in HealthVerity
- P904, an ongoing post-authorization active surveillance safety study using secondary data to monitor real-world safety of mRNA-1273 in Europe, as the booster may become authorized in Europe.

The following ongoing noninterventional studies will capture safety and effectiveness data after any dose, including a booster dose:

- P901, an ongoing real-world study to evaluate mRNA-1273 effectiveness and long-term

effectiveness

The following planned or ongoing noninterventional studies will capture safety data after any dose, including a booster dose:

- P905, an ongoing post-marketing observational safety study of mRNA-1273 vaccine in pregnancy using routinely collected health data in five European countries.
- P902, an ongoing post-marketing observational safety study to evaluate the outcomes of pregnancies and birth in females exposed to mRNA-1273 vaccine during pregnancy and to evaluate infant outcomes.
- P911, a planned post-marketing observational safety study to evaluate long-term sequelae of myocarditis temporally associated with mRNA-1273 vaccination with at least 5 years of follow-up.

Table 5. Ongoing and Planned Non-interventional Studies with mRNA-1273

Study Number, Title, and Categories Status	**Summary of Objectives**	**Safety Concerns Addressed**	**Milestones**	**Due Dates (MM/DD/YYYY)**
Study mRNA-1273-P903 Post Authorisation Safety of SARS-CoV-2 mRNA-1273 Vaccine in the US Study status: Ongoing	Enhanced pharmacovigilance study to provide additional evaluation of AESI (including myocarditis and pericarditis) and emerging validated safety signals. The study has 3 core objectives: -Estimation of background rates for AESI and other outcomes in the cohort -Assessment of observed versus expected rates -Self-controlled risk interval analyses for adverse events that meet specific threshold criteria	Anaphylaxis Myocarditis Pericarditis Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD) Long-term safety AESI and emerging validated safety signals	Final Protocol submission	01/31/2022
			Study completion date	12/31/2022
			Final report submission	06/30/2023
Study mRNA-1273-P904 A Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-	The overarching research question of this study is whether the occurrence of adverse events of special interest (AESI) among persons vaccinated with COVID-19 Vaccine Moderna in Europe is higher than expected.	Anaphylaxis Myocarditis Pericarditis Vaccine-associated enhanced disease (VAED) including	Feasibility assessment	01/31/2021
			Final Protocol submission	11/04/2022
			Study completion date	03/31/2023

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates (MM/DD/YYYY)
1273 Vaccine in the EU Study status: Ongoing	Primary objectives: To estimate incidence rates of the AESI among persons receiving COVID-19 Vaccine Moderna overall and in subgroups of interest To assess whether vaccination with COVID-19 Vaccine Moderna (one dose, two doses, any dose) is associated with an increased rates of the AESI compared with expected overall and in subgroups of interest. Secondary objectives: To estimate incidence rates of the AESI among individuals vaccinated with the COVID-19 Vaccine Moderna, using real-world data, in the following specific subpopulations of COVID-19 Vaccine Moderna recipients: women of childbearing age, patients who are immunocompromised, patients previously diagnosed with COVID-19 infection, patients with unstable health conditions and morbidities, subjects patients with autoimmune or inflammatory disorders, and in age-specific populations (children, adolescents, adults); To assess whether vaccination with COVID-19 Vaccine Moderna is associated with an increased rates of the AESI compared with the expected rates in subpopulations of interest: women of childbearing age, patients who are immunocompromised,	vaccine-associated enhanced respiratory disease (VAERD) Long-term safety Interaction with other vaccines Use in frail subjects with unstable health conditions and co-morbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders) Use in subjects with autoimmune or inflammatory d disorders	Final study report	12/31/2023

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates (MM/DD/YYYY)
	patients previously diagnosed with COVID-19 infection, patients with unstable health conditions and morbidities, subjects patients with autoimmune or inflammatory disorders, and in age-specific populations (children, adolescents, adults).			
Study mRNA-1273-P905 Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely collected health data in five European countries Study status: Ongoing	Electronic database assessment of use in pregnant women	Use in pregnancy	Final Protocol submission	11/04/2021
			Study Completion Date	03/31/2023
			Final study report	12/31/2023
Study mRNA-1273-P902 Observational pregnancy outcome study Study status: Ongoing	Evaluate outcomes of pregnancies and birth in females exposed to mRNA-1273 vaccine during pregnancy. Evaluate infant outcomes.	Use in pregnancy and while breast-feeding	Final Protocol submission	07/31/2021
			Study completion date	09/30/2023
			Final study report	06/30/2024
Study mRNA-1273-P901 Real-world study to	Primary Objectives 1. To evaluate the effectiveness of 2 doses of	Use in immunocompromised subjects	Final Protocol submission	12/20/2021

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates (MM/DD/YYYY)
evaluate mRNA-1273 effectiveness and long-term effectiveness in the U.S. Study Status: Ongoing	Moderna COVID-19 vaccine in preventing COVID-19 diagnosis 2. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing severe COVID-19 disease Secondary Objectives 1. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis by age and by sex 2. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis by race/ethnicity groups 3. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis in individuals with chronic diseases (e.g., chronic kidney disease, lung disease including chronic obstructive pulmonary disease [COPD] and asthma, diabetes) 4. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis in individuals who are immunocompromised (e.g., HIV, cancer, transplant, immunosuppressive medications) 5. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis in individuals with autoimmune conditions (e.g., rheumatoid arthritis, inflammatory bowel disease, psoriasis, psoriatic arthritis, multiple sclerosis, systemic lupus erythematosus) 6. To evaluate the effectiveness of 2 doses of	Interaction with other vaccines, as possible Use in frail subjects with unstable health conditions and co-morbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, cardiovascular disorders) Use in subjects with autoimmune or inflammatory disorders	Study completion date	01/31/2024
			Final study report	04/14/2025

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates (MM/DD/YYYY)
	Moderna COVID-19 vaccine in preventing COVID-19 diagnosis in frail individuals 7. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis in pregnant women 8. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis among individuals with a history of COVID-19 diagnosis 9. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis when given concomitantly with another vaccine 10. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing asymptomatic COVID-19 11. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing symptomatic COVID-19 12. To evaluate the durability of 2 doses of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis 13. To evaluate the durability of 2 doses of Moderna COVID-19 vaccine in preventing severe COVID-19 disease 14. To evaluate the effectiveness of 1 dose of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis 15. To evaluate the effectiveness of 1 dose of Moderna COVID-19 vaccine in preventing severe COVID-19 disease.			

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates (MM/DD/YYYY)
Study mRNA-1273-P911 Long-term outcomes of myocarditis following administration of SPIKEVAX (Moderna COVID-19, mRNA-1273) Study Status: Planned	The overarching goal of this study is to characterize long-term outcomes of myocarditis temporally associated with administration of mRNA-1273 (SPIKEVAX). *Primary objectives:* 1. To characterize the presentation, clinical course of acute post-vaccine myocarditis in children and young adults 2. To characterize potential long-term sequelae of post-vaccine myocarditis, and functional outcomes in children and young adults *Secondary objectives:* 3. To compare long-term effects of post-vaccine myocarditis with those of nonvaccine myocarditis, including myocarditis arising in COVID-infected children and young adults 4. To identify possible risk factors for post-vaccine myocarditis in children and young adults including age, sex, race, ethnicity, obesity, lifestyle factors, and medical history	Myocarditis	Final Protocol Submission Date	04/30/2022
			Study Completion Date	10/31/2027
			Final Study Report	10/31/2028

3.2 Pharmacovigilance Methods

3.2.1 Passive Surveillance

3.2.1.1 mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part III: Pharmacovigilance Plan (Including Post-Authorisation Safety Studies)**

3.2.1.2 Active surveillance

mRNA-1273 Primary Series

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part II.C.2 Other Studies in Post-Authorisation Development Plan**

Refer to Risk Management Plan for SPIKEVAX (COVID-19mRNA vaccine) version 2.2 – **Part VI: Summary of the Risk Management Plan - II.C Post-Authorisation Development Plan**

4. REFERENCES

Gargano JW, Wallace M, Hadler SC, Langley G, Su JR, Oster ME, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the Advisory Committee on Immunization Practices—United States, June 2021. Morbidity and Mortality Weekly Report 2021;70(27):977.

Munoz FM, Cramer JP, Dekker CL, Dudley MZ, Graham BS, Gurwith M, et al. Vaccine-associated enhanced disease: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine 2021;39(22):3053-66.