Part III: Pharmacovigilance Plan (Including Post-Authorisation Safety Studies)

III.1 Routine Pharmacovigilance Activities

Routine pharmacovigilance will be conducted for mRNA-1273 along with the additional actions part of the pharmacovigilance plan. Due to the special circumstances of the pandemic, enhancement of routine activities will be undertaken.

Moderna has a safety surveillance and reporting system in place to organize the collection, data entry in the company global safety database and evaluation of any AEs reported to Moderna.

A call center will be available in countries for vaccine providers (eg, healthcare professionals and individuals who administer the vaccine) and recipients, to assist with medical inquiries, collect product quality complaints and AEs.

All AE/serious AE cases will undergo follow-up and for serious AEs, hospital records including autopsy reports, will be queried to the reporter, as possible.

Routine Pharmacovigilance Activities Beyond Adverse Reactions Reporting and Signal Detection:

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 characterise 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 vaccination.

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 et al 2020).

Table 29: mRNA-1273 Vaccine Signal Data Sources and Frequency of Evaluations

Data Source	Frequency of Safety Evaluations
Company global safety database	Ongoing monitoring of individual cases of Suspected Unexpected Serious Adverse Reaction (SUSAR), safety concerns, and Adverse Events (AE) of Special Interest. Weekly aggregated review of AE cases 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 the mRNA-1273 vaccine. Review of endpoints of interest (ie, 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 Individual Case Safety Reports (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 disproportionality analyses of the combination of AEs as appropriate. In case of disproportionality, Moderna will present these results in the monthly summary safety reports or upcoming Periodic Safety Update Reports (eg, as part of the interval and cumulative number of reports per MedDRA high-level term and system organ class).