



Data Blinding Plan (DBP)

**A 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**

ModernaTX, Inc.

Protocol mRNA-1273-P301

Investigational Medicinal Product: mRNA-1273

Amendment 2

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Version 3.0

DOCUMENT HISTORY

Version	Date	Description of main modifications
1.0	25 August 2020	Original Version (Version 1.0)
2.0	3 November 2020	Amendment 1 (Version 2.0) <ul style="list-style-type: none">• Added Section 5.3.2: Sponsor unblinded team to support regulatory submissions• Added Section 5.5: CRO CSR writing team• Added Section 7.3 Firewall to separate blinded and unblinded sponsor teams• Updated Section 9: Access to unblinded data

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1 PURPOSE AND SCOPE

The purpose of the Data Blinding Plan (DBP) is to lay out the roles and responsibilities of the Sponsor (i.e. Moderna) and the CRO (i.e. PPD) study teams in receiving access to unblinded data during the clinical study.

The DBP ensures that the blinding is maintained during trial execution, and that the dissemination of the resultant unblinded clinical trial data are appropriate to meet all business needs and regulatory and legal requirements. The DBP also ensures simultaneous accuracy of disseminated data, including for submission to Regulatory Agencies and the protection of propriety and confidential information.

The DBP is set up as a study specific master document to describe general and study specific aspects of data blinding management procedures for a study. The DBP does not cover management of randomization lists, unblinding of individual participants (whether accidental or for emergency), or unblinding for regulatory safety reporting, which are managed in accordance with applicable CRO Standard Operating Procedures (SOPs).

2 RESPONSIBILITIES

The DBP is set up by the responsible Sponsor study biostatistician in conjunction with the Sponsor Clinical Operations Lead, and approval is documented in [Section 10](#).

In case of a protocol amendment impacting the blinding level of the study or in any operational change in the study impacting blinding, a revised version of the DBP will be needed. In addition, there should be a review of the DBP list of personnel (i.e. role and organizational membership) that will have access to study unblinded data at each planned analysis to ensure any changes to the study team are reflected in the Plan.

Deviations to the DBP and/or accidental/unplanned unblinding will be escalated per the mRNA-1273-P301 Communication Plan and applicable CRO SOPs and documented and reported accordingly.

The list of personnel both internal and external to Moderna (i.e. role and organizational membership) with access to unblinded study analyses data at specified timepoints is defined in [Section 9](#), Access List to Study Unblinded Analyses Data.

A full list of study team members with study title is maintained by the CRO as specified in the mRNA-1273-P301 Communication Plan.

3 REFERENCE DOCUMENTS

- mRNA-1273-P301 Protocol
- mRNA-1273-P301 Data Safety Monitoring Board (DSMB) Charter and DSMB Analysis Plan
- mRNA-1273-P301 Statistical Analysis Plan
- mRNA-1273-P301 Communication Plan

- mRNA-1273-P301 Protocol Safety Review Team Charter
- PPD Data Import Agreement for Protocol mRNA-1273-P301
- Moderna Data Disclosure Policy and Process

4 STUDY BACKGROUND

mRNA-1273-P301 is a Phase 3, Randomized, Stratified, Observer-Blind, Placebo Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARSCoV-2 Vaccine in Adults Aged 18 Years and Older

5 STUDY BLINDING

5.1 Clinical Site

The study will be conducted in an observer-blinded manner. The Investigational product (IP) is administered by unblinded medical personnel in a manner that shields both the participant and blinded study staff from viewing the IP. The unblinded medical personnel will not participate in any Per-protocol (PP) clinical evaluations. The participant and study personnel responsible for the evaluation of any study endpoint (e.g., safety and reactogenicity) will be blinded to treatment assignment throughout the course of the study. No set of individual codes will be held at the study sites. The study investigator may unblind a study participant's treatment assignment if this information is necessary for clinical care. The investigator must contact the CRO medical monitor or Moderna medical lead to request to unblind and explain the reason. In an emergency the investigator can directly contact the Interactive Response Technology (IRT) system and request to unblind. However, the study investigator must inform the Moderna medical lead of the unblinding within 24 hours.

5.2 CRO and Clinical Site Monitors

5.2.1 Clinical Site Monitors

Separate blinded and unblinded teams will oversee monitoring of the clinical site. The separate unblinded study monitor will be responsible for vaccine accountability. Blinded clinical site monitors will remain blinded until end of study.

5.2.2 CRO blinded Study Biostatistician and Programmer(s)

CRO study biostatistician and statistical programmer(s) supporting mRNA-1273 are blinded to treatment assignment. The CRO study biostatistician and programmer(s) are responsible to

- Develop the study data packages for DSMB review (including the safety data review and the planned interim analyses) using dummy randomization code and will be referred to as the blinded data package

5.2.3 CRO unblinded Biostatistician and Programmer(s) and Medical Monitors

An independent unblinded biostatistician and, as needed, independent unblinded statistical programmer(s) and unblinded medical monitor(s) will be designated by the CRO and/or Moderna to support unblinded analysis for the DSMB and/or to help the Sponsor prepare regulatory submission at the time of interim or final analysis. The unblinded team will have access to the unblinded participant level treatment assignment during the study. The unblinded CRO staff will secure access to unblinded information per CRO Standard Operation Procedures (SOPs) throughout the study.

- The unblinded biostatistician and programmer(s) will have access to participant level treatment assignment data
- The unblinded biostatistician and programmers supporting the DSMB will perform any unblinded analysis for DSMB review. The unblinded analysis will be performed using the blinded data package developed by the blinded study biostatistician, with application of the actual treatment assignment data.
- The unblinded biostatistician supporting the DSMB will provide the unblinded DSMB package to the DSMB members.
- The unblinded biostatistician supporting the DSMB will help prepare presentation of unblinded results to DSMB, participate in both the OPEN session and the CLOSED session of the DSMB meetings, and facilitate with DSMB's questions and requests regarding unblinded data.
- A group of biostatistician and programmers will be unblinded post an interim analysis (IA) should the IA demonstrate early efficacy and result in the Sponsors decision to file regulatory submission.
- The medical monitor will support writing documents and communications with DSMB with oversight by the unblinded Sponsor clinical representative.

5.2.4 Data Safety Monitoring Board (DSMB)

Participant safety will be primarily monitored by an unblinded independent Data Safety Monitoring Board (DSMB) both at specific timepoints as described in the study DSMB Charter and on an ad hoc basis. Details regarding composition, responsibilities and procedures of the DSMB will be presented in the respective charter and the study specific DSMB analysis plan.

5.2.5 Protocol Safety Review Team (PSRT)

The PSRT is a blinded group of medical monitors from Moderna, NIAID, and BARDA who review blinded safety data weekly. The tables and listings originate from the clinical and safety databases. The PSRT is responsible for escalating concerns to the DSMB.

5.3 Sponsor

Blinding of the Sponsor during the study will be conducted as described in the study [protocol Section 6.2.8](#). Depending on the recommendation of the DSMB, the Sponsor may prepare a regulatory submission after an IA. In this case, pre-identified Sponsor members including the analysis and reporting

team will be unblinded to treatment assignments and remain unblinded for the remainder of the study. Participants and investigators will remain blinded. PI will be blinded for IA and will not review or sign the Primary Analysis CSR but, will review and sign the End of Study CSR.

5.3.1 Sponsor unblinded clinical representative to support DSMB

A Sponsor clinical representative will oversee and support interactions between the CRO unblinded Biostatistician and Programmer(s) and unblinded medical monitor and the DSMB prior to the interim or final analysis.

5.3.2 Sponsor unblinded team to support regulatory submissions

The Sponsor unblinded team will include representatives from cross-functional teams (see [Section 9](#) for roles and the blinding/unblinding level and status). This team will be unblinded only when the decision is made to prepare for a regulatory submission post IA; and the purpose for the unblinding is to enable the group to develop regulatory submission documents and to address questions from regulatory agencies during the regulatory review of the submission. After unblinding, this team will not participate in the conduct or execution of the subsequent course of study.

5.3.3 Sponsor blinded team for oversight of ongoing study post interim analysis

If an IA demonstrates early efficacy and results in a decision by the Sponsor to unblind for purpose of a regulatory submission, a dedicated blinded team distinct and separated by a “firewall” ([Section 7.3](#)) from the unblinded team will be responsible for continued conduct and execution of the clinical trial after the interim analysis.

5.4 Laboratory

The laboratory personnel in charge of immunogenicity testing will be blinded to the treatment assignment of the samples tested throughout the course of the study. Immunogenicity results will be transferred from the laboratory to the CRO per the PPD Data Import Agreement for Protocol mRNA-1273-P301. As the data to be imported contains information that could potentially unblind the project team, the laboratory will post the data in the specified unblinded location. Authorization to receive the import will be documented in accordance with the CRO SOP.

5.5 CRO Writing Team

The CRO writing team (medical writers, quality reviewers, compilations, and publishing team members) will be fully unblinded after the release of the IA data for writing up the IA results in regulatory submissions. This writing team will work with the unblinded Sponsor team members (described in [Section 5.3](#)) and unblinded CRO team members listed in [Section 9](#) “Access List To Study Unblinded Analyses Data Prior To Final Database Lock”. A part of the CRO Writing Team may be involved in developing draft mock sections with the unblinded Sponsor team members prior to release of the IA data.

6 STUDY ANALYSES AND RESULTS

There are two (2) planned interim analyses when 35% (53 cases) and 70% (106 cases) of total target cases have been observed across the two treatment groups. The primary analysis will be performed when approximately 151 cases have been observed in the study. These analyses will be conducted on cleaned data. Details of the IA and primary analysis are described in the study [protocol section 9.6](#) and the [SAP](#).

7 LOCATION OF UNBLINDED DATA / UNBLINDED DATA FLOW

7.1 DSMB Data Flow

Unblinded data, listings and minutes from the closed, unblinded DSMB meetings are maintained in a secure DSMB Site and maintained by PPD. Access is restricted to authorized unblinded individuals the CRO and the DSMB members as defined in the mRNA-1273-P301 Data Safety Monitoring Board (DSMB) Charter and analysis plan.

7.2 Data Flow for Primary Analysis and Unblinded Analyses to Support Regulatory Submissions

A secure file transfer path will be decided between the CRO, the SPONSOR, NIAID, to use for the transfer of unblinded study data for DSMB review. Only the CRO independent unblinded biostatistician, unblinded programmer(s), unblinded medical monitor and unblinded Sponsor clinical representative will have access to upload the unblinded data package to the secured file transfer location to be delivered to the DSMB. The unblinded DSMB review include regular safety data review and planned interim analyses.

For the Primary Analysis, the Sponsor Study Lead Biostatistician or delegate will request access to the study specific Unblinded Primary Analysis folder prior to the date of expected data release for the Primary Analysis. Access to the specified (b) (4) location will only be requested for members of the Sponsor statistical team. Once access has been granted, the CRO PM or delegate will confirm with Moderna that the access has been granted.

Before the scheduled date for releasing the unblinded Primary Analysis and/or unblinded IA analysis to support regulatory submissions, the CRO unblinded Biostatistician will send an email to the Sponsor Study Lead Biostatistician or delegate, with the relevant study leads in copy, confirming whether the unblinded analyses results will be ready as scheduled, and seeking approval from the Sponsor to post the unblinded data on the scheduled delivery date.

For the Primary Analysis and the unblinded IA analysis to support regulatory submissions, following approval from the Sponsor's Head of Biostatistics (or delegate) and the Therapeutic Area Head (or delegate), the CRO Lead Biostatistician will notify the CRO Unblinded Statistician. The CRO Unblinded Statistician will upload the unblinded data from the analyses to the designated Unblinded (b) (4) folder on the agreed-upon date. The Sponsor Biostatistician or delegate who will be unblinded post IA or

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Primary Analysis will then upload the Analysis data to the Sponsor unblinded folder and only provide access to the subject-level unblinded Sponsor study team members as specified in this document ([Section 9](#)). Upon the time of unblinding, the unblinded team will cease participation of conduct and execution of the subsequent course of the study. Further dissemination of the unblinded data at the Sponsor will be in accordance with the Sponsor’s Data Disclosure Policy and Process.

7.3 Firewall to Separate Blinded and Unblinded Sponsor Teams

When a decision has been made by the Sponsor to unblind the study prior to study completion, the blinded and unblinded Sponsor staff will be separated by a firewall. This “firewall” consists of 1) folder access restriction – folders containing any unblinded data and documents will be accessible only by the pre-specified unblinded team members according to the pre-specified level of unblinding ([Section 9](#)), and the unblinded folder will have the control and traceability on access and usage monitored by designated digital team member; and 2) communications, both written and verbal, of unblinded data analysis outcome will be insulated from the blinded team. Unblinded team will receive appropriate timely alerts indicating sensitive unblinded information communication.

8 END OF STUDY

The study will be fully unblinded after final database lock.

9 ACCESS LIST TO STUDY UNBLINDED ANALYSES DATA PRIOR TO FINAL DATABASE LOCK

Access to unblinded data is described in the below table and figure.

Role	Organization	Access to Unblinded Data			
		DSMB review (safety data review and Interim analysis) ¹	Primary Analysis		End of Study Analysis
			Treatment Group-Level Unblinded ²	Subject-Level Unblinded ³	
PPD (CRO)					
Project Manager	CRO	NO	NO	NO	YES
Clinical Team Manager		NO	NO	NO	YES
Medical Director		NO	NO	NO	YES
Biostatistics Lead		NO	NO	NO	YES
Lead Programmer		NO	NO	NO	YES
Clinical Data Manager		NO	NO	NO	YES
Unblinded Clinical Research Associate		NO	NO	NO	YES
Unblinded Project Assistant		NO	NO	NO	YES
Unblinded Programmer		YES	YES	YES	YES

Unblinded Biostatistician		YES	YES	YES	YES
Unblinded Medical Monitor		YES	YES	YES	YES
Unblinded Biostatistician to Support Regulatory Submissions		NO	YES	YES	YES
Unblinded Programmer to Support Regulatory Submissions		NO	YES	YES	YES
Medical Writing Team (including Medical Writers, Document Reviewers, and Compilation Specialists)		NO	YES	YES	YES
Principal Safety Specialist/DSMB Coordinator		NO	NO	NO	NA
Moderna					
Sponsor unblinded clinical representative (Florian Schödel)	Sponsor (Moderna)	YES	YES	YES	YES
Chief Medical Officer (Tal Zaks)		NO	YES	NO	YES
Chief Development Officer (Mel Ivarsson)		NO	YES	NO	YES
Therapeutic Area Head, Infectious Disease (Jacqueline Miller)		NO	YES	NO	YES
Program Leader (Hamilton Bennett)		NO	YES	NO	YES
Clinical Development Lead (Brett Leav)		NO	YES	YES	YES
Study Medical Lead, Blinded (Allison August or designee)		NO	NO	NO	YES
Sponsor clinical representative (Karen Slobod)		NO	YES	NO	YES
Sponsor blinded clinical representative, Blinded (b) (6)		NO	NO	NO	YES
Head, Biostatistics (Shu Han)		NO	YES	YES	YES
Study Lead Biostatistician, (Weiping Deng)		NO	YES	YES	YES
Program Lead Biostatistician (Honghong Zhou)		NO	YES	YES	YES
Study Lead Biostatistician, Blinded (b) (6)		NO	NO	NO	YES
Statistical Programming Program Lead (Baoyu Ding)		NO	YES	YES	YES
Statistical Programming Study Lead, Blinded (Xiaoping Zhao)		NO	NO	NO	YES
Head, Pharmacovigilance (David Martin)		NO	YES	YES	YES
Pharmacovigilance Lead (Melissa Rossi)		NO	YES	YES	YES
Pharmacovigilance Lead, Blinded (b) (6)		NO	NO	NO	YES
Study Clinical Operations Lead, Blinded (b) (6)	NO	NO	NO	YES	

Program Clinical Operations Lead, Blinded (Conor Knightly)		NO	NO	NO	YES
Study Medical Writing Lead, (b) (6)		NO	YES	YES	YES
Program Medical Writing Lead, Blinded (Lakshmi Ramkumar)		NO	NO	NO	YES
Study Data Manager, Blinded (b) (6)		NO	NO	NO	YES
Clinical Biomarker Lead, Infectious Disease, Blinded (Rolando Pajon)		NO	NO	NO	YES
Senior Vice President, Regulatory Affairs (Charbel Haber)		NO	YES	NO	YES
VP, Regulatory Affairs Strategy, Infectious Disease (Carla Vinals)		NO	YES	NO	YES
Director, Program Management (b) (6)		NO	YES	NO	YES
Senior Manager, Regulatory Strategy (b) (6)		NO	YES	NO	YES
Senior Manager, Regulatory Operations (b) (6)		NO	YES	NO	YES
Senior Director, Regulatory Operations (b) (6)		NO	YES	NO	YES
Biomedical Advanced Research and Development Authority (BARDA)					
Chief Medical Officer and Director (Robert Walker)		NO	YES	YES	YES

¹If early success is demonstrated at an interim analysis and with DSMB recommendation, the Sponsor decides to unblind select Sponsor team members to prepare for the Emergency Use Authorization (EUA) submission, a CSR, and/or regulatory interaction, that interim analysis would be considered to be the Primary Analysis, and the Access to Unblinded Data at the Primary Analysis will be applied.

²Once unblinded, treatment group unblinded group will have access to aggregate summary statistics by treatment groups, but not to study participants' subject-level treatment information, with exception on SUSAR reporting or information on any death.

³Unblinding at participant level (tables and individual listings)

10 APPROVERS

Approver Role:	Name	Signature and Date
Moderna Chief Development Officer	Melanie Ivarsson	
Moderna Study Lead Biostatistician	Weiping Deng	
Moderna Program Lead Biostatistician	Honghong Zhou	
Moderna Statistical Programming Program Lead	Baoyu Ding	
Moderna Program Medical Lead	Brett Leav	
CRO (PPD) Lead Study Biostatistician – Blinded	(b) (6)	
CRO (PPD) Independent Biostatistician - Unblinded	(b) (6)	