Julius Clinical

Data Management Plan Signature Page

Full project title:	VASCO study (Vaccine Study COvid-19): A population-based prospective cohort study on vaccine effectiveness of COVID-19 vaccines in the Netherlands
Protocol Number:	N76815.056.21
Protocol Versions and Data:	v3.0, 03-Mrt-2021
Sponsor:	Dutch Ministry of Welfare and Sports

Data Management Plan Version:	v1.0
Data Management Plan Date:	05-May-2021
Data Management Plan Author(s):	5.1.2e Julius Clinical

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Data Management Plan Signature Page

The Data Management Plan for the project entitled:

"VASCO study (Vaccine Study COvid-19): A population-based prospective cohort study on vaccine effectiveness of COVID-19 vaccines in the Netherlands"
Short name: VASCO

has been reviewed and approved.

REPRESENTATIVES OF CRO(s)

Having reviewed the Data Management Plan for this project, I approve the procedures and standards as described therein.

5.1.2e

Project Manager - Julius Clinical

Date (dd-Mmm-yyyy) 06-May-2021

Signature 5.1.2e

Lotte Smets

Manager Data Management - Julius Clinical

Date (dd-Mmm-yyyy) 06-May-2021

Signature 5.1.2e

The Data Management Plan will be reviewed yearly by the Julius Clinical Lead Data Manager or when procedures need to be updated.

Data Management Plan

VASCO study

VASCO study (Vaccine Study COvid-19): A population-based prospective cohort study on vaccine effectiveness of COVID-19 vaccines in the Netherlands

Sponsor	Dutch Ministry of Welfare and Sports
Protocol Number	N76815.056.21
Document Version	1.0
Issue Date	05-May-2021
Author	5.1.2e

Review and Approval

The original signature page of the approved Data Management Plan (JC.Template.264-Data Management Signature Page) is filed in the Trial Master File (TMF).

Julius Clinical

Data Management Plan

CONTENTS

Data Management Plan

1. Purpose and Scope

The purpose of the Data Management Plan (DMP) is to describe which Data Management (DM) services will be provided for the VASCO clinical project and how these services will be organised, setup and executed from set-up until clinical project closure.

The DMP describes the underlying DM processes which govern collection, management, review and reporting of data from a clinical project. The content of this plan includes, but is not limited to, timelines, DM procedures including data collection and data flow. It documents as well the validation strategy and tools and its references and responsibilities for different DM tasks.

A DMP is managed by a Data Manager and is provided in addition to the protocol for the VASCO clinical project which contains the overall clinical plan for the project, and the Project Plan, which contains the overall operational plan for the clinical project.

The DMP will be made available for the project team in the Trial Master File (TMF), section Data Management Plan.

2. Data Management Tasks and Timelines

DM tasks applicable for VASCO clinical project refer to service agreement between RIVM and Julius Clinical.

The timelines for DM processes are interconnected with the timelines of the clinical project. A delay in one timeline will cause delays in the subsequent timelines. DM will inform the Julius Clinical Project Manager (PM) about the time necessary to fulfil tasks and also notify the PM when timelines are under pressure.

Additionally, a Data Management Review Log (JC.Template.205a) will be created to document all the data review activities which will be performed by DM for VASCO clinical project and as specified in the Data Review Plan. Any deviations from the review timelines will be documented in this log as well and will be made available in the TMF. The Data management review log will be available in the Trial Master File (TMF), section data management, data review.

3. Data Management Training

The training requirements per project team role are described in Project Specific Training Overview which is located at TMF. It provides an overview of all project specific training that the project team and site staff is required to complete, prior to performing any project related activities.

4. Applicable Procedures

All SOPs and WIs used for this clinical project are listed in the Appendix 1 and throughout the body of the DMP.

Any deviations from the procedures described in this DMP and which cannot be documented on the Data Management Review Log will be documented in a Process Deviation Report (JC.Template.108-Process Deviation Report) which will be forwarded to the Project Compliance Manager (PCM) of Julius Clinical for review and to the Project Manager (PM) for signing off.

In addition to the DMP, a Project Research Plan (PRP) will be available for this clinical project.

5. Project training

Who should be trained, and how training has to be given, for processes and documents regarding DM activities for the VASCO project will be documented in the Project Specific Training overview, see Project Research Plan (PRP). Training on the use of the YourResearch portal is further explained in section 12.1 database user training of the DMP.

6. Risk Management

The DM risks identified during the clinical project's lifecycle will be documented in the Risk Management Plan (JC.Template.002d) by the Responsible Project Lead (PM) with support of DM and evaluated on detectability, likelihood and impact. The (potential) severity of the risk will be calculated automatically. Identified risks that affect the way data is validated will be captured in the DMP.

7. Communication

7.1. Project Team Contact List

For all the project team contacts, please refer to the Project Contact Information list (JC.Template.222) available in the TMF.

7.2. Scheduled Meetings for DM

During the set-up phase of the project, meetings will take place between DM, RIVM, YourResearch, and other project team members as is deemed necessary. The primary goal of such meeting will be to discuss the status of the project with regard to planning and operations as well as strategic considerations concerning the database design. The discussions will result in the final database specifications; therefore no meeting minutes will be taken. Similar process will be followed in case of database changes when required during the study conduct.

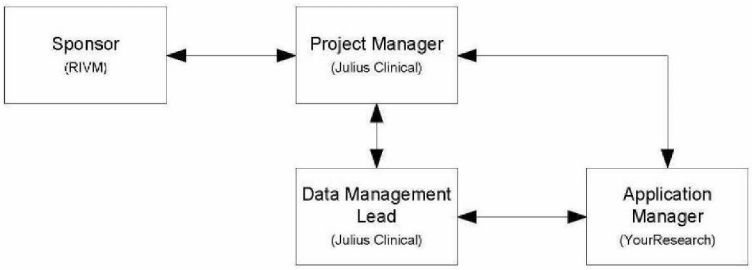
During the conduct phase of the project, meetings with DM, Project team members and YourResearch will be scheduled on an ad-hoc base and only if required.

Any additional meetings involving DM will be described in the Communication Plan which will be maintained and distributed by the Julius Clinical PM.

7.3. Communication/Escalation Plan

In case any issues are discovered by DM that could jeopardize the execution of the project, the Julius Clinical PM will be informed immediately. The PM will decide whether further escalation is needed.

The Data Management team structure and escalation pathways during the clinical project with the EDC vendor (YourResearch) will be as follows:



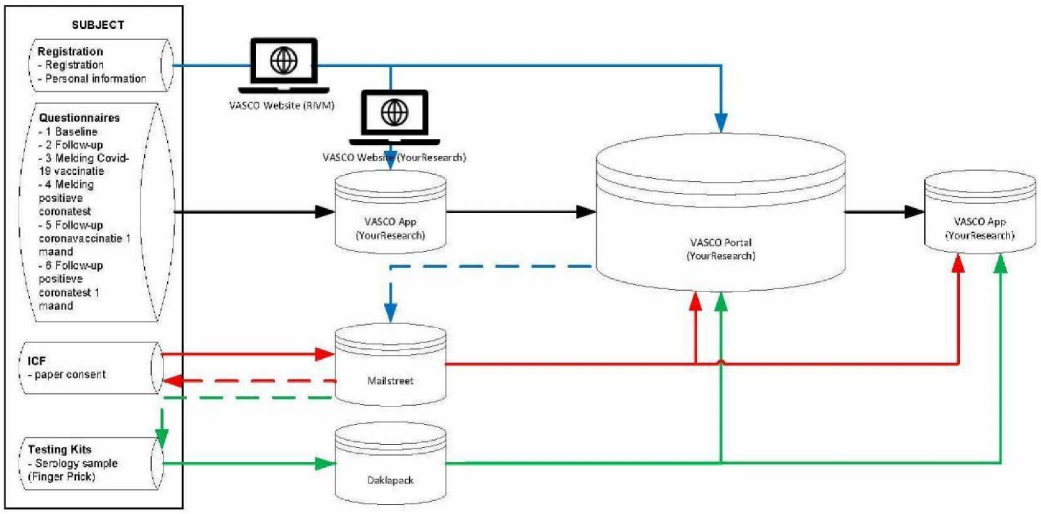
8. Data Management Document Review and Approval

The following Data Management documents require the approval from Julius Clinical PM.

- Database Approval and Release (if applicable according to YourResearch SOPs)
- Database Changes (if applicable according to YourResearch SOPs)
- Data Management Plan
- Data Review Plan
- Data Management Report
- Database Lock Plan
- Database Lock

9. Project Data Flow

9.1. Project Data Flow



9.2. Data Collection Methods

The table below summarizes all data collection methods and agreements as applicable for the VASCO project.

Data Source	Method of Collection/ Transfer	Specifications/ Agreements	Responsible Organisation
Questionnaires	Data Entry, Data import	Database Specifications	YourResearch / Julius Clinical
Finger Prick information	Data Entry, Data Import	Data transfer specifications	Daklapack / Julius Clinical
ICF information	Data Entry, Data Import	Data transfer specifications	Mailstreet / Julius Clinical

9.3. Data Collection Help

A YourResearch User Manual will be made available by YourResearch before the start of the project. The YourResearch User Manual will be maintained by the DM team throughout the project. The manual will serve as a reference document for the day-to-day activities performed by the project team.

10. Database Design

YourResearch will set-up the clinical database using the YourResearch app and platform. For the VASCO project, only blinded information will be stored in the clinical database.

10.1. Database Set up

Julius Clinical will subcontract the design and set-up of the database to YourResearch. Julius Clinical will manage subcontracted activities by scheduling regular meetings, tracking of progress and escalation of issues to ensure agreed timelines are met and required quality standards are adhered to. YourResearch will develop the app/platform in accordance with their own procedures. JC.SOP.018-Database Design will only be applicable for User Acceptance testing (UAT).

10.2. Database Testing and UAT

YourResearch is responsible for testing and validating the database before releasing it for User Acceptance Testing (UAT). UAT will be performed by Julius Clinical / RIVM / UMCU project team and the respective end users.

The UAT test plan will be described in more detail in the UAT Plan (JC.Template.267).

10.3. Database Changes

In case the database needs to be modified due to a protocol amendment, or any other reason, YourResearch and/or Julius Clinical DM will be responsible for implementing the modifications. The change process from YourResearch will be followed when incorporating the changes. Approval by the PM is required before implementation of the changes into the live database.

10.4. Subject Enrolment

Subject ID

Data for all subjects participating in the project will be entered into the YourResearch platform. Subject numbers will be assigned automatically by the EDC according to predefined subject numbering convention which will be specified in the Project Research Plan.

11. System Availability and Assistance Plan

YourResearch has the right to take its systems, services, networks or parts out of operation for the purpose of maintenance, adjustment or improvement. YourResearch will notify Julius Clinical in due time of this scheduled taking out of service and will attempt to schedule it as much as possible outside working hours. The aforementioned limited intervals shall not be applicable in situations wherein longer downtimes are necessary for the security of YourResearch's systems, the service or the data – e.g. (attempted) hacking. Emergency maintenance (e.g. updating essential security software) may be performed by YourResearch at any time. Further details are described in the Service Level Agreement (SLA) between YourResearch and JuliusClinical.

12. Database Training, Database Access and User Management

YourResarch's SOPs will be followed for setup of database access and user management. The VASCO platform will be accessible via role-based permissions, as defined in Database Roles Specifications. Database Roles Specifications will be filed in the TMF.

12.1. Database User Training

Before being granted access to the database, project team members must complete the YourResearch training. Except for users that require Read-Only access to the EDC system, then approval from the Julius Clinical PM is sufficient.

The training requirements per project team role are described in Project Specific Training Overview (JC.Template.277) which is located in the Trial Master File (TMF), section Global Training. Completed training will be tracked in the Project Specific Staff Training Record (JC.Template.077) by the Julius Clinical DM and will be located in the Trial Master File (TMF).

YourResearch will provide accompanying training materials to PCM who will ensure that these training materials are available to the team in the TMF.

12.2. Database User Management Process

12.2.1. Creation and Activation of User Accounts

Access to the YR platform should be requested according to the below procedure:

- Project team: Access for project team members (internal/external) should be requested by the Julius Clinical PM via email (5.1.2i Functionele emailadressen@juliusclinical.com) after confirmation that the applicable training is completed and documented appropriately.

For eCRF account creation the following information needs to be provided per user:

- First name
- Last name
- E-mail address
- YourReasarch user role

Based on the provided information Julius Clinical DM will update VASCO User activation tracker.

12.2.2. Changes/Deactivation of User Accounts

In case the eCRF account needs to be changed/deactivated (when staff is leaving the project for example) the following procedure should be followed:

- Project team: The user account change/deactivation should be requested by the Julius Clinical PM via email (5.1.2i Functionele emailadressen@juliusclinical.com).

Based on the provided information Julius Clinical DM will update VASCO User Activation Tracker and deactivate the account. The user account will be deactivated within one working day.

12.3. Database Help (helpdesk/technical support)

First level support for the participants will be provided by a Julius clinical helpdesk. In case of any issues or questions raised by participants, they should contact the helpdesk to follow up on the issue. The helpdesk can be contacted via email 2i Functionele emailadres@juliusclinical.com or telephone (+31(0)5.1.2e 5.1.2e during the Julius Clinical working hours (08:30 – 17:00)

Items that cannot be solved at the first level support will be escalated to Julius Clinical Data Management. If DM cannot resolve the issue, they will escalate to YourResearch. YourResearch will be available during European business hours (09:00 – 17:00) Monday to Friday except public holidays. YourResearch will inform JC DM of days when the office is closed and any other periods when second level support may not be available.

13. Data Collection and Data Review

Data collection and data review will be performed according to JC.SOP.021-Data Collection and Data Review. A Data Review Plan (DRP) (JC.Template.047) will be developed, before the first data review/monitoring activities start, in which all data review activities being performed by the project team will be described. In the DRP the applicable tools, procedures/instructions and quality control steps will be outlined per activity and the responsible party, including data review performed by DM. In addition, the DRP will specify the actions to be taken during the data review process and will provide the clean data definition. The DRP will be filed in the TMF.

14. Database Lock and Export

14.1. Database Lock

Database lock will be performed according to JC.SOP.023-Database Lock upon approval from the Sponsor. Database lock will be performed at the end of the project when all project data is entered into the YR platform and all review activities are completed. All the necessary steps taken before the Database lock will be listed on Database Lock checklist (JC.Template.049).

After the Database Lock is completed the Data Management Report (JC.Template.205) will be finalised. The Data Management Report (DMR) will summarize the execution of the DM activities performed for VASCO project and verify the actual conduct of these activities against the agreements as set forth in the project DM specific plans that were effective during the lifecycle of the project.

In the DMR any deviations from the final DMP will be documented as well in order to illustrate further the status and quality of the data in the database during the time of database lock. Any mutually upon agreed outstanding/irresolvable data issues, data anomalies, missing data, etc. (inclusive of external third party/Safety data) will be also documented accordingly in the DMR. The DMR will require approval from Merck and Julius Clinical PM.

14.2. Database Unlock

In case any changes are required to the database after it has been locked, the database will be unlocked upon approval from the Julius Clinical PM. Only those changes that are deemed critical or significant errors that may affect the overall analysis will be considered for unlocking the database. Unlocking the database will be documented by the DM on Database Lock checklist.

14.3. Database Export

YourReseach's SOPs will be followed for the database export and distributing the datasets. Final datasets will be exported by YourRearch and/or Julius Clinical DM from the YourReasarch platform and filled in the TMF. Final datasets will be provided to the Sponsor and Statistician via MS Teams.

15. Reports

Data Management will provide project metric reports and listings to UMC Utrecht, RIVM and the VASCO project team during the conduct phase of the project. DM will responsible for compiling and distributing project metric reports according to the agreements made throughout the project. An overview of all the reports and metrics created will be attached to DMR.

16. Filing and Archiving

JC.SOP.057-Data Management Project Closure will be followed for the project closeout.

16.1. Documentation Filing and Archiving

Each party involved in executing the DM activities shall be responsible for maintaining accurate and complete essential project specific documentation. Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. Julius Clinical DM shall maintain documentation in the TMF in accordance with the guidelines and file structure as outlined in the PRP.

In addition, YourResearch will provide a copy of the final YR set-up and QC documentation to Julius Clinical. This includes, but is not limited to, the specifications, validation/test documentation and sign-offs.

16.2. Data Filing and Archiving

The complete data from the YourResearch platform and its audit trail will be provided by YourResearch to Julius Clinical on secure electronic storage media prior to decommissioning of the systems and as per agreements specified in Archiving Files Specifications (JC.Template.207). Thereafter the database will be decommissioned (JC.Template.206).

17. Backup and Security

For the backup and security of the Julius Clinical systems used in the VASCO project JC.SOP.009-Backup and Restore will be followed.

The YourResearch platform will be hosted by Microsoft Azure which maintains highest standards for back-up and security of the system applications and data. Unauthorised access to the systems and data will be prevented by maintaining adequate security measures by Microsoft Azure, YourResearch and Julius Clinical, which include restricted access to hardware locations, instalment of firewalls and virus detection/prevention software and access restriction via authorised username and password restrictions. The YourResearch platform will be accessible via role-based permissions, as defined in Database Roles Specifications. Database Roles Specifications will be filed in TMF.

18. Abbreviations and Definitions

Abbreviation	Explanation
CRA	Clinical Research Associate
DLP	Database Lock Plan
DM	Data Management / Data Manager
DMP	Data Management Plan
DMR	Data Management Report
DRP	Data Review Plan
JC	Julius Clinical
PM	Project Manager
PRP	Project Research Plan
SOP	Standard Operating Procedure
TMF	Trial Master File
UAT	User Acceptance Testing

Term	Explanation
YourResearch Platform	YourResearch platform, this system will be used to collect the clinical data.

19. Revision History

Version	Author	Issue Date	Changes To Previous Version
1.0	5.1.2e	05-May-2021	Not applicable, initial version

Julius Clinical

Data Management Plan

Appendix 1

This Data Management Plan is based on the following procedures:

Standard Operating Procedures (SOPs)

Internal Reference	Full title
JC.SOP.009	Backup, Restore
JC.SOP.016	Data Management Project Set-up
JC.SOP.018	Database Design (partially)
JC.SOP.021	Data Collection and Data Review
JC.SOP.023	Database Lock
JC.SOP.032	Project Document Management
JC.SOP.057	Data Management Project Closure

External Reference	Full title
NA	NA

Working Instructions (WIs)

Not applicable

Manuals

Not applicable

Other

Not applicable

In case new versions are released of the Julius Clinical, YourResearch, 3rd party SOPs, WIs, other procedures or accompanying document templates that are used for the development of the Data Management Plan, the impact on the Data Management Plan is assessed by the PCM, with support of DM and the PM, and it will be decided if the new version(s) will be implemented for this project. This will be documented on the Impact Assessment Form (JC.Template.144) and shared with the PM.

In case no PCM is assigned to the project, the PM will perform the impact assessment with support of Data Management.