NOR-WGS-NIPH

D3.1:

Evaluation plan

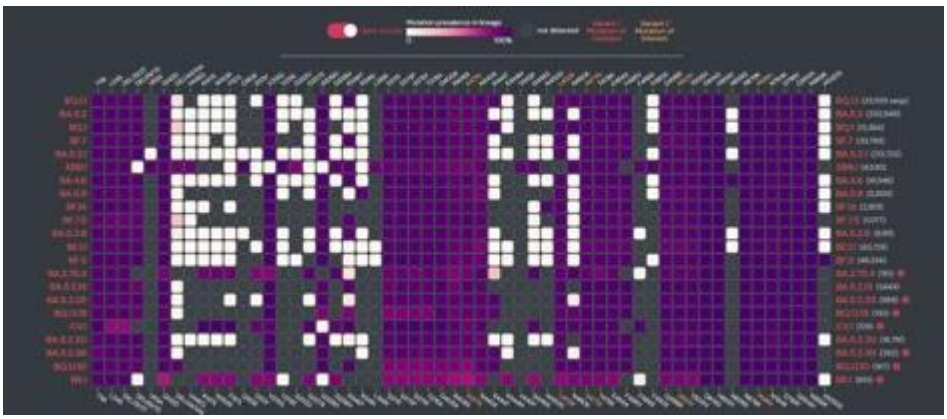

Photo: Visualization of the outbreak investigation

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List of acronyms / abbreviations

Abbreviation	
D	Deliverable
ISO	International Organization for Standardization
IT	Information technology
LIMS	Laboratory Information system
M	Month
MS	Milestone
NOR-WGS-NIPH	Consolidation of the HERA-WGS-infrastructure and capacity building at NIPH to enhance microbial surveillance and preparedness
SOP	Standard Operating Procedure
PCR	Polymerase chain reaction
QA	Quality Assurance
WP	Work Package

1 Introduction

1.1 Background

The Norwegian Institute of Public Health (NIPH) is the national infection control institute in Norway and is the national reference laboratory for a total of 30 bacteria and viruses. Microbial surveillance is an essential part of the NIPH laboratory activity. The role as reference laboratory covers research, laboratory-based surveillance and characterization of pathogens, outbreak investigations and response, as well as specialized microbiological assays.

We received in 2021/2022 a grant from HERA for enhancement of whole genome sequencing (WGS) infrastructure and capacity at our institute, with COVID-19 response as the main aim. Within the HERA-financed project, we have focused on laboratory automation and digitalization. We have purchased pipetting robots and barcoding system, and we have worked with integration of laboratory instrumentation in the SARS-CoV-2 WGS workflow with our laboratory information management system (LIMS). In addition, we have further developed our LIMS to serve as a database for all laboratory results for more efficient downstream sequence analysis.

We aim to consolidate the achieved deliverables from the HERA grant on SARS-CoV-2, and further strengthen and expand our microbial WGS as well as other genomic based analyses. As described in the application we will do this by:

- automation of our laboratory workflow, including digitalisation of instrument data,
- expanding the current WGS activity to several pathogens
- developing downstream visualisation and reporting platforms

The project is organised into seven work packages (WP1-7). The main monitoring and project management tasks are organized under WP1, which overarches the entire project. WP2-4 will ensure that the activities and results from the three technical WP's (WP5-7) are also executed in a way that we can disseminate our activities (WP2), evaluate the project progress and effectiveness (WP3), and ensure sustained value also after the funding period (WP4).

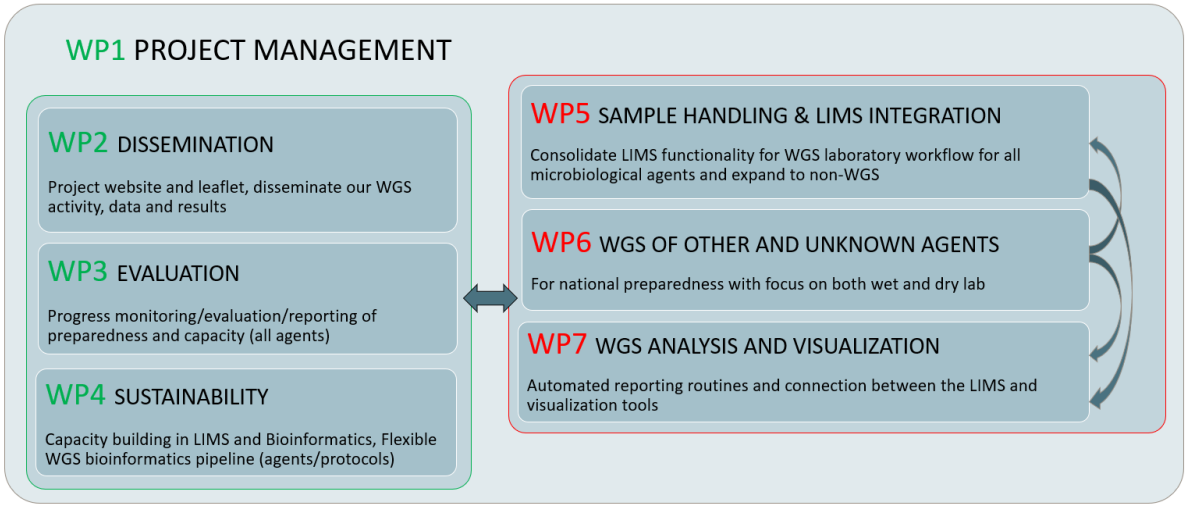

Figure 1 Overview of the project structure

1.2 Purpose and scope of the evaluation plan

This evaluation plan describes how progress monitoring and evaluation of the achievements in the projectis going to be carried out. The document will be updated when necessary throughout the project lifetime to reflect changes and clarifications.

Evaluation (WP3) aims to

I. measure the progress of the project by monitoring that tasks, milestones and deliverables are progressing according to plan and completed on time.
II. measure the effectiveness/outcomes of the project in meeting the specific objectives, especially LIMS functionality regarding data in/out and laboratory workflow.

2 Progress monitoring and evaluation

2.1 Roles and responsibilities

Evaluation activities will be mostly carried out by the project staff. In addition, the Project Steering Committee (PSC) composed of coordinators and WP leaders will be involved in the evaluation activities and will present and discuss the evaluation results at the regular SB meetings. They will also prepare progress monitoring and evaluation reports as well as carry out risk assessment and organise evaluation workshops.

2.2 Progress monitoring and reporting

Progress monitoring entails regular meetings and progress reporting by the project staff and the PSC. Project monitoring will be carried out quarterly to evaluate and document the progress.

The progress report includes:

- Monitoring tasks, milestones and deliverables according to plan (table 1-3). Tasks are indicated as according to plan (light green), completed (dark green), started (yellow), if initiated before plan, and delayed (red). If delayed, a risk assessment must be conducted and measures must be considered.
- Specific achievements for the respective reporting period.
- Training (D4.1), validation (D4.2) and SOPs (D4.3).
- Any deviations from the plan.

For monitoring progress in WP5, which is a complex WP with many actors involved, risk assessment will be performed monthly and reported along with a progress update to the digitalisation project management at NIPH. This format is used for all digitization projects in NIPH and is only included in the quarterly progress report in case of deviation.

The workgroup for WP5, have weekly meetings for all involved, where issues and progress is discussed. Subcontractors are followed up through weekly meetings. The coordinator raises matters to the project board if they can’t be resolved within the WP.

2.3 Evaluation

The automation in lab is related to improved LIMS functionality, by direct import of results to LIMS for all NGS analyses from scripts and instruments, support for laboratory workflow like selection and priority of samples, indexes, calculations, and export of data from LIMS to down-stream processing and analysis. Molecular methods such as PCR may be a part of the NGS workflow or separate workflow with direct import of results. The effectiveness and outcome of the new functionality will be monitored by key performance indicators (KPI's) as defined in table 1. These specific key indicators shall facilitate monitoring and evaluation of the project activities implementation by setting up baseline and target. The expected outcome is time and resources saved for data handling, better quality by reducing manual registration and generation of more comprehensive data into LIMS. This will be addressed in the LIMS integration report (D5.1), indicators related to sequence capacity and sharing of sequences will be addressed in the Sequence data sharing report (D7.3). Baseline is defined as before October 1 st 2022. The baseline values are further defined in table footnotes.

TABLE 1 – KEY PERFORMANCE INDICATORS (KPIS) AND ASSOCIATED SPECIFIC OBJECTIVES.

Indicators (KPIs)	Baseline	Target	Related Specific Objectives	Responsible WP
Number of WGS workflows and microbiological agents implemented in LIMS	0	Influenza, HCV & SARS-CoV-2, all 14 bacterial WGS work-flows	Consolidate LIMS functionality for WGS	WP5
Number of reported deviations in registration of data[1]	12	0 by M18, 0 by M39	Quality in results	WP5
Reduction in time for data handling HCV-WGS (minutes)	Manual typing of HCV-results, 15 min per sample	Automated import to LIMS, < 1 min	Registration of results in LIMS	WP5
Number of genomic based workflows (non WGS) that have been implemented into our LabWare LIMS	1	All pathogens using the Rotorgene PCR instrument	Develop LIMS functionality	WP5
Reduction in time for data handling PCR (minutes)	Manual typing in sample sheets and LIMS, 1 hrs per run	Automated import to LIMS, < 1 min	Develop LIMS functionality to support the data handling	WP5
Number of external labs that are connected through the LIMS-LIMS integration for electronic export of laboratory analysis results	0	2 by M18, 4 by M39	Develop LIMS functionality to support electronic export to external laboratories.	WP5
Number of external labs that are connected through the LIMS-LIMS integration for electronic requisitions	0	0 by M18, 2 by M39	Develop LIMS functionality to support electronic requisition from external laboratories.	
Number of pathogens for which we have a working WGS protocol [2]	16	17 by M18, 20 by M39	Develop WGS protocols for agents with severe outbreak or disease potential.	WP6

Processing time for NGS protocols[3]	X hours/days Hands-on time	X hours/days Hands-on time	Establish reporting and visualization routines for WGS related metrics and results.	WP5, WP7

[1] From 1st September to 31st December 2022 there were 7 deviation, from 1st of January 2023 until 31st of August there were 4 deviation and 1 external complain.

[2]Number of pathogens for which we have a working WGS protocol are 16 at baseline (SARS-CoV, HCV and 14 bacterial agents), by M18 rotavirus will be implemented and by M39 unknown pathogen protocol, HBV, Rotavirus and enteroviruses will be implemented.

[3] For processing time there will be an indicator for time from batch to registration of results and hands-on time per sample from sample registration to results for WGS workflow.

2.3 Evaluation reports

The main aim of the evaluation is to assess achievements in the laboratory workflow, in particular new functionality of the Laboratory Information Management System development (LIMS). The evaluation is divided into two periods resulting in two evaluation reports. The Midterm evaluation, D3.2 is due in month 20 and the End of Project evaluation, D3.3 is due in month 39. In addition, there are the LIMS integration report and sequence sharing report that will further describe the impact of the project.

Table 2 - List of deliverables related to evaluation and their content.

Deliverable	*Description of content*	*Due date*
D3.1 Evaluation plan	*Evaluation plan*	*Month 12*
D3.2 Midterm evaluation	Evaluation of the project, based on progress report Q2 2024 (2.1), identifying any needs for adjustments to the project progress, including, risk management and list of training actives, validations and SOPs, effectiveness (2.2)	*Month 20*
D3.3 End of project evaluation	Evaluation of the project, based on progress report Q2 2024 (2.1), including, risk management and list of training actives, validations and SOPs, effectiveness (2.2), as well as the impact of the various outcomes	*Month 39*
D5.1 LIMS integration report	Description and overall results /tasks under LIMS integration.	*Month 39*
D7.3 Sequence in public domin	Sequence data sharing report. (ENG)	*Month 33*

2.4 Implementation of high quality

Laboratory quality assurance

The laboratory follows a quality assurance (QA) system that is based on the ISO 17025 standard to ensure quality and traceability of all procedures in the laboratory. All new methods that are implemented in the laboratory require a validation plan (Template in Annex 1) before starting the validation, as well as a validation report (Template in Annex 2) before implementation of the protocol. The validation is based on a set of criteria defined in the quality assurance system. In addition, all

laboratory analytic tests are supported by a Method description (Template in Annex 3), SOP (called AR in our system) (template in Annex 4) and worksheets.

Validation of IT-systems is also validated as part of the quality assurance system using a separate IT-specific template. All these documents are handled in "Documentum" with restricted access and in Norwegian.

Validation reports and SOPs for new laboratory analysis and/or LIMS functionality are deliverables in the projects, as they are documentation for the implementation of these, as well as ensures the quality of the deliverable. The QA system has defined roles so that competent and responsible personnel approve the reports.

The laboratory has an own system for registration of improvements and deviations. All deviations from protocols are registered in the system. In case of a deviation, the deviation is registered in our deviation management system. Briefly, the process includes uncover and evaluate cause and consequences, implement action/measure, and then evaluate the result of the measure. If implemented measure has satisfactory result the deviation case can be closed (Figure 2). The deviation management system also includes processing of deviations, planned deviations (fravik) and complaints. More details about the process can be found in our SOP 710-FE-AR-001.

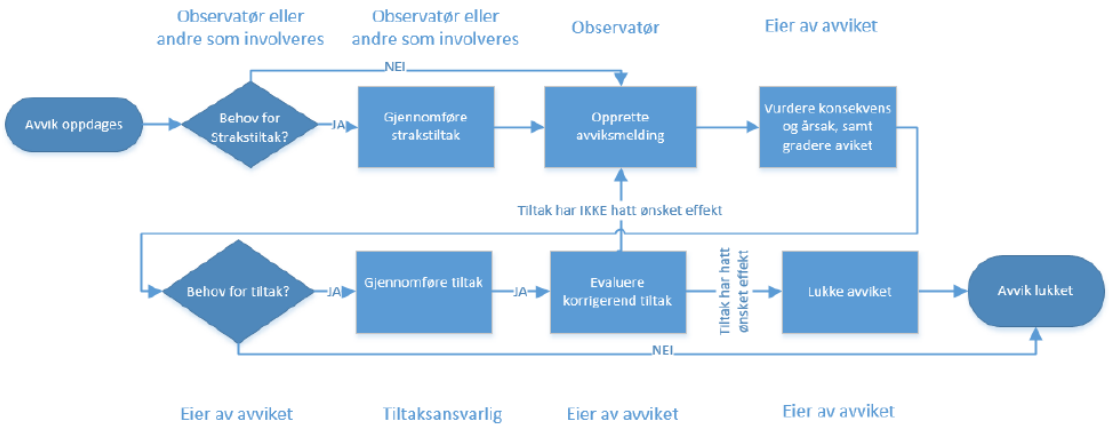

Figure 2: Flow chart of the deviation management process from QA document 710-FE-AR-001

LIMS functionality

All functionality in LIMS (WP5) will be tested by users and the lab coordinator in a test environment before implementation and hence reporting of results. The process is described in a validation plan and followed up in validation report for each package when deployed.

1 Template validation plan
2 Template validation report
3 Template method description
4 Template for SOP (AR)