



# D3.1 Baseline evaluation report on national needs

## Work Package 3: Enhancement & Consolidation of WGS- & PCR-based Methods for Public Health Action

Author(s): Irena Tabain, Ivana Ferenčak



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<b>Other authors</b>	Irena Tabain			
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## 1. EXECUTIVE SUMMARY

In the course of the first project round, the focus on national infrastructure and capacity up-scaling enhancing WGS and/or RT-PCR to respond to the COVID-19 pandemic and future health threats set a solid but challenging basis for the enhancement of processes in national health agencies and public analytic facilities. The priorities are now to consolidate these new processes. The consolidation of WGS and RT-PCR activities aims to ensure the sustainable use and integration of enhanced infrastructure into routine surveillance and outbreak investigation activities, in synergy with relevant ongoing work at the international level is the key priority.

The COVID-19 pandemic aggravated the existing shortcomings that have to be tackled as soon as possible to improve the WGS workflow in terms of speed, efficiency, costs, and high-throughput analysis in general but also in terms of preparedness for future epidemics and pandemics.

This deliverable D3.1. “Baseline evaluation report on national needs“ is based on a survey that the Consortium conducted. The survey was distributed between partners and relevant stakeholders to evaluate different national needs and possible gaps for laboratory-integrated surveillance for respiratory and gastrointestinal diseases through a systematic and objective assessment of the relevance, efficiency, effectiveness, and sustainability of the existing systems.

## 2. LIST OF ABBREVIATIONS

<b>EU</b>	European Union
<b>NGS</b>	Next Generation Sequencing
<b>RT-PCR</b>	Reverse Transcription Polymerase Chain Reaction
<b>WGS</b>	Whole Genome Sequencing
<b>WHO</b>	World Health Organization
<b>ECDC</b>	European Centre for Disease Prevention and Control
<b>AMR</b>	Antimicrobial Resistance
<b>ILI</b>	Influenza-like Disease
<b>SARI</b>	Severe Acute Respiratory illness

## 3. BACKGROUND OF THE PROJECT

The goal of this 42-month-long project is to establish stable WGS and RT-PCR processes in four relevant national institutions under the One Health approach with the aim of a more effective response to all current and future challenges during the outbreak, monitoring, and resolution of epidemics and other crises in public health.

The cooperation of these professional public health institutions will enable an interdisciplinary approach to global and One Health, aimed at mutual encouragement and the establishment of new highly specialized work processes.

The objectives of work package 3 are to sustain the increased RT-PCR capacity for COVID-19 diagnosis/pre-screening for circulating SARS-CoV-2 variants of concern and the established WGS capacity for the genomic surveillance of SARS-CoV-2, and the expansion to other pathogens for both surveillance and outbreak investigation purposes; to evaluate the different national needs for both outbreak investigation and surveillance using PCR/WGS as a baseline and post-project status; to enhance the clinical sentinel surveillance of ILI/SARI and gastrointestinal diseases with laboratory surveillance; to enhance the outbreak investigation of respiratory and gastrointestinal pathogens using PCR/WGS according to national needs; WGS-derived data on the resistome and resistance plasmids in outbreak strains from both clinical and environmental samples and WGS-based AMR monitoring via in-silico AMR-gene detection.

## **4. OBJECTIVES AND CONTENTS**

One of the objectives of work package 3 is to evaluate the different national needs and possible gaps for laboratory-integrated surveillance for respiratory and gastrointestinal diseases through a systematic and objective assessment of the relevance, efficiency, effectiveness, and sustainability of the existing systems. This deliverable describes the needs of the consortium partners regarding PCR and sequencing at the start of the project.

## **5. TOOLS**

The results of the survey were analyzed among partners and used in the creation of this deliverable.

## **6. PARTNERS' STATUS AT THE BEGINNING OF THE PROJECT**

The public health division at AGES established WGS to improve the detection and characterization of bacterial pathogens for surveillance and outbreak investigation. The number of sequenced and analyzed samples has been increasing constantly with slight adaptations of equipment and IT infrastructure. The task now is to develop a process for this new structure that incorporates past experience and outcomes and allows for optimal operations. The proposed measures to automate and upgrade the IT infrastructure (taking into account possible future upgrades in sequencing capacity) will enable high-capacity WGS, reduce costs, improve quality,

speed up analysis, and speed up reporting, leading to faster reporting and decision-making on measurements in case of public health threats.

CIPH participated in the HERA 1 grant to establish WGS as a public health tool for improving the detection and characterization of viral and bacterial pathogens for surveillance and outbreak investigation. This objective has been only partially met since procurement of equipment and consumables took a significant part of the project and Croatia implemented only SARS-CoV-2 surveillance. Through the HERA 2 project, CIPH will consolidate the infrastructure and develop new pipelines for pathogens of interest. Croatia will also implement a system that will tackle outbreaks and mainly cross-border threats. In addition, Croatia aims to develop an information system that enables public health to communicate and connect information, protocols, and results more efficiently.

NNK will continue the implementation and harmonization of the different standard operating procedures for the production and analysis of WGS data and bioinformatics tools previously developed for the identification of the different pathogens, using the infrastructure already set up in HERA 1. The aim is to expand and increase the current whole genome sequencing capacity and sequence-based surveillance. According to these goals, it is important to improve the quality and effectiveness of the analysis and speed up the diagnostic workflow and reporting process as well. This project will improve the diagnostic capacity, together with timely reporting of the information at the national and EU/EEA/WHO level.

In Greece, through the application for the HERA-Grant, both the central as well as the regional public health laboratories have been gradually equipped with the required infrastructure for RT-PCR and WGS, and have hired and adequately trained staff to implement RT-PCR and WGS protocols for the detection, diagnosis, and genomic surveillance of SARS-CoV-2. However, due to some unexpected delays in the procurement process and the subcontracting for the web-based platform, the overall design, development, and implementation have to be further optimized. With HERA 2, EODY will be supported to further develop a sustainable, efficient, and high-capacity RT-PCR and WGS infrastructure for national public health microbiology laboratories to provide timely and reliable surveillance for infectious threats and cooperate with the other three countries of the consortium to enhance the preparedness for future cross border epidemics.

## **7. DIFFERENCES AND SIMILARITIES**

Austria and Hungary already implemented genomic surveillance of certain pathogens and used HERA1 to expand their capacities with equipment, personnel, and IT infrastructure. Their focus now is on expanding, consolidating, and enhancing current workflows and establishing new ones.

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Croatia and Greece used the HERA 1 grant to kickstart their genomic surveillance path. Both Croatia and Greece managed to acquire the necessary WGS equipment and IT infrastructure for high throughput SARS-CoV-2 sequencing and employ and educate personnel for wet lab and dry lab analysis. Both countries are planning to expand their capacities for molecular diagnosis and NGS analysis for other pathogens as well.

Taking into account the different levels of implementation of the genomic surveillance of outbreaks, cross-border threats, and the implementation of RT-PCR and WGS methodology between the consortium partners, we do not aim to achieve the same level of public health readiness for outbreaks but rather to substantially improve current status through common efforts and knowledge sharing.

While the specific objectives are identical for all partners, as each aspect will be leveled up, enhancements of different scales will be facilitated, and strong impulses for the further development of these areas are an essential part of the grant concerning consolidation and harmonization.

As was observed through inter-consortial communication, the prices of the same sequencing instruments and reagents across different EU countries are highly variable. For this deliverable, we tried to compare the prices of a couple of instruments and reagents of the same manufacturer that all partners own and use (VAT excluded). The analysis showed that the same instrument is in one partner country almost 30% more expensive than in others. With reagents are differences even more obvious, as, for example, the price for the main disposable unit of the same instrument is more than 50% different across partner countries.

## 8. NATIONAL NEEDS ANALYSIS

Resources		AGES	CIPH	EODY	NNK
Equipment					
	RT-PCR	There is no need for additional equipment.	There is no need for additional equipment.	There is no need for additional equipment.	There is no need for additional equipment.
	Short-read sequencing	Fully equipped (MiniSeq, NextSeq 2000 and Miseq)	Fully equipped (MiniSeq, NextSeq 550)	Fully equipped (MiSeq, NextSeq 2000, Ion Torrent S5)	Fully equipped (MiSeq, Nextseq550, ISeq)
	Long read sequencing	Fully equipped (1 Gridion, 5	There is a need for high-throughput	Only two of the regional public health	Mk1C and Gridion devices are available



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		Minion) at the moment	equipment to lower the cost per sample.	laboratories have Minion, so there is a need for the Central Public Health Laboratory to obtain one as well.	
	Additional equipment	If demand for long-read sequencing increases, Promethion or another Gridion will be needed.	Bio-bank organizers for an efficient sample and isolate storage.	Complete the integration of software tools, for automated submission of the results.	
Reagents		Reagents for all phases of the analytical workflow are needed.	Reagents for all phases of the analytical workflow are needed.	Reagents for all phases of the analytical workflow are needed.	Reagents for all phases of the analytical workflow are needed.
Personnel		There is need for trained personnel in the wet lab but also for sequence analysis. This include microbiologists with genomics knowledge and bioinformaticians.	Sufficiently staffed for current and additional workflow.	as Greek partners are a consortium of three public health laboratories, there is a need for more than a dozen additional personnel, namely junior technicians and bioinformaticians.	Senior scientists, Junior scientists and bioinformaticians needed.
IT Infrastructure		As the obsolescence of IT tools is highly variable, continuous improvement is necessary.	As the obsolescence of IT tools is highly variable, continuous improvement is necessary.	As the obsolescence of IT tools is highly variable, continuous improvement is necessary.	As the obsolescence of IT tools is highly variable, continuous improvement is necessary.

## **9. CONCLUSIONS AND NEXT STEPS**

The conducted survey showed that the consortium partners' baseline start is different and consequentially are their needs. This difference is also visible in the individual budget plans. The next step is to connect the data from this deliverable with implementation plans, to start with procurements, and to work toward the project's final goals, which are to develop reliable RT-PCR and WGS protocols, bioinformatic pipelines, and data-sharing platforms. The different instrument and reagents prices also have an effect on national needs and we believe that this is an issue that needs to be addressed at the EU level.