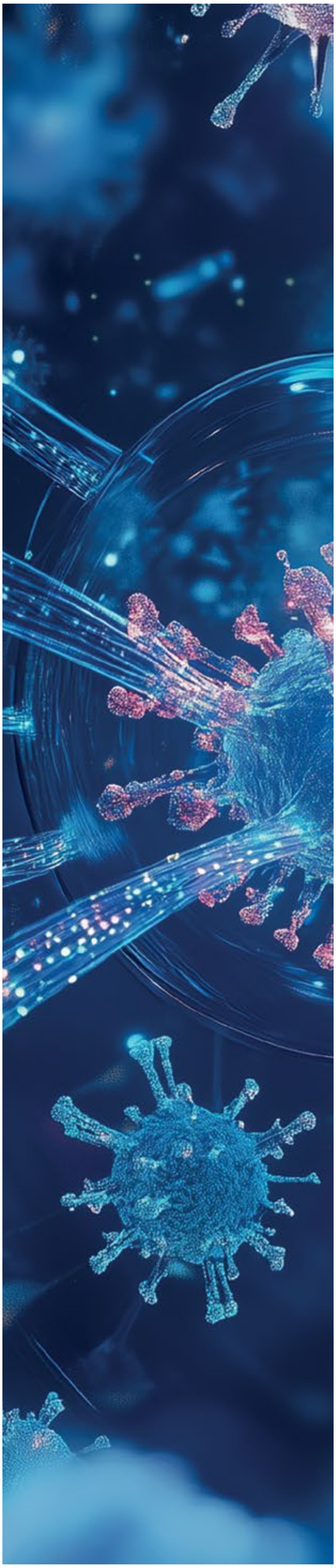
GENOMIC SURVEILLANCE

SEQ4EPI

STRENGTHENING PATHOGEN SURVEILLANCE THROUGH SEQUENCING

Co-funded by
the European Union

EU4HEALTH programme funded by the European Commission. Approval no.: 101113174



SEQ4EPI: improving integration of genomics into epidemiological surveillance

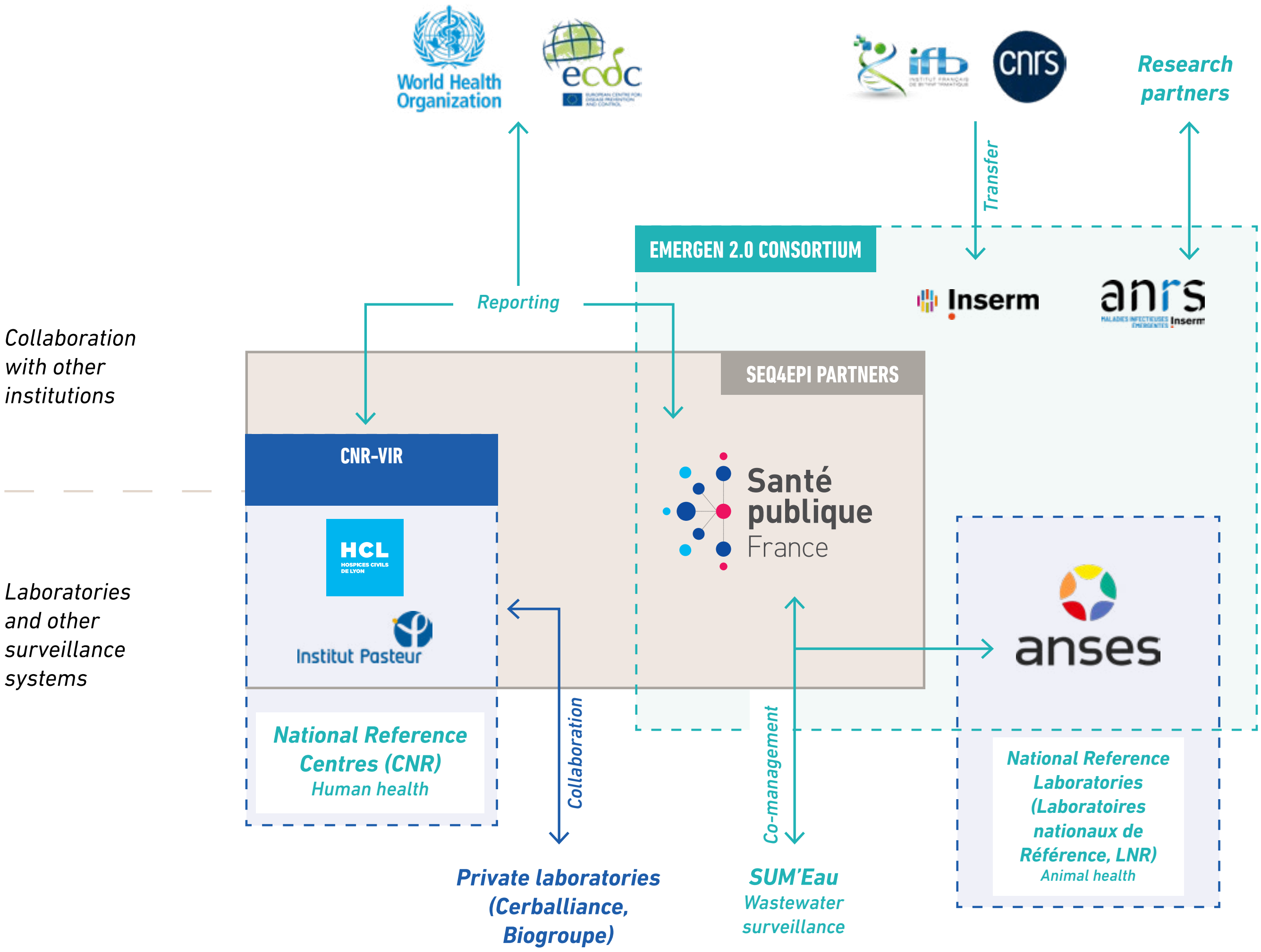
SEQ4EPI (sequencing of pathogens for epidemiology), a project led by Santé publique France and the National Reference Centre for Respiratory Infection Viruses (Centre national de référence des virus des infections respiratoires, CNR-VIR), is funded by the European Commission. Its objective is to enhance the surveillance of infectious diseases in France by using pathogen sequencing. In concrete terms, this means analysing the genetic material of viruses and other microbes to help improve our understanding of their spread and evolution.

To this end, SEQ4EPI relies on a structured network of French laboratories and institutions and partnerships with, in particular, the ANRS Emerging Infectious Diseases (Maladies infectieuses émergentes, MIE) and the French Agency for Food, Environmental and Occupational Health and Safety (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail, ANSES), as well as with international institutions. The objectives of this collaborative approach are to scale up the coordination of genomic surveillance projects and develop bioinformatic, phylogenetic and phylodynamic analysis tools to improve monitoring of viral epidemics. It also aims to maintain a team of epidemiologists working to coordinate this network of partners and integrate this data for monitoring, alert investigation and risk analysis.

By building on the achievements of the EMERGEN consortium created in January 2021 to respond to the challenges of the COVID-19 crisis, SEQ4EPI is helping to widen its aims to cover other pathogens, leading to improved anticipation of health risks and preparation of responses to future epidemics.

The goal of SEQ4EPI is to improve how data from pathogen sequencing is integrated with epidemiological data so that we can continue to improve the detection and monitoring of infectious diseases in France and respond rapidly to future health crises.

The EMERGEN consortium was set up in 2021 during the COVID-19 epidemic to monitor the genetic evolution of SARS-CoV-2 and detect the emergence and spatio-temporal distribution of variants of this virus. Coordinated by Santé publique France and the ANRS-MIE, it relied on a network of public and private laboratories and a centralised database (EMERGEN-DB). It led to the deployment of genomic surveillance capabilities throughout France to complement and strengthen those of the National Reference Centre for Respiratory Infection Viruses. It brought together both monitoring and research activities.

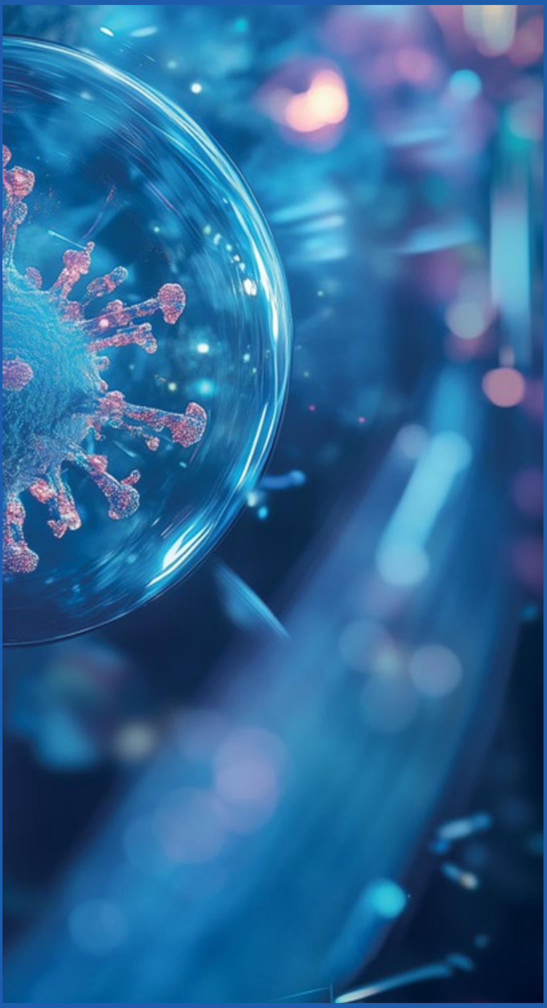


The French national reference centres (CNR) are laboratories of excellence appointed for five years by order of the Minister for Health, after Santé publique France has conducted a call for applications process and their CNR committee has issued an opinion. They provide advice and expertise and contribute to the surveillance and alert process for one or more specific pathogens (viruses, bacteria or parasites of interest in France). Their activities include identifying and characterising strains, genomic sequencing, detecting variants or treatment-resistant strains, monitoring the circulation of these pathogens, detecting emerging threats and supporting health authorities in implementing control measures. During the COVID-19 crisis, the CNR for Respiratory Infection Viruses played a key role in analysing samples, monitoring SARS-CoV-2 variants and supporting public health policies.

Objectives of SEQ4EPI

SEQ4EPI is a three-year project, running from 1 October 2022 to 30 September 2025. During the first two years, it enabled the **genomic surveillance of SARS-CoV-2** that the EMERGEN consortium had been working on to continue, gradually reintegrating the operations involved into the CNR-VIR's routine activity and showing how continuing this can be seen as an essential component of integrated and multi-source surveillance of acute respiratory infections (ARI).

The project's objective for 2023 to 2025 is to **extend this system to other emerging pathogens,** starting with other viruses such as Monkeypox (declared a public health emergency of international concern by the WHO in August 2024) and influenza (given an increased risk of emergence of zoonotic origin).



Actions already taken

Between 1 January 2022 and 31 July 2024, the genomic surveillance system for SARS-CoV-2 introduced in 2021 was consolidated and strengthened. Beginning in 2021, 135 prevalence surveys ("Flash Surveys") were conducted to monitor the spread of its different variants. Every week, laboratories across France sent a random selection of samples testing positive for SARS-CoV-2 by RT-PCR to be sequenced.

These **sequencing data for SARS-CoV-2 variants have been used and included in several scientific publications:**

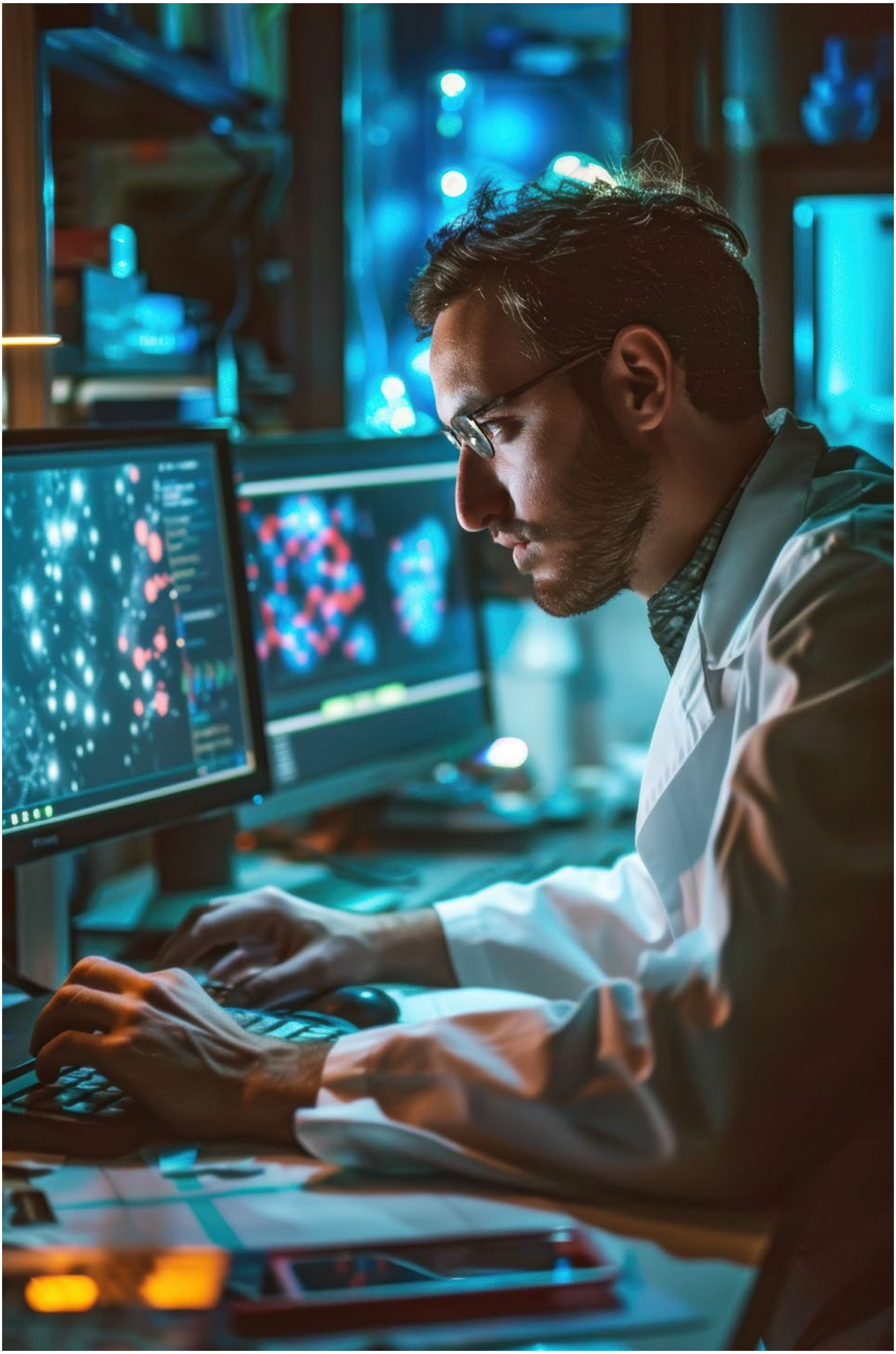
193	**regional EMERGEN feedback bulletins** produced for local monitoring stakeholders;
61	**national epidemiology bulletins** (COVID-19 followed by acute respiratory infections - ARI), split into regional editions depending on the context;
55	**monthly risk analyses** on emerging SARS-CoV-2 variants produced to 15 September 2024;
9	**regional COVID-19 public health bulletins** (2020–2023 Review);
4	scientific articles:

_First cases of Omicron in France are exhibiting mild symptoms, November 2021-January 2022, Maisa & al., Infectious Diseases Now 2022.

_Rapid investigation of BA.4/BA.5 cases in France, Kouamen & al., Frontiers in Public Health 2022.

_Emergence, spread and characterisation of the SARS-CoV-2 variant B.1.640 circulating in France, October 2021 to February 2022, Picard & al., Eurosurveillance 2023.

_Monitoring SARS-CoV-2 variants with complementary surveillance systems: risk evaluation of Omicron JN.1 variant in France, August 2023 to January 2024, Traoré & al., Eurosurveillance 2025.

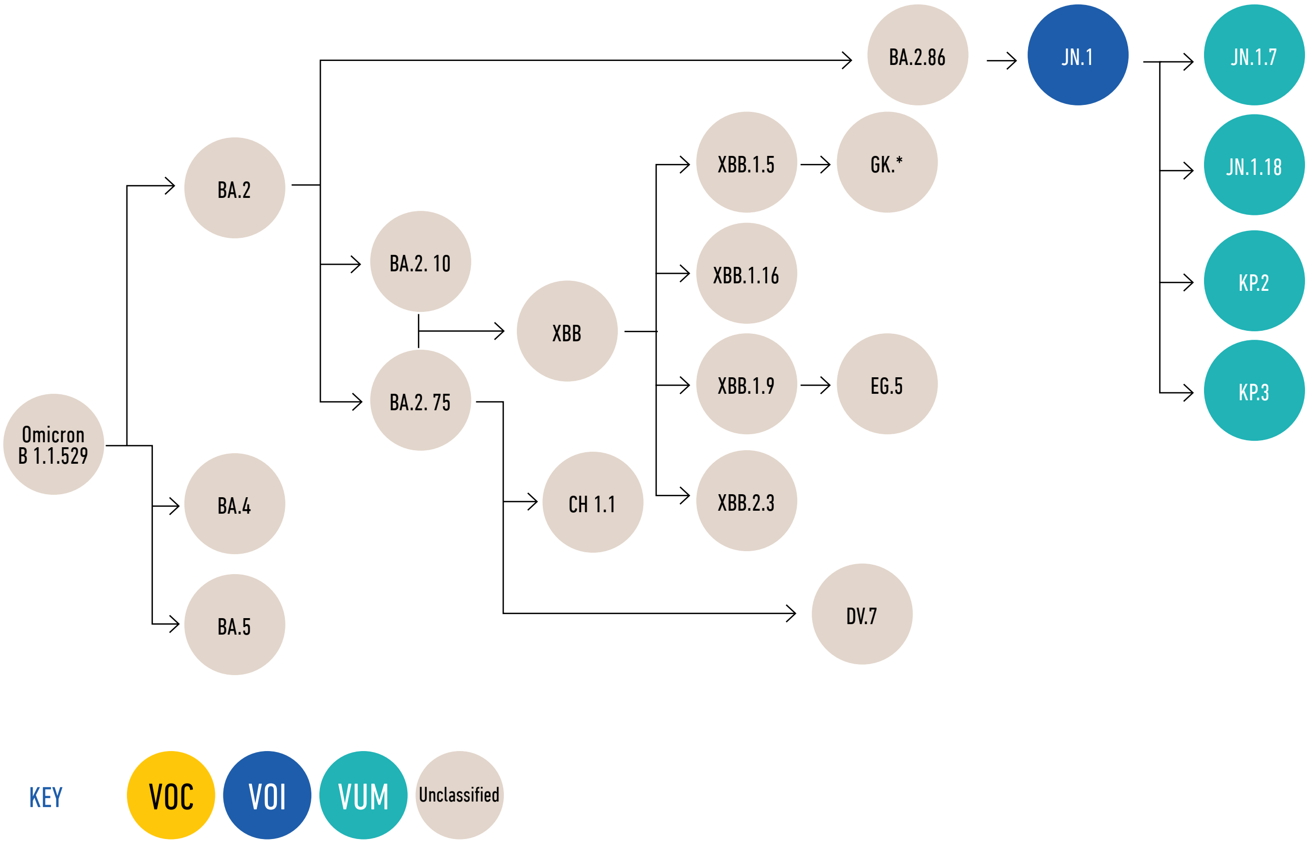


To help different sectors understand and adopt genomic surveillance, various diagrams and infographics were developed:

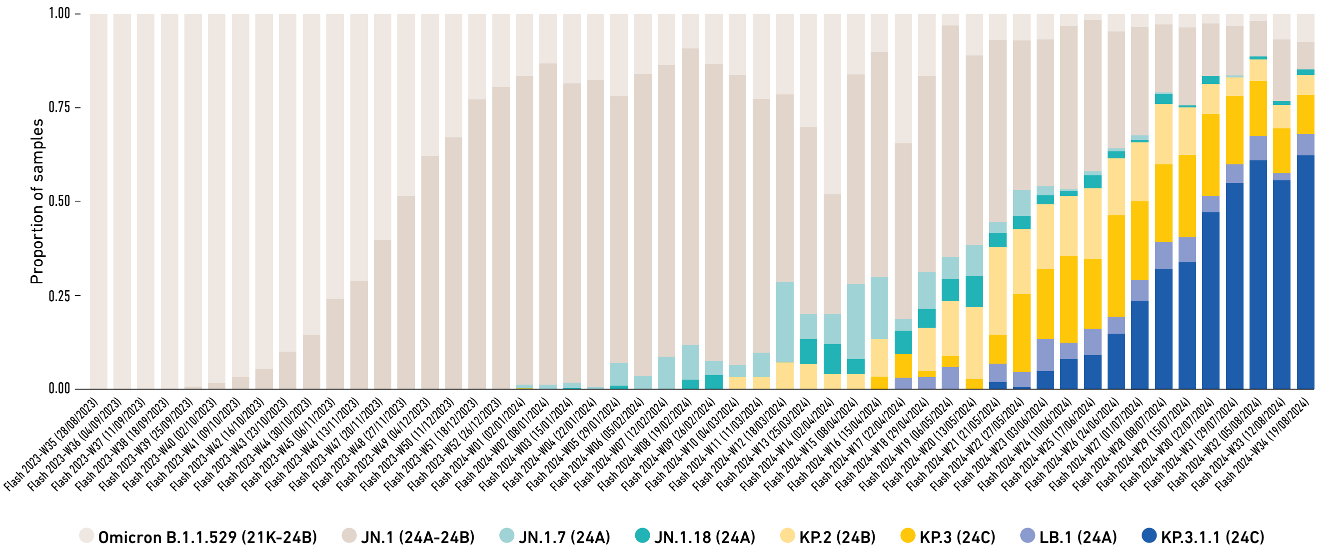
- A diagram illustrating the genetic filiation between SARS-CoV-2 variants was designed to improve understanding of the lineages mentioned in the analyses, in response to diversification of SARS-CoV-2 variants and lineages over time.
- An infographic showing the distribution of variants during the Flash Surveys was produced and integrated into several scientific publications in order to provide a clear view of the variants in circulation.
- A table was created to summarise the risk analyses each month, classifying the variants of interest into three categories: variant of concern (VOC), variant of interest (VOI) and variant under monitoring (VUM). This presentation made it easier for decision-makers to identify variants posing a risk.

RT-PCR *(reverse transcription polymerase chain reaction)* is a laboratory technique that produces a polymerase chain reaction (PCR) from an RNA sample. This amplifies traces of the genetic material of the virus so they can be detected. A positive SARS-CoV-2 RT-PCR result means that the test detected the virus responsible for COVID-19 in the sample (often taken from the nose or throat), signalling that the person is (or has recently been) infected. It does not indicate whether the person is contagious or has symptoms but only that they have been in contact with the virus.

SCHEMATIC REPRESENTATION OF THE GENETIC FILIATION OF THE CLASSIFIED OMICRON VARIANTS (EXAMPLE FROM THE RISK ANALYSIS OF 9 SEPTEMBER 2024)



PROPORTION OF VARIANTS AND LINEAGES DETECTED DURING THE FLASH SURVEYS AMONG INTERPRETABLE SEQUENCES, FIGURE PRODUCED ON 9 SEPTEMBER 2024



CLASSIFICATION OF VARIANTS IN FRANCE (MAINLAND AND OVERSEAS TERRITORIES) FROM THE 9 SEPTEMBER 2024 RISK ANALYSIS

Variants of concern (VOC)	Variants of interest (VOI)	Variants under monitoring (VUM)
	JN.1 (24A-24B)[1] **18%**	**KP.3.1.1 (24C)** **56%**
		KP.3 (24C)[2] **16%**
		KP.2 (24B) **5%**
		LB.1 (24A) **3%**
		JN.1.18 (24A) **Not detected in W33-2024**
		JN.1.7 (24A) **Not detected since Flash W27-2024**

Flash Survey W33-2024 of 12 August 2024 (latest consolidated data): 109 interpretable sequences.
The nomenclature has been adjusted in line with the changes in the WHO classification in effect on 19 July 2024, described above.
Each classified lineage includes all its sub-lineages without a specific classification.

On 1 October 2024, the monitoring of SARS-CoV-2 became part of normal operations. This genomic surveillance is now carried out by the CNR-VIR.

---

[1] JN.1.7, JN.1.18, KP.2, KP.3, KP.3.1.1 and LB.1 excluded
[2] KP.3.1.1 excluded

Ongoing actions and expected results

SEQ4EPI involves various actions to better monitor epidemics of viral origin: supporting the development of various analysis tools based on bioinformatics and phylogenetic techniques, working on an inventory of the sequencing capacities and needs of CNRs, reporting on the progress of the project on the Santé publique France website and organising seminars with its various partners.

Creation of bioinformatics tools

ClusterFinder

https://github.com/genepii/SEQ4EPI/tree/main

Developed by the CNR-VIR, ClusterFinder makes it possible to identify clusters from viral genomic data based on phylogenetic analysis. The molecular results provide solid evidence to support epidemiological investigations, meaning that potential clusters can be confirmed or refuted in near real time. It is to be customised to analyse three respiratory viruses: SARS-CoV-2, influenza and respiratory syncytial virus (RSV).

In epidemiology, a cluster refers to a grouping of cases of a disease in a given place and time that seems unusual. These may be cases linked to one another by a common source of infection (such as contamination in a healthcare facility, workplace, family, or a multi-person event) or close human-to-human transmission. Rapid identification of clusters means that control measures (isolation, targeted screening, etc.) can be put in place to limit the spread of the virus.

SARSProbeMonitor

https://gitlab.pasteur.fr/cnrvir/projects/seq4epi

SARSProbeMonitor is used to identify and evaluate the emergence of mutations that could affect the detection of SARS-CoV-2 using available sequencing primers. It provides an assessment of sequencing performance for circulating variants, allowing adjustments and improvements to be made as needed. Adaptation for influenza viruses and RSV is to be evaluated.

Epidemiological work

Inventory of sequencing capabilities and needs of the French national reference centres (CNR)

An assessment of the genomic surveillance capabilities, activities and needs of the 43 French CNRs was conducted as part of the project. Its findings will help guide future national genomic surveillance strategies.

A web page has been created with information for the public about the project and its progress

French version

https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/projet-seq4epi

English version

https://www.santepubliquefrance.fr/en/seq4epi-project

Extension of the EMERGEN infrastructure to other pathogens such as the Mpox virus

On 14 August 2024, in response to the Mpox (formerly known as monkeypox) epidemic caused by the new clade Ib of the Mpox virus in West Africa, the World Health Organization (WHO) declared a public health emergency of international concern (PHEIC). In this context, genomic surveillance of the Mpox virus, based on the EMERGEN infrastructure, has been strengthened. Work has been undertaken to create a national database centralising Mpox sequences and bolster the sequencing capacities of the CNR for Orthopoxvirus to be prepared for the potential introduction and spread of the virus in France.

Strengthening the “One Health” focus with the ANSES

This process will begin with a study of zoonotic influenza viruses, in the current context of epizootic disease in birds and the emergence of new clades in cattle in the United States. This preparatory work will be carried out in collaboration with the ANSES in line with a “One Health” approach. It will involve setting up a common database, procedures and tools to analyse and compare animal and human sequences. The objective is to incorporate genomic surveillance data into epidemiological practices and quickly be able to produce knowledge on emerging pathogens that will be useful for public health decision-making.

Seminars

Every year, a seminar bringing together the partners of the SEQ4EPI project is organised to encourage exchanges between the various parties involved in the project. Two seminars have already taken place. The first, in Paris in June 2023, aimed to encourage discussions on regional actions carried out and highlight the contribution of genomics to public health. The second, in Lyon in June 2024, included presentations and workshops on the question “Where are we with genomic surveillance of SARS-CoV-2 in France?”. The April 2025 seminar in Marseille provided an opportunity to discuss the project's sustainability with our partners.

Find out more

EMERGEN

History of the creation of the EMERGEN consortium

https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/consortium-emergen

Network of National Reference Centres (CNR)

https://www.santepubliquefrance.fr/a-propos/nos-principes-fondateurs/centres-nationaux-de-reference-pour-la-lutte-contre-les-maladies-transmissibles-cnr

CNR-VIR (National Reference Centre for Respiratory Infection Viruses) - Institut Pasteur

https://www.pasteur.fr/fr/sante-publique/tous-cnr/virus-infections-respiratoires-dont-grippe-sars-cov-2

CNR-VIR Lyon Public Hospitals

https://teamhcl.chu-lyon.fr/cnr-virus-des-infections-respiratoires-grippe-sars-cov-2

Santé publique France

https://www.santepubliquefrance.fr/

ANRS-MIE (French National Agency for AIDS and Viral Hepatitis Research - Emerging Infectious Diseases), an independent INSERM agency

https://anrs.fr/fr/qui-sommes-nous/lagence-en-bref/

INSERM (French National Institute of Health and Medical Research)

https://www.inserm.fr/

ANSES (French National Agency for Food, Environmental and Occupational Health and Safety)

https://www.anses.fr/fr

European projects

SEQ4EPI (sequencing pathogens for epidemiology)

https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/projet-seq4epi

HERA, European Health Emergency Preparedness and Response Authority

https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/project-enhancing-whole-genome-sequencing-wgs-and-or-reverse-transcription-polymerase-chain-reaction-rt-pcr-national-infrastructures-and-capaci

SARS-CoV-2 variants

COVID-19 special report

https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19

SARS-CoV-2 variant surveillance

https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/coronavirus-circulation-des-variants-du-sars-cov-2

EMERGEN database

https://www.emergen.cloud/fr/

Bioinformatics analysis tools

https://gitlab.pasteur.fr/cnrvir/projects/seq4epi

Scientific publications

Funding: European Union

SEQ4EPI: a European project to strengthen
pathogen surveillance through sequencing.
Saint-Maurice: Santé publique France, 2025.
12 p. Visit URL: www.santepubliquefrance.fr

ISBN-NET: 979-10-289-0981-9 - LEGAL FILING: JULY 2025
Design: Infectious Diseases Department, Santé publique France; Formatting: **Luciole**