25es journées annuelles de santé publique

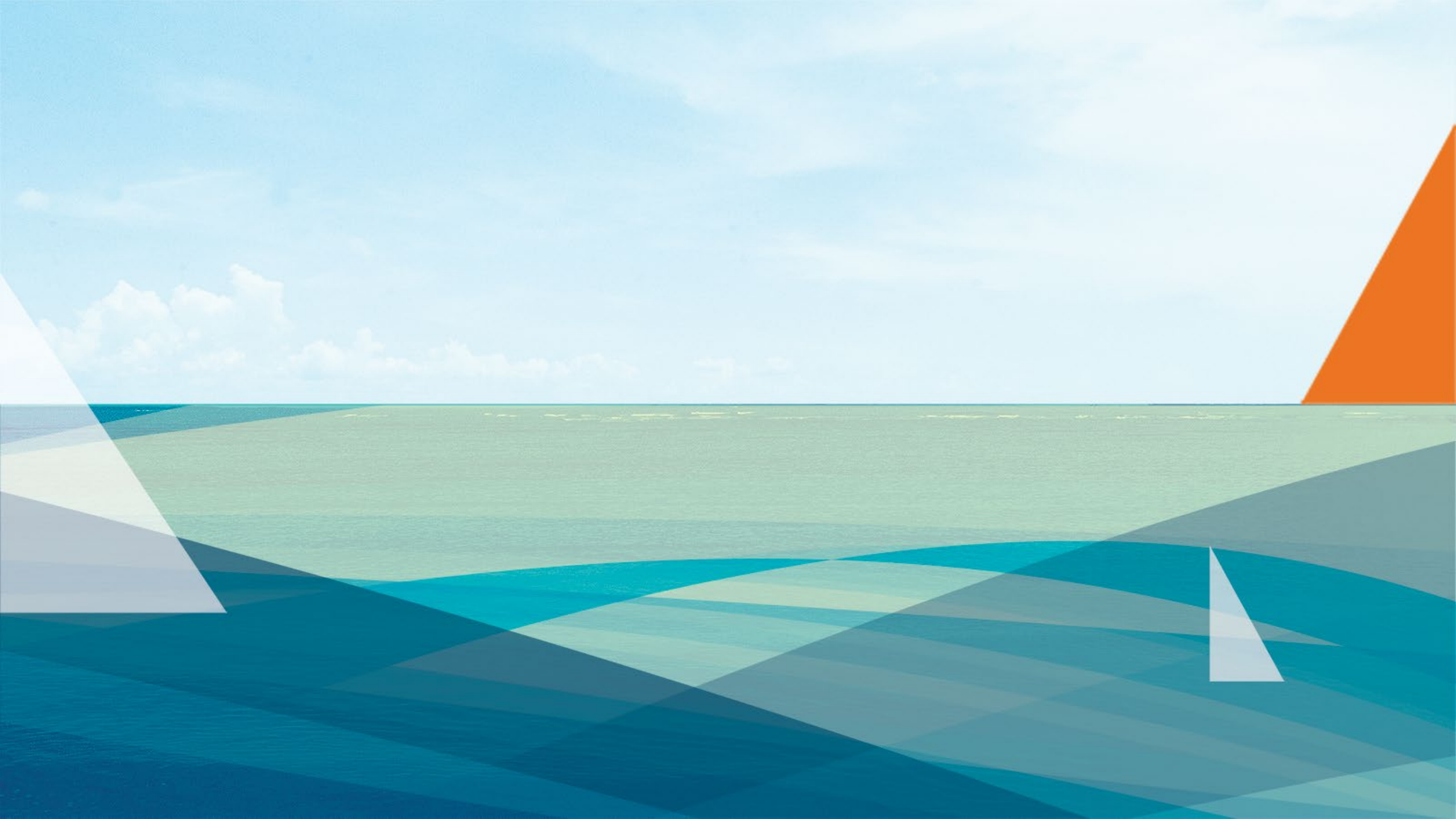
Santé publique France

Implementation of a National Surveillance System for SARS-Cov-2 and Its Variants in France

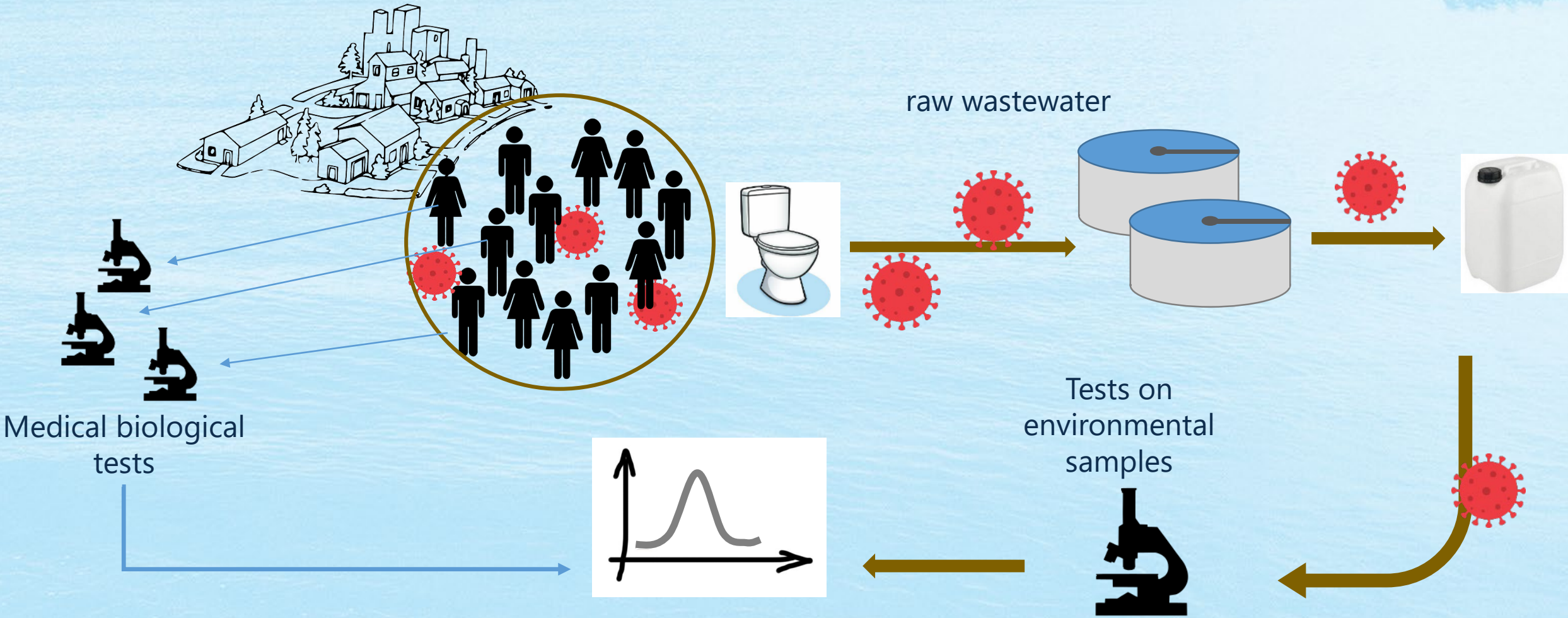
Frédéric Jourdain, Santé publique France

With the contribution of Benoît Gassilloud (Anses) and Damien Mouly (SpF)

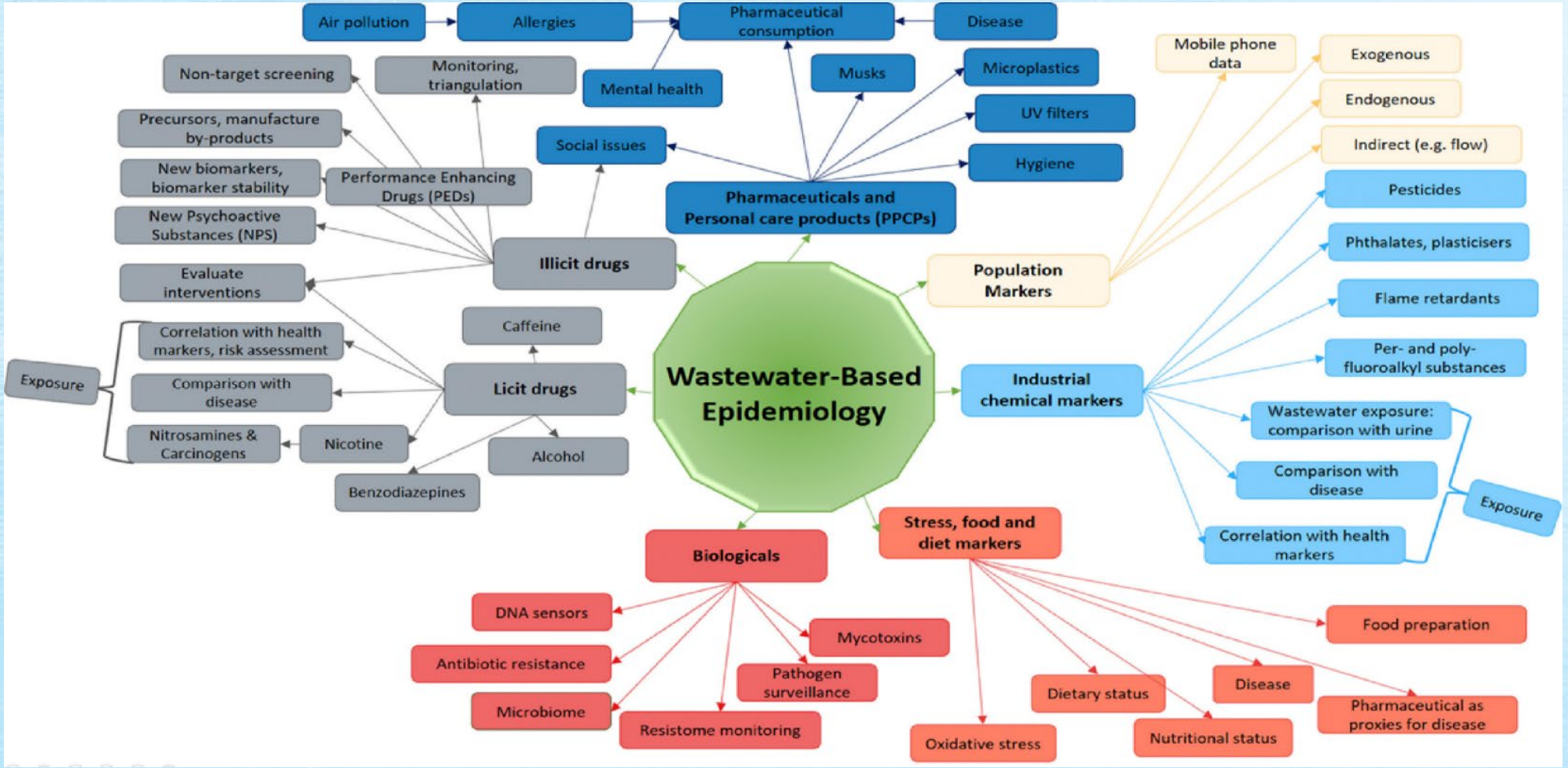
November 29, 2022



Principles of wastewater surveillance



Wastewater, an "integrative" matrix



Choi et al., 2,018. *TrAC Trends in Analytical Chemistry* –Wastewater-Based Epidemiology Biomarkers: Past, Present and Future

Numerous scientific studies on the detection of pathogens in wastewater and sludge from treatment plants

57

R.S.I. 1. 1951.

THE DETECTION OF ENTERIC CARRIERS IN TOWNS BY MEANS OF SEWAGE EXAMINATION*

by B. MOORE, B.SC., M.B., B.CH., B.A.O.,

irector of the Public Health Laboratory, Exeter.

POLIOMYELITIC VIRUS IN SEWAGE

JOHN R. PAUL JAMES D. TRASK C. S. CULOTTA

SEPTEMBER 15, 1939

SCIENCE

AMERICAN JOURNAL OF EPIDEMIOLOGY

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STRATEGIC VIRAL SURVEILLANCE OF SEWAGE DURING AND FOLLOWING AN ORAL POLIOVIRUS VACCINE CAMPAIGN

DONALD B. NELSON, RICHARD CIRCO AND ALFRED S. EVANS[1]

(Received for publication April 25, 1967)

Environmental Surveillance for Polioviruses in the Global Polio Eradication Initiative

Humayun Asghar,[1] Ousmane M. Diop,[3] Goitom Weldegebriel,[4] Farzana Malik,[6] Sushmitha Shetty,[8] Laila El Bassioni,[2] Adefunke O. Akande,[5] Eman Al Maamoun,[2] Sohail Zaidi,[7] Adekunle J. Adeniji,[5] Cara C. Burns,[9] Jagadish Deshpand

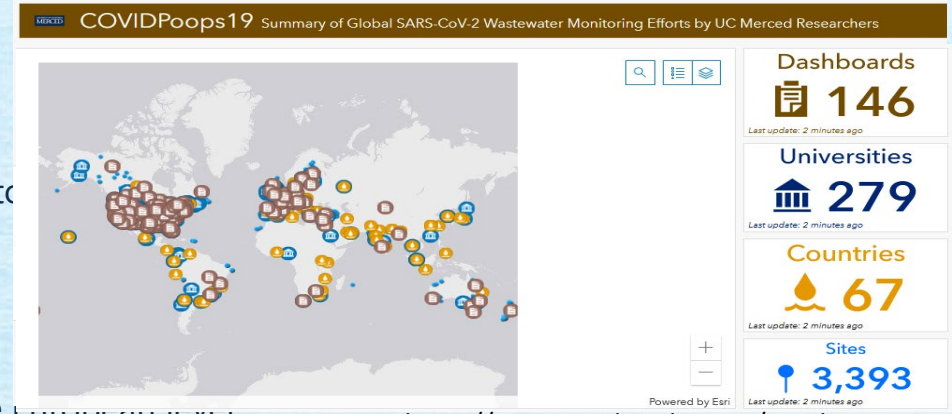
J. Infect. Dis., Volume 210 Issue suppl 1, Nov 2014

WHO

Guidelines for environmental surveillance of poliovirus circulation

SARS-CoV-2 and wastewater: an interest driving many initiatives

- at the international level
  - different structures (agencies, universities…) were involved very early on in the monito
- At the European Commission level
  - Implementation of an initiative designed to propose a harmonized framework at the European level
- In France, starting in March 2020
  - Many public and private projects
    - GIS Obépine
    - COMETE (Marins-pompiers de Marseille)
    - Covid-19 City Watch (Suez), Vigie Covid-19 (Veolia)
    - And many others…



https://www.covid19wbec.org/covidpoops19

RECOMMANDATION (UE) 2021/472 DE LA COMMISSION

du 17 mars 2021

concernant une approche commune pour la mise en place d'une surveillance systématique de la présence du SARS-CoV-2 et de ses variants dans les eaux usées de l'Union européenne

"The reason for collecting, analyzing, and disseminating information on a disease is to control that disease. Collection and analysis should not be allowed to consume resources if action does not follow."

—William Foege, 1976

Photo: Kay Hinton, Emory University

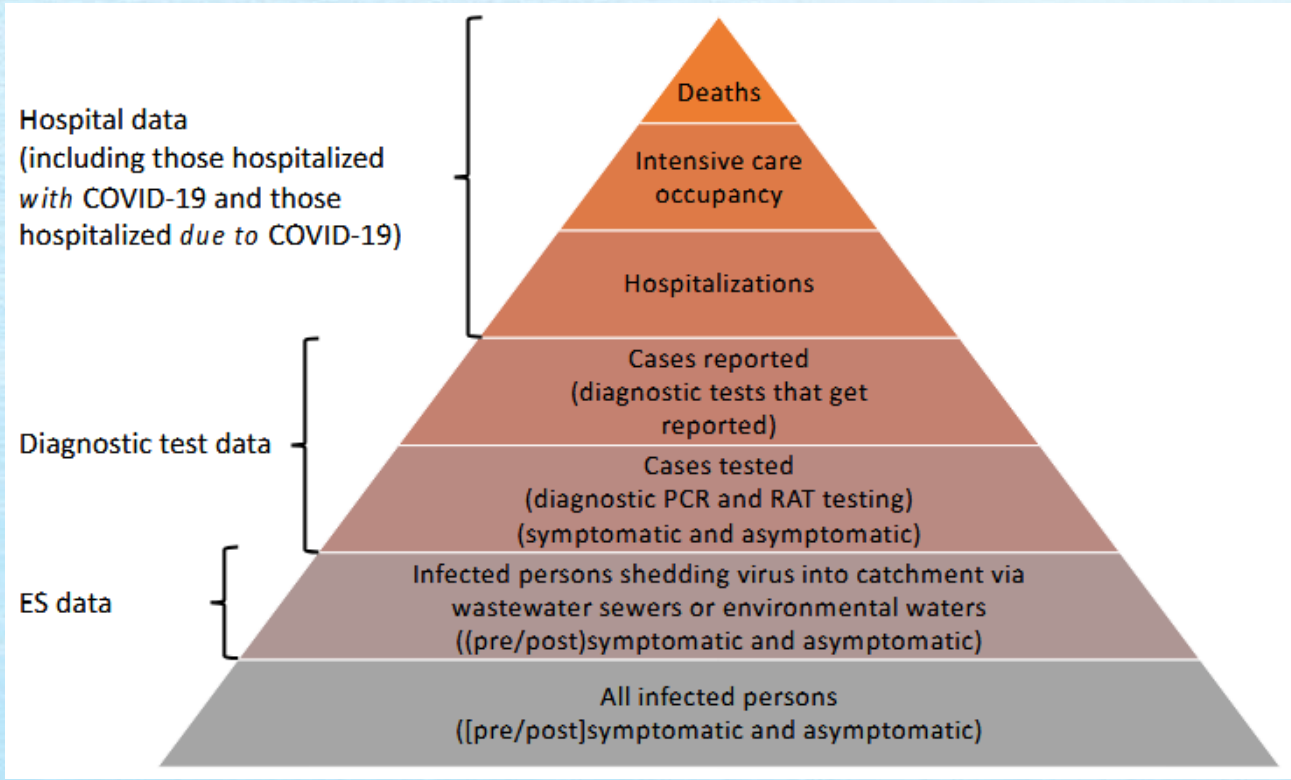
Foege WH, Hogan RC, Newton LH. Surveillance projects for selected diseases. Int J Epidemiol 1976;5:29–37.

Objectives of SARS-CoV-2 wastewater surveillance for public health purposes

- Early detection of the SARS-CoV-2 genome and variants in the general population
- Monitor trends in viral circulation in a population

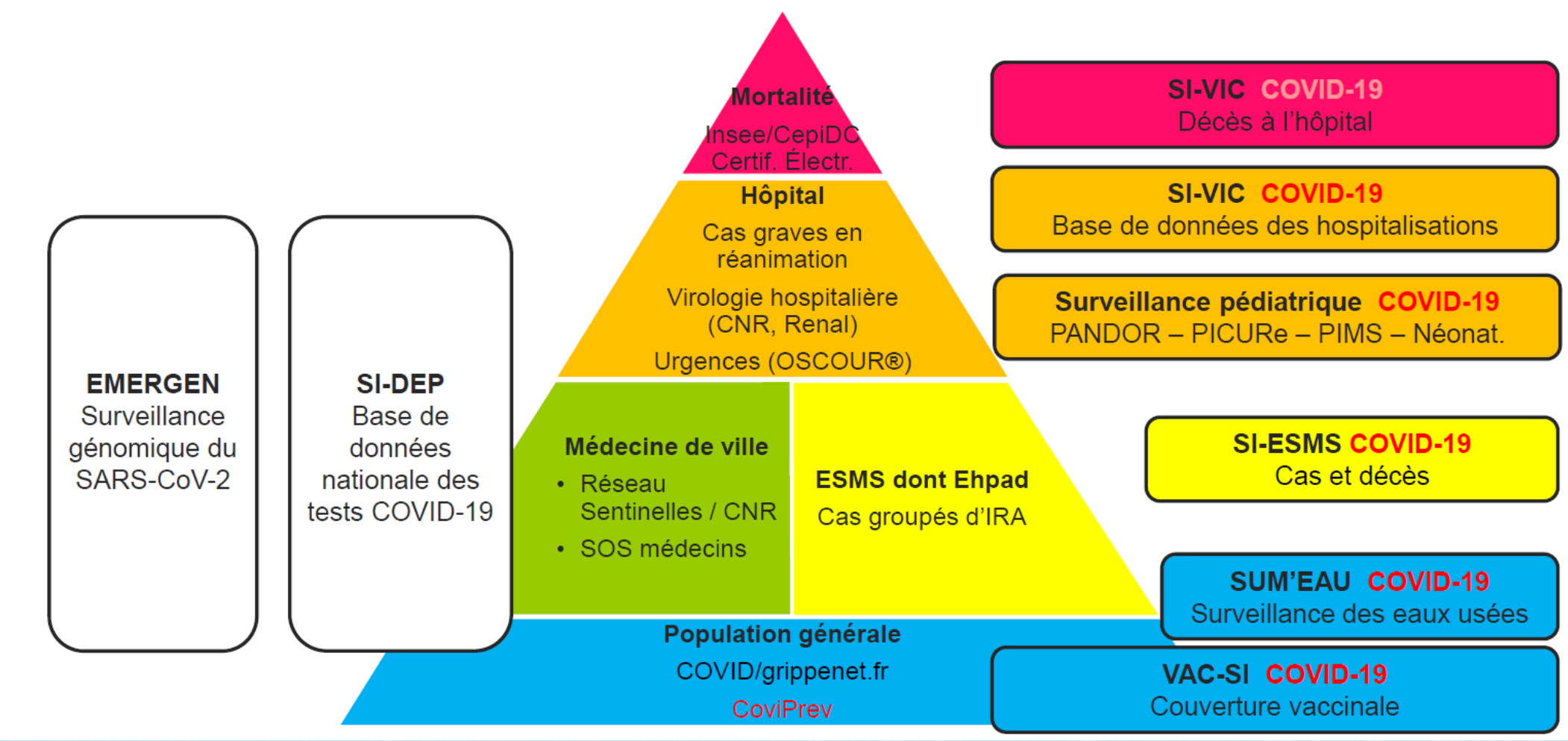
What place for wastewater surveillance?

- Aggregate indicator for low-cost virological surveillance
- early detection (viral circulation, emergence of a variant, and study of genetic diversity)
- population-based health surveillance tool, independent of screening strategies
- complementary surveillance of existing systems



WHO 2022 Environmental surveillance for SARS-CoV-2. Interim guidance

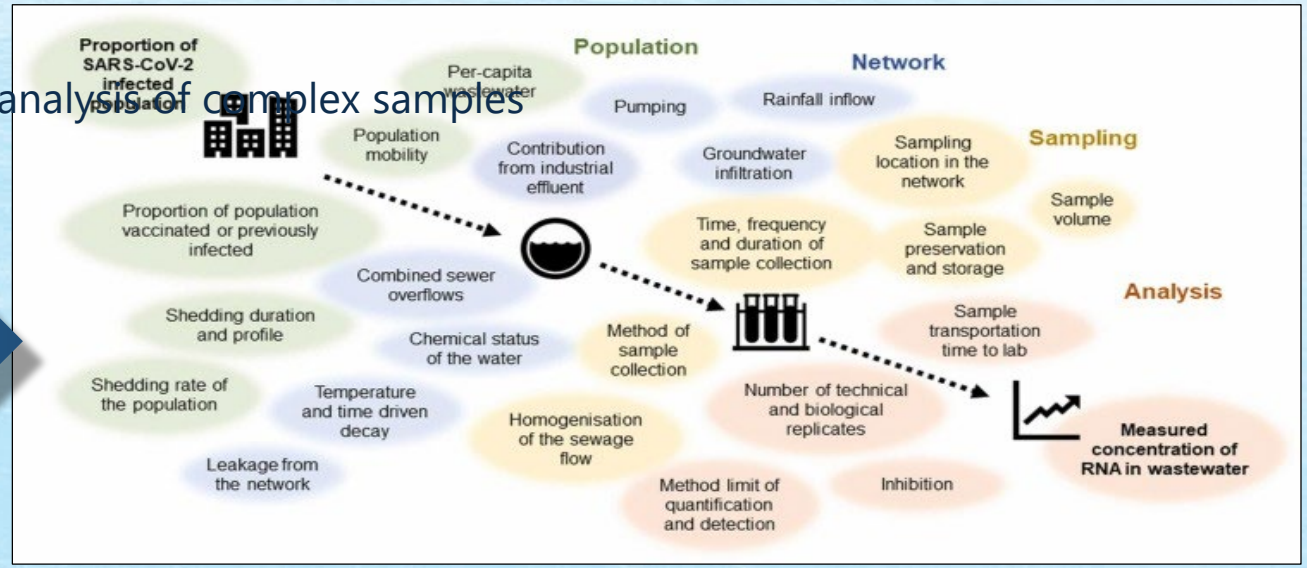
What place for wastewater surveillance?



Limits of wastewater surveillance

- Does not allow for an accurate estimate of the number of infected individuals
- Impossibility of locating clusters in a precise way if we stay at the WWTP level
- Sensitivity is difficult to estimate and may vary by site
- Diversity of sanitation systems installed across the territory
- Complexity of the wastewater matrix, necessary standardization of results
- Detection tools available but not yet standardized
- Variant characterization method(s) to be developed for the analysis of complex samples
- ….

Different aspects to be considered
for accurate epidemiological monitoring



Wade et al., 2022, *Journal of Hazardous Materials*

In France, monitoring was set up within the framework of the SUM'EAU network (Surveillance microbio des eaux usées)

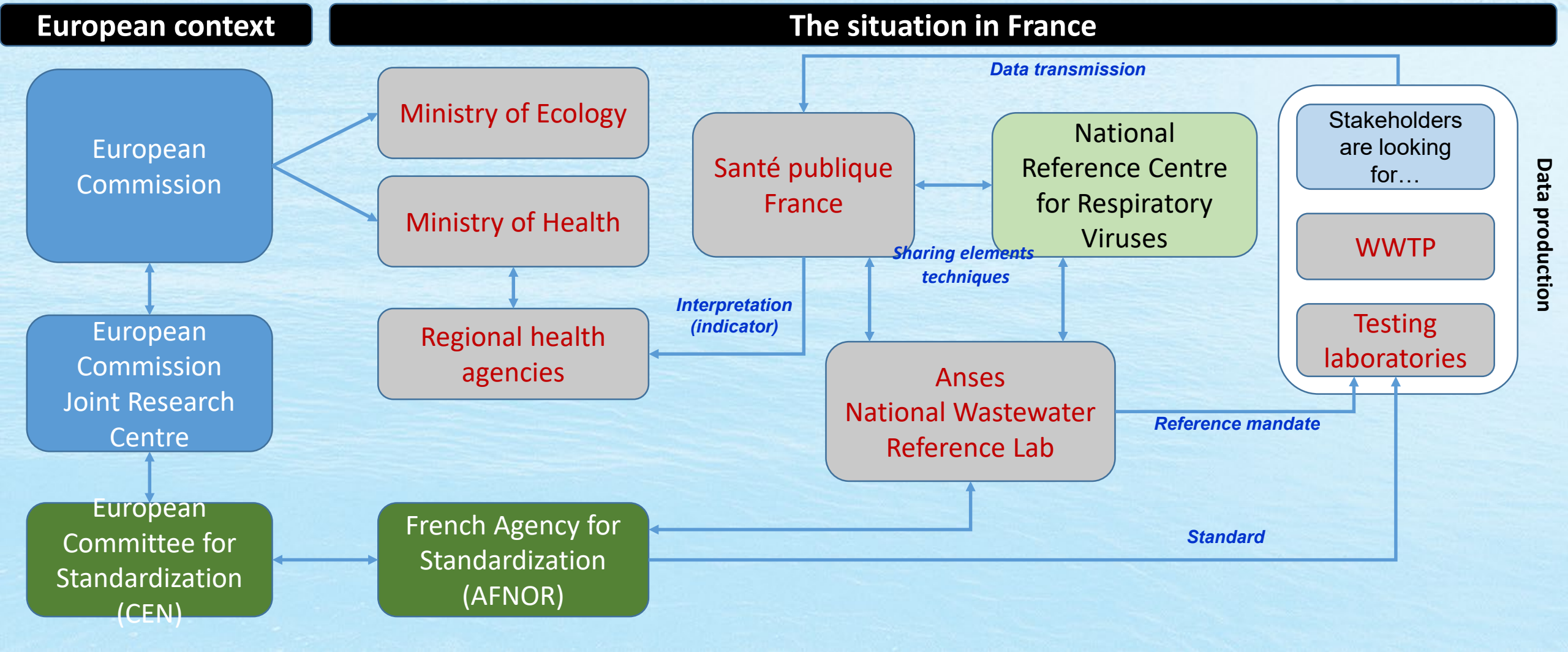
RECOMMANDATION (UE) 2021/472 DE LA COMMISSION

du 17 mars 2021

concernant une approche commune pour la mise en place d'une surveillance systématique de la présence du SARS-CoV-2 et de ses variants dans les eaux usées de l'Union européenne

- Preliminary work launched in July 2021 under the aegis of the Ministries of Health and Ecology in conjunction with the public health agencies (SpF, ANSES), divided into 4 themes:
  - Sampling strategy
  - Analytical methods
  - Production of indicators
  - Research and innovation

Stakeholders



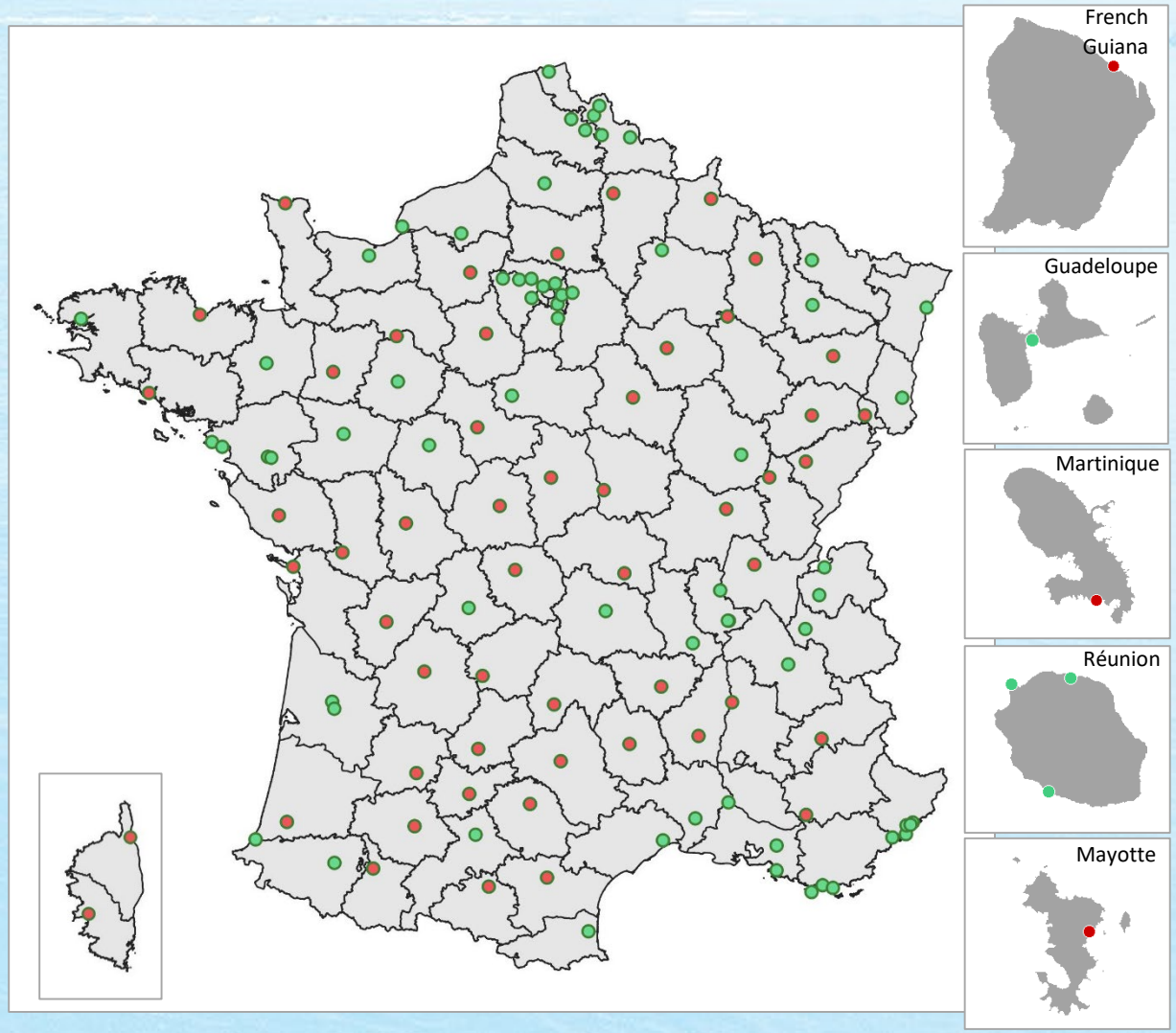
Sampling strategy: spatial resolution

- Objective: to have a network of sentinel stations representative of the national territory

- Identification of a network based on 2 criteria:
  - Population size (see EC recommendation)
  - Territorial representation (see risk management framework)

Proposal of a target network

- Target network of 126 WWTPs
  - 70 in metropolitan areas of more than 150,000 inhabitants
  - 56 to ensure territorial coverage



Sampling strategy: temporal resolution

- Objective: sampling plan adapted to the monitoring of the evolution of SARS CoV-2 circulation in wastewater.
- Challenges
  - intra-day variations: integrated 24-hour sampling.
  - Inter-day variations: adaptation according to the objectives pursued and the epidemiological situation.

Sampling strategy: temporal resolution

Epidemiological situation	Objective of the monitoring	Sampling frequency
Absence of virus circulation	Detection	1/week
Risk of emergence (international alert, large gatherings)	Detection	1/week
Initiation (occurrence of clusters or sporadic cases)	Detection	2–3/week (according to risk level)
Dissemination (propagation)	Estimation of circulation patterns (temporal and spatial)	2–3/week
Identification of variants	Detection	1/week
Circulation of different variants	Estimation of circulation patterns	1–2/week depending on intensity of circulation (sensitivity)

Analytical methods: detection and quantification of SARS-CoV-2

- Protocols adapted to allow for the detection & quantification of SARS CoV-2 in wastewater. National survey of laboratory capacity
  - Important diversity of methods (globally, three main analytical fields)
  - Specificity: in France some analyses are performed on small volumes
  - Difficulty of comparison due to lack of crossover tests.
- Implementation of a pilot intercomparison study financed by the DGS within the framework of the SUM'EAU network and organized by the LHN

Objective: Carry out a dynamic intercomparison of the methods of detection and quantification of the SARS-CoV-2 genome on wastewater samples through the use of the majority analytical channels at the national level thanks to a panel of 10 laboratories (scoping note): to define a reference method adapted to the targeted objectives.

  - Dynamic intercomparison of SARS-CoV-2 detection and quantification methods using the analytical methods most commonly applied at the national level, thanks to a panel of 10 laboratories
  - Selection of 12 wastewater treatment plants across the territory
  - 10 laboratories participated in the study (including the LHN) and analyzed the 12 samples weekly, for 11 weeks (from March to June 2022) in the descending phase of the 5th wave to evaluate the methods on a decreasing range of viruses

Analytical methods: assessing laboratory competence

- Implementation of validation and proficiency tests on wastewater samples to assess the ability of laboratories to detect and quantify SARS CoV-2 virus particles in this complex matrix.
  - Take into account the analytical capacities (number of laboratories) and the _____
  - Take into account specificities related to the matrix
  - Representativeness of samples sent to the laboratory
  - Organization following proven guidelines
- First Test: ILT validation
  - 31 participating laboratories from late June to early July 2022
  - 3 separate samples
  - Very large number of results processed

Production of indicators

- Data standardization:
  - From the flow rate
  - From ammoniacal nitrogen
- Production of qualitative trend indicators
  - Moving average
  - Variation of the slope of the linear regression

Transitional monitoring phase

Monitoring the circulation of SARS CoV-2 across the territory by genome quantification using molecular tools (RT-PCR)

- Upstream phase of the network implementation
- Genomic targets monitored: E and N1 genes of SARS-CoV-2
- 12 wastewater treatment plants
- 1 sample/week
- Standardization from ammonia nitrogen and daily flow measurement data

Construction of monitoring indicators

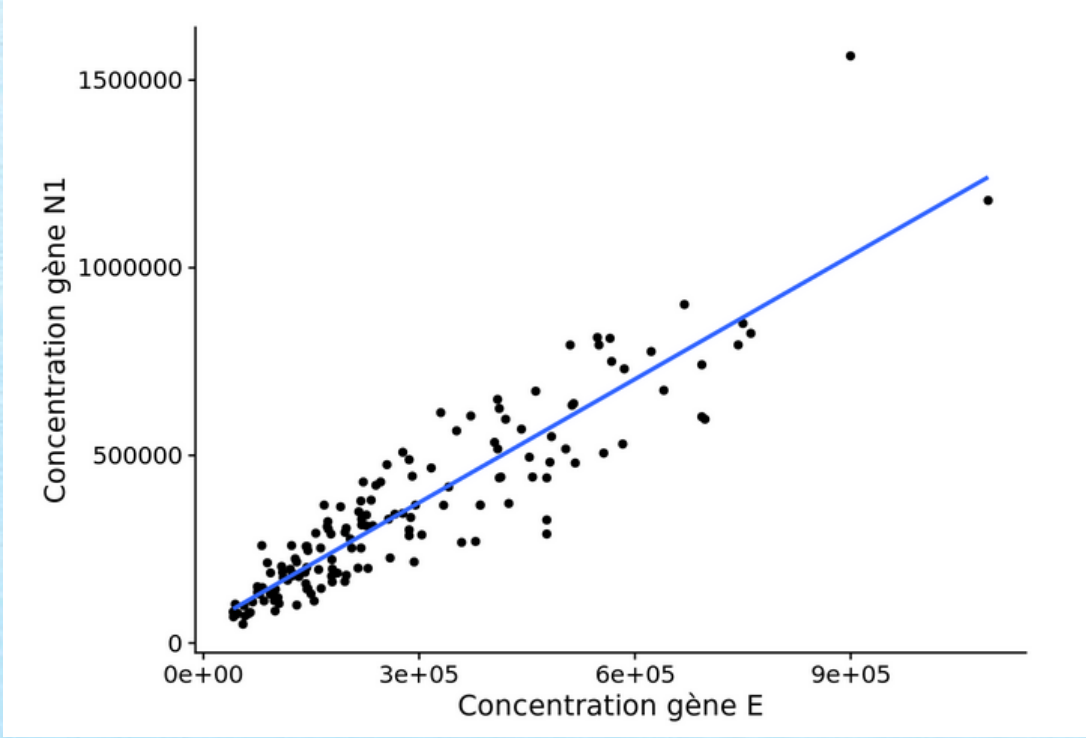
SARS-CoV-2 measurements

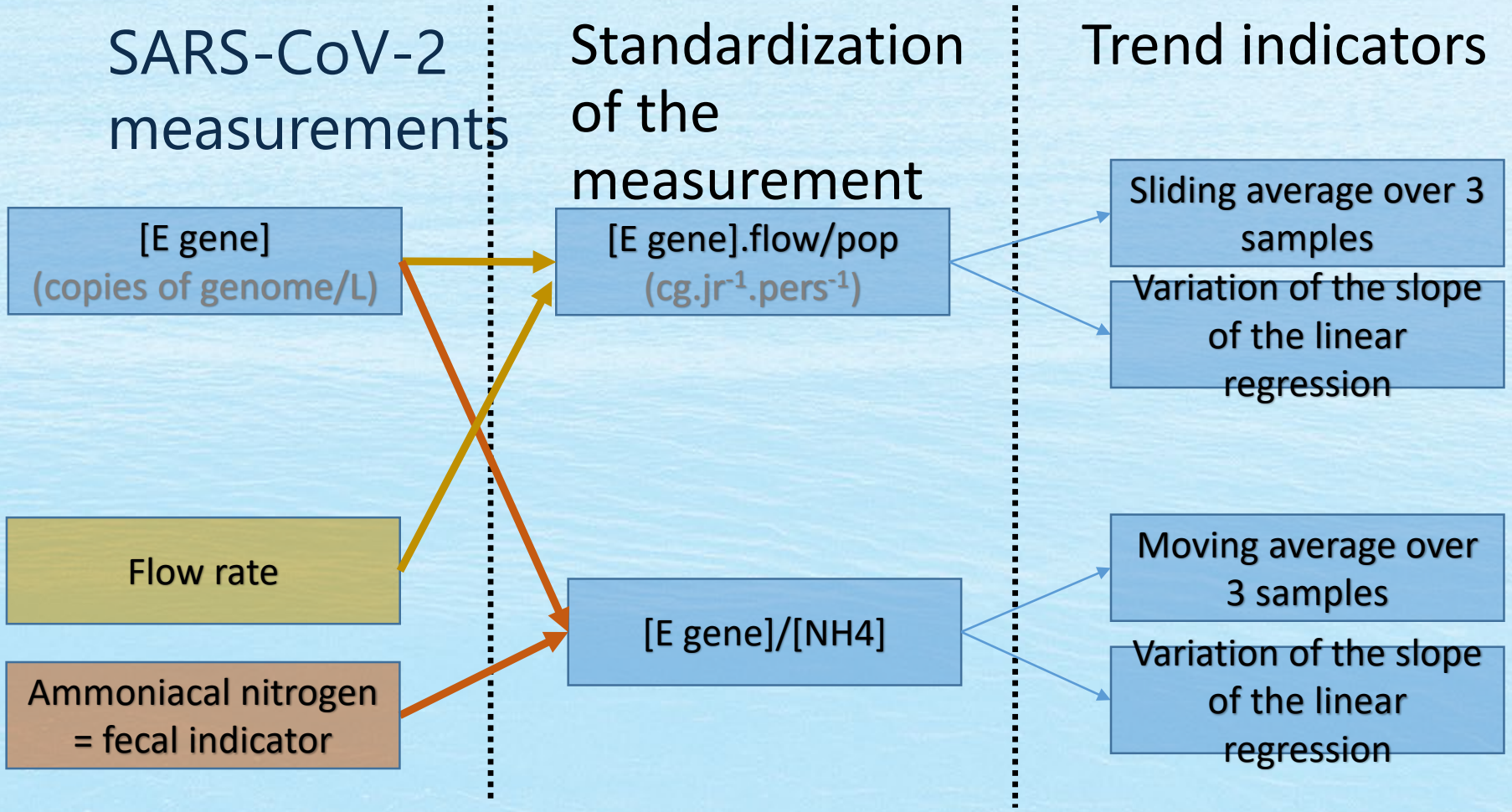
[E gene]
(copies of genome/L)

[N1 gene]
(copies of genome/L)

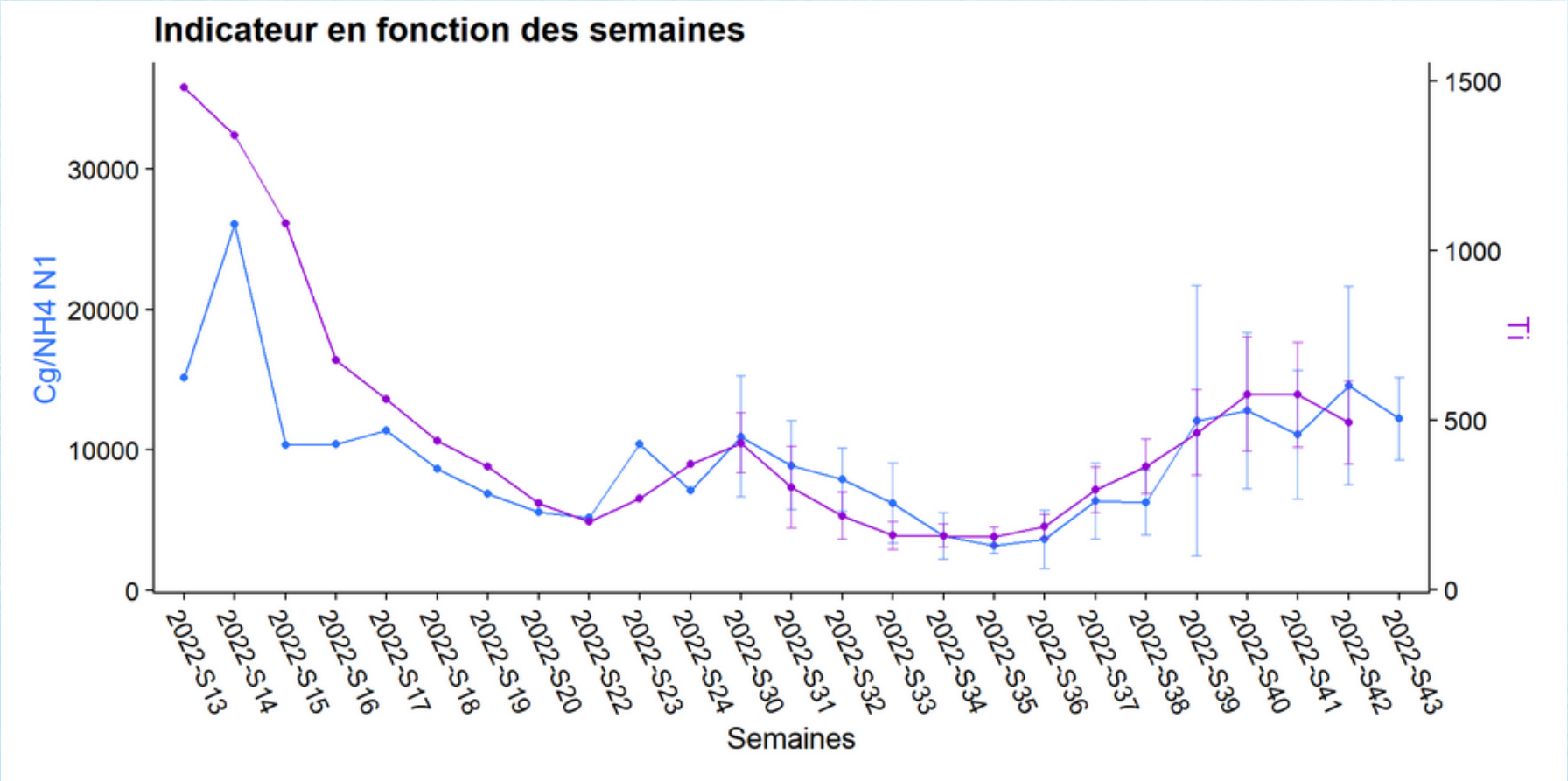
Flow rate

Ammoniacal nitrogen
= fecal indicator

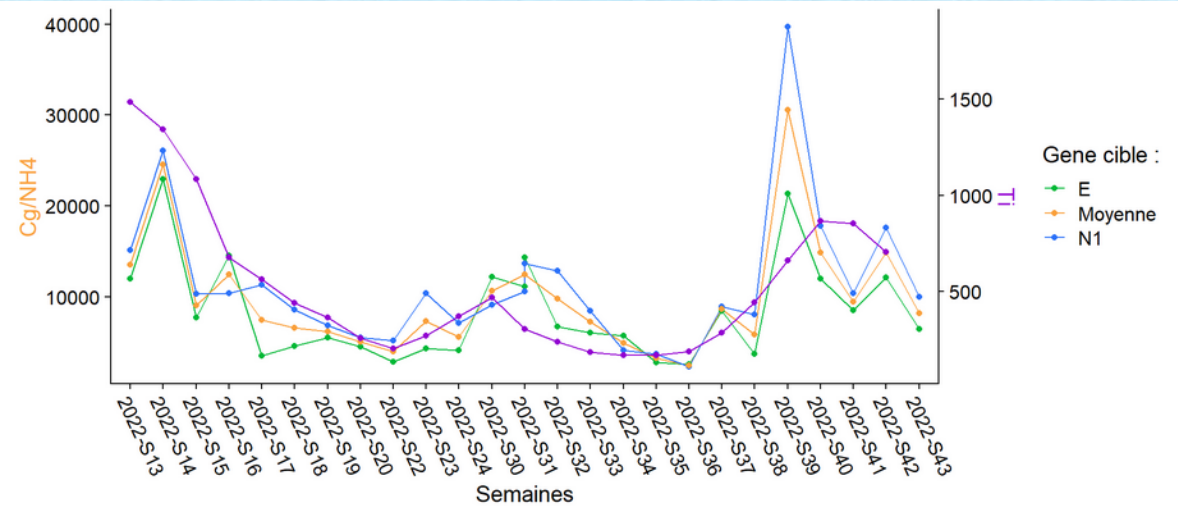



SARS-CoV-2 measurements
Standardization of the measurement
Trend indicators
[E gene] (copies of genome/L)
Flow rate
Ammoniacal nitrogen = fecal indicator
[E gene].flow/pop (cg.jr-1.pers-1)
[E gene]/[NH4]
Sliding average over 3 samples
Variation of the slope of the linear regression
Moving average over 3 samples
Variation of the slope of the linear regression

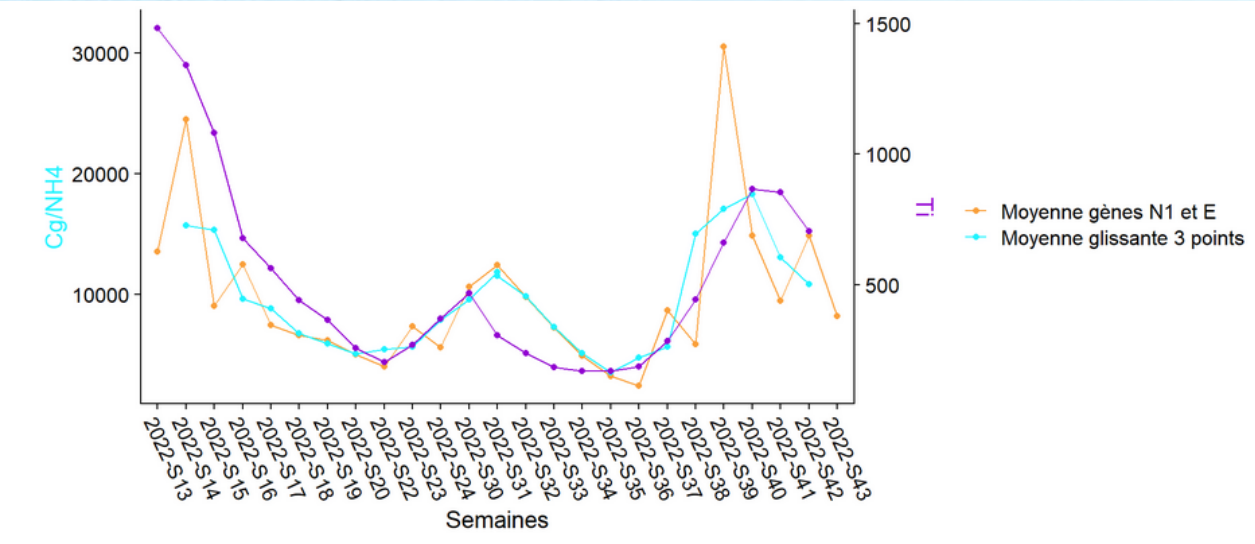
Results for all WWTPs



Results by WWTP



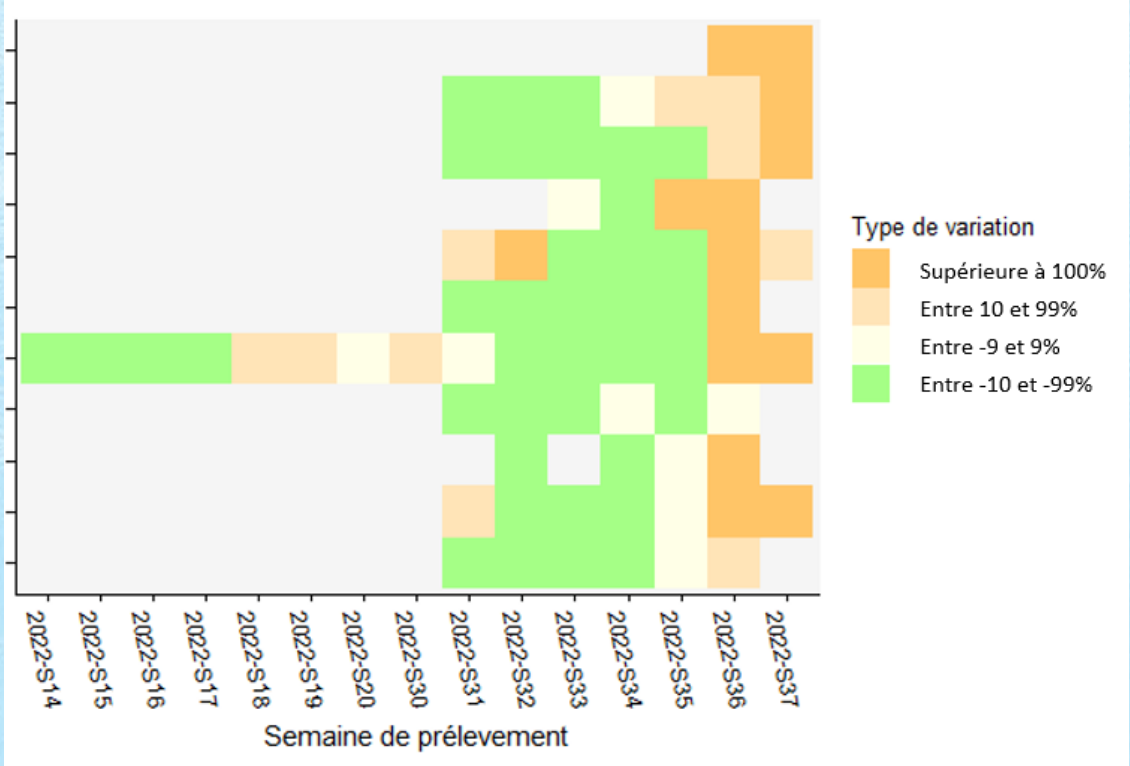
Comparison of E and N1 gene measurements standardized to incidence rate



Comparison of 3-point moving average to incidence rate

Qualitative trend indicator for the 12 WWTPs monitored

- Daily percentage change, obtained from the slope of the linear regression over the last 3 measurement points



Next steps before integration of wastewater indicators and dissemination of results

- Finalization/validation of indicators
  - Smoothing techniques
  - Treatment of outliers
- Selection of laboratories to reach the target network
- Implementation of a dedicated IS
- Restitution of indicators towards different targets

Conclusions and prospects

- Results that become more refined as time series are built up
- Overall assessment quite positive: 8/11 WWTPs consistent with screening data
- Increase the sampling frequency to compensate for variability
- Importance of analyzing the results in an integrated manner, with other available epidemiological indicators
- Introduction of indicators of measure validity (flow rates, [gene]/incidence ratio)
- Reflection on extending to other pathogens according to identified public health objectives (influenza, RSV, MKP, PV, arboviruses?)

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Caroline Huot, Géraldine Patey, **INSPQ**

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Thank you for your time