Global Influenza Hospital Surveillance Network

Foundation for Influenza Epidemiology

Call for proposal: Year-round surveillance 2025-26

GLOBAL INFLUENZA HOSPITAL SURVEILLANCE NETWORK: LINKING EPIDEMIOLOGICAL AND CLINICAL DATA TO VIROLOGICAL INFORMATION

OBJECTIVE

The Foundation for Influenza Epidemiology seeks to support hospital-based sentinel surveillance sites that can improve our understanding of influenza epidemiology and other respiratory viruses and contribute to the WHO's vaccine strain selection process by monitoring influenza virus circulation and hospital-associated disease burden as part of the Global Influenza Hospital Surveillance Network (GIHSN).

We are looking for non-profit institutions with experience in hospital-based surveillance for influenza and other respiratory viruses that would be willing to participate in the GIHSN using a standardized protocol[1] for case ascertainment and respiratory sample collection.

The Global Influenza Hospital Surveillance Network (GIHSN) is a platform that collects standardized data from hospitalized patients with severe acute respiratory illnesses across countries, including low-, middle-, and high-income countries from both hemispheres. 28 sites and 113 hospitals in 24 countries are participating in the GIHSN for the influenza season 2024-2025.

The GIHSN has evolved over the last 12 years to focus on linking epidemiologic and clinical data with Whole Genome Sequencing (WGS) information to facilitate exploring viral phenotypes as they relate to severity or vaccine breakthrough cases. This information is shared with local public health authorities, the World Health Organization (WHO) and the scientific community at large.

The GIHSN is the largest network of its kind and is currently scaling up. A Memorandum of Understanding with WHO was established in 2023 to strengthen collaboration with GISRS.

Although influenza surveillance is critical for GIHSN, the network supports sites to include other respiratory viruses as part of their surveillance, if laboratory capacity exists locally. The COVID-19 pandemic has highlighted the importance of rapid sharing of surveillance data, not only in the context of a pandemic but also to understand the circulation and burden of other common respiratory viruses that could guide public health decision making.

The following specific objectives are underscored for the year-round surveillance Call for proposal 2025-26:

- Screening and inclusion of hospitalized patients with respiratory illness meeting protocol case definition[1] year-round (from November 1st, 2025, to October 31st, 2026).
- Collection of epidemiologic and clinical data for all participating patients, with a standardized questionnaire administered at enrolment and a chart abstraction at patient discharge (or death).
- Enrolled patients would have respiratory specimen collected shortly after hospital admission and sent for testing at the local and/or reference laboratory or National Influenza Centre.

[1] See the protocol on the GIHSN website: Protocol and questionnaire

- PCR test for influenza as a priority. If multiplex PCR and/or wet assay for SARS-COV-2 (and RSV and other respiratory viruses) can be performed in addition, it would be a strong added value.

- Storage (-20C or -70C) of respiratory samples (swabs) from all enrolled patients for a minimum of one year. This will assure sample availability for additional retrospective investigations, pathogen discovery research, or evaluation of new diagnostic tool if necessary.

- Whole Genome Sequencing of a minimum of 50 to 100 influenza viruses will be expected. If number of influenza positive cases are low, sites are encouraged to complete WGS of SARS-COV-2. WGS data will be uploaded to GISAID by site in a reasonable timeframe so that results are available for the WHO Vaccine Composition Meeting (VCM). A GIHSN tag will be included to allow future analysis, and the GISAID accession number will be reported in the clinical questionnaire to allow linkage of WGS information with clinical data.

BENEFICIARIES' ELIGIBILITY CRITERIA

Applicants should be non-profit institutions and will be asked to provide substantiating documentation when submitting their application. *(See How to apply)*

All sites must show **an excellent connection between a hospital surveillance platform and a virology laboratory** in their country, allowing for influenza testing by RT-PCR and subsequent sequencing (subtype/lineage) of the positive specimens within 7 days from sample collection.

If a site has no capacity to generate WGS, the site is offered the possibility to ship its specimens to the GIHSN sequencing platform at the National Influenza Centre in Lyon, France, or to another GIHSN partner having sequencing capacity and located closer to the site, under the Terms of Reference for sharing materials in GISRS. Shipment expenses will be borne by the GIHSN.

All sites must have the capacity to submit WGS at a minimum consensus data of the HA and NA segments to the GISAID EpiFlu™ database[2]. Clinical information should be captured in the current questionnaire used by the GIHSN (possibly e-CRF) and will include the link with GISAID sequence.

SELECTION PROCESS

Applications from Institutions meeting the eligibility criteria will be reviewed and evaluated by the Independent Scientific Committee of the Foundation according to predefined quality criteria.

Main evaluation criteria are:

- **Description of study settings**: Clear description of the surveillance population and settings, number of hospital facilities, link with a virology laboratory with testing capacity (see below), whether data are shared with the National Influenza Centre or WHO reference centres.

- **Laboratory capacities**: Availability of RT-PCR testing for influenza viruses, including subtyping for influenza A and lineage for influenza B. The existing full genome sequencing capacities on site or proposed referral system to sequence influenza viruses (or SARS-COV-2) should be described. Sites should mention if they will test samples for other respiratory viruses and, if so, describe the strategy for testing (e.g., all samples tested for all viruses, including influenza

[2] https://gisaid.org/

and SARS-COV-2 or a random subset of samples tested for other respiratory viruses after influenza testing is done, or other options).

- **Surveillance period**: Sites are expected to run the surveillance year-round (from November 1st to October 31st the following year). If expected number of cases to be screened is too high, site should explain a strategy to systematically assess patients over the surveillance period. See suggested **Sampling Strategy** in Appendix 3.

- **Targeted sample size for WGS**: The estimated number of sequenced samples expected to be shared via the GISAID platform during the season is at a minimum 50-100 and will depend on the site's capacity and number of potential influenza or SARS-COV-2 cases identified. If site proceeds with sequencing of RSV samples, results can be shared in the GIHSN but RSV sequencing is not covered by the GIHSN grant.

- **Clinical information data collection capacities**: The proposal needs to include detailed description about the way the site will identify eligible patients, their local staff capacity to interview and collect information from charts (please indicate if electronical medical chart abstraction will be done), and whether they expect to collect clinical and respiratory samples from all patients or propose a sampling frame if the expected number of patients to be screened is too high. The sampling scheme should be focused on influenza. Other respiratory viruses can be incorporated in the same sampling frame according to resources available and/or use of multiplex testing tools. Sites that can generate information for other respiratory viruses (especially SARS-COV2 and RSV) will be strong applicants, to ensure global monitoring and awareness of respiratory virus circulation after the disrupted seasons seen in 2020/21 and 2021/22. Applicants should clearly describe their proposal screening, enrolment, and testing strategies, including if testing for other respiratory viruses will be performed, and how they can meet the year-round surveillance requirements. This should consider local capacity and resources. See suggested **Sampling Strategy** in Appendix 3.

- **Timelines of the data availability**: Sites should be able to upload data from the questionnaire using the e-CRF or through regular uploads using excel files to share data on enrolled patients (regardless of test results). The preferable approach should be clearly described in the proposal. If sharing data by excel batches, data would be expected to be uploaded every last Wednesday of each month.

  Sites with sequencing capacity should upload genome sequencing data in GISAID as soon as they have results available. Sites using the GIHSN sequencing platform or another GIHSN partner with sequencing capacity should be able to have their samples shipped in regular batches along the year-round surveillance and at least 4 weeks before each WHO strain selection meeting (February and September each year). The proposal should describe the site's ability to manage data uploads and shipments and expected timelines for shipments. If the suggested timelines for data sharing or sample shipments cannot be met, site should explain the rationale.

- **Geographical representativeness**: sites in regions under-represented in the GIHSN will be given funding priority.

- **Cost-effectiveness**: the relevance of the cost in relation to expected sample size will be considered when reviewing applications. The Foundation is providing catalytic funding and is not expected to fund the full cost of the surveillance system (clinical and sequencing data

collection). The Foundation encourages sites to seek for national or other sources of funding to guarantee the sustainability of their surveillance.

In September each year, the Executive Committee of the Foundation will select institutions and decide the amount of the grant provided during the season to support the implementation. For sites already participating in the GIHSN, the selection will be conditional to data transfer completion in the previous season.

A formal letter from the Foundation describing grant modalities (in cash contribution) and payment milestones will be sent to the selected sites in October 2025. Kick off meetings or calls with sites to review generic protocol and operational details will be organized in October and November. **Sites are expected to implement the year-round surveillance starting November 1st for a one-year duration**.

HOW TO APPLY AND HIGHLIGHTS

The Call for proposal is published on the GIHSN website www.gihsn.org

All applications must be submitted on-line on the GIHSN website, using the dedicated application form. Deadline for submission of all applications is July 23rd, 2025, EOB.

⇒ New sites to the GIHSN: Please create your personal space on-line on the GIHSN website to proceed. Fulfil your application on-line.

⇒ Recurrent sites (previous year(s) contribution to the GIHSN): Please connect to your personal space on-line on the GIHSN website and update your previous application form to account for change, if any, in study implementation and budget.

HIGHLIGHTS

- Applicants should be non-profit institutions engaged in respiratory virus hospital-based surveillance. Applicants should demonstrate a strong connection between one or several hospital facilities and a virology laboratory with testing capacities.
- Sites are expected to do **YEAR-ROUND surveillance** for respiratory illness hospitalizations (from November 1st to October 31st the following year).
- Sites should use a **SYSTEMATIC screening** approach (e.g., assess eligibility of patients **everyday, week-days**, or **3 times/week**) and **explain their strategy in the application** because it is important to understand the sampling frame used by each site (i.e., how and when patients are approached) to allow for data analysis and interpretation of results.
- Sites should **apply case definition** (there is a list of slightly modified case definitions in the protocol and questionnaire (e.g., WHO SARI case definition).
- Sites should perform **SYSTEMATIC testing for all enrolled patients** using PCR for Influenza and when possible, testing for other respiratory viruses (multiplex-PCR).
- Sites should **SYSTEMATICALLY complete a questionnaire for all enrolled patients** to capture information on the entire continuum of influenza illness, from pre-hospital signs, symptoms and management to hospital documented disease severity, as well as treatment and clinical outcomes.
- Sites should perform **Whole Genome Sequencing of a minimum of 50 to 100 influenza viruses** (lower CT values increase the chance for sequencing) or alternatively send those samples to the NIC's sequencing platform in Lyon, France, or to the WHO Collaborating Centers.
- Sites should **share their data EVERY MONTH**, preferably every last Wednesday of each month, even if some patients have incomplete data to follow an incremental data management process.

The following documents should be provided along with the proposal to attest the above status:

- ☐ Last annual report of institution applying (administrative document of the institution)
- ☐ Financial report (including earnings and balance sheet) of the previous year
- ☐ Bank account number (official bank document – with swift number)
- ☐ List of the members of the board of governors (i.e., group of people who jointly oversee the activities of the laboratory)
- ☐ Copy of the decree of creation (i.e., Statutory act returned by the president of the republic or the head of government)

A GIHSN data sharing agreement *(See appendix 2)* will be requested to be signed by the selected sites at the start of the season.

Should you have any question, please do not hesitate to reach out to us: contact@gihsn.org

Abbreviations

GIHSN: Global Influenza Hospital Surveillance Network
GISAID: Global Initiative on Sharing All Influenza Data
GISRS: Global Influenza Surveillance and Response System
IFPMA: International Federation of Pharmaceutical Manufacturers & Associations
WHO: World Health Organisation

Appendix 1: How the GIHSN operates?

The GIHSN is operated and supported by a dedicated fund, the Foundation for Influenza Epidemiology, under the auspices of Fondation de France, a leading philanthropy network in France. As of January 2025, donors of the Foundation included Sanofi, Seqirus, Pfizer, Abbott Diagnostics. Donors do not have access to the data and there is no commercial use of the data.

Scientific oversight of the GIHSN is ensured by an Independent Scientific Committee composed of world leading experts in epidemiology, virology, and public health, including representatives from WHO and field-based experts, investigators from GIHSN sites.

Coordination of the GIHSN, supervision of implementation and data management/data hosting are supported by Impact Healthcare, an independent organization based in Paris, France, specializing in the strategic and operational management of large innovative projects in Digital Health and the use of Health data, both in France and internationally.

Learn more: https://gihsn.org/the-foundation-for-influenza-epidemiology/

Appendix 2: GIHSN data sharing agreement

Sites participating in the GIHSN share data with the GIHSN under the terms of a Data Sharing Agreement.

Data collected by sites receiving funding remains the proprietary of the site. There is no commercial use of the data. The data is transferred through a secured channel and the site has full access to the data that was shared, through a secured platform managed by Impact Healthcare.

The GIHSN database is hosted in a secure environment (certified secured hosting for health personal data). Data is processed in full accordance with the European General Data Protection Regulation (GDPR) and French data protection regulations.

Aggregated surveillance data by site is reported on a yearly basis in the GIHSN Annual Report. It is also displayed in the form of aggregated indicators and graphs accessible via the GIHSN website.

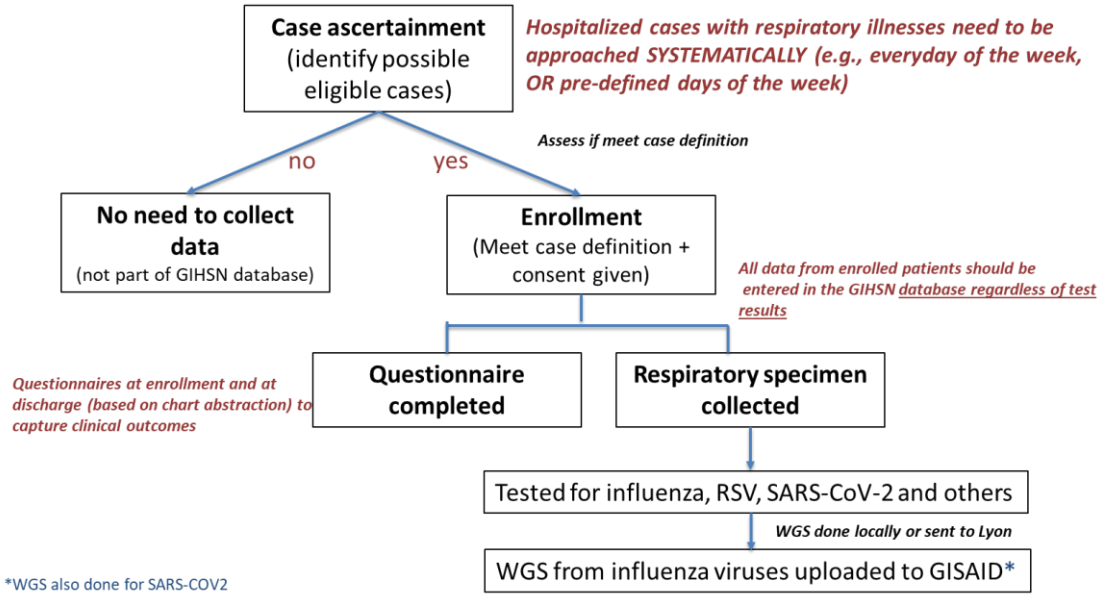
Analysis results are submitted for publication. Scientific publications and communications will mention contributing sites, with investigators names in the authorship, in line with the ICMJE rules.

Sites will be informed upfront for any planned data analysis and they have the possibility to opt-out. Any research project leveraging on the GIHSN data must be approved beforehand by the Scientific Committee of the GIHSN and the Foundation for Influenza Epidemiology. Only anonymised data is shared.

Download GIHSN data sharing agreement: https://gihsn.org/data-management-and-ethics/

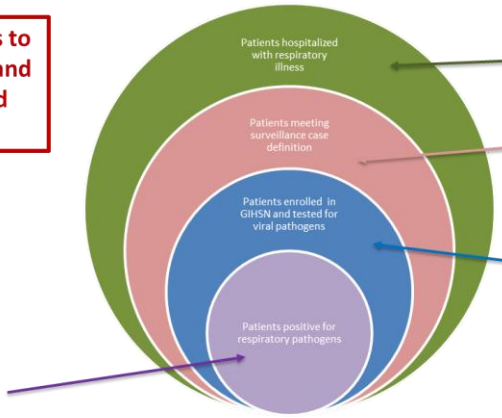
Appendix 3: Patient screening and enrollment

PROCESS FOR IDENTIFICATION OF CASES AND DATA COLLECTION - GIHSN



SAMPLING STRATEGY

Sampling strategy needs to be done systematically and done in a way to avoid potential biases



Full universe of cases hospitalized with respiratory illness Includes all the potentially eligible cases but not all cases will meet Case Definition for enrollment

It is challenging to approach every patient that meet Case Definition This is why we need to apply a sampling frame that could represent this pool of patients, minimizing selection bias (i.e., systematically applied)

Patients included in GIHSN database (with questionnaire and specimen collection – regardless of test results) They represent a sample of the cases hospitalized that met GIHSN surveillance case definition that were approached for enrollment and accepted inclusion

WHY DO WE NEED SYSTEMATIC SAMPLING?

If we only have virus-positive patients, we will not tell a complete story about these viruses...We need positive and negative patients (Blue + Purple)

Describe the percentage positivity for the various pathogens would also be important to understand/document virus circulation year-round

Sampling strategy suggestion for year-round surveillance:

- Depending on the local circumstances, if number of screened and enrolled participants are expected to overwhelm local hospital capacity, the site can develop a sampling strategy to keep the surveillance throughout the year (from November 1st to October 31st the following year). We suggest that, in this situation, the site can define 3 days of the week for systematic screening and enrolment of patients. Respiratory samples would also be collected during these days of the week from all patients who meet the case definition and consent to participate in the surveillance. Clinical information would be collected from all enrolled patients (independently of laboratory results)

- It is important to avoid selecting patients for enrolment based on severity or vaccination status. This is because we want to be able to pool data for analysis. To be able to describe the cases based on disease presentation and distribution of epidemiologic and clinical characteristics, the selection of participants cannot be biased

Appendix 4: Timeline

GIHSN timeline	2025								2026											
	May	June	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	March	Apr	May	June	July	Aug	Sep	Oct	Nov	Dec
Site selection and engagement																				
Call for proposal released on GIHSN website																				
Submission of applications																				
Evaluation of applications by Scientific Committee																				
Decision on site selection and grant allocation																				
Letter of Engagement sent to selected sites & first settlement																				
Onboarding of selected sites																				
Implementation of year-round surveillance																				
Start patient enrollement - all year-round (Nov 1st, 2025 up till Oct 31st, 2026)																				
Collect and share clinical data with GIHSN on a regular basis (monthly) - all year-round																				
Proceed with WGS and share results on a regular basis - at least twice a year before VCM																				
Finalise data collection 2025-26 prior to cut-of and preparation of Annual Report																				