Call for proposal - 2022/23 Influenza Season

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 GIHSN has been around for the past 10 years, covering influenza circulation in the Northern and Southern Hemispheres. The network has changed over time, focusing on linking epidemiologic and clinical data with WGS information during the 2019/2020 season. During the 2020/21 season, due to the COVID-19 pandemic, changes in patterns of influenza and other respiratory viruses were observed, with substantial reduction in detection of non-COVID-19 respiratory cases. These changes in the epidemiology of other respiratory viruses need to be carefully monitored. The reduction in infectious diseases associated with influenza and RSV, for instance, could lead to an increase in the number of susceptible populations, facilitating large or unforeseen outbreaks in the communities. During the 2021-22, the GIHSN has proposed a year-round surveillance for the monitoring of respiratory viruses. For the 2022-23, the GIHSN will similarly continue supporting public health officials’ effort to understand the circulation and evolution of respiratory viruses, especially influenza.

Although influenza surveillance is critical for GIHSN, the network supports sites to include other respiratory viruses as part of their surveillance if laboratory capacity exist locally. The COVID-19 pandemic has highlighted the importance of rapid sharing of surveillance data, not only in the context of the pandemic but also to understand the circulation and burden of other common respiratory viruses that could guide public health decision making. The GIHSN promotes sharing of surveillance data with local health authorities, WHO and the scientific community at large. Currently, laboratory data on WGS are also actively shared by being uploaded into GISAID – a global initiative that provides open-access to genomic data from influenza and SARS-COV-2 viruses.

As such, the following specific objectives are underscored for the 2022-23 season call for tender:

- **Screening and inclusion of hospitalized patients with respiratory illness** meeting protocol case definition\(^1\) year-round (From November 2022 to October 2023).

- **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).

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\(^1\) See the protocol on the GIHSN website [www.gihsn.org](http://www.gihsn.org)
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.

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, site is 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 link to the WGS and the clinical data will be uploaded to GISAID to allow future analysis.

**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 should be able to ship its specimens to the GIHSN sequencing platform at the National Influenza Center in Lyon, France, 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. 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 facilities, infrastructure, 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.

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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 2022 - October 2023). 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 box below.

- **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.

- **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 box below.

- **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. 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 should be able to have their samples shipped in regular batches at least 3 weeks before the WHO strain selection meeting. 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 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).
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 (i.e., November 2022 – October 2023). 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.

At the end of August/early September 2022, 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 participating sites, the selection will be conditional to data transfer completion of the 2021-22 season.

A formal letter from the Foundation describing grant modalities (in cash contribution) and payment milestones will be sent to the selected sites.

HOW TO APPLY

The call has been posted on the [www.gihsn.org](http://www.gihsn.org) website on May 11th, 2022. All applications must be submitted on-line on the GIHSN website before June 29th, 2022, via the application template.

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

- Last annual report (administrative document of the institution)
- Financial report (including earnings and balance sheet) from last 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)

The data sharing modality document (*See appendix 2*) will be requested to be signed by the selected sites at the start of the season.
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: Governance of the Foundation for Influenza Epidemiology

The governance of the Foundation for Influenza Epidemiology is ensured by an Executive Committee (EC). The Executive Committee is the decision maker, in charge of the strategic directions related to the project. Based on pre-established criteria, the Executive Committee selects applicant sites for funding allocation each year. The Executive Committee is composed of 5 scientific specialists from the donors (Sanofi Pasteur, Seqirus, Illumina and IFPMA) and three independent experts (members of the Independent Scientific Committee).

An Independent Scientific Committee composed of 12 experts provide recommendations for technical, scientific and related ethical aspects to the Foundation. 3 of these experts are members of the Executive Committee.

Impact HealthCare is a subcontractor of the Foundation for Influenza Epidemiology and supports GIHSN operations.

More details on the Foundation are available on www.gihsn.org.

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3 Independent experts: Bruno LINA, University of Lyon, France (Chair); John PAGET, Nivel, Netherlands; Justin ORTIZ, University of Maryland, USA; John McCACLEY, Crick Institute London, UK; Arnaud FONTANET, Institut Pasteur, France; Christian HAPPY, Harvard Medical School, USA; Joe BRESEE, Task Force for Global Health, USA; Wenqing ZHANG, Head of GIP, WHO, Geneva (Observer) – Sites representatives: Melissa K ANDREW, Canadian Serious Outcomes Surveillance Network, Halifax, Canada; Elena BURTSEVA, FSBI « N.F. Gamaleya NRCEM », Moscow, Russia; Marta NUNES, University of the Witwatersrand, South Africa – Foundation for Influenza Epidemiology representative : Sandra Chaves, Scientific executive officer (Observer)
Appendix 2: Global Influenza Hospital Surveillance Network (GIHSN) data sharing agreement

Sites implementing the GIHSN protocol should be compliant with their ethical and national regulations for conducting the surveillance.

With respect to existing WHO surveillance capacities, I understand that all data collected through the GIHSN Study questionnaires will be shared with corresponding National Influenza Centers and/or with WHO Collaborating Centers for Reference and Research on Influenza. Influenza strain genetic sequencing data will be shared via GISAID.

Impact HealthCare based in France, is responsible for the coordination of the GIHSN network on behalf of the Foundation for Influenza Epidemiology and is proposing an online data collection tool to ensure timely data display on the GIHSN website. Any obligation related to data protection and data transfer to the Impact HealthCare Company platform should be anticipated.

Data collected by sites receiving funding remains the proprietary of the site. There is no commercial use of the data. Donors (Sanofi, Seqirus, Illumina, IFPMA) do not have access to the data. The data are transferred through a secured channel and the site has full access to the data through a secured platform managed by Impact HealthCare Company.

Impact HealthCare Company is given access to the GIHSN data for epidemiologic research fulfilling the three following conditions:

- Analyses can only be performed for research purposes in line with the mandate of the Foundation (i.e. surveillance and monitoring of influenza and other respiratory virus)
- Analyses are exclusively performed with pseudonymised data
- Any analyses plan will need to be approved beforehand by the Independent Scientific Committee of the Foundation

Analysis results will be 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 beyond the routine annual pooled analysis and they have the possibility to opt-out.
Considering these rules and in order to allow for continued analysis of both historical and current seasonal data, I hereby agree to share with Impact HealthCare Company the data collected at site level.

| Main investigator  
First and Last Name |
|---------------------|
| Name and address of  
institution          |
| Country/region      |

Date

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Signature

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