



Call For proposal- 2019-2020 Influenza Season

LINKING CLINICAL TO VIROLOGICAL AND GENETIC DATA IN EXISTING INFLUENZA SURVEILLANCE NETWORKS

INTRODUCTION

The biannual seasonal influenza vaccine strain selection process which drives the vaccine composition decisions remain challenging and enhanced data from surveillance monitoring and virology sequencing (timeliness, geographic representativeness, clinical relevance) are most needed.

After seven years supporting active surveillance of influenza at hospital level through the implementation of the Global Influenza Hospital Surveillance Network (GIHSN), the Foundation for Influenza Epidemiology (see governance in *Appendix 1*) is evolving toward the development of capacities to link clinical and virological data in Influenza positive patients.

Participation of experienced hospital surveillance sites and virology laboratories with sequencing capacities is sought.

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RESEARCH OBJECTIVES

Research objectives of the 2019 Call for Proposal aims at supporting international capacities developed through the Global Influenza Surveillance and Response System (GISRS) of laboratories to increase the availability of clinical information linked with genetic sequencing of influenza strains to expand the support of the biannual vaccine strain selection process of the WHO's formal recommendation for the composition of human influenza vaccines.

ELIGIBILITY CRITERIA

Applicants should be non-profit public 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 the possibility for confirmed influenza by RT-PCR and subsequent sequencing of the positive specimens in less than 7 days. If no capacities to generate genetic sequence data (GSD) are available, the site may 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 GSD, and submit at a minimum consensus data of the HA and NA segments to the GISAID EpiFlu™ database¹. Clinical information will be captured in the current e-CRF used by the GIHSN (see *Appendix 2*) and includes the link with the GSD and other metadata shared through [GISAID](#).

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:

- Laboratory capacities: The existing full genome sequencing capacities on site or proposed referral system to sequence Influenza positive samples should be described.
- Targeted sample size: The estimated number of sequenced samples expected to be shared via the GISAID platform during the Influenza season is between 50 and 100.
- Clinical information data collection capacities: The site needs to describe the way and the method to access clinical information (using laboratory referral system or using targeted clinical sampling).
- Timelines of the data availability: Sites should be able to upload data into the e-CRF on a weekly basis. Sites with sequencing capacity should upload data in GISAID on a weekly basis. 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.
- Geographical representativeness: sites in countries under-represented in GISAID will be given funding priority.

Cost-effectiveness: the relevance of the cost in relation to expected sample size will be considered. The Foundation is providing catalytic funding and is not expected to fund the full cost of the clinical and sequencing data collection. In September, the Executive committee of the Foundation will select

¹ [GISAID - from Vision to Reality Eurosurveillance, 22\(13\) doi:10.2807/1560-7917.ES.2017.22.13.30494](#) ;

institutions and the amount of the grant provided during the season in order to support the implementation.

A formal letter from the Foundation describing grant modalities and payment milestones will be sent to the sites selected by mid October 2019.

HOW TO APPLY

The call has been posted on the www.gihsn.org website on May 30th, 2019.

All applications have to be submitted on-line on the GIHSN website **before July 15th, 2019** via the application template.

Requirements for applicants:

To be eligible, applicants should be not-for-profit public institutions.

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

- Last annual report
- 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 3*) 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

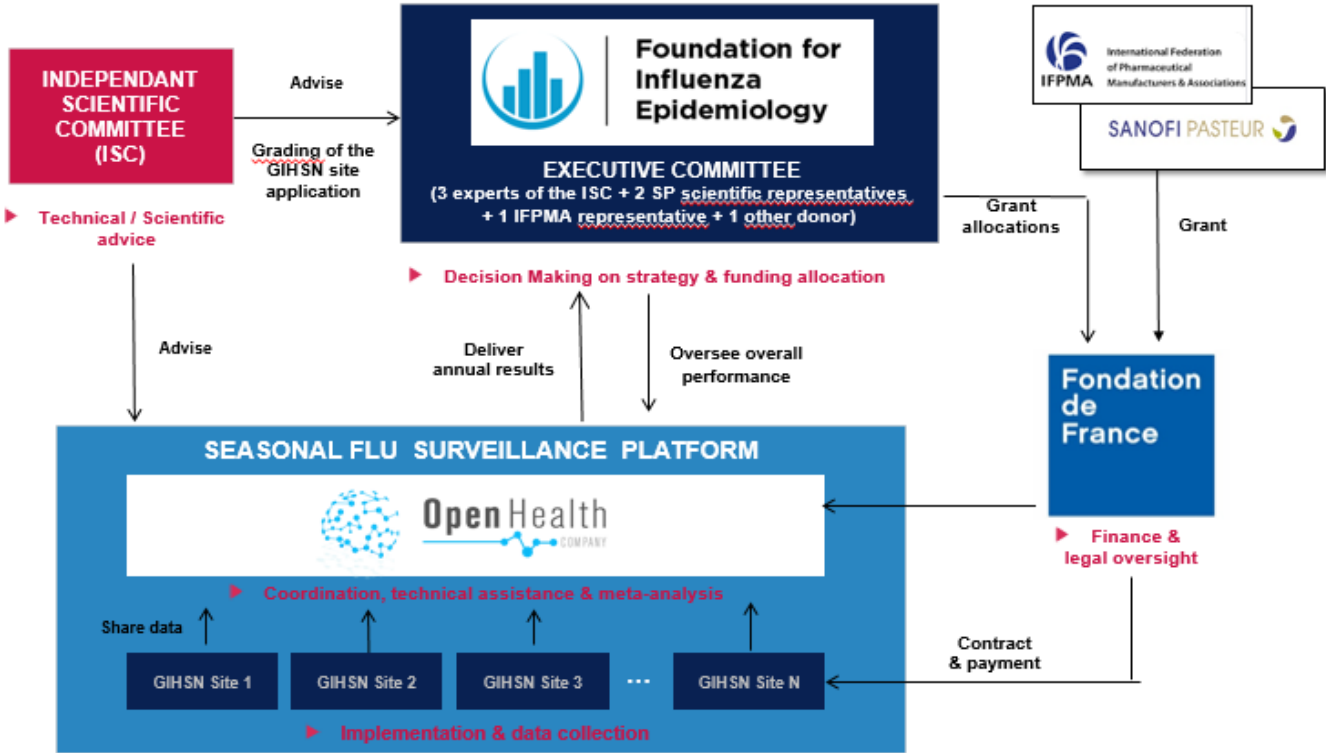
WHO World Health Organisation

Appendix 1: Governance of the Foundation for Influenza Epidemiology

The governance of the Foundation for Influenza Epidemiology is ensured by an Executive Committee, composed of three independent influenza experts, two Sanofi Pasteur scientists and one IFPMA representative observer. The main role is to select applicant sites for funding allocation each year. Following decisions from the Executive Committee in September, grants are provided directly from the Foundation for Influenza Epidemiology to institutions or laboratories responsible for the study implementation.

An Independent Scientific Committee composed of 11 experts² provide recommendations for technical, scientific and related ethical aspects to the Foundation. 3 of these experts are members of the Executive Committee.

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



² Melissa Andrew (GIHSN Canada investigator), Elena Burtseva (GIHSN Moscow investigator), Allen Cheng (Monash Univ, Australia), Jill Ferdinand (CDC, USA), Bruno Lina (Univ of Lyon, France), Feng Luzhao (CDC, China), Marta Nunes (GIHSN South Africa investigator), Justin Ortiz (Univ of Maryland, USA), John Paget (NIVEL, Nederland) , Bobby Reiner (IHME, USA)
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Appendix 2: Main clinical variables to be collected for Influenza positive cases

Description	Rules
Admission diagnosis (letter/code.subcode)	If comp_a_diag = No, must be empty If comp_a_diag = Yes, must be one fo the value from annex 1 of the questionnaire, other values (including empty or NULL value) are not permitted
ICD used	If comp_a_diag = No, must be empty If comp_a_diag = Yes, must be 0 (= ICD-9) or 1 (= ICD-10), other values (including empty or NULL value) are not permitted
Date of admission (yyyy-mm-dd)	Mandatory Must be a valid date, other values (including empty or NULL value) are not permitted
What is the hospital ID?	Mandatory
Patient study identification number	Mandatory For a given season and a given site, (id_hospital+id_patient) must be unique
Sex	Mandatory 0 = male, 1 = female, other values (including empty or NULL value) are not permitted
Age (Years)	Mandatory Must be a valid Integer and >=5, other values (including empty or NULL value) are not permitted
Smoking habits	Must be one the following values. Other values (including empty or NULL value) are not permitted 1 = Current tobacco smoker or quit less than 1 year ago (>100 cigs in a lifetime); 2 = Past tobacco smoker (>100 cigs in a lifetime & stopped at least 1 year before inclusion in the study); 3 = Never Smoker (<100 cigs in a lifetime)
Pregnancy status	Must be one the following values. Other values (including empty or NULL value) are not permitted 0= No; 1 = Yes; 2 = Non Applicable
If yes, pregnancy weeks:	if < 1 week, use the value 0, if you don't know, use the value NA must be a valid integer
Do you have any chronic conditions?If yes, indicate which ones	Must be one the following values. Other values (including empty or NULL value) are not permitted 0= No; 1 = Yes;
Cardiovascular disease / High blood pressure	0 = No, 1 = Yes
Chronic obstructive pulmonary disease	0 = No, 1 = Yes
Asthma	0 = No, 1 = Yes
Diabetes	0 = No, 1 = Yes
Immunodeficiency (except HIV) / Organ transplant	0 = No, 1 = Yes
Renal impairment	0 = No, 1 = Yes
Rheumatologic disease / Autoimmune disease	0 = No, 1 = Yes

Neurological or neuromuscular disease	0 = No, 1 = Yes
Cirrhosis / Liver disease	0 = No, 1 = Yes
Neoplasm	0 = No, 1 = Yes
Obesity	0 = No, 1 = Yes
Active tuberculosis	0 = No, 1 = Yes
HIV infection	0 = No, 1 = Yes
Other	0 = No, 1 = Yes
Prescriptions of antiviral for the current episode	0 = No, 1 = Yes, other values (including empty or NULL value) are not permitted
Starting Date (yyyy-mm-dd)	Must be a valid date
Influenza vaccination for the current season	0 = No, 1 = Yes, 2 = Do not know, other values (including empty or NULL value) are not permitted
Vaccine type	Split, Subunit, Trivalent, Quadrivalent or Do not Know
Vaccinated more than 14 days before onset of the ILI symptoms	0 = No, 1 = Yes, 2 = Do not know
Date of swabbing (yyyy-mm-dd)	Must be a valid date, other values (including empty or NULL value) are not permitted. If you don't know, result = NA
Supplemental oxygen without mechanical ventilation	0 = No, 1 = Yes, 2 = Do not know, other values (including empty or NULL value) are not permitted
Vasopressor support	0 = No, 1 = Yes, 2 = Do not know, other values (including empty or NULL value) are not permitted
ICU admission	0 = No, 1 = Yes, 2 = Do not know, other values (including empty or NULL value) are not permitted
Mechanical ventilation	0 = No, 1 = Yes, 2 = Do not know, other values (including empty or NULL value) are not permitted
Death while hospitalized	0 = No, 1 = Yes, 2 = Do not know, other values (including empty or NULL value) are not permitted
Discharge/death date (yyyy-mm-dd)	Must be a valid date, other values (including empty or NULL value) are not permitted
Main diagnose at discharge/death (letter/code.subcode)	Must be a valid ICD9 code or ICD10 code
Secondary 1 diagnose at discharge/death (letter/code.subcode)	Optional Must be a valid ICD9 code or ICD10 code
Secondary 2 diagnose at discharge/death (letter/code.subcode)	Optional Must be a valid ICD9 code or ICD10 code. NULL if d_diag2 is NULL
ICD used	Must be 0 (= ICD-9) or 1 (= ICD-10), other values (including empty or NULL value) are not permitted
A/H1N1pdm09	0 = No, 1 = Yes
A/ H3N2	0 = No, 1 = Yes
B/Yamagata	0 = No, 1 = Yes
B/Victoria	0 = No, 1 = Yes
Influenza A no lineage	0 = No, 1 = Yes
Influenza B no lineage	0 = No, 1 = Yes
Corona virus	0 = No, 1 = Yes
Metaneumovirus	0 = No, 1 = Yes
Respiratory syncytial virus	0 = No, 1 = Yes
Adenovirus	0 = No, 1 = Yes

Bocavirus	0 = No, 1 = Yes
Parainfluenza virus	0 = No, 1 = Yes
Rhinovirus	0 = No, 1 = Yes
GISAID Accession Number (EPI_ISL)	Should be completed for the data linkage (Clinical/Sequencing) http://gisaid.org/EPI_ISL/123456

Appendix 3: 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](#).

Open Health Company 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 Open Health 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. Sanofi Pasteur does 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 Open Health Company.

Open Health Company is given **access** to the GIHSN data for epidemiological 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 viruses)
- Analyses are exclusively performed with strictly anonymous and aggregated 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 Open Health Company the data collected at site level.

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

Date

Signature
