WELCOME TO THE GIHSN COMMUNITY!
ORGANISATION OF THE MEETING

❖ 19 OCTOBER 12:00–14:00 CET – PLENARY SESSION
  ▪ Update on the GIHSN and discussion of the Global Results for the 2019/2020 season.
  ▪ With an external speech from Dr Wenqing Zhang, WHO, on GISRS and the Covid impact

❖ 20 OCTOBER 9:00–12:00 & 14:00–17:00 CET – 2 REGION SPECIFIC SESSIONS
  ▪ Results by site
  ▪ Covid impact and implementation challenges for the coming season
WEBINAR RULES

Except for the Speakers & Moderators, all attendees will be in “Listening only” mode.

Your questions should be submitted using the Q&A button.

Questions will be discussed after the presentations.

Key questions not answered during the Q&A sessions will be answered in Day 2 sessions if relevant or via email after the webinar.

Thank you for your cooperation!
# Plenary Session 19
**October 12:00-14:00 CET**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker(s)</th>
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</thead>
<tbody>
<tr>
<td>12:00</td>
<td>Welcome &amp; Opening of the Meeting</td>
<td>C Mahé (Foundation)</td>
</tr>
<tr>
<td>12:00-12:10</td>
<td>Welcome messages from all sites (video)</td>
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<tr>
<td>12:00-12:10</td>
<td>Objectives of the Meeting</td>
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<tr>
<td>12:10</td>
<td>Foundation Update: Strategy &amp; Governance</td>
<td>C Mahé</td>
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<tr>
<td>12:10-12:25</td>
<td>Participating sites for the Next Season</td>
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<tr>
<td>12:10-12:25</td>
<td>Presentation followed by Q&amp;A</td>
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<tr>
<td>12:25</td>
<td>GISRS and COVID-19 impact</td>
<td>W Zhang (WHO)</td>
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<tr>
<td>12:25-12:45</td>
<td>Presentation followed by Q&amp;A</td>
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<tr>
<td>12:25-12:45</td>
<td>Moderated by J W McCauley (WHO CC)</td>
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<tr>
<td>12:45</td>
<td>GISAID: Update on Covid-19</td>
<td>S Maurer-Stroh (GISAID)</td>
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<td>12:45-12:55</td>
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<tr>
<td>12:55</td>
<td>GIHSN Update: Last Year Activities &amp; Results</td>
<td>M Andrew (ISC)</td>
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<tr>
<td>12:55-13:35</td>
<td>Presentation followed by Q&amp;A</td>
<td>B Lina (ISC)</td>
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<tr>
<td>13:35</td>
<td>GIHSN Updated Protocol for the Next Season</td>
<td>S Chaves (Foundation)</td>
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<tr>
<td>13:35-13:55</td>
<td>Presentation followed by Q&amp;A</td>
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<tr>
<td>13:55</td>
<td>Closure of the Plenary Session &amp; Introduction to Day 2 Sessions</td>
<td>C Mahé</td>
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<tr>
<td>13:55-14:00</td>
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GIHSN 8TH ANNUAL MEETING, 19-20 OCTOBER 2020

FOUNDATION UPDATE: VISION & GOVERNANCE

Cédric MAHE, President, Foundation for Influenza Epidemiology
Effective influenza surveillance is essential for vaccine strain selection and pandemic preparedness

WHO Global Influenza Surveillance and Response System (GISRS) relies on successful 70 years partnership with collaborating centers & NICs worldwide

Nonetheless, additional components could strengthen GISRS:
- Catalytic funding not to rely only on national funds (see COVID impact)
- Additional focus on Severe Acute Respiratory Infection (essential part of WHO preferred product characteristics for flu vaccines in LMICs)
- Linkage between virus genetic sequencing and clinical significance (better strain selection?)
- Multiple respiratory pathogens detection (e.g. COVID, RSV) for economy of scale
- Advanced analytics

Private sector shares same goals regarding optimization of vaccine performance and the importance of awareness about severe respiratory outcomes → untapped potential for collaboration, synergistic funding

Toward a PPP funding mechanism for respiratory virus surveillance and control
LATEST DEVELOPMENTS

• **Dialog with WHO GIP**
  - provision of data for the annual vaccine strain selection (NGS + clinical data)
  - Potential use the GIHSN to generate COVID-19 data: site feasibility conducted in April

• **Diversification of funding**: 2 new donors (Illumina and Seqirus) in addition of Sanofi Pasteur and IFPMA provide catalytic funding which complete national investments

• **Expansion of the sequencing activities**: strain sequencing platform, GISAID partnership

• **Discussion of a collaboration in respiratory virus surveillance and epidemiology with Institut Pasteur**

• **Potential link with Alliance for Influenza Pandemic Preparedness**. The Foundation is part of the Alliance and could be involved in the action plan (burden of disease awareness)
EXECUTIVE COMMITTEE MEMBERS

Executive Committee Members:
• Cédric Mahé, Sanofi Pasteur
• Erica Dueger, Sanofi Pasteur
• Mendel Haag, Seqirus
• Volker Liebenberg, Illumina
• Paula Barbosa, IFPMA
• Bruno Lina, Independent Scientific Committee
• John Paget, Independent Scientific Committee
• Melissa Andrew, Independent Scientific Committee
INDEPENDENT SCIENTIFIC COMMITTEE

Mandate

➢ Review and advise on the scientific deliverables such as the protocol, analyses, interpretation of results, report(s), scientific communication and publications
➢ Advises on technical and scientific topics and provides specific recommendations
➢ Grading of the proposal to the tender
➢ 3 designated representatives at the Executive Committee

Composition

➢ The Committee is composed of 5 to 8 independent experts and 2-3 investigators from the GIHSN network
➢ Membership currently under renewal
FOUNDATION GOVERNANCE

**EXECUTIVE COMMITTEE**
(3 ISC + 2 Sanofi Pasteur + Illumina + Seqirus)

- Decision Making on strategy & funding allocation

**COORDINATION TEAM**
(Chair ISC + SP + CRO)

- Deliver annual results
- Oversee overall performance

**INDEPENDANT SCIENTIFIC COMMITTEE**
(include 3 site representatives)

- Technical/Scientific advice

**SEASONAL FLU SURVEILLANCE PLATFORM**

- Coordination, technical assistance & meta-analysis
- Implementation & data collection

**Coordinating CRO**

- Share data

**GIHSN Site**
1 2 3 N

**GIHSN Site**

**Coordination team**
(Co-chaired ISC + SP + CRO)

**Fondation de France**

- Funding
- Grant allocations
- Finance & legal oversight

- Coordinating contract

**SHARE DATA**

- GIHSN Site 1
- GIHSN Site 2
- GIHSN Site 3
- GIHSN Site N
Contribution of FTEs from SP staff (during this contribution, they do not represent SP interest)

- Sandra Chaves (0.1 FTE - scientific)
- Laurence Torcel-Pagnon (0.2 FTE - coordination)
- Cédric Mahé (0.1 FTE - strategy & partnerships)
- Myriam Beigeaud (0.1 FTE - admin)
SITES PARTICIPATING TO THE GIHSN IN THE 2019-2020 & 2020-2021 SEASON

North America
Canada
Mexico

South America
Brazil
Argentina
Peru

Eurasia
Romania
Serbia
France-Paris
France-Lyon
Ukraine
Spain
Russia (2)

Africa
Ivory-Coast
South Africa
Kenya
Morocco

Middle East
Lebanon
Turkey

Asia/Pacific
China-Fudan
China-Wuhan
India
Nepal
Bangladesh

2019-2020
2019-2020 & 2020-2021
2020-2021
GISRS AND COVID-19 IMPACT

Dr Wenqing ZHANG, Head of Global Influenza Program, WHO
GISRS and COVID-19 impact

Wenqing Zhang

GIHSN Global Annual Meeting 2020
19-20 October • Virtual meeting
Response to COVID-19 pandemic:

GISRS in action since day 1 of the identification of SARS-CoV-2
TOP URGENT: GSD (Genetic sequence data) sharing

• GSD sharing – critical for diagnostic development, risk assessment ….
• ABS – Access and Benefit Sharing
• GISAID – the GISRS mechanism for influenza GSD sharing

• 2020-01-10 1st GSD shared via GISAID (< 48 hours)

EpiFlu™ → EpiCoV™

• ~118K whole genomes of SARS-CoV-2 as of 2 Oct 2020
TOP URGENT: EQAP (external quality assessment program)

- Evaluate lab diagnostic quality of the novel virus SARS-CoV-2; understand the global capacity
- GISRS mechanism of annual EQAP for influenza since 2007
- Influenza EQAP → WHO COVID-19 EQAP
  - 8 Feb initiated discussion
  - Confirmed contract 15 March – 31 August
  - 16 April – 1st shipment going out

164 countries (233 labs) participated:
  - 94% participating labs all correct
  - 95% participating countries with all correctness full capacity in place
  - 96% of labs with 2019 influenza EQAP all correct record, all correct for COVID-19 virus
Capacity built through influenza readily \rightarrow COVID-19 response

- **FluMart** \rightarrow CoVMart: COVID data reporting
- GISRS influenza **shipping mechanism** \rightarrow COVID-19 virus materials shipping
- Influenza pandemic **special study** protocols \rightarrow COVID-19 serology and early investigation protocols
- ~90% national COVID-19 labs are **NICs** or labs associated with GISRS
- **GISRS mechanisms** e.g. TORs of H5RefLabs \rightarrow COVID-19 Reference Labs

- **COVID-19 sentinel surveillance by GISRS**

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Operational considerations for COVID-19 surveillance using GISRS

Interim guidance
26 March 2020

**World Health Organization**
Impact on influenza surveillance and monitoring

Reporting to FluNet - global
Specimens processed for influenza by WHO Region

AFR

AMR

EMR

EUR

SEAR

WPR
Shipments to WHO Collaborating Centres (via SFP)
Impact on influenza surveillance and monitoring

**Reporting indicators of PISA**

**Total responses (n=31)**
(from AFRO, AMRO, SEARO and WPRO)

Influenza sentinel hospitals (e.g. SARI surveillance) repurposed to COVID-19 designated hospitals?
WHO guidance - how to address the issue

Preparation of GISRS for the upcoming influenza seasons during the COVID-19 pandemic – practical considerations

Interim guidance
26 May 2020

Influenza
Preparing GISRS for the upcoming influenza seasons

In the context of the COVID-19 pandemic, GISRS, regional influenza networks, and national influenza surveillance systems should prepare for the co-circulation of influenza and SARS-CoV-2 viruses in the upcoming and subsequent influenza seasons and for the possible emergence of influenza viruses of pandemic potential. This document summarizes operational considerations to continue monitoring the persistent influenza threat and maintain influenza surveillance while responding to the current COVID-19 pandemic.

Read the document

https://www.who.int/influenza/gisrs_laboratory/upcoming_flu_season/en/

- For the persistent influenza threat: continuous surveillance, monitoring, and timely assessment of associated risks of seasonal, zoonotic, and pandemic influenza as specified in the WHO Terms of Reference of GISRS.

- For the current COVID-19 response: continued leverage of GISRS and associated surveillance systems for COVID-19 sentinel surveillance.
Optimize the use of GISRS influenza systems

- Enhance **vigilance** for the threat of influenza
- Surveillance for **co-circulation** of influenza and COVID-19
  - Utilize existing influenza sentinel surveillance systems – sustainable, practical
  - Atypical seasonality 2020 – strategies for inter-seasonal periods

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>Myanmar</th>
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<tbody>
<tr>
<td>COVID % positivity among sentinel samples</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Universal COVID % positivity (Our World in Data)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID cases reported to WHO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sentinel samples tested per week</td>
<td>46 - 210</td>
<td>161 - 324,226</td>
</tr>
<tr>
<td>universal testing per week</td>
<td>4 - 730</td>
<td>441 - 20,755</td>
</tr>
</tbody>
</table>
COVID-19 sentinel surveillance

Between week 26-39: 17 ~ 33 countries reported timely
COVID-19 sentinel surveillance by WHO Region

AFRO

PAHO

EMRO

EURO

SEARO

WPRO

Countries, areas, territories

Week

Non-sentinel sites
Sentinel sites
Not reporting
Samples >50 at sentinel
WHO e-Consultation 6-8 October
- main outcomes and observations

• Reassured **common ground** of a global system → GISRS and associated surveillance systems → influenza and COVID-19

• **Consensus** on essential components of the global systems for influenza and COVID-19 sentinel surveillance e.g. case definition, testing algorithms:
  - Primary roles and responsibility: influenza surveillance and monitoring
  - Whenever possible, add SARS-COVID-2 in sentinel surveillance
  - Clearer vision on how to function GISRS systems in the upcoming next 6-12 months
  - Real experience from Southern Hemisphere 2020 valuable

• Challenges real; **importance and benefits** of GISRS for both influenza and COVID-19 **not** fully understood by decision-making levels in many countries

• Importance of reporting to FluNet and FluID (for both influenza and COVID-19 surveillance data) **not** fully understood by some countries

• High expectation for **Multiplex** influenza+SARS-CoV-2 – *vs* – limited supply
  - CDC supply limited; commercial kits with constraints
What GIHSN can support

- Sustain sentinel surveillance
  - Secure 150 (minimum 50) per week of **quality** SARI/ILI/ARI specimens

- Test for influenza and SARS-COVID-2
  - When resource allows, test for both

- Report the aggregated results through same influenza reporting channel, same timing
  - Additional data fields already built into FluNet/FluID, including potential co-infections

- Vigilant of influenza threat
  - Continue GISRS function on influenza, especially now!
Acknowledgement

• **WHO GISRS** (Global Influenza Surveillance and Response System)
• GISRS associated **national/sub-national surveillance systems**
• **Countries** hosting GISRS institutions

• WHO Global Influenza Programme
Thank You
GIHSN 8TH ANNUAL MEETING, 19-20 OCTOBER 2020

GISAID: UPDATE ON COVID-19

Sebastian MAURER-STROH, GISAID
“GISAID was a well-oiled machine when the Coronavirus hit”

BBC and PRI the World

Dr. Sebastian Maurer-Stroh
Bioinformatics Institute (BII)/A*STAR

Near Real-Time Data Sharing begins 2009

Sharing the first and all subsequent genomes of the pandemic H1N1 influenza virus via GISAID (2009)

Rebecca Garten et al, U.S. CDC
Near Real-Time Data Sharing continues, e.g. 2013

Sharing the first and all subsequent genomes of the novel, highly pathogenic H7N9 avian influenza virus via GISAID

Tian Bai et al, China CDC
GISAID was ready for Disease X ==＞ newly emerging coronavirus

Viral pneumonia cases reported in central China

14-Jan-2020

31-Dec-2019

Whole genome sequences for the novel coronavirus (2019-nCoV) from the Chinese authorities were shared with WHO and have also been submitted by Chinese authorities to the GISAID platform so that they can be accessed by public health authorities, laboratories and researchers.

CORONAVIRUS
(2019-nCoV)

World Health Organization Western Pacific and South East Asia (WHO)

Whole genome sequences for the novel coronavirus (2019-nCoV) from the Chinese authorities were shared with WHO and have also been submitted by Chinese authorities to the GISAID platform so that they can be accessed by public health authorities, laboratories and researchers.

CORONAVIRUS
(2019-nCoV)

World Health Organization Western Pacific and South East Asia (WHO)

Complete genomes sequenced

Less than 48 hours

Shared with the world via GISAID

2020-01-08

EPI_ISL_402119 via GISAID EpiCoV™

EpiCoV™

2020-01-10
GISAID Data instantly yields Results for Targeted Response

1. Development of first diagnostics kits and refinement through ongoing surveillance for mutations

2. Identification of potential drug and vaccine targets on hCoV-19 through repurposing

3. Genomic epidemiology of hCoV-19, allows analysis of the exportation and importation events of viruses between countries, contact-tracing in countries, or identification of transmission chains

4. Evidence that the virus has not drifted to significant strain difference, with in particular the cell receptor binding pocket being followed closely

5. Identification of animal precursors of hCoV-19 (in bats and pangolins)
Real-time data sharing is not achieved by governmental Regulations
... it is incentivized by the confidence in transparent sharing mechanisms
Where did it come from?

Light Orange ... previous bat CoVs
Orange ... previous closest bat precursor (Yunnan 2013)
Red ... new bat CoVs (Yunnan 2019)
Light blue ... hCoV-19 2019-2020
Green ... pangolin CoV (Southern China 2019)
Blue ... SARS CoV

Southern China 2019: precursors in 2 species
Early outbreak genomes showed very low diversity, only a handful of mutations over 30,000 bases

Thailand: First full genomes outside of China were still identical to the Wuhan consensus

Nucleotide (base) differences among early outbreak strains
How can you detect it?

**PCR-based (RNA amplification)**

- For active viral infection
- Highly specific
- Quick to develop
- Lab-based

**Serology-based (Antibody binding)**

1. For later stage of infection
2. After infection (immune memory)

- Slow to develop
- Can become point-of-care

Antibody binding region (epitope)

by BII/GIS, A*STAR Singapore
Mutations leading to split into genetic groups (clades)

Full genome tree derived from all outbreak sequences 2020-10-16

Notable changes:

- 135707 full genomes (+3834) (excluding low coverage, out of 145201 entries)
- Updated clades:
  - S clade 6358 (+70)
  - L clade 4181 (+53)
  - V clade 5251 (+48)
  - G clade [S477X] 30972 [92] (+1329 [+0])
  - GR clade [S477X] 53178 [7351] (+1115 [+5])
  - GH clade [S477X] 31930 [618] (+1151 [+52])
  - Other clades 3837 (+32)

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

Blue: new from Asia
Green: new from Oceania
Magenta: new from Americas
Red: new from Europe
Yellow: new from Africa
Grey: from previous updates
CoVsurver tool to analyse mutations – example spike S477N

Protein: Spike
Coronavirus type: SARS-CoV-2 (2019)
Mutation (as in paper): S477N
neutral AA: S
mut. AA: N
Effect: Host Change

Comment:
In a deep mutational scanning experiment that expresses Spike S2O in a yeast-display platform, S477N mildly increases the binding to ACE2 (apparent dissociation constant delta-log10 value: 0.34).

Literature reference:
Spike S477N in the paper is at an equivalent position of the mutation in Sars CoV-2.
Surface antigen mutations appear random and not driven by antigenic selection (sites on top) so far.

**How can you treat it?**

**Vaccines, mAbs**

- **Common spike mutations within the outbreak – Sep 2020**
- **Mutations with occurrence >100**
- **Mutations with occurrence >10**

**Trimer complex of viral spike glycoprotein**

**Small molecule drugs**

- **Polymerase hCoV-19 vs SARS**
  - nsp12 (gray=identical, red=mutated) complex with nsp7 (yellow) and nsp8 (cyan, green)

Inhibitors developed against the SARS-CoV polymerase have good potential to bind similarly to hCoV-19 -> **Drug repurposing**

**Remdesivir**
2 of 4 reinfection cases have mutations possibly interfering with the structural conformation of glycosylation sites in a region that is also broadly recognized by antibodies which would provide a hypothetical mechanism for immune escape potentially contributing to permitting second infection. However, this doesn’t apply to all cases and many other factors could play a role too. Importantly, these mutations are rare and occur sporadically without causing large clusters so far.
Summary – GISAID contributes to...

1. Development of first diagnostics kits and refinement through ongoing surveillance for mutations
2. Identification of potential drug and vaccine targets on hCoV-19 through repurposing
3. Genomic epidemiology of hCoV-19, allows analysis of the exportation and importation events of viruses between countries, contact-tracing in countries, or identification of transmission chains
4. Evidence that the virus has not drifted to significant strain difference, with in particular the cell receptor binding pocket being followed closely
5. Identification of animal precursors of hCoV-19 (in bats and pangolins)

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence and meta data.
2019/2020: 20 SITES HAVE SHARED THEIR DATA ON THE GIHSN PLATFORM

#included = 14,429

#LCI = 4,326

#sequenced = 753

#ORV+ = 2,298
All sites apply a standardized protocol

- Key focus: Link clinical and virologic data (including whole genome sequence) from hospitalized patients with acute respiratory infections, with emphasis on lab-confirmed influenza cases

Trained study staff on site collect relevant information

- 2 questionnaires (<5 years old / 5 years old and more)

All patients meeting the inclusion criteria and providing consent will be swabbed. Samples are sent to reference laboratory for RT-PCR or tested on site.

WGS must be generated for a minimum of 50-100 flu positive specimens.

- If the site has no WGS capacity, specimens can be sent to the National Influenza Center in Lyon, France, under Terms of Reference for sharing materials
Results of WGS are shared on the GISAID platform with a “GIHSN” tag.

Epi data are collected for positive samples that have been sequenced and, if possible, for all positive cases and negative cases (for sequenced specimens, the questionnaires include a GISAID number to allow linkage between WGS results and clinical information).

Questionnaires are uploaded on the GIHSN Data platform using a e-CRF or excel files.
Descriptive analysis and outcomes

(Data as of 9/10)
GLOBAL PATIENT INCLUSION
– NEARLY 90,000 PATIENTS OVER 8 YEARS

N=87,253

*sequenced samples shared with GISAID
CONTRIBUTION BY HEMISPHERE
SEASON 2019-2020

13 SITES:
- CANADA
- CHINA
- FRANCE – LYON & PARIS
- LEBANON
- MEXICO
- ROMANIA
- RUSSIA – MOSCOW & ST PETERSBURG
- SERBIA
- SPAIN
- TURKEY
- UKRAINE

4 SITES:
- INDIA
- IVORY COAST
- NEPAL
- PERU

3 SITES:
- BRAZIL
- KENYA
- SOUTH AFRICA
  (ANALYSIS PENDING)

11,349
87%
3,778
2,022
739
955
77
48
0
2,125
471
228
14

N= 14,429

- # Included
- # LCI
- # ORV+
- #Sequenced
2019-2020 GLOBAL AGE DISTRIBUTION & VACCINATION RATE

N = 14,429
2019-2020 EVOLUTION OF INFLUENZA CASES NORTHERN HEMISPHERE

Flu season: W45 early November 2019 – W16 early April 2020

Peak W5 end January

N = 11,349
2019-2020 EVOLUTION OF INFLUENZA CASES
SOUTHERN HEMISPHERE

« Season » : W2 mid January – W12 mid March

Peak W11
mid March

N= 955
2019-2020 EVOLUTION OF INFLUENZA CASES
INTERTROPICAL HEMISPHERE

Peak W6 early February

Year-round surveillance

N= 2 125
INFLUENZA VIRUS STRAIN EVOLUTION OVER MULTIPLE SEASONS: NORTHERN HEMISPHERE
INFLUENZA VIRUS STRAIN EVOLUTION: INTERTROPICAL REGIONS
INFLUENZA VIRUS STRAIN EVOLUTION: SOUTHERN HEMISPHERE

Virus distribution per time period
Population: LCI (582)
2019-2020 INFLUENZA VIRUS STRAIN DISTRIBUTION PER AGE GROUP - NORTHERN HEMISPHERE
2019-2020 INFLUENZA VIRUS STRAIN DISTRIBUTION PER AGE GROUP - INTERTROPICAL HEMISPHERE

Virus distribution by age
Population: N=471

- A-Not Subtyped
- A/H1N1
- A/H3N2
- B-Not Subtyped
- B/Victoria
- B/Yamagata
- Mixed
OTHER RESPIRATORY VIRUS STRAINS EVOLUTION OVER MULTIPLE SEASONS: NORTHERN HEMISPHERE

N=15,734
OTHER RESPIRATORY VIRUS STRAIN EVOLUTION: INTERTROPICAL REGIONS

Virus distribution per time period
Population: ORV (~997)

- Adenovirus
- Bocavirus
- Corona virus
- Metaneumovirus
- Mixed
- Parainfluenza virus
- Respiratory syncytial virus
- Rhinovirus

N=997
OTHER RESPIRATORY VIRUS STRAINS EVOLUTION: SOUTHERN HEMISPHERE

Virus distribution per time period
Population: ORV+ (1 807)

- Adenovirus
- Bocavirus
- Coronavirus
- Metameunovirus
- Mixed
- Parainfluenza virus
- Respiratory syncytial virus
- Rhinovirus

N=1 807
2019-2020 OTHER VIRUS STRAIN DISTRIBUTION PER AGE GROUP - NORTHERN HEMISPHERE

Virus distribution by age
Population: 2022

N=2,022
2019-2020 OTHER VIRUS STRAIN DISTRIBUTION PER AGE GROUP - INTERTROPICAL REGIONS

N=228
CHRONIC CONDITIONS LCI+ VS ORV+
PATIENTS <5

- Immunodeficiency/organ transplant
- Neoplasm
- HIV exposure
- Congenital Heart Disease
- Asthma
- Cardiovascular disease
- Obesity
- Malnutrition
- Prematurity
- Neuromuscular disease
- Other

N= 2,629

#Patient LCI+
#Patient ORV+
CHRONIC CONDITIONS LCI+ VS ORV+
PATIENTS >=5

- Immunodeficiency/organ transplant
- Rheumatologic autoimmune disease
- Neuromuscular disease
- Asthma
- Renal impairment
- Neoplasm
- Obesity
- Chronic obstructive pulmonary disease
- Diabetes
- Cardiovascular disease
- Other

N=3 995
ICU ADMISSION PER AGE GROUP
LCI+ VS ORV+

- < 5 yo: 5% LCI+, 7% ORV+
- 5 - < 18: 4% LCI+, 8% ORV+
- 18 - < 45: 3% LCI+, 3% ORV+
- 45 - < 65: 10% LCI+, 7% ORV+
- 65 - < 80: 12% LCI+, 6% ORV+
- 80+: 7% LCI+, 9% ORV+

N=16 434
MORTALITY PER AGE GROUP
LCI+ VS ORV+

N=16 434
GIHSN 8TH ANNUAL MEETING, 19-20 OCTOBER 2020

STRAIN SEQUENCING 2019/2020

Bruno LINA, University of Lyon, GIHSN Independent Scientific Committee
**Shipment:**
- Transport by World Courrier (organized Open Health)
- Predefined dates were not applicable
- Additional extra sequences not always used

**Material:**
- Extracted RNA (volume 60μL per specimen, ct<30 and below)

**Documentation:**
- Excel table called « GISAID epiflu uploader » with completed mandatory fields
GIHSN STRAIN SEQUENCING PERSPECTIVES FOR 2019-2020

<table>
<thead>
<tr>
<th>Country</th>
<th>Quantity</th>
<th>Shipments</th>
<th>Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>100</td>
<td>3 shipments</td>
<td>Nov 4, Jan 1, Mar</td>
</tr>
<tr>
<td>Nepal</td>
<td>65</td>
<td>3 shipments</td>
<td>Nov 4, Jan 1, Mar</td>
</tr>
<tr>
<td>Kenya</td>
<td>100</td>
<td>3 shipments</td>
<td>Dec 1, Jan, Mar</td>
</tr>
<tr>
<td>France – Lyon</td>
<td>50</td>
<td>(real-time)</td>
<td></td>
</tr>
<tr>
<td>France – Paris*</td>
<td>100</td>
<td>3 shipments</td>
<td>Dec 2, Jan, Mar</td>
</tr>
<tr>
<td>Russia – Moscow</td>
<td>60</td>
<td>3 shipments</td>
<td>Dec 2, Jan, Mar</td>
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<td>100</td>
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<td>60</td>
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<td>Dec 2, Jan, Mar</td>
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<tr>
<td>Peru</td>
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<td>3 shipments</td>
<td>Jan 1, Jul, Sept</td>
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<td>100 HN-HS</td>
<td>3 shipments</td>
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<tr>
<td>Argentina</td>
<td>75 HS</td>
<td>3 shipments</td>
<td>May 2, Jul, Sept</td>
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</table>

TOTAL / 860 incl 250HS
GIHSN STRAIN SEQUENCING REALITY FOR 2019-2020

- India (111) 3 shipments: week 4 of Jan, week 2 of Feb
- Nepal (0) 0 shipment
- Kenya (63) 2 shipments week 2 Feb, week 2 Sept
- France – Lyon (42) (almost real-time)
- France - Paris (33) 1 shipments week 2 Sept
- Russia – Moscow (0) 0 shipment
- Serbia (50) 2 shipments week 2 Jan, week 1 Mar
- Ukraine (61) 3 shipments week 2 Jan, week 1 mar, week 4 Jun
- Lebanon (87) week 2 Jul
- Peru (14) 1 shipments week 1 sept
- Bangladesh (0) 0 shipments
- Ivory Coast (pending)
- Argentina (0) 0 shipments

TOTAL / 461 plus 215 off-site
GIHSN SHIPMENT PERSPECTIVES FOR 2019-2020

Prepared 2019-2020 calendar for shipments/data sharing

2019

Shipments on Tuesdays

2020
GIHSN SHIPMENT REALITY FOR 2019-2020

Prepared 2019-2020 calendar for shipments/data sharing

2019

Shipments on Tuesdays

2020
# SUMMARY OF GIHSN SEQUENCE ANALYSIS

<table>
<thead>
<tr>
<th>Pays d'origine</th>
<th>Date réception</th>
<th>Nbre de séquences reçues</th>
<th>Nbre de séquences validées au CRMT</th>
<th>Nbre de séquences non séquences / Ahec</th>
<th>GI SAO</th>
<th>Nbre de séquences non séquences / Ahec / double muco</th>
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<th>seq en cours</th>
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</table>

676
Majority of A(H1N1)pdm09, a minority of A(H3N2) viruses.

B Victoria strains majority of the detected B viruses, no B Yamagata detected in the network.

Phylogenetic analysis not completed:
- sequences from off-sites not all received
- sequencing of the last strains still pending (late arrivals)
PRELIMINARY COMPARISON GISRS – GIHSN : H1N1PDM09

K130N, N156K, L161I, V250A in HA1
PHYLOGENY OF RECENT H1N1PDM09 (INCL 6B1.A/156K)
PHYLOGENY OF RECENT GIHSN H1N1PDM09
(INCL 6B1.A/156K)
Same diversity (T135K-A and T135K-B), but limited number of viruses. New viruses to be sequenced.
PHYLOGENY OF RECENT H3N2
(3C.2A1B SUBCLADES)
PHYLOGENY OF RECENT GIHSN H3N2 (3C.2A1B SUBCLADES)

Clade 3c.2A1b
PRELIMINARY COMPARISON GISRS – GIHSN: B VICTORIA

Δ162-164, K136E, G133R

B/Washington/02/2019

E128K → ?
PHYLOGENY OF RECENT B VICTORIA
(Δ162-164 1A SUBCLADE)
PHYLOGENY OF RECENT GIHSN B VICTORIA
(Δ162-164 1A SUBCLADE)
SUMMARY

• More input from the sites than last year
• Some very participative labs
• Completion of the data not finished yet
• Overall 500 sequences generated from the Lyon lab

• Very large representation of the A(H1N1)pdm09 and B Victoria from hospital cases
• Sharing of sequence data and GISAID upload satisfactory
• Good feedback from sites

• Improvement in TaT for sequence production and sharing
• Improvement in shipment of material
EVOLUTION OF THE ENVIRONMENT

Acquisition of a Mosquito platform
• Reduction of cost per sequence
• Better preparation for the sequencing (automation)

Illumina nextseq on site (confirmed)
• Improved TaT
• dedicated staff

Hiring of a Bio-Ingeneer (Hadrien REGUES) and a PhD student (Gregory QUEROMES)
• Provide analytical and comparison tools
• involved in the wet and dry lab
• Development of a website for better interaction with the sites
ACKNOWLEDGEMENTS

Staff from Lyon NIC

Gwendoline Burfin
Hadrien Regue
Solene Brun
Marine Jourdain
Maude Bouscambert
Laurence Josset
Martine Valette

Surveillance GISRS Data

John McCauley
GISRS network

System for Data collection

GISAID

Source of Data

GIHSN sites
GIHSN SURVEILLANCE PROTOCOL 2020/21

Sandra CHAVES, MD, MSc, Executive Officer Foundation for Influenza Epidemiology
OBJECTIVES

• Expand international laboratory and surveillance capacity and data sharing
• Support the biannual WHO vaccine strain selection process
• Link clinical and virologic (including whole genome sequence) data from hospitalized patients with acute respiratory infections
• Describe the distribution of the different influenza strains (A/H1N1, A/H3N2, B/Yamagata, B/Victoria) among these severe cases over a wide range of geographic areas
ELIGIBILITY CRITERIA

• Patients with an acute process
• Patients whose indication for admission was any of a predefined set of conditions, described as possibly associated with a recent influenza infection (list provide to sites)
• Study nurse or attending clinician will identify eligible cases in the hospital admission log, chart review or available records
• All eligible patients hospitalized in the previous 72 hours with hospital stay of at least 1 night would be screened
INCLUSION CRITERIA

• Patients ≥5 years will be included in the study if they are hospitalized within 7 days of community onset influenza like-illness, defined as

**Modified ECDC definition of influenza like-illness (ILI)**
Combination of:
At least one of the following four systemic symptoms (ICD-9-CM code): Fever or feverishness (780.6), headache (784.0), myalgia, (729.1) or malaise (780.79);
**AND**
At least one of the following four respiratory symptoms (ICD-9-CM code): Cough (786.2), sore throat (787.2), shortness of breath (786.05), or nasal congestion (478.19)

• Patients <5 years will be included if admission associated with any of the conditions listed as part of eligibility criteria – if onset within 7 days from admission
SAMPLE COLLECTION

Each patient meeting the inclusion criteria and providing consent would have the following specimens collected:

- A nasopharyngeal (NP) or nasal swab combined with an oropharyngeal (OP) swab in a viral transport media (VTM)

Samples are sent to reference laboratory for RT-PCR or tested on site

**Note**: There may be some variation on specimen collected by site that need to be captured

- Nasal and throat swabs combined are well accepted and the yield is like NP/OP combined

WGS must be generated for a **minimum of 50-100 flu positive specimens**

- If the site has no WGS capacity, specimens can be sent to the National Influenza Center in Lyon, France, under Terms of Reference for sharing materials
SAMPLE MANAGEMENT AND LABORATORY PROCEDURES

• Samples kept at –20ºC until sent to reference laboratory. Multiplex real-time RT-PCR
• Influenza A/B viruses (influenza A subtyped and influenza B lineage identified)
• **Testing for SARS-CoV-2 simultaneously (?)**
  • Other respiratory pathogens (human coronavirus, metapneumovirus, bocavirus, respiratory syncytial viruses, adenovirus, parainfluenza viruses, rhinovirus) optional
    ✓ Analysis for respiratory viruses other than influenza can be carried out after the study ends (if samples are stored appropriately)

• Storage (-20C or -70C) of all influenza positive and negative study samples for a minimum of one year
• All influenza positive (and SARS-CoV-2 positive, if performed) samples plus a subset of 30% of negative samples should be stored for an additional 3 years
  ✓ This will assure sample availability for additional retrospective investigations (e.g. SARS-CoV-2, testing of lab diagnostic tools or investigation of emerging new pathogens)
GENOME SEQUENCING

• Whole genome sequencing (WGS) must be generated for a **minimum of 50-100 influenza positive specimens**
• Samples for WGS will be selected using specific criteria to be agreed upon by the GIHSN Independent Scientific Committee (ISC) prior to the start of the 2020/21 influenza season
• If the site has no WGS capacity, specimens can be sent to the National Influenza Center in Lyon, France, under Terms of Reference for sharing materials in GISRS
  ✓ Shipments are organized by OpenHealth

<table>
<thead>
<tr>
<th>Hemisphere</th>
<th>Early season</th>
<th>ICU/deaths and vaccine failures</th>
<th>Samples per month</th>
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</thead>
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<tr>
<td>Northern</td>
<td>all samples until 15 January</td>
<td>All</td>
<td>10-30 (during season)</td>
</tr>
<tr>
<td>Southern</td>
<td>all samples until 15 July</td>
<td>All</td>
<td>10-30 (during season)</td>
</tr>
<tr>
<td>Intertropical</td>
<td>NA</td>
<td>All</td>
<td>5-15 (all year)</td>
</tr>
</tbody>
</table>
EPI AND CLINICAL DATA COLLECTION

- Trained study staff collect relevant information by a combination of face-to-face interview with patient or caretaker and attending physicians, and by reviewing clinical records (to capture clinical outcome data).
- Influenza vaccination status is self-reported (patient or caretaker/representative):
  - If patient had received the influenza vaccine for the current season, date of vaccination is captured.
  - Whenever possible vaccination information will be validated by existing registries, vaccination cards or through contacting the place where the vaccine was administered.
• Two questionnaires still available (children <5 years vs. those ≥5 years)
• Capture information on testing for specific pathogens (including SARS-CoV-2)

• In the ≥5 years questionnaire
  ✓ Added few extra variables to assess clinical presentation (nausea and vomiting, diarrhea, new loss or taste or smell, chest pain)
  ✓ Clarify severity questions to be captured at admission and frailty score to be done in all patients 50 years and older

• In the <5 years questionnaire
  ✓ Added signs and symptoms for acute episode (not collected before), accommodating also those associated with COVID-19
QUESTIONS?

WE’re MEETING TO TALK ABOUT COL-

WHAT’S “COL”? 

IT LOOKS LIKE HIS SCREEN FROZE.

SHOULD WE WAIT?

YEAH, LET’S WAIT.

I WAS ON MUTE... I AGREE. 

HI, SORRY I'M LATE. WHAT DID I MISS?

-LABORATION.

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GIHSN 8TH ANNUAL MEETING, 19-20 OCTOBER 2020

CLOSURE & INTRODUCTION TO DAY 2

Cédric MAHE, Foundation for Influenza Epidemiology
20 OCTOBER: 2 REGION SPECIFIC SESSIONS - DISCUSS SITE RESULTS & IMPLEMENTATION CHALLENGES

9:00–12:00 CET
SITES SESSION 1

CHINA - FUDAN
CHINA - WUHAN
INDIA
BANGLADESH
NEPAL
LEBANON
TURKEY
RUSSIA - ST PETERSBURG
RUSSIA – MOSCOW
UKRAINE
SERBIA
ROMANIA

14:00–17:00 CET
SITES SESSION 2

CANADA
MEXICO
BRAZIL
ARGENTINA
PERU
SOUTH AFRICA
KENYA
IVORY COAST
SPAIN
FRANCE - PARIS
FRANCE - LYON
THANK YOU!