

Scientific Advisory Group on the Origins of Novel Pathogens (SAGO)

SAGO was formed in the context of the continued threat of the emergence or re-emergence of pathogens with epidemic and pandemic potential

Addressing needs

- A global framework to study future emerging and re-emerging pathogens, including
 - Comprehensive and coordinated studies
 - A holistic approach to study the emergence of high threat zoonotic pathogens including the animal human interface, environmental safety, biosafety and biosecurity
 - An established framework for studying emerging pathogens where and when they emerge.

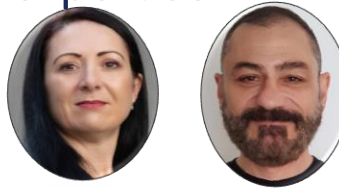
Addressing gaps

- A scientific advisory group to advise WHO on technical and scientific considerations regarding origins of emerging and re-emerging pathogens:

The Scientific Advisory Group for the Origins of Novel Pathogens (SAGO)

Meetings and Organization of the SAGO

- Creation of SAGO: November 2021
- 21 plenary SAGO meetings held to date
- 27 members with significant and diverse expertise
- Chair: Professor Marietjie Venter
- Vice-Chair: Dr Jean-Claude Manuguerra
- Observers
 - 6 working groups
 - Human, epidemiology
 - Animal/Human Interface
 - Environment/Ecological
 - Early Investigation/Anthropology
 - Biosafety/Biosecurity
 - Genomics/Phylogenetics



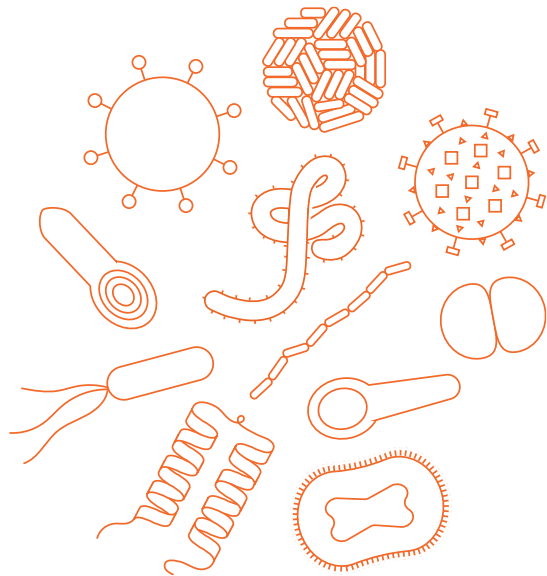
Food and Agriculture
Organization of the
United Nations



World Organisation
for Animal Health
Founded as OIE



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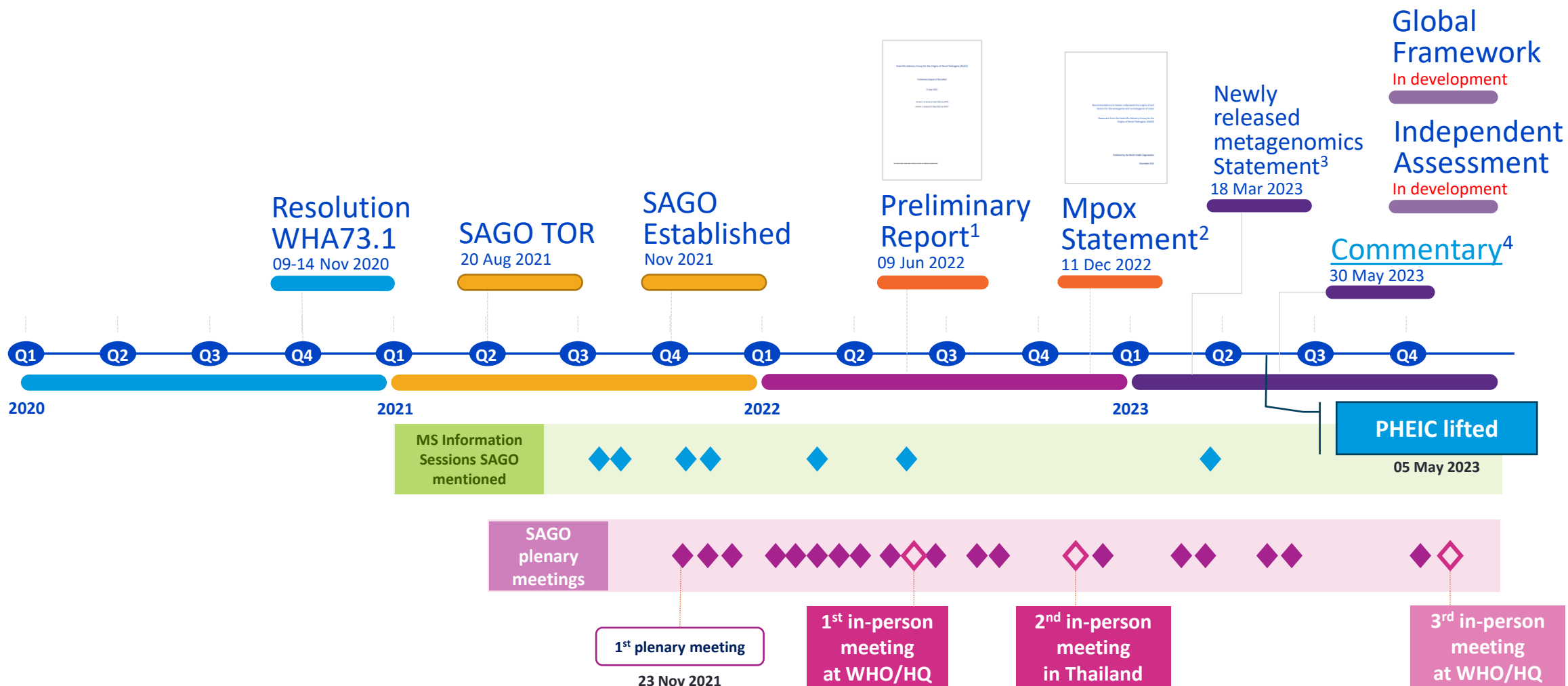


In its capacity as an advisory body to WHO, the SAGO will follow the terms of reference as initially outlined and shall have the following functions:

1. To advise WHO on the development of a **WHO global framework** to define and guide studies into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential
2. To advise WHO on **prioritizing studies and field investigations into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential**, in accordance with the WHO global framework described in point (1) above; 2
3. In the context of **SARS-CoV-2 origins**:
 - a. To provide an **independent evaluation** of all available **scientific and technical findings** from global studies on the **origins of SARS-CoV-2**;
 - b. To advise the WHO Secretariat regarding **developing, monitoring and supporting the next series of studies** into the origins of SARS-CoV-2
4. To provide additional advice and support to WHO, as requested by the WHO Secretariat, which may include participation in future WHO-international missions to study the origins of SARS-CoV-2 or for other emerging pathogens.

SAGO Timeline

(as of January 2024)



1. Scientific Advisory Group for the Origins of Novel Pathogens. Preliminary Report for the Scientific Advisory Group for the Origins of Novel Pathogens (SAGO). Geneva, Switzerland: World Health Organization; 2022 (<https://www.who.int/publications/m/item/scientific-advisory-group-on-the-origins-of-novel-pathogens-report>).

2. Scientific Advisory Group for the Origins of Novel Pathogens. Recommendations to better understand the origins of and factors for the emergence and re-emergence of mpox. Geneva, Switzerland: World Health Organization; 2022 (<https://www.who.int/publications/m/item/recommendations-to-better-understand-the-origins-of-and-factors-for-the-emergence-and-reemergence-of-mpox>).

3. Scientific Advisory Group for the Origins of Novel Pathogens. SAGO statement on newly released SARS-CoV-2 metagenomics data from China CDC on GISAID. Geneva, Switzerland: World Health Organization; 2023 (<https://www.who.int/news/item/18-03-2023-sago-statement-on-newly-released-sars-cov-2-metagenomics-data-from-china-cdc-on-gisaid>).

4. Venter M. Why the world needs more transparency on the origins of novel pathogens. Nature. 2023;618:27-9.

Update: Global Framework

WHO global framework to define and guide studies into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential

- Rationale
 - Prior to SAGO - lack of a unified and structured approach to standardize origins investigations globally
 - Global framework to study origins of emerging and re-emerging pathogens using a One Health approach
- Significance of the Framework



Improve the **understanding of the pathogen's origins.**



Improve the **global preparedness and response** to emerging pathogens of similar origin



Improve the **speed, quality, consistency, coordination, and comprehensiveness** of investigations



Foreground the commitment of **international health regulations (IHR)**



Consider the **diverse specializations and expertise** via a participatory and integrative approach

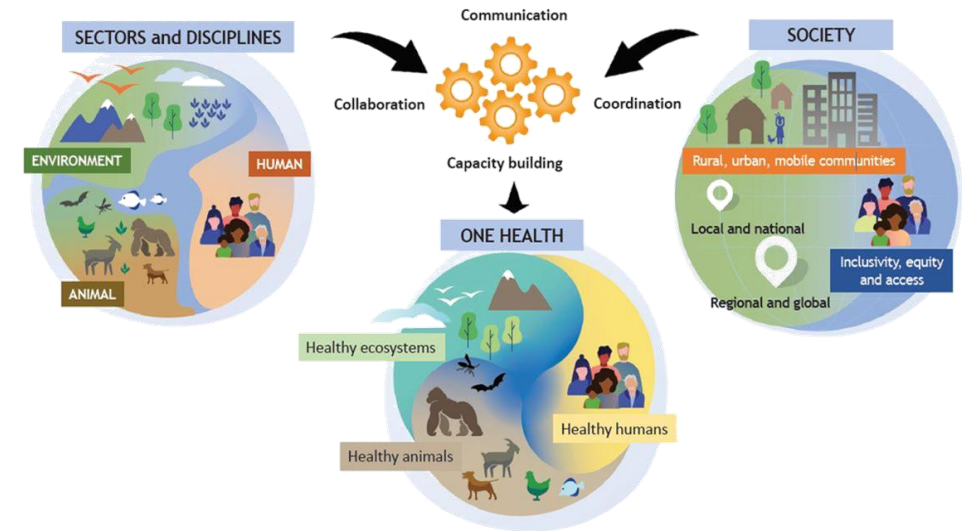
WHO global framework to define and guide studies into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential

Goal

- Identify the origins of a novel pathogen (or re-emerging pathogen) through a series of comprehensive scientific studies investigations, working collaboratively across disciplines using a One Health approach, with national and international partners to inform public health actions and limit further spread and prevent future outbreaks.

Objectives

- To obtain an early and comprehensive understanding of the source of the pathogen; whether it is zoonotic spill over or another route into human population(s)
- To facilitate the understanding of the epidemiological characteristics of the outbreak and clinical manifestations of the disease
- To determine the transmission routes through an intermediate host, be it an animal reservoir, vector or environmental source to allow public health action to be taken to implement appropriate prevention and control measures in order to mitigate continued reintroduction
- To contribute to the development of treatments, vaccines and control strategies by providing critical scientific evidence on the characteristics of the pathogen and its transmission



WHO global framework to define and guide studies into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential

Six key technical components of the comprehensive scientific studies and investigations



Early investigations following the emergence



Human studies: epidemiology



Human/Animal Interface studies



Environmental/Ecological studies



Genomics/Phylogenetics



Biosafety/Biosecurity

Requirements in Member States to facilitate the successful implementation of the framework

Systems and capacities needed to conduct recommended scientific investigations

General requirements	<ul style="list-style-type: none">• Multidisciplinary team for rapid investigation, including international experts.• Systems for early sample collection (clinical, human, animal, environmental) and storage for extensive testing and analysis.
Early Investigations	<ul style="list-style-type: none">• Outbreak investigation around early cases to trace the source. Systems for collection and storage of samples (human, animal and environmental) as well as diagnostic testing and sequencing (including pathogen isolation and molecular characterization)
Human Studies	<ul style="list-style-type: none">• Existing syndromic surveillance programs for routine sample collection and screening.• Epidemiology data collection to define clinical presentations.
Animal/human interface	<ul style="list-style-type: none">• Secure platforms for comprehensive epidemiological and laboratory data on animal cases and environmental samples, including genomics and metadata.• Syndromic surveillance systems on farms and markets for detecting clinical syndromes in animals in contact with humans; Identification of reservoir species, intermediate hosts; reverse zoonoses
Environmental	<ul style="list-style-type: none">• Surveillance system for sampling and testing environmental samples, e.g. wastewater and vectors.
Genomics	<ul style="list-style-type: none">• Laboratory systems ready for rapid pathogen identification, including genomic sequencing; sharing of sequencing data to public databases (GISAID; GENBANK etc.)
Biosafety and biosecurity element	<ul style="list-style-type: none">• Biosafety and biosecurity rules, governance, and oversight structures to enable assessment during outbreaks.• Accurate laboratory records for tracing pathogen types, safety protocols, and health records.



Early investigations

- **Objectives:** To trace the origins of a pathogen and identify possible early human cases preceding the pathogen's initial detection.
- **Methodology:** Collect information from diverse sources, including environmental, clinical, and samples from animals or insect vectors around early cases.
- **Key Areas:**
 - Identify earliest cases in humans and animals, and positive environmental samples.
 - Assess laboratories working with similar viruses.
- **Goals:**
 - Determine the timeline of the pathogen's presence.
 - Understand potential transmission modes.
- **Examples of recommended studies:**
 - All investigations should ensure early specimen collection and contribute to biobanking (humans, animals, environment) samples.
 - **Humans:** Biological material and epidemiology data from early human cases and individuals during site visits.
 - **Animals and Vectors:** Samples from animals, animal products and vectors caught in vicinity in cases of suspected exposure.
 - **Environment:** Samples from surfaces, drainages, animal cages, and wastewater in suspected exposure sites.
- **Examples of studies from SARS-CoV-2**
 - The original group who investigating SARS-CoV-2 from the China and WHO joint mission reviewed several data sources from routine surveillance of morbidity and mortality in the period prior to December 2019, as well as reviewed records from medical institutions, neither provided any further evidence suggestive of substantial circulation of SARS-CoV-2 in Wuhan.



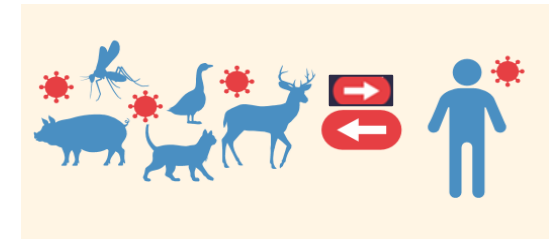
Human studies

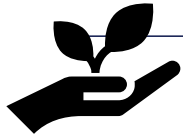
- **Objective:** To investigate illness in humans due to novel pathogens and understanding origins and health threats.
- **Methodology:**
 - Develop specific case definitions based on signs and symptoms.
 - Collect specimen materials for microbiological analysis.
- **Goals:**
 - Evaluate symptoms, signs, and severity in early cases.
 - Use cases and samples to develop diagnostic assays.
 - Continuously update case definitions with new information.
- **Examples from the recommended studies:**
 - Evaluate the symptoms, signs and severity of early human cases of the new disease and the status of their contacts to gain an understanding of the range of clinical illness
 - Develop and validate sensitive, specific molecular assays following sharing of sequencing data on SARSCOV2 from early cases (e.g. RT-PCR) for rapid case identification after initial pathogen detection, and distribute internationally to track its broader spread."
- **Examples from SARS-CoV-2**
 - Scientists around the world quickly developed and shared protocols and reagents for RT-PCR tests, as well as other types of molecular assays, to enable rapid diagnosis and surveillance of the pandemic.



Human/Animal Interface studies

- **Objective:** To investigate chains of transmission involving wild and domestic animals, including potential or known ancestral and intermediate hosts, and their interactions with humans.
- **Methodology:** Employ a One Health approach to assess exposures from wild and domestic animals.
- **Key Areas:**
 - Explore transmission chains from animal hosts to humans.
 - Assess potential zoonotic spillover events.
 - Conduct serosurveys in animals and humans in affected areas.
 - Study behavioural risks at the human-animal-environment interface.
 - Investigate reverse zoonoses in trade animals to identify susceptible hosts.
- **Examples from the recommended studies:**
 - Studies aimed at virus discovery to detect potential zoonotic pathogens in wildlife and domestic animals
 - Screen species from the initial outbreak area, including animals from the epicenter and upstream farms, using specific molecular or serological assays.
- **Examples from SARS-CoV-2**
 - Reverse zoonosis of SARS-CoV-2 from humans to animals has been detected in both wild, farmed and zoo animals; WOAHA reported 699 outbreaks, affecting 26 species across 36 countries by December 2022
 - Ex: White tailed deer (*Odocoileus virginianus*), farmed American mink (*Neogale vison*) and European minks (*Mustela lutreola*) and various zoo animal (eg. Lions, tigers, primates etc)





Environmental/Ecological studies

- **Objective:** To identify transmission pathways for early preventive and control measures, environmental contamination from animals and humans and population scale surveillance.
- **Methodology:** Determine transmission pathways, including surface contamination, droplets, aerosols, airborne particles, water-borne, food-borne pathways, and arthropod vectors.
- **Key Areas:**
 - Evaluate vector potential and host preferences.
 - Assess pathogen viability in various environments.
 - Conduct retrospective and prospective wastewater surveillance studies.
- **Examples from the recommended studies:**
 - Determine vector distribution and densities at outbreak sites to establish identities and diversity of potential disease vectors and population threshold for disease transmission –eg Zika and West Nile emergence in Americas.
 - Perform studies on wastewater collected for other programmes or purposes for population scale surveillance.
- **Examples from SARS-CoV-2**
 - Investigation of environmental surveillance samples from November/December 2019 from Brazil and Italy (wastewater samples) provided some important information about SARS-CoV-2 global distribution, however, further metagenomic studies needed to determine if samples match those circulating in China during that period (Nov/Dec 2019).



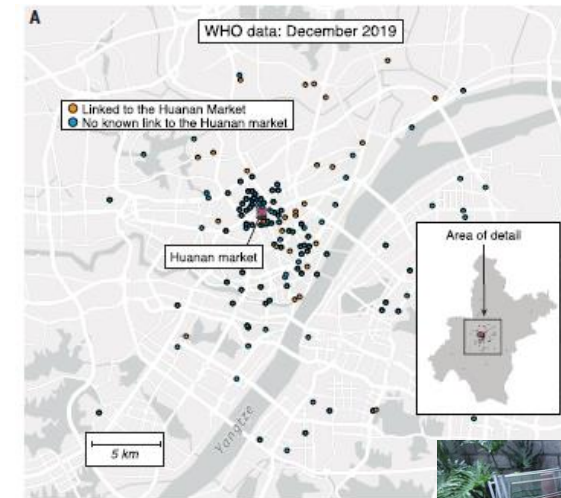


Genomics/Phylogenetics

- **Objective:** To identify the origins of novel pathogens using genomic and phylogenetic information.
- **Methodology:** Analyse genomics and phylogenetic data across animal hosts, human samples, and environmental sources, and explore evolutionary mechanisms
- **Key Areas:**
 - Sequence infected samples in early outbreak stages
 - Identify virus population dynamics and spread rates.
 - Cluster transmission chains to trace back virus emergence.
 - Utilize databases for genome sequences and data sharing.
- **Examples from the recommended studies:**
 - Collect human and animal clinical samples, and environmental samples at emergence.
 - Perform genomic surveillance to track source, evolution and identify variants of concern.
- **Example from SARS-CoV-2:**
 - Sequencing data on bats trace precursor viruses in China and Laos;
 - Chinese scientist provide genome sequencing data of early cases and environmental samples from Huanan Seafood Market
 - Allow independent researchers to analyzed the publicly available metagenomic sequencing data uploaded to GISAID by China.

Genetic tracing of market wildlife and viruses at the epicenter of the COVID-19 pandemic

Authors: Alexander Crits-Christoph, Joshua I. Levy, Jonathan E. Pekar, Stephen A. Goldstein, Reema Singh, Zach Hensel, Karthik Gangavarapu, Matthew B. Rogers, Niema Moshiri, Robert F. Garry, Edward C. Holmes, Marion P. G. Koopmans, Philippe Lemey, Saskia Popescu, Andrew Rambaut, David L. Robertson, Marc A. Suchard, Joel O. Wertheim, Angela L. Rasmussen, Kristian G. Andersen*, Michael Worobey*, Florence Débarre*.



SAGO statement on newly released SARS-CoV-2 metagenomics data from China CDC on GISAID

18 March 2023 | Statement | Reading time: 3 min (751 words)

On 12 March 2023, WHO was made aware of new SARS-CoV-2 sequences and metagenomics data associated with samples collected in the Huanan Seafood Wholesale Market, Wuhan, China, from January 2020, that became available on GISAID for a short period of time. The data had subsequently been downloaded by a number of researchers from several countries. Access was restricted shortly after, apparently to allow further data updates by China CDC. WHO then immediately reached out to China CDC and to the Chair and Vice-Chair of SAGO. Upon discussions between WHO and Chinese colleagues, it was explained that the genomic data are the basis for an expected update to the existing Liu et al. 2022 preprint (1), which is in the process of being re-submitted for publication to Nature by China CDC.





Biosafety/Biosecurity

- **Objective:** To ascertain if initial disease clusters are related to laboratory incidents.
- **Methodology:**
 - Evaluate biological risk management systems, SOPs, training, and health monitoring.
 - Investigate accidental events, procedural or engineering failures leading to pathogen release.
 - Assess risks in laboratory environments and field settings.
- **Examples from the recommended studies:**
 - Analyse all available information and documentation on the biological risk management system in place for the facilities according to the topics covered by national/regional legislation or the WHO Laboratory Biosafety Manual, 4th edition
 - Perform an investigation at a laboratory to better understand the biological risk management system in place
- **Examples from SARS-CoV-2**
 - SAGO provided recommendations in its Preliminary Report (June 2022) for the need for onsite assessments of the Wuhan institutes, interviews with lab staff, and those responsible for managing biosafety/biosecurity

Sharing Findings in Investigating Origins of Emerging and Re-Emerging Pathogens

- Investigating the pathogen's origins requires a dynamic, non-linear approach where findings are shared rapidly and transparently to guide the next steps.

This process:

- **Guides Immediate Responses:** Shared insights are crucial for implementing measures to halt further transmission and prevent new spillover events.
- **Facilitates adaptive studies:** Leveraging current findings accelerates and refines ongoing and future investigations, allowing research to adapt swiftly to new information.
- **Promotes transparency:** Sharing results with the international community throughout the investigation fosters transparency and facilitates international collaboration. The framework encourages results are shared as they are finalized, not waiting for a final report.

Next steps for SAGO

- Finalization and publication of **the Global Framework**; currently undergoing editing, and will then be pushed through for internal WHO approvals
 - Expected publication timeline: end of Q1 2024
- Finalization and publication of SAGO's “**Independent assessment of the origins of SARS-CoV-2: What does the science say?**”
 - WHO Secretariat will organize a separate briefing to MS when ready
 - Publication to be expected end of Q1 2024

The SAGO remains open to all scientific evidence that becomes available in the future to allow for comprehensive testing of all reasonable hypotheses.