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

Update to Member States
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Scientific Advisory Group on Novel Origins (SAGO)

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

The Need

• 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 a gap

• 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)
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

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.

Source: SAGO TOR
Timeline of Development

- **August 2021**: WHO Open Call
- **September 2021**: Secretariat undergoes selection process for members
- **October 2021**: SAGO Secretariat confirms membership list.
- **November 2021**: First meeting of the SAGO
- **December-January 2021-2022**: 4 more SAGO meetings took place.
- **February 2022**: First SAGO Report
Meetings and Organization of the SAGO

- First meeting November 2021
- 7 Plenary SAGO meetings held to date
- 27 Members with significant and diverse expertise
- Chair and vice-chair
- 2 Observers
- 6 sub-working groups were formed and are meeting regularly;
  - Human, epidemiology
  - Animal/Human Interface,
  - Environment/Ecological,
  - Early Investigation/Anthropology,
  - Biosafety/Biosecurity, and
  - Genomics/Phylogenetics

Current Main Areas of Focus

1. Provide recommendations to establish a **Global Framework for** studying the origins of emerging and re-emerging pathogens
2. Review available evidence studying **emergence of SARS-CoV-2** and provide recommendations for studies urgently needed
3. Provide preliminary recommendations to study the **emergence of SARS-CoV-2 VOCs**
Presentations to the SAGO in Plenary and subsequent meetings

- Overview of the work of WHO for high threat zoonotic pathogens, including SARS, MERS, VHF, Arboviruses, COVID-19 (SAGO Secretariat)
- Overview of the work of WHO related to biosafety and biosecurity (SAGO Secretariat)
- Summary of the findings and recommendations from the March 2021 Joint WHO-China mission report (SAGO member)
- Overview of pre-pandemic 2019 studies (WHO Secretariat)
- Overview of the emergence of SARS-CoV-2 variant of concern Omicron (SAGO Member)
- Overview of SARS-CoV-2 and SARS-CoV-like virus circulation in animals (WHO Secretariat)
- Update from Chinese Scientists on the implementation of studies recommended in March 2021 WHO-China Joint report
- Overview of SARS-CoV-2 literature review (WHO Secretariat)
SAGO discussions of Global Framework for Emerging and Re-emerging Diseases

• **Meeting the need**
  • The rapid emergence and spread of SARS-CoV-2 has highlighted the importance of being prepared for any future event. The need to be able to quickly identify novel pathogens early and to identify the risk factors that contribute to their emergence and spread.

• **Discussions of framework involve**
  • Early investigations following the emergence
  • Human studies: epidemiology
  • Human/Animal Interface studies
  • Retrospective sampling of pre-outbreak samples
  • Environmental/Ecological studies
  • Biosafety/Biosecurity
  • Genomics/Phylogenetics

• **Applying this framework to SARS-CoV-2 variants of concern: e.g., Omicron**
Critical elements for the Global Framework for Emerging and Re-emerging Diseases

- Early investigations following the emergence
- Human studies: epidemiology
- Human/Animal Interface studies
- Retrospective sampling of pre-outbreak samples
- Environmental/Ecological studies
- Biosafety
- Biosecurity
- Genomics/Phylogenetics
WHO secretariat conducted systematic literature review on available evidence pertaining to the origins of SARS-CoV-2 from 2019 to date using a comprehensive search strategy, assessing grey literature, foreign language, published and pre-print articles.

Using the WHO COVID-19 research literature database which reviews 70 online databases and approximately 500,000 citations:

- Animal susceptibility
- Molecular epidemiology
- Review articles
- Hypothesis
- Surveillance
- Early suspect or known cases in China
- Positive samples from 2019
- Market tracing and/or animal trade
- Gain of function experiments
- Field acquired infection
- Laboratory acquired infection
- Biosafety and biosecurity
- Review studies
SARS-CoV-2 is likely to be a coronavirus of bat origin, with the closest viral genome found in *Rhinolophus affinis* bats (RatG13 bat strain in Yunnan, China, 96.1% (2020); BANAL-52, 96.8%, Laos (2021)).

Rhinolophus species are abundant and diverse in South China and across Asia, the Middle East, Africa and Europe; Apart from China, SARS-CoV-2 related coronaviruses have also been isolated from bats in Southeast Asia.

Two other closely-related coronaviruses with 85.5% to 92.4% sequence similarity to SARS-CoV-2 were sequenced from custom-seIZED trafficked Malayan pangolins that were housed in rehabilitation facilities in China.

Earliest market related cases in Wuhan already some diversity suggesting original spill over event to humans may not have happened at the market itself.

Several decades of evolutionary distance between most similar viruses from bats and SARS-CoV-2 suggests the need for search of intermediaries.
Presentations to SAGO: SARS-CoV-2 Animal Susceptibility Studies

Susceptibility of animal species

- Direct contact with humans
- Proximity/indirect contact with humans
- Lab

Adapted from Michelitsch et al.; Adv Virus Res. 2021
• WHO review of pre-pandemic testing of samples or referral of samples for confirmatory testing to external laboratories for validation

• Systematically reached out to authors of published/pre-print studies with positive test results in pre-pandemic biological samples (2019 and early January 2020):

  • Examples: Germany, US, Scotland, Italy, Canada, Netherlands, and Japan have tested biobanked samples from respiratory samples, wastewater – all negative

  • Spain, Italy, France, US, Brazil tested respiratory pathogens, serum from blood donations, measles samples, skin samples, wastewater etc – some positive results
    • Requested and arranged referral testing for confirmation
    • Requested information on follow up or investigations planned or underway
    • Requested respiratory materials for virus sequence processing

• Further testing/verification of biological samples is ongoing in Italy.
Presentations to SAGO: Overview of findings of the WHO-China Joint Mission Report 2021

Zoonotic

Zoonotic + intermediate host

(Cold) food chain related

Laboratory related
The SAGO secretariat has requested further information from Chinese scientists on the status of the implementation of studies recommended in the March 2021 report.

**SAVO received two presentations from invited Chinese scientists**

- Overview of the findings of the recommended studies outlined in the March 2021 Joint China-WHO March mission report
- Update on the implementation of studies recommended in March 2021 WHO-China Joint report
- Information gathering is ongoing.

Next steps

• Continue to meet in plenary and as working groups to meet objectives set out in TORs

• Finalize SAGO First Report to WHO *(anticipated in the coming weeks)*
  • Establishment of SAGO, aims and objectives, organization, meetings
  • Preliminary recommendations by the SAGO
    1. General considerations for the scope of the global framework
    2. Preliminary recommendations on studies needed to better understand the origins of SARS-CoV-2
       • Epidemiology and molecular epidemiology recommendations
       • Animal and environmental studies
       • Introduction of SARS-CoV-2 to the human population through a laboratory accident or incident
    3. Initial recommendations for studies on the source of the Omicron variant
  • Outline Next steps of SAGO to meet TORs