Update from the Secretariat
Scientific Advisory Group for the Origins of Novel Pathogens
Update on studies into the origin of SARS-CoV-2
Establishment of the Scientific Advisory Group for the Origins of Novel Pathogens

SGAO
Human health, animal health and the state of ecosystems are inextricably linked with 70-80% of emerging and re-emerging infectious diseases known to be of zoonotic origin.

Source: adapted from multiple sources
Scientific Advisory Group on Novel Origins (SAGO)

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)
Functions of the SAGO

1. To advise WHO on the development of a 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 framework described above

3. To advise WHO on the development of a detailed work plan of the SAGO
4. **In the context of SARS-CoV-2;**

   a) To provide the WHO Secretariat with 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, including rapid advice on WHO's operational plans to implement the next series of global studies into the origins of SARS-CoV-2, as outlined in the Joint WHO-China Global Study of Origins of SARS-CoV-2: China Part report published on 30 March 2021, and advise on additional studies as needed; and

5. 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 - Composition

• Up to 25 members

• Members must have significant expertise in one or more of the following technical disciplines:

  infectious disease epidemiology and conducting epidemiological studies, field research, virology, ecology, molecular epidemiology, sero-epidemiology, medicine, bioinformatics, outbreak analytics, health statistics, microbiology, veterinary medicine, food safety, bacteriology, environmental science, biosafety, biosecurity, occupational health and safety, or laboratory safety and security, ethics and social sciences, or other activities related to the emergence or re-emergence of pathogens of pandemic potential.

• Geographic representation, gender balance, declaration of interest

• Members of the SAGO shall be appointed to serve for a period of 2 years and shall be eligible for reappointment
Update on studies into the origin of SARS-CoV-2
Global spread of SARS-CoV-2: findings from phylogenetic analyses

Current TMRCA estimates: November 2019 (95% credible interval October - December 2019)

Source: Nextstrain.org
SARS-CoV-2 and other SARS-related CoVs

- SARS-CoV-2 is likely to be a coronavirus of bat origin, with the closest viral genome (RaTG13, 96.2% homology) found in *Rhinolophus affinis* bats in Yunnan, China.

- 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.

https://www.who.int/health-topics/coronavirus/origins-of-the-virus
Coronaviruses closely related to the pandemic virus discovered in Japan and Cambodia

The viruses, both found in bats stored in laboratory freezers, are the first SARS-CoV-2 relatives to be found outside China.

Identification of a novel lineage bat SARS-related coronaviruses that use bat ACE2 receptor

Hua Guo, Ben Hu, Hao-rui Si, Yan Zhu, Wei Zhang, Bei Li, Ang Li, Rong Geng, Hao-Feng Lin, Xing-Lou Yang, Peng Zhou, Zheng-Li Shi

doi: https://doi.org/10.1101/2021.05.21.445091
Susceptibility of several animal species to SARS-CoV-2 has been confirmed, including pets and (farmed) wildlife

366 animals from 27 countries*
- Cats: 161
- Dogs: 149
- Tigers: 19
- Lions: 19
- Asian small-clawed otters: 5
- Snow leopards: 5
- Cougar: 3
- Gorillas: 3
- Wild caught mink: 1
- Pet ferret: 1
- White tailed deer (30% sero+)

435 mink farms in 12 countries

*Does not include individual numbers of positive farmed mink

Source: OIE, FAO, UDA APHIS
Animal species experimentally infected with SARS-CoV-2

- Cats*
- Dogs
- Ferrets*
- Mink*
- Hamsters†
- Deer mice*
- Rabbits
- Tree shrews
- Raccoon dogs*
- Cattle

- Non-human primates‡
- Egyptian fruit bats*
- White-tailed deer*
- Striped skunks
- Raccoons
- Bushy-tailed woodrats
- Bank voles
- Striped skunks
- Raccoons

* Transmission to other animals of the same species reported
†Hamster species include Chinese hamsters and golden Syrian hamsters
‡Non-human primate species include African green monkeys, baboons, common marmosets, cynomolgus macaques, pigtail macaques, rhesus macaques, and savanna monkeys

Source: OIE, FAO, References included in CDC’s One Health Scientific Publication Tracker- One Health and Animal Studies
Animal sales from Wuhan wet markets immediately prior to the COVID-19 pandemic

Xiao Xiaolong, Chris Newman, Christina D. Buesching, David W. Macdonald & Zhao-Min Zhou

Here we document 47,381 individuals from 38 species, including 33 protected species sold between May 2017 and November 2019 in Wuhan’s markets. We note that no pangolins (or bats) were traded, supporting reformulated opinion that pangolins were not likely the spillover host at the source of the current coronavirus (COVID-19) pandemic. While we caution against the misattribution of COVID-19’s origins, the wild animals on sale in Wuhan suffered poor welfare and hygiene conditions and we detail a range of other zoonotic infections that may potentially vector. Nevertheless, in a precautionary response to COVID-19, China’s Ministries temporarily banned all wildlife trade on 26th Jan 2020, and permanently banned eating and trading terrestrial wild (non-livestock) animals for food on 24 Feb 2020. These interventions, intended to protect human health, redress previous trading and husbandry inconsistencies, and will have collateral benefits for global biodiversity conservation and animal welfare.

https://www.nature.com/articles/s41598-021-91470-2
SARS-CoV-2 testing in samples from 2019

• Literature screening and review (including preprints)

• Laboratory Reference Network discussions with experts

• WHO Lab Network – review of pre-pandemic testing of samples or referral of samples for confirmatory testing to external laboratories
### Testing of pre-pandemic samples – negative results

<table>
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<tr>
<th>Countries</th>
<th>Study period</th>
<th>Sample type</th>
<th>Population</th>
<th>Results for samples</th>
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<tr>
<td>Germany¹</td>
<td>December 2019 – April 2020</td>
<td>Respiratory specimens</td>
<td>Patients with pneumonia</td>
<td>No positive results before March 2020. N=195</td>
</tr>
<tr>
<td>UK²</td>
<td>January 2020</td>
<td>Respiratory specimens</td>
<td>Patients with pneumonia</td>
<td>No positive results before February 2020. N=1,378</td>
</tr>
<tr>
<td>Scotland³</td>
<td>December 2019 – February 2020</td>
<td>Respiratory specimens</td>
<td>ICU admitted patients</td>
<td>No positive results before March 2020. N=148</td>
</tr>
<tr>
<td>US⁴</td>
<td>December 2019 – June 2020</td>
<td>Respiratory specimens</td>
<td>Patients, BAL samples, dept. defense</td>
<td>No positive samples found before January 2020. N=7,000</td>
</tr>
<tr>
<td>Italy⁵</td>
<td>November 2019 – March 2020</td>
<td>Respiratory specimens</td>
<td>Patients, SARI</td>
<td>No positive results. N=166</td>
</tr>
<tr>
<td>Italy⁶</td>
<td>December 2019 – March 2020</td>
<td>Respiratory specimens</td>
<td>Patients with respiratory symptoms</td>
<td>No positive results. N=906</td>
</tr>
<tr>
<td>Canada⁷</td>
<td>August 2019</td>
<td>Wastewater</td>
<td>NA</td>
<td>Negative</td>
</tr>
<tr>
<td>Netherlands⁸</td>
<td>February 2020</td>
<td>Wastewater</td>
<td>NA</td>
<td>Negative</td>
</tr>
<tr>
<td>US⁹</td>
<td>January – April 2020</td>
<td>Wastewater</td>
<td>NA</td>
<td>Negative</td>
</tr>
</tbody>
</table>

### Testing of pre-pandemic samples – positive results

<table>
<thead>
<tr>
<th>Countries</th>
<th>Study Period</th>
<th>Sample type</th>
<th>Population</th>
<th>Results</th>
<th>Dates of positive samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>France¹</td>
<td>December 2019 – January 2020</td>
<td>Respiratory sample</td>
<td>ICU admitted patients</td>
<td>1/14 tested positive (PCR)</td>
<td>December 2019</td>
</tr>
<tr>
<td>Italy³,⁴,⁵,⁶</td>
<td>September 2019 – February 2020</td>
<td>Oropharyngeal</td>
<td>Measles-suspected patients</td>
<td>1/39 tested positive (in house PCR)</td>
<td>December 2019</td>
</tr>
<tr>
<td></td>
<td>August 2019 – February 2020</td>
<td>Oropharyngeal</td>
<td>Measles-suspected patients</td>
<td>11/44 tested positive (in house PCR) *</td>
<td>September-December 2019</td>
</tr>
<tr>
<td></td>
<td>November 2019</td>
<td>Dermatosis sample</td>
<td>Patients with skin manifestations</td>
<td>1 tested positive (in house assay)</td>
<td>November 2019</td>
</tr>
<tr>
<td></td>
<td>December 2019</td>
<td>Wastewater</td>
<td>-</td>
<td>Tested positive (PCR)</td>
<td>December 2019</td>
</tr>
<tr>
<td>Brazil⁷</td>
<td>October 2019 – March 2020</td>
<td>Wastewater</td>
<td>NA</td>
<td>Tested positive (PCR)</td>
<td>November, December 2019</td>
</tr>
<tr>
<td>Spain⁸</td>
<td>2019</td>
<td>Wastewater</td>
<td>NA</td>
<td>Tested positive but cannot be verified</td>
<td>March 2019</td>
</tr>
<tr>
<td>Italy⁹</td>
<td>September 2019 – March 2020</td>
<td>Serum</td>
<td>Cancer screening trials</td>
<td>Initially positive, negative upon re-testing 6/959 (neutralization)</td>
<td>October – December 2019</td>
</tr>
</tbody>
</table>

¹Deslandes et al., 2020; 10.1016/j.intantimicag.2020.106006
²Basavaraju et al., 2020; 10.1093/cid/czaa1785
³Amendola et al., 2020; 10.3201/eid2702.2004632
⁴Amendola et al., 2021; 10.2139/ssrn.3883274
⁵Gianotti et al., 2021; 10.1131/1d.19804
⁶La Rosa et al., 2021, 10.1016/j.watres.2021.117104
⁷Fongaro et al., 2021; 10.1038/s41467-021-146196
⁸Chavarria-Miro et al. 10.1101/2020.06.13.20129627
⁹Apolone et al. 10.1177/0009921X20974755

*followed up
Collaborations and verification of early results

• Italy - after notification of a positive signal retrieved from a lung cancer screening trial in October-December 2019, a collaboration was established between researchers in Italy, the UK and the Netherlands

• Samples were shared with an external site from the WHO lab network - Erasmus Medical Centre in Netherlands for re-testing, the initial results have not been verified.
Summary of pre-pandemic sampling

• Many negative signals from retrospective studies testing respiratory and serum samples from Germany, France, Italy, UK and the US.

• Some serological and molecular evidence of SARS-CoV-2 circulation in late 2019 (France, US, Italy, Brazil), verification is ongoing.

• No study was able to generate a whole genome sequence from a 2019 sample thus far.
SAGO - Open Call & Selection Process

- Open call – circulation of open call to Member States, existing WHO networks, GOARN, and available on WHO website

- Interested individuals will be asked to register their interest to SAGO@who.int and include:
  - A cover letter
  - Curriculum vitae
  - A signed and completed Declaration of Interests (DOI) form for WHO Experts, available at https://www.who.int/about/ethics/declarations-of-interest

- All applications will be assessed by the WHO secretariat in accordance with the WHO procedures, based on their technical expertise, taking into consideration diverse perspectives from different regions, especially from low and middle-income countries, and for gender balance