

Open Letter to the World Health Organization and the Members of its Executive Board

April 30, 2021

Understanding the origins of the pandemic is essential to addressing our vulnerabilities and preventing future crises. Unfortunately, as outlined in previous open letters released on [March 4](#) and [April 7](#), structural, procedural, and analytical shortcomings of the WHO-convened joint study into COVID-19 origins have created unnecessary barriers to this understanding.

On March 30, 2021, World Health Organization Director General Tedros Adhanom made a number of [important assertions](#) following the release of the WHO-convened [joint study report](#). These include:

- “I do not believe that [the joint’s team] assessment [of a possible lab incident] was extensive enough. Further data and studies will be needed to reach more robust conclusions... potentially with additional missions involving specialist experts, which I am ready to deploy.”
- “As far as WHO is concerned all hypotheses remain on the table... We have not yet found the source of the virus, and we must continue to follow the science and leave no stone unturned as we do... It is clear that we need more research across a range of areas, which will entail further field visits.”

As scientists and science communicators, we welcome this courageous defense of the scientific method and of the WHO's integrity. We also hope that Dr. Tedros’s clear articulation of critical next steps will be fully supported by all concerned countries and parties. This open letter lays out specific recommendations for what a full investigation into pandemic origins should entail.

Objective of further Studies:

The stated objective of the further studies recommended by Dr. Tedros must be “*to investigate all possible origins of the COVID-19 pandemic*, including an exclusively “natural” zoonosis in the wild, human contamination in an animal farm, and a research-related accident.

This would contrast with the reductive language of [World Health Assembly](#) resolution 73.1, which tasked the WHO “to work closely with the World Organisation for Animal Health and

the Food and Agriculture Organization of the United Nations, and countries, as part of the One Health approach, to identify the *zoonotic* source of the virus.”

Additionally the WHO has [previously stated](#) that the mission’s objectives were only to recommend, help design, and review scientific studies. As later confirmed by a [joint-team member](#), this meant that performing an investigation, let alone a forensic audit of laboratories, was beyond the remit of the joint mission.

To address this shortcoming, we recommend that the stated objective be reformulated as: *to conduct a full scientific and forensic investigation into all possible origins of COVID-19, be it zoonotic or not.* Such a reformulation of the objective would ensure compliance with the scientific method of deriving the conclusion from data and facts, not the reverse.

Methods and Protocols:

Given the stakes, the “COVID-19 origins investigation” must follow the highest standards of data-driven, peer-reviewed science. To make this possible in the next phase of the COVID-19 origins study, we recommend:

- ❑ Clearly listing the possible paths for virus evolution and human infection (Annexes A and B below provide a succinct review of such possible paths).
- ❑ Allocating proper time and efforts to examining all hypotheses without any *a priori* assumptions.
- ❑ Ensuring all assumptions and key steps in the analysis are supported by factual data.
- ❑ Guaranteeing access to required raw data (relevant records, samples, project applications, project reports, personnel information, field trip information, relevant emails, laboratory notebooks, etc.) and not solely semi-aggregated data or summaries.
- ❑ Sharing of all relevant medical records, anonymized according to local laws for confidentiality protection, with the joint study team.
- ❑ Ensuring that the team of scientists and specialists is able to undertake their studies at key meetings and visits with no [unnecessary presence](#) of host government non-scientific personnel.
- ❑ Ensuring mission members can conduct interviews, as needed, confidentially and/or anonymously, and with assistance of translators appointed by the WHO if necessary.

Team Selection:

The Terms of Reference for the initial joint study gave Chinese authorities an effective veto over participation in the international team, thereby compromising its independence. In order to support the revised objectives of the further studies, we recommend that:

- ❑ Any veto power be removed and the selection process of the members be made transparent to the WHO Executive Board.

- ❑ International experts with conflicts of interest, including those who may have served in the first phase of the study, should not be included in the WHO-organized independent committee going forward.
- ❑ The selection process should ensure that the team has the skill sets required to assess all pandemic origin hypotheses and to conduct any necessary scientific and forensic audit. This requires the inclusion of biosafety and biosecurity experts, biodata analysts, and forensic investigators, as the WHO previously very successfully did following the SARS lab-leaks in Singapore and Taiwan in 2003/04.

Essential Resources:

The joint-study work has suffered from limited access to granular data, relevant records and samples. We recommend that this type and level of access should be mandated for the next phase of the joint-study work, with specific mention of the following key resources:

- ❑ Anonymized data and biological samples from early COVID-19 patients, close contacts and possibly infected persons.
- ❑ Records of laboratories and institutions involved in coronavirus research in Wuhan.
- ❑ Key databases of pathogens, samples and isolates. These databases are essential as they contain data about viruses not yet published, and some of these viruses may be closely related to SARS-CoV-2. We recommend access to the histories of changes and the previous versions since 2018 for:
 - The 62MB MySQL [database](#) batvirus.whiov.ac.cn, including access to the password-protected private section.
 - The www.virus.org.cn portal and its underlying 15 databases.
- ❑ The full sequence of the 8 coronaviruses sampled in the Mojiang mine several years ago, which are some of the closest relatives of SARS-CoV-2 and were mentioned in an [Addendum](#) to a Nature paper published in November 2020.
- ❑ Documents previously prepared (grant applications, detailed progress reports, final reports, scientific publications) by the researchers involved in the following research projects:
 - USA National Institute of Health research projects entitled “Understanding the Risk of Bat Coronavirus Emergence”: [1R01AI110964-01](#) and [2R01AI110964-06](#).
 - USA research projects whose goal is to strengthen global capacity for detection of viruses with pandemic potential: [PREDICT](#) and [PREDICT 2](#).
 - Research projects in China investigating various coronaviruses: [31770175](#), [31800142](#), [2013FY113500](#), [81290341](#), [XDPB0301](#), [XDB20101010](#).
 - The July 2019 [tender](#) of China's Ministry of Science and Technology, which aimed to isolate new viral pathogens, standardize their preservation and establish a shared database.

- Research [project](#) initiated by the Chinese Academy of Sciences in 2018 to study several viruses and develop vaccines.
- [China Virome Project](#), also named [China National Global Virome Initiative](#) (CNGVI), which aims to identify unknown viruses from wildlife and is part of the [Global Virome Project](#).

Essential Questions

Because the first phase of the joint study process focused primarily on examining the zoonosis hypothesis, commensurate efforts should now be expended in the next phase of the study examining the possibility of a lab-related incident, including by addressing the following questions:

1. In April 2012, after clearing bat guano in an abandoned mine in Mojiang (Yunnan), six men contracted [severe pneumonia with COVID-19-like symptoms](#). All were sent to Kunming hospital where three eventually died. An on-duty doctor at the hospital at the time [reported](#) a 'potential epidemic outbreak' of unknown pneumonia to the local Center for Disease Control, on arrival of the 5th patient. Unspecified samples from these patients were sent to the Wuhan Institute of Virology and other labs in 2012. Dr. Shi Zhengli recently announced that the [WIV tested the serum samples again](#).
 - Why were these six miners sent to clean guano in the mine in April 2012? Who hired them and sent them all to the same distant Kunming hospital?
 - Why are these pneumonia cases absent from the Chinese CDC statistics for 2012 and why were they not reported to the WHO, despite a 'potential epidemic outbreak' alert having been reported to the local CDC?
 - Why were these lethal pneumonia cases not mentioned in any scientific research article after 2014, despite the [PREDICT](#) program showing a high [interest](#) for potential coronavirus disease outbreaks via bat guano shortly after these events?
 - Were any SARS-like coronaviruses isolated from the patient samples?
 - What samples were taken from these six patients and sent to the WIV and other labs? Are any of these samples available for independent analysis?
 - Is it possible to interview the three surviving miners, their relatives and some Mojiang villagers - and also to take serum samples from them - in order to better understand in which condition these miners fell sick and what their exact pathology was?
2. To this day all the coronaviruses most closely related to SARS-CoV-2 come from that Mojiang mine. Some scientists who went sampling at the mine had their [samples confiscated](#) while investigative journalists have been systematically turned away.
 - Can Chinese authorities offer unfettered access to the mine to international scientists for the required continued sampling effort?

3. Animal sampling and testing is the only way to establish a zoonotic origin, be it in the wild or in a farm. This data should be shared with the international scientific community.
 - Which animals were, are and will be tested in China, in which wild ecosystems and in which breeding farms?
 - Can the full data for these tests be shared with international experts and the scientific community?
4. Chinese authorities have asserted difficulties sharing human health data with the international members of the WHO-China joint team because of strict domestic privacy laws. However informed consent can normally be waived when de-identified data is used, as was done for instance in this recent Chinese [publication](#) involving 35,040 Wuhan citizens tested for COVID-19.
 - Why was such a waiver not available when requests for very similar data were made by the joint-mission team members?
 - Can this type of waiver be made now?
5. Dr. Shi Zhengli has stated that Wuhan Institute of Virology virus databases were taken offline [during the pandemic](#). However the key [bat virus database](#) was taken offline in September 2019, three months before the official start of the outbreak.
 - Can Chinese officials explain this contradiction?
 - Can Chinese officials explain why the [scientific paper](#) describing the [key database](#) (digital object identifier: [10.11922/csdata.2019.0018.zh](#)) was taken [offline](#) from the corresponding Chinese journal website “China Science Data” in mid-2020?
 - Can Chinese officials also explain why the [full website](#) of “China Science Data”, where the database was described, became [inaccessible](#) in March-April 2021?
 - Can these databases, in their form as of September 2019, be shared with the WHO study group?
6. A bat coronavirus sampled in the Mojiang mine in 2013 (‘RaTG13’) is still the virus most closely-related to SARS-CoV-2. Dr. Shi Zhengli and Yanyi Wang, director of the WIV, said in interviews that there is “[no more sample](#)” of RaTG13, so that no further sequencing is possible, and that the virus was no longer “[in our lab](#).” Based on the raw data provided, it has unfortunately not been possible to [assemble](#) the RaTG13 genome sequence.
 - When was the RaTG13 sample fully depleted?
 - How was the RaTG13 genome sequence assembled and how was the [5’ end](#) sequence determined?
 - Did the WIV or any other laboratory ever attempt to recreate RaTG13 or any other coronaviruses by assembling them from synthetic gene sequences?

- Why are a few of the [RaTG13 amplicons dated as June 2017](#) and named “7896”, which is the [name](#) of another closely related virus collected in the same mine?
 - Given that RaTG13 shows [weak binding](#) to bat receptor ACE-2 and binds only to one of the ACE2 orthologs of *Rhinolophus affinis*, is RaTG13 the true whole genome sequence of the sample BtCoV/4991 collected in 2013 by the WIV?
7. A striking feature of the SARS-CoV-2 genome which increases its pathogenicity, is the presence of a so-called “furin cleavage site”. This site was noted as a “cleavage site” in a January 2020 [publication](#) by Dr. Shi Zheng-Li and colleagues.
- Why was this so-called “furin cleavage site,” clearly an important and novel feature of the SARS-CoV-2 virus, not mentioned in the February 2020 Nature [publication](#)?
8. WIV acknowledged [isolating three strains of live SARS-related coronaviruses](#), but based on the WIV naming [convention](#) for their live viruses isolates it appears that the WIV did not disclose two potential isolates, WIV6 (not WIV06) and [WIV15](#), as these names are not mentioned anywhere in the literature.
- Do these isolates exist? If no, what is the explanation for why these isolate names were skipped in the series?
 - In any case, can the sequences, additional relevant data and the live isolates themselves for all viruses?, plus their clones and mutants (if any) be provided to the WHO Study Group?
9. WIV laboratories were involved in specific government-sponsored research projects in 2019, in collaboration with [EcoHealth Alliance](#). The key objective for one of these [projects](#) (‘bat coronavirus surveillance’) was to identify potentially dangerous viruses based on their spike proteins and involved so-called “gain of functions” experiments, in which viruses were specifically manipulated to acquire new pathogenic features.
- Can Chinese authorities provide the laboratory notebooks and electronic records of the WIV and of any other laboratory that was involved in virus “gain of function” research, as well as any results, including related sequences and isolates?
 - Can [Peter Daszak](#), President of EcoHealth Alliance and also a member of the [joint study team](#), clarify the context of the [experiments](#) he was referring to in late 2019 and make all relevant records available to the study team?
10. The influenza diagnosis and treatment [plan](#) issued by China's National Health Commission on 13 November 2019 advised against isolating virus specimens from patients who did not test positive for influenza, while the [2018 plan](#) had previously encouraged it. This change in policy may have had the unfortunate consequence of facilitating an unreported circulation of SARS-CoV-2 in the last few weeks of 2019.
- What was the reason for this change in policy?

11. Chinese authorities have stated [that staff at four Wuhan labs](#) all tested negative for SARS-CoV-2 antibodies.
 - How many people were tested, in which Wuhan labs, on which days, and as part of which teams or services within these labs?
 - Were any of these serum samples retained?
 - Are independent international investigators able to retest the samples of the lab staff to confirm the results?

12. [Dr. Shi Zhengli](#) and Dr. [Yuan Zhiming](#) have both stated that ‘all staff tested negative for SARS-CoV-2 antibodies’ at the WIV in March 2020. Yet, this is statistically unlikely (roughly less than one chance in a billion) given that there are more than 590 staff and students at the WIV and about 4.4% of the Wuhan urban population [tested positive](#) at around that time. Even if only 85 people were tested, the chance of no positive test would still be less than 4%.
 - How can this contradiction be explained?
 - Can Chinese authorities make available the anonymized raw data of these tests and the test samples for further examination?

Next Steps:

As terrible as COVID-19 has been, this is almost certainly not the last pandemic we will face -- and possibly not even the worst. Taking all necessary measures to understand the origins of this pandemic as an essential foundation for addressing our dangerous vulnerabilities is therefore a matter of great urgency. Doing so will also establish an important precedent for fully and transparently investigating any such outbreaks in the future wherever and however they might originate.

We call on the World Health Organization and its Executive Board to fully address the recommendations and questions raised in this letter as a critical step toward protecting everyone on earth and future generations.

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Annex A: Lab-related Accident scenarios

Lab-Related Accident Scenario:	Field sampling accident LS1	Lab acquired infection (LAI) of Wuhan lab personnel LS2	Lab escape without LAI LS3
Description	Infection during field sampling by or on behalf of a Wuhan laboratory	Infection inside a Wuhan institution with laboratories	Infection outside a Wuhan institution with laboratories
Index case	Personnel present at field sampling site, went back to Wuhan or infected someone who went back to Wuhan	Can be lab personnel, staff, student, or anybody present in the institution (including temporary worker or visitor).	Someone out of the lab, in proximity typically, or in relation to lab activities (such as waste processing)
Actual Biosafety Level	Very limited to equivalent of Biosafety Level 2 (BSL-2) laboratory, full PPE commonly not worn	Bat SARS-related coronaviruses research officially performed at BSL-2 & BSL-3 levels	Bat SARS-related coronaviruses research officially performed at BSL-2 & BSL-3 levels
Incident	Either via contact with animal hosts or animal waste on site	Either: - infection in lab suite handling virus - infection in common facilities shared with lab suite handling virus - infection in institution precinct via aerosols, wastes or stray lab animal	Either - infection via aerosol outside lab precinct - infection via incompletely neutralized liquid or solid lab wastes outside lab - infection via stray lab animal
Virus [See Annex B on virus genesis]	Present in nature	Either present in nature or a lab product	Either present in nature or a lab product
First person infected in a lab/institution?	Possibly - could also be employee, contractor, contract worker, collaborator, associate, or visitor, accompanying university student	Probably - could be employee, contractor, contract worker, collaborator, associate, or visitor	First person is infected outside of lab/institution
Virus in field samples?	Not necessarily. Could be an infection from a bat that may not even have been sampled	Not if virus is a lab product, or from live bat collected in nature and bred in lab	Not if virus is a lab product, or from live bat collected in nature and bred in lab
Virus isolated? (cell culture)	Not necessarily. May not be in a field sample, and, even if the virus is in a field sample, the field sample may not have been processed yet	Not necessarily. Could be from non-processed field sample or a non isolated lab construct	Not necessarily. Could be from non-processed field sample or a non isolated lab construct

Virus sequenced?	Not necessarily. May not be in a field sample, and, even if the virus is in a field sample, the field sample may not have been processed yet	Not necessarily. Could be from non-processed field sample or a non isolated or non sequenced lab construct	Not necessarily. Could be from non-processed field sample or a non isolated or non sequenced lab construct
Argument #1: SARS-CoV-2 not present in lab	Irrelevant	Relevant only in case of a sequenced virus	Relevant only in case of a sequenced virus
Argument #2: No lab-employee tested positive for SARS-CoV-2 antibodies (igG)	Irrelevant (unless all field sampling personnel, contractors, contract workers, associates, and visitors were tested)	Irrelevant (unless all lab personnel, contractors, contract workers, associates, and visitors were tested)	Irrelevant

Annex B: Virus genesis scenarios

Virus Scenario:	Found in nature	Routine processing in lab	Serial passage in lab, Gain of function selected	Genetic manipulation in lab, Gain of function created and selected
	VS1	VS2	VS3	VS4
Lab Product?	No	Yes	Yes	Yes
Description	Virus arose in nature	Virus arose naturally in lab via mutations or recombinations (without artificial selection)	Virus arose in lab through serial passage (directed evolution), artificially selected mutations or recombinations	Virus arose in lab through genetic manipulation via mutations and recombinations created and selected
Host	Natural host (bat or other animal)	Lab cultures and/or lab animals	Lab cultures and/or lab animals	Lab cultures and/or lab animals

Note that all combinations of VS2, VS3 and VS4 are also possible, for instance VS3 followed by VS2.