Notice of Award

RESEARCH **Issue Date:** 05/27/2014

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 1R01AI110964-01
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Aleksei
President
460 West 34th Street
17th Floor
New York, NY 100012317

Award e-mailed to: [redacted]

Budget Period: 06/01/2014 – 05/31/2015
Project Period: 06/01/2014 – 05/31/2019

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $666,442 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Laura A. Pone
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 1R01AI110964-01

Award Calculation (U.S. Dollars)

Salaries and Wages	$167,708
Fringe Benefits	$54,168
Supplies	$21,400
Travel Costs	$35,918
Other Costs	$10,000
Consortium/Contractual Cost	$227,663
Federal Direct Costs	$516,857
Federal F&A Costs	$149,585
Approved Budget	$666,442
Federal Share	$666,442
TOTAL FEDERAL AWARD AMOUNT	$666,442
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$666,442

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
1	$666,442	$666,442
2	$630,445	$630,445
3	$611,090	$611,090
4	$597,112	$597,112
5	$581,646	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2014

IC	CAN	2014	2015	2016	2017	2018
AI	8472350	$666,442	$630,445	$611,090	$597,112	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C / **OC**: 414A / **Released**: AMIDONL 05/20/2014
Award Processed: 05/08/2014 01:52:21 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1R01AI110964-01

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 1R01AI110964-01

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.

b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.
d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the Central Contractor Registration. Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 1R01AI110964-01

THIS AWARD CONTAINS GRANT SPECIFIC RESTRICTIONS. THESE RESTRICTIONS MAY ONLY BE LIFTED BY A REVISED NOTICE OF AWARD.

RESTRICTION: This award is issued with the knowledge that subjects may be involved within the period of support, but definite plans were not set forth in the application as per 45 CFR 46.118. No human subjects may be involved in any project supported by this award until all requirements for Human Subjects research as identified in the PHS398/SF424 Instructions have been provided to and approved by NIH.

RESTRICTION: The present award is being made without a currently valid certification of IRB approval for this project with the following restriction: Only activities that are clearly severable and independent from activities that involve human subjects may be conducted pending the NIAID's acceptance of the certification of IRB review and approval.

No funds may be drawn down from the payment system and no obligations may be made against Federal funds for any research involving human subjects prior to the NIAID's notification to the grantee that the identified issues have been resolved and this restriction removed.

~~~~~~~~~
This award includes funds for subcontract/consortium activity with Wuhan Institute of Virology, CHINA and is budgeted as follows:

	-Yr 1	-Yr 2	-Yr 3	-Yr 4	-Yr 5
Total Direct Costs	$123,699	$128,718	$147,335	$147,335	$147,335
F&A Costs @ 8%(MTDC)	$9,896	$10,297	$11,787	$11,787	$11,787
TOTAL COSTS	$133,595	$139,015	$159,122	$159,122	$159,122

Consortiums are to be established and administered as described in the NIH Grants Policy Statement. This written agreement with the consortium must address the negotiated arrangements for meeting the scientific, administrative, financial, and reporting requirements for this grant.
~~~~~~~~~
This award includes funds for subcontract/consortium activity with East China Normal University, CHINA and is budgeted as follows:

	-Yr 1	-Yr 2	-Yr 3	-Yr 4	-Yr 5
Total Direct Costs	$87,100	$67,300	$50,108	$39,167	$14,850
F&A Costs @ 8%(MTDC)	$6,968	$5,384	$4,009	$3,133	$2,404
TOTAL COSTS	$94,068	$72,684	$54,117	$42,300	$32,454

Consortiums are to be established and administered as described in the NIH Grants Policy Statement. This written agreement with the consortium must address the negotiated arrangements for meeting the scientific, administrative, financial, and reporting requirements for this grant.
~~~~~~~~~
Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.
~~~~~~~~~

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

o A list of the new and/or additional Agent(s) that will be studied;
o A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Laura A. Pone
Email: [redacted] **Phone**: [redacted] **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: [redacted] **Phone**: [redacted]

SPREADSHEET SUMMARY
GRANT NUMBER: 1R01AI110964-01

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 1	Year 2	Year 3	Year 4	Year 5
Salaries and Wages	$167,708	$167,708	$167,708	$167,708	$167,708
Fringe Benefits	$54,168	$54,168	$54,168	$54,168	$54,168
Supplies	$21,400	$19,250	$7,250	$7,000	$3,500
Travel Costs	$35,918	$35,918	$35,918	$35,918	$35,918
Other Costs	$10,000	$13,550	$11,050	$9,800	$9,400
Consortium/Contractual Cost	$227,663	$211,699	$213,239	$201,422	$191,576
TOTAL FEDERAL DC	$516,857	$502,293	$489,333	$476,016	$462,270
TOTAL FEDERAL F&A	$149,585	$128,152	$121,757	$121,096	$119,376
TOTAL COST	$666,442	$630,445	$611,090	$597,112	$581,646

Facilities and Administrative Costs	Year 1	Year 2	Year 3	Year 4	Year 5
F&A Cost Rate 1	44.1%	44.1%	44.1%	44.1%	44.1%
F&A Cost Base 1	$339,194	$290,594	$276,094	$274,594	$270,694
F&A Costs 1	$149,585	$128,152	$121,757	$121,096	$119,376

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

May 28, 2016

Mr. Aleksei Chmura
Senior Coordinator of Operations
EcoHealth Alliance
460 West 34th Street – 17th Floor
New York, NY 10001

RE: 5R01AI110964-03

Dear Mr. Chmura:

Based upon information in the most recent progress report, NIAID has determined that the above referenced grant may include Gain of Function (GoF) research that is subject to the U.S. Government funding pause (http://www.phe.gov/s3/dualuse/Documents/gain-of-function.pdf), issued on October 17, 2014. The following specific aims appear to involve research covered under the pause:

Aim 3: Testing predictions of CoV inter-species transmission

As per the funding pause announcement, new USG funding will not be released for GoF research projects that may be reasonably anticipated to confer attributes to influenza, MERS, or SARS viruses such that the virus would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route. Therefore, the next non-competing segment of the award that starts June 1, 2016 cannot be released until a determination is reached based on the receipt and review of the information requested below. The research funding pause would not apply to characterization or testing of naturally occurring influenza, MERS, or SARS viruses, unless the tests are reasonably anticipated to increase transmissibility and/or pathogenicity.

NIAID requests that you provide the following information within 15 days of the date of this letter:

- **Determination as to whether the above research does or does not include GoF work subject to the funding pause.** Please provide a detailed explanation for this determination, including, but not limited to, descriptions of the MERS and MERS-like chimeric CoVs that you propose to create, and detailed descriptions of the experiments you plan to conduct. Your determination should also include whether each chimeric virus is reasonably anticipated to exhibit enhanced pathogenicity and/or transmissibility in mammals via the respiratory route compared to wild type MERS-CoV.

- **In addition, your progress report makes reference to two chimeric bat SARS-like CoVs constructed on a WIV-1 backbone.** NIAID requests additional information on these strains of SARS-like CoVs, including: the dates the strains were created; whether the chimeric viruses exhibit enhanced pathogenicity and/or transmissibility in mammals via the respiratory route compared to wild type SARS-CoV; and what research plans you have for these chimeric viruses.
- **If it is determined that the above research <u>DOES</u> include GoF work subject to the funding pause, provide detailed information on what research will remain viable with the removal of the GoF work and appropriate budget adjustments. Options include:**
    - For the specific aims that propose GoF work, provide a detailed description of changes that can be made to remove the GoF work but maintain the specific aim(s); or
    - Remove the specific aims and experiments that are subject to the pause from the Research Plan and request to have the award budget renegotiated.

If you have any questions about this matter please do not hesitate to contact the NIAID Program Officer.

Sincerely,

[redacted]

Jenny Greer
Grants Management Specialist
NIAID/NIH/DHHS

[redacted]

[redacted], Ph.D.
Program Officer
Division of Microbiology and Infectious Diseases
NIAID/NIH/DHHS

CC: Dr. Peter Daszak
Ms. Mary Kirker
Dr. Irene Glowinski
Dr. Andrew Ford

EcoHealth Alliance

Dear Drs. Greer and Stemmy,

June 8, 2016

We appreciate your rapid review of our proposed work for year 3 of our R01 (5R01AI110964-03). We have provided the details you requested, below, including alternative strategies if we remove work that could be deemed gain of function. We look forward to your response and will modify our workplan accordingly. In the meantime, please rest assured that none of the proposed work for Specific Aim #3 that you have requested information about will begin.

Determination as to whether the above research does or does not include GoF work subject to the funding pause. Please provide a detailed explanation for this determination, including, but not limited to, descriptions of the MERS and MERS-like chimeric CoVs that you propose to create, and detailed descriptions of the experiments you plan to conduct. Your determination should also include whether each chimeric virus is reasonably anticipated to exhibit enhanced pathogenicity and/or transmissibility in mammals via the respiratory route compared to wild type MERS-CoV.

Firstly, we would like to reiterate that this work is *proposed* for year 3, and none has been conducted to date. Furthermore, we will not proceed with any of this unless we are given the go-ahead by NIAID. The goal of our proposed work to construct MERS and MERS-like chimeric CoVs is to understand the potential origins of MERS-CoV in bats by studying bat MERS-like CoVs in detail. The chimeric viruses will be used to ascertain receptor usage and infectivity of bat MERS-related CoVs *in vitro* and in a mouse model. To achieve this purpose, our aim is to firstly construct a MERS-CoV infectious clone based on the genomic sequence of EMC2012 (GenBank no. NC_019843) and then chimeric CoVs with the replacement of the spike envelope genes from bat derived MERS-like CoVs. We have very recently discovered a small number (9 different strains) of bat MERS-like CoVs in 99 samples from bats in Guangxi, Guangdong, and Szechuan provinces. Phylogenetically, these bat viruses are not very close to MERS-CoV (only 63-66% homology to the S-protein of MERS-CoV).

We aim to test the chimeric viruses for receptor usage of DPP4 (the MERS-CoV receptor) in cells and then in DPP4 transgenic mice, to see if these bat viruses have any capacity to use the same receptor. That said, given the phylogenetic distance from MERS-CoV, we believe it is *highly unlikely* that these bat spike proteins attach to DPP4, and if so, that they would have any pathogenic potential. Finally, should any of these recombinants show evidence of enhanced virus growth >1 log in cells expressing the human, bat, mouse or other DPP4 receptor over wildtype parental backbone MERS-CoV strain or grow more efficiently in human airway epithelial cells, we will immediately: i) stop all experiments with the mutant, ii) inform our NIAID Program Officer and the UNC IBC of these results and iii) participate in decision making trees to decide appropriate paths forward.

In addition, your progress report makes reference to two chimeric bat SARS-like CoVs constructed on a WIV-1 backbone.
NIAID requests additional information on these strains of SARS-like CoVs, including: the dates the strains were created; whether the chimeric viruses exhibit enhanced pathogenicity and/or transmissibility in

EcoHealth Alliance
460 West 34th Street, 17th Floor
New York, NY 10001-2320
[redacted]
EcoHealthAlliance.org

mammals via the respiratory route compared to wild type SARS-CoV; and what research plans you have for these chimeric viruses.

These two chimeric bat-like CoVs were constructed on September 24, 2015. They use the backbone of a group 2b SARS-like bat CoV WIV1 and the spike proteins of two newly discovered bat SL-CoVs (Rs7327 and RsSHC014). The construction of these chimeric viruses aims to understand the receptor usage and infectivity of bat SL-CoVs that may be progenitors of SARS-CoV. We have not yet tested the pathogenicity of these viruses in animals.

We believe that this work would not be considered GoF because the pause specifically targeted experiments that altered the pathogenicity or transmissibility of SARS-CoV, MERS-CoV and any influenza virus. Our molecular clone is WIV1, which is a group 2b SARS-like bat coronavirus that has never been demonstrated to infect humans or cause human disease. It is about 10% different from SARS-CoV. Thus, we feel that introducing other group 2b SARS-like bat coronavirus spike glycoproteins into WIV1 is not subject to the pause. Moreover, we are introducing progressively more distant S glycoproteins into WIV1 (The RBD of Rs7327 differs from WIV1 in several amino acid residues while RsSHC014 is even more distantly related phylogenetically), so it seems progressively less likely that any of these viruses would be more pathogenic or transmissible than the SARS-CoV. This is further supported by the fact that Prof. Ralph Baric's group (Menacherya *et al*, 2015, Nature Medicine, 21 (12):1508-1512; Menacherya *et al*., 2016, PNAS, 113 (11): 3048-3053) took WIV1 spike and inserted it onto a SARS-CoV backbone and showed reduced pathogenicity in mice with human ACE-2 relative to SARS-CoV (mortality rates were much lower, therefore this is *loss-of-function*). This strongly suggests that the chimeric bat spike/bat backbone viruses should not have enhanced pathogenicity in animals.

Finally, as proposed above for the MERS-like viruses, should any of these recombinants show evidence of enhanced virus growth >1 log in cells expressing the human, bat, mouse or civet receptor over wildtype parental backbone SARS-CoV strain or grow more efficiently in human airway epithelial cells, we will immediately: i) stop all experiments with the mutant, ii) inform our NIAID Program Officer and the UNC IBC of these results and iii) participate in decision making trees to decide appropriate paths forward.

If it is determined that the above research DOES include GoF work subject to the funding pause, provide detailed information on what research will remain viable with the removal of the GoF work and appropriate budget adjustments. Options include:

o For the specific aims that propose GoF work, provide a detailed description of changes that can be made to remove the GoF work but maintain the specific aim(s); or

o Remove the specific aims and experiments that are subject to the pause from the Research Plan and request to have the award budget renegotiated.

If these proposed activities within Specific Aim #3 are considered gain of function, we would propose changing them as follows:

1) Instead of the proposed work on MERS-like chimeric CoVs, we would
   a. model the 3-D structure of bat MERS-like CoV spike to assess its potential to bond to DPP4; and
   b. build pseudoviruses with MERS-like CoV spike to conduct experiments for DPP4 binding.

2) Instead of the proposed work on SARS-like chimeric bat CoVs, we would build pseudoviruses with the spike proteins from these viruses and assess receptor binding *in vitro*.

We look forward to your response to our letter and will not conduct any of this proposed work until we hear back from you.

Yours sincerely,

[redacted]

Dr. Peter Daszak

PI
President and Chief Scientist
EcoHealth Alliance

Tel: [redacted]
e-mail: [redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

July 7, 2016

Mr. Aleksei Chmura
Senior Coordinator of Operations
EcoHealth Alliance
460 W. 34th Street – 17th Floor
New York, NY 10001

RE: 5 R01AI110964-03

Dear Mr. Chmura:

Thank you for your correspondence of June 28th, 2016, regarding the October 17, 2014 White House announcement of a U.S. Government-wide pause on certain gain-of-function (GoF) experiments and its potential impact on your research (http://www.whitehouse.gov/blog/2014/10/17/doing-diligence-assess-risks-and-benefits-life-sciences-gain-function-research). The research funding pause pertains to GoF research projects that may be reasonably anticipated to confer attributes to influenza, MERS, or SARS viruses such that the resulting virus would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route.

NIAID reviewed the original grant application, and the additional information provided by you, and made the following assessments regarding Aim 3 of the above-referenced grant:

- NIAID is in agreement that the work proposed under Aim 3 to generate MERS-like or SARS-like chimeric coronaviruses (CoVs) is not subject to the GoF research funding pause. This determination is based on the following: (1) the chimeras will contain only S glycoprotein genes from phylogenetically distant bat CoVs; and (2) recently published work demonstrating that similar chimeric viruses exhibited reduced pathogenicity. Therefore it is not reasonably anticipated that these chimeric viruses will have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route.
- NIAID acknowledges that if any of the MERS-like or SARS-like chimeras generated under this grant show evidence of enhanced virus growth greater than 1 log over the parental backbone strain, Dr. Daszak will immediately stop all experiments with these viruses and provide the NIAID Program Officer and Grants Management Specialist, and Wuhan Institute of Virology Institutional Biosafety Committee, with the relevant data and information related to these unanticipated outcomes.

Please remember that the institution must comply in full with all terms and conditions placed on this grant. As indicated above, NIAID determinations are based on information from multiple sources, but primarily on our communication with you about the details of your proposed experiments and your research results. Should NIAID's determination change based on information obtained through the U.S. Government GoF deliberative process, described here http://www.phe.gov/s3/dualuse/Documents/gain-of-function.pdf, you will be notified; however, until such time, or until the GoF research funding pause is lifted, NIAID's determination, indicated above, is final.

Please let us know if you have any questions, or if you require additional information.

Sincerely,

[redacted]

Jenny Greer
Grants Management Specialist
NIAID/NIH/DHHS

[redacted]

Erik J. Stemmy, Ph.D.
Program Officer
Division of Microbiology and Infectious Diseases
NIAID/NIH/DHHS

CC: Dr. Peter Daszak
Ms. Mary Kirker
Dr. Irene Glowinski
Dr. Andrew Ford

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 11/30/2016

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 5R01AI110964-03 REVISED
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Aleksei Chmura
President
460 West 34th Street
17th Floor
New York, NY 100012317

Award e-mailed to: [redacted]

Period Of Performance:
Budget Period: 06/01/2016 – 05/31/2017
Project Period: 06/01/2014 – 05/31/2019

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Jenny L. Greer
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 5R01AI110964-03 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$167,708
Fringe Benefits	$54,168
Personnel Costs (Subtotal)	$221,876
Materials & Supplies	$7,250
Travel	$35,918
Other	$11,050
Subawards/Consortium/Contractual Costs	$213,239
Federal Direct Costs	$489,333
Federal F&A Costs	$121,757
Approved Budget	$611,090
Total Amount of Federal Funds Obligated (Federal Share)	$611,090
TOTAL FEDERAL AWARD AMOUNT	$611,090
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
3	$611,090	$611,090
4	$597,112	$597,112
5	$581,646	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy, Immunology and Transplantation Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2016

IC	CAN	2016	2017	2018
AI	8472350	$611,090	$597,112	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C / **OC**: 414E / **Released**: GREERJL 11/29/2016
Award Processed: 11/30/2016 12:01:30 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01AI110964-03 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5R01AI110964-03 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants

Policy Statement, including addenda in effect as of the beginning date of the budget period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

REVISED AWARD: This Notice of Award is revised to provide approval for collaboration with the **Wuhan University School of Public Health** (**CHINA**) in accordance with the request submitted by Aleksei Chmura, Ecohealth Alliance, Inc. on October 6, 2016.

Supersedes previous Notice of Award dated **7/26/2016**.

****

No funds are provided and no funds can be used to support gain-of-function research covered under the October 17, 2014 White House Announcement (NIH Guide Notice NOT-OD-15-011).

Per the letter dated July 7, 2016 to Mr. Aleksei Chmura at EcoHealth Alliance, should any of the MERS-like or SARS-like chimeras generated under this grant show evidence of enhanced virus growth greater than 1 log over the parental backbone strain you must stop all experiments with these viruses and provide the NIAID Program Officer and Grants Management Specialist, and Wuhan Institute of Virology Institutional Biosafety Committee with the relevant data and information related to these unanticipated outcomes.

*****

This Notice of Award (NoA) includes funds for consortium activity with:

- **Wuhan Institute of Virology - CHINA** awarded in the Total Costs amount of **$159,122** (**$147,335** Direct Costs + **$11,787** F&A Costs). Future year commitments are as follows: Year 4 Total Costs: $159,122 and Year 5 Total Costs: $159,122
- **East China Normal University - CHINA** awarded in the Total Costs amount of **$54,117** (**$50,108** Direct Costs + **$4,009** F&A Costs). Future year commitments are as follows: Year 4 Total Costs: $42,300 and Year 5 Total Costs: $32,454

Consortiums are to be established and administered as described in the NIH Grants Policy Statement (NIH GPS). The referenced section of the NIH Grants Policy Statement is available at http://grants.nih.gov/grants/policy/nihgps_2013/nihgps_ch15.htm#_Toc271265264.

The written agreement with the consortium must address the negotiated arrangements for meeting the scientific, administrative, financial and reporting requirements for this grant.

No foreign performance site may be added to this project without prior approval of the National Institute of Allergy and Infectious Diseases.

Although a specific amount has been awarded for each consortium, the grantee retains standard rebudgeting authorities.

*****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

*****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:

NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Jenny L. Greer
Email: [redacted] **Phone**: [redacted] **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: [redacted] **Phone**: [redacted]

SPREADSHEET SUMMARY
GRANT NUMBER: 5R01AI110964-03 REVISED

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 3	Year 4	Year 5
Salaries and Wages	$167,708	$167,708	$167,708
Fringe Benefits	$54,168	$54,168	$54,168
Personnel Costs (Subtotal)	$221,876	$221,876	$221,876

Materials & Supplies	$7,250	$7,000	$3,500
Travel	$35,918	$35,918	$35,918
Other	$11,050	$9,800	$9,400
Subawards/Consortium/Contractual Costs	$213,239	$201,422	$191,576
TOTAL FEDERAL DC	$489,333	$476,016	$462,270
TOTAL FEDERAL F&A	$121,757	$121,096	$119,376
TOTAL COST	$611,090	$597,112	$581,646

Facilities and Administrative Costs	Year 3	Year 4	Year 5
F&A Cost Rate 1	44.1%	44.1%	44.1%
F&A Cost Base 1	$276,094	$274,594	$270,694
F&A Costs 1	$121,757	$121,096	$119,376

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 05/26/2017

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 5R01AI110964-04
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Aleksei Chmura
President
460 West 34th Street
17th Floor
New York, NY 100012317

Award e-mailed to: [redacted]

Period Of Performance:
Budget Period: 06/01/2017 – 05/31/2018
Project Period: 06/01/2014 – 05/31/2019

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $597,112 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Laura A. Pone
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 5R01AI110964-04

Award Calculation (U.S. Dollars)

Salaries and Wages	$167,708
Fringe Benefits	$54,168
Personnel Costs (Subtotal)	$221,876
Materials & Supplies	$7,000
Travel	$35,918
Other	$9,800
Subawards/Consortium/Contractual Costs	$201,422
Federal Direct Costs	$476,016
Federal F&A Costs	$121,096
Approved Budget	$597,112
Total Amount of Federal Funds Obligated (Federal Share)	$597,112
TOTAL FEDERAL AWARD AMOUNT	$597,112
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$597,112

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
4	$597,112	$597,112
5	$581,646	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2017

IC	CAN	2017	2018
AI	8472350	$597,112	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C / **OC**: 414E / **Released**: AMIDONL 05/25/2017
Award Processed: 05/26/2017 12:05:11 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01AI110964-04

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5R01AI110964-04

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget

period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V: Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

San Pya Clinic, BURMA
Institut Pasteur du Cambodge, CAMBODIA
Primate Research Center at Bogor Agricultural University, INDONESIA
Conservation Medicine, Ltd, MALAYSIA
King Chulalongkorn Memorial Hospital, THAILAND
Hanoi Agricultural University, VIETNAM
National Animal Health Laboratory, LAOS

****

This Notice of Award (NoA) includes collaboration with **Wuhan University School of Public Health, CHINA.**

****

This Notice of Award (NoA) includes funds for activity with **Wuhan Institute of Virology, CHINA.**

****

This Notice of Award (NoA) includes funds for activity with **(East China Normal University.**

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

This award is subject to the Clinical Terms of Award included in Monitoring of Clinical Trials and Studies - NIAID (see NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032). These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- o A list of the new and/or additional Agent(s) that will be studied;
- o A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Carine Normil
Email: [redacted] **Phone**: [redacted] **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: [redacted] **Phone**: [redacted]

SPREADSHEET SUMMARY
GRANT NUMBER: 5R01AI110964-04

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 4	Year 5
Salaries and Wages	$167,708	$167,708
Fringe Benefits	$54,168	$54,168
Personnel Costs (Subtotal)	$221,876	$221,876
Materials & Supplies	$7,000	$3,500
Travel	$35,918	$35,918
Other	$9,800	$9,400
Subawards/Consortium/Contractual Costs	$201,422	$191,576
TOTAL FEDERAL DC	$476,016	$462,270
TOTAL FEDERAL F&A	$121,096	$119,376
TOTAL COST	$597,112	$581,646

Facilities and Administrative Costs	Year 4	Year 5
F&A Cost Rate 1	44.1%	44.1%
F&A Cost Base 1	$274,594	$270,694
F&A Costs 1	$121,096	$119,376

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 06/18/2018

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 5R01AI110964-05
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Aleksei Chmura
President
460 West 34th Street
17th Floor
New York, NY 100012317

Award e-mailed to: [redacted]

Period Of Performance:
Budget Period: 06/01/2018 – 05/31/2019
Project Period: 06/01/2014 – 05/31/2019

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $581,646 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Tseday G Girma
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 5R01AI110964-05

Award Calculation (U.S. Dollars)

Salaries and Wages	$167,708
Fringe Benefits	$54,168
Personnel Costs (Subtotal)	$221,876
Materials & Supplies	$3,500
Travel	$35,918
Other	$9,400
Subawards/Consortium/Contractual Costs	$191,576
Federal Direct Costs	$462,270
Federal F&A Costs	$119,376
Approved Budget	$581,646
Total Amount of Federal Funds Obligated (Federal Share)	$581,646
TOTAL FEDERAL AWARD AMOUNT	$581,646
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$581,646

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
5	$581,646	$581,646

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2018

IC	CAN	2018
AI	8472350	$581,646

NIH Administrative Data:
PCC: M51C / **OC**: 414E / **Released**: GIRMATG 06/15/2018
Award Processed: 06/18/2018 12:02:35 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01AI110964-05

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5R01AI110964-05

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award represents the final year of the competitive segment for this grant. See the NIH Grants Policy Statement Section 8.6 Closeout for complete closeout requirements at: http://grants.nih.gov/grants/policy/policy.htm#gps.

A final expenditure Federal Financial Report (FFR) (SF 425) must be submitted through the eRA Commons (Commons) within 120 days of the period of performance end date; see the NIH Grants Policy Statement Section 8.6.1 Financial Reports, http://grants.nih.gov/grants/policy/policy.htm#gps, for additional information on this submission requirement. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) quarterly cash transaction data. A final quarterly federal cash transaction report is not required for awards in PMS B subaccounts (i.e., awards to foreign entities and to Federal agencies). NIH will close the awards using the last recorded cash drawdown level in PMS for awards that do not require a final FFR on expenditures or quarterly federal cash transaction reporting. It is important to note that for financial closeout, if a grantee fails to submit a required final expenditure FFR, NIH will close the grant using the last recorded cash drawdown level. If the grantee submits a final expenditure FFR but does not reconcile any discrepancies between expenditures reported on the final expenditure FFR and the last cash report to PMS, NIH will close the award at the lower amount. This could be considered a debt or result in disallowed costs.

A Final Invention Statement and Certification form (HHS 568), (not applicable to training, construction, conference or cancer education grants) must be submitted within 120 days of the expiration date. The HHS 568 form may be downloaded at: http://grants.nih.gov/grants/forms.htm. This paragraph does not apply to Training grants, Fellowships, and certain other programs—i.e., activity codes C06, D42, D43, D71, DP7, G07, G08, G11, K12, K16, K30, P09, P40, P41, P51, R13, R25, R28, R30, R90, RL5, RL9, S10, S14, S15, U13, U14, U41, U42, U45, UC6, UC7, UR2, X01, X02.

Unless an application for competitive renewal is submitted, a Final Research Performance Progress Report (Final RPPR) must also be submitted within 120 days of the period of performance end date. If a competitive renewal application is submitted prior to that date, then an Interim RPPR must be submitted by that date as well. Instructions for preparing an Interim or Final RPPR are at: https://grants.nih.gov/grants/rppr/rppr_instruction_guide.pdf. Any other specific requirements set forth in the terms and conditions of the award must also be addressed in the Interim or Final RPPR. *Note that data reported within Section I of the Interim and Final RPPR forms will be made public and should be written for a lay person audience.*

NIH strongly encourages electronic submission of the final invention statement through the Closeout feature in the Commons, but will accept an email or hard copy submission as indicated below.

Email: The final invention statement may be e-mailed as PDF attachments to: NIHCloseoutCenter@mail.nih.gov.

Hard copy: Paper submissions of the final invention statement may be faxed to the NIH Division of Central Grants Processing, Grants Closeout Center, at 301-480-2304, or mailed to:

National Institutes of Health
Office of Extramural Research
Division of Central Grants Processing
Grants Closeout Center
6705 Rockledge Drive
Suite 5016, MSC 7986
Bethesda, MD 20892-7986 (for regular or U.S. Postal Service Express mail)
Bethesda, MD 20817 (for other courier/express deliveries only)

NOTE: If this is the final year of a competitive segment due to the transfer of the grant to another institution, then a Final RPPR is not required. However, a final expenditure FFR is required and should be submitted electronically as noted above. If not already submitted, the Final Invention Statement is required and should be sent directly to the assigned Grants Management Specialist.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 5R01AI110964-05

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

If any experiments proposed in this award result in a virus with enhanced growth by more than 1 log compared to wild type strains, you must notify your NIAID Program Officer and Grants Management Specialist immediately. Further research involving the resulting virus(es) may require review by the Department of Health and Human Services in accordance with the Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (https://www.phe.gov/s3/dualuse/Documents/P3CO.pdf).

****

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

San Pya Clinic, BURMA
Institut Pasteur du Cambodge, CAMBODIA
Primate Research Center at Bogor Agricultural University, INDONESIA
Conservation Medicine, Ltd, MALAYSIA
King Chulalongkorn Memorial Hospital, THAILAND
Hanoi Agricultural University, VIETNAM
National Animal Health Laboratory, LAOS

****

This Notice of Award (NoA) includes collaboration with **Wuhan University School of Public Health, CHINA.**

****

This Notice of Award (NoA) includes funds for activity with **Wuhan Institute of Virology, CHINA.**

****

This Notice of Award (NoA) includes funds for activity with **East China Normal University.**

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

This award is subject to the Clinical Terms of Award included in Monitoring of Clinical Trials and Studies - NIAID (see NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032). These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Adam Graham
Email [redacted] **Phone**: [redacted] **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: [redacted] **Phone**: [redacted]

SPREADSHEET SUMMARY
GRANT NUMBER: 5R01AI110964-05

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 5
Salaries and Wages	$167,708
Fringe Benefits	$54,168
Personnel Costs (Subtotal)	$221,876
Materials & Supplies	$3,500
Travel	$35,918
Other	$9,400
Subawards/Consortium/Contractual Costs	$191,576
TOTAL FEDERAL DC	$462,270
TOTAL FEDERAL F&A	$119,376
TOTAL COST	$581,646

Facilities and Administrative Costs	Year 5
F&A Cost Rate 1	44.1%
F&A Cost Base 1	$270,694

F&A Costs 1	$119,376

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 07/24/2019

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 2R01AI110964-06
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Dr. Daszak, Peter
PD/PI
460 West 34th Street
Suite 1701
New York, NY 100012320

Award e-mailed to: [redacted]

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2020
Project Period: 06/01/2014 – 06/30/2024

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $733,750 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Tseday G Girma
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 2R01AI110964-06

Award Calculation (U.S. Dollars)

Salaries and Wages	$170,123
Fringe Benefits	$53,590
Personnel Costs (Subtotal)	$223,713
Consultant Services	$79,750
Materials & Supplies	$20,850
Travel	$39,398
Subawards/Consortium/Contractual Costs	$229,651
Federal Direct Costs	$593,362
Federal F&A Costs	$140,388
Approved Budget	$733,750
Total Amount of Federal Funds Obligated (Federal Share)	$733,750
TOTAL FEDERAL AWARD AMOUNT	$733,750
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$733,750

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
6	$733,750	$733,750
7	$709,750	$709,750
8	$709,750	$709,750
9	$709,750	$709,750
10	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021	2022	2023
AI	8472364	$733,750	$709,750	$709,750	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 414B / **Released**: GIRMATG 07/18/2019
Award Processed: 07/24/2019 12:03:26 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01AI110964-06

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 2R01AI110964-06

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.

c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 2R01AI110964-06

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

This Notice of Award (NoA) includes funds for activity with **The University of North Carolina at Chapel Hill** in the amount of **$77,750** (**$50,000** direct costs + **$27,750**F&A costs).

This Notice of Award (NoA) includes funds for activity with **Wuhan Institute of Virology** in the amount of **$76,301** (**$70,649** direct costs + **$5,652** F&A costs).

This Notice of Award (NoA) includes funds for activity with **Institute of Pathogen Biology** in the amount of **$75,600** (**$70,000** direct costs + **$5,600** F&A costs).

****

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

Wuhan Institute of Virology, CHINA

Institute of Pathogen Biology, CHINA

East China Normal University, CHINA

Duke-NUS Medical School, SINGAPORE

****

This award reflects current Federal policies regarding Facilities & Administrative (F&A) Costs for foreign grantees including foreign sub-awardees, and domestic awards with foreign sub-awardees. Please see: Chapter 16 Grants to Foreign Organizations, International Organizations, and Domestic Grants with Foreign Components, Section 16.6 "Allowable and Unallowable Cost" of the NIH Grants Policy.

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

The budget period anniversary start date for future year(s) will be **July** 1.

****

Dissemination of study data will be in accord with the Recipient's accepted genomic data sharing plan as stated in the page(s) **203** of the application. Failure to adhere to the sharing plan as mutually agreed upon by the Recipient and the NIAID may result in Enforcement Actions as described in the NIH Grants Policy Statement.

****

This award is subject to the Clinical Terms of Award referenced in the NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032. These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Tseday G Girma
Email: [redacted] **Phone**: [redacted] **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: [redacted] **Phone**: [redacted]

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01AI110964-06

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 6	Year 7	Year 8	Year 9	Year 10
Salaries and Wages	$170,123	$170,123	$170,123	$170,123	$170,123
Fringe Benefits	$53,590	$53,590	$53,590	$53,590	$53,590
Personnel Costs (Subtotal)	$223,713	$223,713	$223,713	$223,713	$223,713
Consultant Services	$79,750	$79,750	$79,750	$79,750	$79,750
Materials & Supplies	$20,850	$14,850	$14,850	$14,850	$14,850
Travel	$39,398	$39,398	$39,398	$39,398	$39,398
Subawards/Consortium/Contractual Costs	$229,651	$229,651	$229,651	$229,651	$229,651
Publication Costs		$6,000	$6,000	$6,000	$6,000
TOTAL FEDERAL DC	$593,362	$593,362	$593,362	$593,362	$593,362
TOTAL FEDERAL F&A	$140,388	$116,388	$116,388	$116,388	$116,388
TOTAL COST	$733,750	$709,750	$709,750	$709,750	$709,750

Facilities and Administrative Costs	Year 6	Year 7	Year 8	Year 9	Year 10
F&A Cost Rate 1	32%	32%	32%	32%	32%
F&A Cost Base 1	$438,711	$363,711	$363,711	$363,711	$363,711
F&A Costs 1	$140,388	$116,388	$116,388	$116,388	$116,388

Date: April 19, 2020

From: Michael S Lauer, MD
NIH Deputy Director for Extramural Research

[redacted]

To: Kevin Olival, PhD
Vice-President for Research
EcoHealth Alliance
[redacted]

Naomi Schrag, JD
Vice-President for Research Compliance, Training, and Policy
Columbia University
[redacted]

Subject: Project Number 2R01AI110964-06

Dear Dr. Olival and Ms. Schrag:

EcoHealth Alliance, Inc. is the recipient, as grantee, of an NIH grant entitled "Understanding the Risk of Bat Coronavirus Emergence." It is our understanding that one of the sub-recipients of the grant funds is the Wuhan Institute of Virology ("WIV"). It is our understanding that WIV studies the interaction between coronaviruses and bats. The scientific community believes that the coronavirus causing COVID-19 jumped from bats to humans likely in Wuhan where the COVID-19 pandemic began. There are now allegations that the current crisis was precipitated by the release from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs.

While we review these allegations during the period of suspension, you are instructed to cease providing any funds from the above noted grant to the WIV. This temporary action is authorized by 45 C.F.R. § 75.371(d) ("Initiate suspension or debarment proceedings as authorized under 2 C.F.R. part 180"). The incorporated OMB provision provides that the funding agency may, through suspension, immediately and temporarily exclude from Federal programs persons who are not presently responsible where "immediate action is necessary to protect the public interest." 2 C.F.R. § 180.700(c). It is in the public interest that NIH ensure that a sub-recipient has taken all appropriate precautions to prevent the release of pathogens that it is studying. This suspension of the sub-recipient does not affect the remainder of your grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

24 April 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: Termination of NIH Grant R01 AI 110964

Dear Drs. Chmura and Daszak:

I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS) has elected to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI110964, for convenience. This grant project was issued under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284). This grant was funded as a discretionary grant as outlined in the NIH Grants Policy Statement, which states that the decision not to award a grant, or to award a grant at a particular funding level, is at the discretion of the agency, in accordance with NIH's dual review system.

At this time, NIH does not believe that the current project outcomes align with the program goals and agency priorities. NIAID has determined there are no animal and human ethical considerations, as this project is not a clinical trial, but rather an observational study.

As a result of this termination, a total of $369,819.56 will be remitted to NIAID and additional drawdowns will not be supported. The remaining funds have been restricted in the HHS Payment Management System, effective immediately.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

cc: Dr. Erik Stemmy
Ms. Emily Linde

Tarter Krinsky & Drogin LLP
1350 Broadway
New York, NY 10018
P 212.216.8000
F 212.216.8001
www.tarterkrinsky.com

Andrew N. Krinsky, *Partner*
[redacted] *Direct Dial*
[redacted]

May 22, 2020

Via Email, Certified Mail, & FedEx
[redacted]

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research
National Institutes of Health
National Institute of Allergy and Infectious Diseases
1 Center Drive, Building 1, Room 144
Bethesda, Maryland 20892

Re: Termination of NIH Grant 2R01 AI 110964-6

Dear Dr. Lauer:

This firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance") with regard to the post-award decision by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institute of Health ("NIH"), under the Department of Health and Human Services ("HHS"), to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI 110964, on April 24, 2020 (the "Termination").

This letter, pursuant to NIH Grants Policy Statement Section 8.7 and 42 CFR 50, Subpart D, constitutes EcoHealth Alliance's first-level appeal of the Termination, which was "for convenience." As set forth in more detail below, the Termination is not authorized under the NIH Grants Policy Statement, arbitrary and capricious and an indefensible attack on public health and welfare given that it undermines a pivotal 10-year research project involving the origins, spread and threat of emerging bat coronaviruses during the peak of an unprecedented worldwide coronavirus pandemic. Accordingly, EcoHealth Alliance hereby demands that grant 2R01 AI 110964-6 be reinstated immediately.

BACKGROUND

A. EcoHealth Alliance

EcoHealth Alliance is a prominent New York-based nonprofit institution dedicated to protecting the health of people, animals, and the environment from emerging zoonotic diseases. For more than a decade, EcoHealth Alliance has been conducting cutting edge scientific research to identify hundreds of new coronaviruses ("CoVs") in bats and to study the capacity of these viruses to infect human cells. The purpose of this research is to identify high risk populations so international actors can leverage their resources to address potential pandemics. In cooperation with a global network of over seventy partners, including academic institutions, intergovernmental

and governmental agencies, infectious disease surveillance laboratories, and other international and national organizations in over thirty countries, EcoHealth Alliance's work has led to numerous scientific papers published in high impact journals. These publications have been critical in raising awareness of the threat that CoVs pose to global health, the global economy, and U.S. National Security.

EcoHealth Alliance has a long history of successful cooperation with NIH including multiple Research Project Grant R01 awards. In particular, Peter Daszak, EcoHealth Alliance's President and Chief Scientist, has been the Principal Investigator on five multidisciplinary R01s. All of these projects used modeling, epidemiology, laboratory, and field science to test hypotheses on the emergence of wildlife-origin viral zoonoses, including SARS-CoV, the Nipah and Hendra viruses, Avian influenza, and other bat-origin viruses. EcoHealth Alliance, a 501(c)(3) organization, is unique in that it goes one step further by leveraging its research goals to create an alliance of international collaborators that can advocate for real-world changes to protect high risk populations.

Notably, in collaboration with virologists in China, EcoHealth Alliance isolated and characterized SARSr-CoVs from bats that use the same human host cell receptor (ACE2) as SARS-CoV. This work provided critical reagents and resources that have advanced scientific understanding of virus-host binding and contributed to vaccine development. For example, the genetic sequences of the bat viruses that EcoHealth Alliance discovered under its NIH research funding, which were published online (Genbank & GISAID), have been used to test the effectiveness of the drug Remdesivir against not only SARS-CoV, but also MERS, and other potentially zoonotic or pre-pandemic bat CoVs. Significantly, this type of testing can be performed without the need for viral cultures or shipping viruses internationally.

B. NIH Awards And Extends EcoHealth Alliance Research Grant R01 AI 110964

In 2014, NIH issued EcoHealth Alliance a five-year research award for the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI 110964 (the "Project"). EcoHealth Alliance received additional awards for the Project each year between 2015 and 2018. Between 2015 and 2019, the Project resulted in the publication of more than twenty papers.

In 2019, EcoHealth Alliance submitted a renewal application to NIH through NIAID to extend the Project period for an additional five years. Upon filing of its renewal application, the Project was ranked as an "extremely high priority" (in the top 3%) by NIAID during its external review process. In light of its success and the importance of EcoHealth Alliance's work, on July 24, 2019, NIH reauthorized grant R01 AI 110964 and increased EcoHealth Alliance's funding. EcoHealth Alliance was issued a notice of award in the amount of $733,750.00 (the "2019 Award"). The notice of award also extended the Project period for an additional five years to 2024. A copy of the notice of award is attached hereto as Exhibit A.

C. EcoHealth Alliance Agrees Not To Fund The Wuhan Institute Of Virology

During the pendency of the Project, in December of 2019, China reported a cluster of cases of pneumonia in Wuhan, Hubei Province. It was later determined that the cause of this pneumonia

was a novel CoV, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease (COVID-19). Thereafter, SARS-CoV-2 spread to nearly every country throughout the world. In response, EcoHealth Alliance has prioritized its efforts in conducting research that will be integral to developing an effective strategy to combat SARS-CoV-2.

On April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH regarding a laboratory in China, the Wuhan Institute of Virology ("WIV"). WIV was a prior sub-recipient of a small portion of the R01 AI 110964 grant funds. The letter stated that, given allegations that COVID-19 "was precipitated by the release from WIV of the coronavirus responsible for COVID-19", NIH was pursuing suspension of WIV from participating in Federal programs. However, Mr. Lauer assured EcoHealth Alliance that "[t]his suspension of the sub-recipient does not affect the remainder of [EcoHealth Alliance's] grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension." A copy of the letter is attached hereto as Exhibit B.

On April 21, 2020, Dr. Daszak of EcoHealth Alliance responded by email to Dr. Lauer stating that he could "categorically state that no funds from [sic] 2R01 AI 110964-6 have been sent to Wuhan Institute of Virology, nor has any contract been signed." Dr. Daszak further represented that EcoHealth Alliance would comply with all NIAID requirements. Dr. Lauer acknowledged (1) that no monies from grant 2R01 AI 110964-6 had gone to WIV and no contract between EcoHealth Alliance and WIV had been signed and (2) EcoHealth Alliance's agreement that it would not provide any funds to WIV until and unless directed otherwise by NIH. A copy of the email correspondence between NIH and EcoHealth Alliance is attached hereto as Exhibit C.

D. NIH Abruptly Terminates Research Grant 2R01 AI 110964-6 "For Convenience"

Notwithstanding NIH's representation that suspension of WIV would not affect the remainder of EcoHealth Alliance's 2019 Award, on April 24, 2020, NIH notified EcoHealth Alliance by letter that, effective immediately, the 2019 Award had been terminated by NIAID. The stated grounds for the Termination were: (1) convenience; (2) NIH's discretion not to award a grant, or to award a grant at a particular funding level; and (3) NIH's belief that the Project outcomes did not align with the program goals and agency priorities. A copy of the Termination is attached hereto as Exhibit D.

ARGUMENT

A. NIH Research Grants Are Not Subject To Termination For Convenience

"Termination for convenience" refers to the exercise of the government's right to bring to an end the performance of all or part of the work provided for under a contract prior to the expiration of the contract "when it is in the Government's interest" to do so. Federal agencies typically incorporate clauses in their procurement contracts which give them the right to terminate for convenience. Here, there is no clause in the terms and conditions applicable to the 2019 Award, or in the NIH Grants Policy Statement, that permits NIAID or NIH to issue a post-award decision to terminate a NIH research grant award "for convenience."

Moreover, the unprecedented assertion by NIH that active research grants can be terminated "for convenience" during the subject budget period renders Section 8.5.2 of the NIH Grants Policy Statement meaningless. *See, e.g., Li v. Eddy*, 324 F.3d 1109, 1110 (9th Cir. 2003) (rejecting suggested statutory interpretation on the grounds that the interpretation ran squarely against the canon of construction that courts interpret statutes so as not to render any section meaningless). Section 8.5.2 of the NIH Grants Policy Statement governs, *inter alia*, modification or termination of an award for misconduct. If NIH grants were terminable for convenience, NIH could always choose to terminate for convenience to avoid (1) the "for cause" restriction on grant terminations and (2) the labor intensive task of enforcing compliance through disallowing costs, withholding further awards, or wholly suspending the grant, pending corrective action.

B. NIH's Discretion Not To Award A Grant, Or To Award a Grant At A Particular Funding Level, Does Not Authorize A Post-Award Decision To Terminate

NIH's discretion regarding the "decision not to award a grant, or to award a grant at a particular funding level" does not give NIH the authority to issue a post-award decision terminating a duly awarded grant during the budget period. This purported discretion, which is based on language in the last paragraph of NIH Grants Policy Statement Section 2.4.4, entitled *Disposition of Applications*, concerns NIH's authority to reject incomplete or otherwise undesirable grant applications in the first instance only. The provisions of Section 2, generally, have no bearing on post-award decisions affecting duly approved grants for which specified funds have already been allocated. As the 2019 Grant in the amount of $733,750.00 was awarded to EcoHealth Alliance on July 24, 2019, NIH's authority to deny initial grant applications does not allow NIH to terminate the 2019 Grant.

C. The Research Goals Of EcoHealth Alliance And NIAID Are Virtually Identical

NIH's contention that the Project's outcomes do not align with the agency's priorities is demonstrably false. First, the Project was ranked as "extremely high priority" on external review by NIAID less than nine months ago, before the discovery of SARS-CoV-2. Since this discovery, NIH has promulgated new grants seeking applicants to conduct research on the same issues covered by the Project and the 2019 Award.

In addition, there is substantial overlap between the four strategic research priorities on page 1 of NIAID's Strategic Plan for COVID-19 Research, published April 22, 2020, and the three Specific Aims of the Project. Both NIAID and EcoHealth Alliance seek to: (1) improve fundamental knowledge of SARS-Cov-2; (2) develop methods to assess the rate of infection and disease incidence; (3) contribute to the development of an effective vaccine; and (4) increase public health preparedness. Copies of the Project's Specific Aims and the NIAID Strategic Plan's four strategic research priorities for COVID-19 research are attached hereto as Exhibit E.

D. There Is No Rational Basis To Terminate The 2019 Award For Cause

The grounds and procedures for suspension and termination of awards are specified in NIH Grants Policy Statement Section 8.5.2 and 45 CFR Parts 75.371 through 75.373. Notably, Section

8.5.2 provides, *inter alia*, that NIH will generally suspend (rather than immediately terminate) a grant and allow the recipient an opportunity to take appropriate corrective action before NIH makes a termination decision. Through this lens, 45 CFR 75.372 provides that NIH may terminate a Federal award, in whole or in part, if: (1) the non-Federal entity fails to comply with the terms and conditions of the award; (2) for cause; (3) by the HHS awarding agency or pass-through entity with the consent of the non-Federal entity; or (4) by the non-Federal entity upon written notice to the HHS awarding agency setting forth the reasons for such termination and other information. None of the foregoing predicate conditions exist here.

As of the date of the Termination, EcoHealth Alliance had not received any notice from NIH, NIAID, or HHS that it either failed to comply with any of the terms or conditions of the 2019 Award, or committed any misconduct in connection with the award. To the contrary, in email correspondence following EcoHealth Alliance's representation that it had not and would not give any funds from the 2019 Award to WIV, Aleksei Chmura, EcoHealth Alliance's Chief of Staff, memorialized the mutual agreement between NIH and EcoHealth Alliance that EcoHealth Alliance was in compliance with all requests. (Ex. C, # 8). To be clear, EcoHealth Alliance clearly and unequivocally stated that it had not and will not distribute any funds from the 2019 Award to WIV.

In sum, there is no statutory, regulatory, or contractual basis for NIAID's termination of the Project, *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant 2R01 AI 110964-6. However, please note that this letter is not intended to provide an exhaustive list of all possible grounds for reversal of the Termination and may not reflect all arguments and claims that EcoHealth Alliance will assert in the event that a formal second-level appeal of the Termination is required.

Should you wish to present evidence in an effort to refute any of the factual assertions made in this letter and/or to engage in good faith negotiations regarding appropriate terms and conditions for the resumption of funding for grant 2R01 AI 110964-6, we are prepared to review such evidence and to participate in such negotiations.

We await your response to this letter.

Very truly yours,

[redacted]

Andrew R. Krinsky

[redacted]

cc: (*by email*)

Dr. Erik Stemmy [redacted]
Ms. Emily Linde [redacted]

Exhibit A

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 07/24/2019

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 2R01AI110964-06
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Dr. Daszak, Peter
PD/PI
460 West 34th Street
Suite 1701
New York, NY 100012320

Award e-mailed to: [redacted]

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2020
Project Period: 06/01/2014 – 06/30/2024

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $733,750 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Tseday G Girma
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 2R01AI110964-06

[redacted]

[redacted]

Approved Budget	$733,750
Total Amount of Federal Funds Obligated (Federal Share)	$733,750
TOTAL FEDERAL AWARD AMOUNT	$733,750
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$733,750

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
6	$733,750	$733,750
7	$709,750	$709,750
8	$709,750	$709,750
9	$709,750	$709,750
10	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021	2022	2023
AI	8472364	$733,750	$709,750	$709,750	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 414B / **Released**: GIRMATG 07/18/2019
Award Processed: 07/24/2019 12:03:26 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01AI110964-06

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 2R01AI110964-06

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.

c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 2R01AI110964-06

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

[redacted]

****

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

[redacted]

****

This award reflects current Federal policies regarding Facilities & Administrative (F&A) Costs for foreign grantees including foreign sub-awardees, and domestic awards with foreign sub-awardees. Please see: Chapter 16 Grants to Foreign Organizations, International Organizations, and Domestic Grants with Foreign Components, Section 16.6 "Allowable and Unallowable Cost" of the NIH Grants Policy.

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

The budget period anniversary start date for future year(s) will be **July** 1.

****

Dissemination of study data will be in accord with the Recipient's accepted genomic data sharing plan as stated in the page(s) **203** of the application. Failure to adhere to the sharing plan as mutually agreed upon by the Recipient and the NIAID may result in Enforcement Actions as described in the NIH Grants Policy Statement.

****

This award is subject to the Clinical Terms of Award referenced in the NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032. These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Tseday G Girma
Email: [redacted] **Phone**: [redacted] **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: [redacted] **Phone**: [redacted]

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01AI110964-06

INSTITUTION: ECOHEALTH ALLIANCE, INC.

[redacted]					
TOTAL COST	$733,750	$709,750	$709,750	$709,750	$709,750

Facilities and Administrative Costs	Year 6	Year 7	Year 8	Year 9	Year 10
F&A Cost Rate 1	32%	32%	32%	32%	32%
F&A Cost Base 1	$438,711	$363,711	$363,711	$363,711	$363,711
F&A Costs 1	$140,388	$116,388	$116,388	$116,388	$116,388

Exhibit B

[redacted]

Date: April 19, 2020

From: Michael S Lauer, MD
NIH Deputy Director for Extramural Research

[redacted]

To: Kevin Olival, PhD
Vice-President for Research
EcoHealth Alliance
[redacted]

Naomi Schrag, JD
Vice-President for Research Compliance, Training, and Policy
Columbia University
[redacted]

Subject: Project Number 2R01AI110964-06

Dear Dr. Olival and Ms. Schrag:

EcoHealth Alliance, Inc. is the recipient, as grantee, of an NIH grant entitled "Understanding the Risk of Bat Coronavirus Emergence." It is our understanding that one of the sub-recipients of the grant funds is the Wuhan Institute of Virology ("WIV"). It is our understanding that WIV studies the interaction between corona viruses and bats. The scientific community believes that the coronavirus causing COVID-19 jumped from bats to humans likely in Wuhan where the COVID-19 pandemic began. There are now allegations that the current crisis was precipitated by the release from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs.

While we review these allegations during the period of suspension, you are instructed to cease providing any funds from the above noted grant to the WIV. This temporary action is authorized by 45 C.F.R. § 75.371(d) ("Initiate suspension or debarment proceedings as authorized under 2 C.F.R. part 180"). The incorporated OMB provision provides that the funding agency may, through suspension, immediately and temporarily exclude from Federal programs persons who are not presently responsible where "immediate action is necessary to protect the public interest." 2 C.F.R. § 180.700(c). It is in the public interest that NIH ensure that a sub-recipient has taken all appropriate precautions to prevent the release of pathogens that it is studying. This suspension of the sub-recipient does not affect the remainder of your grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension.

[redacted]

[redacted]

[redacted]

[redacted]

Exhibit C

~~I Michael Lauer~~ email 20 April 2020

From: Lauer, Michael (NIH/OD) [E] <[redacted]>
Sent: Sunday, April 19, 2020 11:00 AM
To: [redacted] Naomi Schrag <[redacted]>
Cc: Black, Jodi (NIH/OD) [E] <[redacted]>
Subject: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Importance: High

Dear Dr. Olival and Ms. Schrag

Please see attached. (Referring to Exhibit B)

Many thanks, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: [redacted]
Email: [redacted]

2 Kevin Olival email on 20 April 2020

From: Kevin Olival <[redacted]>
Subject: **Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06**
Date: April 20, 2020 at 4:12:28 PM EDT
To: "Lauer, Michael (NIH/OD) [E]" [redacted]
Cc: Naomi Schrag <[redacted], "Black, Jodi (NIH/OD) [E]" [redacted]

Dear Mike,

I received the attached letter, however please note:

1. I am not the PI on this award. You should contact Dr. Peter Daszak [redacted] who is the PI and leading this project for EcoHealth Alliance.
2. Columbia University is not involved in this NIH project, and it is not clear to me why Naomi and Columbia University were included.

Thank you,
Kevin

Kevin J. Olival, PhD
Vice President for Research

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

1.[redacted](direct)
1.[redacted](mobile)
1.212.380.4465 (fax)
www.ecohealthalliance.org

3 Michael Lauer email on 20 April 2020

Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

Lauer, Michael (NIH/OD) [E] <[redacted]>

Mon 4/20/2020 4:31 PM

To: Kevin Olival <[redacted]>; Peter Daszak [redacted]

Cc: Naomi Schrag [redacted]; Black, Jodi (NIH/OD) [E] [redacted] Lauer, Michael (NIH/OD) [E] [redacted]

Importance: High

2 attachments

Screen Shot 2020-04-20 at 4.23.38 PM.png; EcoHealth Alliance re AI grant 4 19 20.pdf;

Thank you Kevin

- We need to work with a senior responsible business official – usually PI's and senior business officials are different people.
- When I looked you up on the web, I see the Columbia logo (see attached screenshot). Specifically, it appears to be Columbia University > Ecology, Evolution, and Environmental Biology > EcoHealth Alliance (labeled as an "Affiliation/Department"). Thus the web profile makes it look to me as if EcoHealth Alliance is linked to Columbia University.
- In any case, I'm looping in Dr. Daszak.
- We need to know all sites in China that have been in any way linked to this award (Type 1 and Type 2). We have data in NIH, but we want to make absolutely sure that we're of the same understanding.

We greatly appreciate your prompt attention to this matter.

Best, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: [redacted]
Email: [redacted]

Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

4 Michael Lauer email on 20 April 2020

Lauer, Michael (NIH/OD) [E] [redacted]

Mon 4/20/2020 6:34 PM

To: Naomi Schrag [redacted]; Kevin Olival [redacted]; Peter Daszak [redacted]

Cc: Black, Jodi (NIH/OD) [E] [redacted]; Lauer, Michael (NIH/OD) [E] [redacted]

1 attachment

Screen Shot 2020-04-20 at 4.23.38 PM.png;

Thanks Naomi – not the impression an observer would get looking at the website (see screen shot), but we understand about the grant.

If they "are entirely separate entities" then why does Columbia identify EcoHealth Alliance as an "Affiliation/Department" on its website.

Maybe with the label "Affiliation/Department" you would have a clearly visible disclaimer that says, "EcoHealth Alliance is not affiliated with nor a department of Columbia"? – although even that is internally contradictory.

Best, Mike

From: Naomi Schrag [redacted]
Date: Monday, April 20, 2020 at 5:19 PM
To: "Lauer, Michael (NIH/OD) [E]" [redacted], Kevin Olival [redacted]
Cc: Naomi Schrag [redacted], "Black, Jodi (NIH/OD) [E]" [redacted]
Subject: RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

Dear Dr. Lauer,
Columbia and EcoHealth Alliance are entirely separate entities. Some individuals affiliated with EcoHealth Alliance do have adjunct appointments in Columbia's Ecology, Evolution, and Environmental Biology ("E3B") department, but we are not aware of any Columbia involvement with the referenced grant, and have found no agreement on record in our grants system to the contrary.

We would be happy to answer any additional questions. Thank you.
Sincerely,
Naomi Schrag

Naomi J. Schrag

Vice President for Research Compliance, Training and Policy
Office of Research Compliance and Training
475 Riverside Drive, Suite 840
New York, New York 10115
[redacted]
www.researchcompliance.columbia.edu

RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

5 Peter Daszak email on 21 April 2020

Peter Daszak

Tue 4/21/2020 1:32 AM

To:Lauer, Michael (NIH/OD) [E] [redacted]; Naomi Schrag [redacted]; Kevin Olival [redacted]

Cc:Black, Jodi (NIH/OD) [E] [redacted];

Dear Michael Lauer & Jodi Black – I now have your email and will deal with it directly with you and your staff. Naomi is correct that there is no involvement of Columbia University in this grant. I'm sure NIH has records to confirm that.

From this moment on, I will not cc any staff at Columbia as part of this discussion, and I hope you will also honor that. Respectfully, the discussion of whether or not EHA is an affiliate of CU is entirely irrelevant to the request that you contacted us about, and should remain a private matter between EcoHealth Alliance and Columbia University.

I'll look over your email and respond tomorrow.

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: [redacted]
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

6 Peter Daszak email on 21 April 2020

Peter Daszak

Tue 4/21/2020 7:03 PM

To:Lauer, Michael (NIH/OD) [E] [redacted]

Cc:Black, Jodi (NIH/OD) [E] [redacted] Aleksei Chmura [redacted];
Stemmy, Erik (NIH/NIAID) [E] [redacted]; [redacted]

Importance: High

1 attachment

EcoHealth Alliance re AI grant 4 19 20.pdf;

Dear Michael – Confirming receipt of your email. I'm also cc'ing the following people so they're aware of this request:

1. Our AOR – Dr. Aleksei Chmura, who has access to all our records
2. My Program Officer for this award, Dr. Erik Stemmy & the Division Director (DMID), Dr. Emily Erberding, so they are informed and aware of the request and our response.

That said we need some time to go through the request for information and will provide this as quickly as we can.

However, **I can categorically state that no funds form 2R01AI110964-06 have been sent to Wuhan Institute of Virology, nor has any contract been signed.** Furthermore, we will comply with NIAID requirements, of course.
Concerning the request for information on all of the sites linked to this award in China, you should be aware that these are documented in our progress reports over the course of the grant. As you can understand we are under enormous pressure to generate data related to the current pandemic, and we do not want to divert staff to this effort. We are hoping the previously filed reports will satisfy this request.

We are well aware of the political concerns over the origins of this outbreak. Our collaboration with Wuhan Institute of Virology has been scientific and we have been consistently impressed with the scientific capabilities of that laboratory and its research staff. Our joint work has led to a series of critical papers published in high impact journals that served to raise awareness of the future threat coronaviruses pose for global health and therefore US national security. Scientific insights with epidemiological significance have been jointly published and our relationship has always been open and transparent and with one concern only, scientific validity. We are concerned that current actions may jeopardize 15 years of fruitful collaboration with colleagues in Wuhan, who are working at the leading edge to design vaccines and drugs that could help us fight this new threat in future years. It is quite remarkable that of the 5 vaccine candidates listed by WHO that are already in human trials, 3 have been developed in China. That said, we of course will

do all we can to make sure any further questions from NIH or any Federal agency are addressed to our fullest knowledge.

Yours sincerely,

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: [redacted]
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

7 Michael Lauer email on 21 April 2020

From: **Lauer, Michael (NIH/OD) [E]** [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 21, 2020 at 19:28
To: Peter Daszak [redacted]
Cc: Black, Jodi (NIH/OD) [E] [redacted] Aleksei Chmura [redacted] Stemmy, Erik (NIH/NIAID) [E] [redacted] Erbelding, Emily (NIH/NIAID) [E] [redacted] Lauer, Michael (NIH/OD) [E] [redacted]

ML

Many thanks Peter for your response.

We note that:

- No monies have gone to WIV on the Type 2 award and no contract has been signed.
- You agree that you will not provide any funds to WIV until and unless directed otherwise by NIH.
- All foreign sites for the Type 1 and Type 2 awards have been documented in the progress reports submitted to NIH.

We appreciate your working with us.

Best, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: [redacted]
Email: [redacted]

8 Aleksei Chmura email on 21 April 2020

From: **Aleksei Chmura** [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 23, 2020 at 13:50
To: Lauer, Michael (NIH/OD) [E] [redacted]
Cc: Peter Daszak [redacted] Black, Jodi (NIH/OD) [E] [redacted] Erik Stemmy [redacted]
Erbelding, Emily (NIH/NIAID) [E] [redacted]

Dear Mike,

I read that we are in agreement and in compliance with all requests. Please let us know if anything further is required. We will continue in our usual close communication with our Program Officer Erik Stemmy.

Sincerely,

-Aleksei

Aleksei Chmura
Chief of Staff &
Authorized Organizational Representative

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

[redacted] (office)
(mobile)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

From: **Lauer, Michael (NIH/OD) [E]** [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 23, 2020 at 13:59
To: Aleksei Chmura [redacted]
Cc: Peter Daszak [redacted] Black, Jodi (NIH/OD) [E] [redacted] Stemmy, Erik (NIH/NIAID) [E] [redacted] Erbelding, Emily (NIH/NIAID) [E] [redacted] Lauer, Michael (NIH/OD) [E] [redacted] Compliance Review [redacted]

Many thanks Aleksei.

9 Michael Lauer email on 21 April 2020

Best, Mike

From: **Lauer, Michael (NIH/OD) [E]** [redacted]
Subject: PLEASE READ -- Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 24, 2020 at 16:47
To: Aleksei Chmura [redacted] Peter Daszak [redacted]
Cc: Black, Jodi (NIH/OD) [E] [redacted] Stemmy, Erik (NIH/NIAID) [E] [redacted]
Erbelding, Emily (NIH/NIAID) [E] [redacted] Linde, Emily (NIH/NIAID) [E]
Lauer, Michael (NIH/OD) [E] [redacted] Bulls, Michelle G. (NIH/OD) [E] [redacted]

10 Michael Lauer email on 24 April 2020

Dear Dr. Chmura and Dr. Daszak

Please see attached. (Referring to Exhibit D)

Sincerely,
Michael S Lauer, MD

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: [redacted]
Email: [redacted]

From: **Aleksei Chmura** [redacted]
Subject: Re: PLEASE READ -- Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 27, 2020 at 23:57
To: Lauer, Michael (NIH/OD) [E] [redacted]
Cc: Peter Daszak [redacted] Black, Jodi (NIH/OD) [E] [redacted] Erik Stemmy [redacted]
Emily Erbelding [redacted] Linde, Emily (NIH/NIAID) [E] [redacted] Bulls, Michelle G. (NIH/OD) [E]
[redacted] Alison Andre [redacted]

Dear Michael,

Could Peter and I have a quick chat with you sometime tomorrow (Tuesday) about your email, below?

Sincerely,

11 Aleksei Chmura email on 27 April 2020

-Aleksei

Aleksei Chmura, PhD
Chief of Staff

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

[redacted](office)
(mobile)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

Exhibit D

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

24 April 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: Termination of NIH Grant R01 AI 110964

Dear Drs. Chmura and Daszak:

I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS) has elected to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI110964, for convenience. This grant project was issued under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284). This grant was funded as a discretionary grant as outlined in the NIH Grants Policy Statement, which states that the decision not to award a grant, or to award a grant at a particular funding level, is at the discretion of the agency, in accordance with NIH's dual review system.

At this time, NIH does not believe that the current project outcomes align with the program goals and agency priorities. NIAID has determined there are no animal and human ethical considerations, as this project is not a clinical trial, but rather an observational study.

As a result of this termination, a total of $369,819.56 will be remitted to NIAID and additional drawdowns will not be supported. The remaining funds have been restricted in the HHS Payment Management System, effective immediately.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

cc: Dr. Erik Stemmy
Ms. Emily Linde

Exhibit E

SPECIFIC AIMS

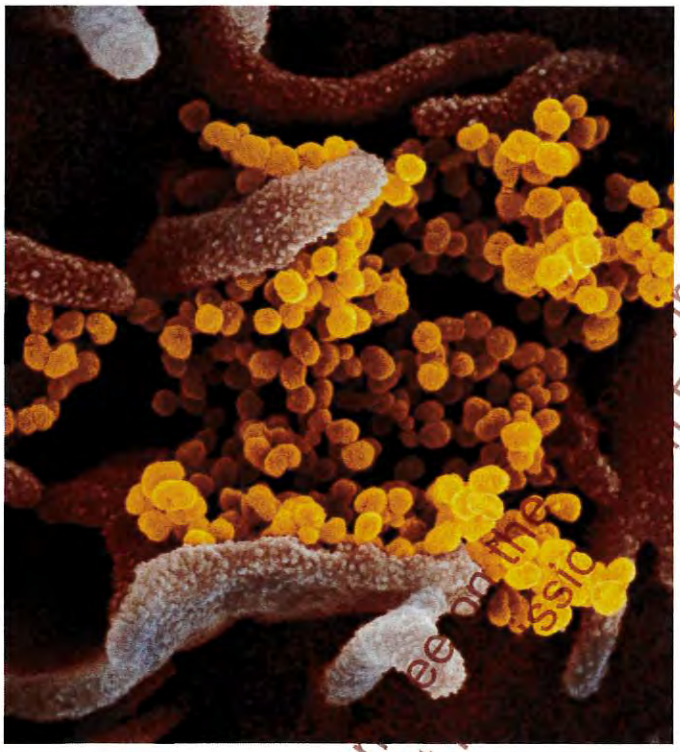
Zoonotic coronaviruses are a significant threat to global health, as demonstrated with the emergence of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) in 2002, and the continuing spread of Middle East Respiratory Syndrome (MERS-CoV). The wildlife reservoirs of SARS-CoV were identified by our group as bat species, and since then we have sequenced dozens of novel SARS-related CoV (SARSr-CoV) strains. Our previous R01 work demonstrates that bats in southern China harbor an extraordinary diversity of SARSr-CoVs, some of which are able to use human ACE2 to enter into human cells, can infect humanized mouse models to cause SARS-like illness, and evade available therapies or vaccines. We found that the bat hosts of SARSr-CoVs appear to no longer be traded in wildlife markets, and that people living close to bat habitats are the primary risk groups for spillover. At one of these sites, we found diverse SARSr-CoVs containing every genetic element of the wild-type SARS-CoV genome, and serological evidence of human exposure among people living nearby. Thus, there is significant potential for future spillover of SARSr-CoVs, and of public health impacts. *Yet salient questions remain: Are there specific bat communities and sites that harbor CoV strains with higher risk for bat-to-human spillover? Which human behaviors drive risk of bat SARSr-CoV exposure that could lead to infection? Does human exposure to these viruses cause SARS-like or other illness? Can we characterize viral strain diversity, bat traits and human behaviors to assess risk of potential future CoV spillover?* **The proposed work in this renewal R01 builds on these findings** to address these issues by conducting: **1)** focused sampling of bats in southern China to **identify viral strains with high predicted risk of spillover**; **2)** community-based, and clinic-based syndromic, sampling of people to **identify spillover, and assess behavioral risk factors and evidence of illness**; and **3)** conduct *in vitro* and *in vivo* viral characterization and analyze epidemiological data **to identify hotspots of future CoV spillover risk**. This work will follow 3 specific aims:

Aim 1: Characterize the diversity and distribution of high spillover-risk SARSr-CoVs in bats in southern China. We will conduct targeted bat sampling at sites where we predict that undiscovered high risk SARSr-CoV strains exist. Bat sampling will be targeted geographically and by host species to test predictions about evolutionary diversity of SARSr-CoV. We will analyze RdRp and S protein sequences to test their capacity for spillover to people in Aim 3.

Aim 2: Community- and clinic-based surveillance to capture SARSr-CoV spillover, routes of exposure and potential public health consequences. We will conduct focused, targeted human surveys and sampling to identify key risk factors for SARSr-CoV spillover and evidence of illness. To maximize our opportunity of capturing human exposure to bat CoVs, we will conduct community-based surveillance in regions with high SARSr-CoV prevalence and diversity, and individuals having contact with bats. We will assess bat-CoV seropositive status against a small number of questions about human-wildlife contact and exposure. We will conduct clinic-based syndromic surveillance close to these sites to identify patients presenting with influenza-like illness and severe acute respiratory illness, assess their exposure to bats via a questionnaire, and test samples for PCR- and serological evidence of SARSr-CoV infection. We will conduct follow-up sampling to capture patients who had not yet seroconverted at the time of clinic visit.

Aim 3: *In vitro* and *in vivo* characterization of SARSr-CoV spillover risk, coupled with spatial and phylogenetic analyses to identify the regions and viruses of public health concern. We will characterize the propensity of novel SARSr-CoVs to infect people *in vitro* using primary human airway epithelial cells and *in vivo* using the transgenic hACE2 mouse model. We will use mAb and vaccine treatments to test our hypothesis that SARSr-CoVs with 10-25% divergence in S protein sequences from SARS-CoV are likely able to infect human cells, and to evade mAb therapeutics and vaccines. We will then map the geographic distribution of their bat hosts and other ecological risk factors to identify the key 'hotspots' of risk for future spillover.

Overall, our SARSr-CoV program serves as a model platform to integrate virologic, molecular and ecologic factors contributing to CoV emergence while informing high impact strategies to intervene and prevent future pandemics. This includes providing critical reagents, therapeutic interventions and recombinant viruses for future SARSr-CoV pandemic and public health preparedness.



This scanning electron microscope image shows SARS-CoV-2 (yellow), the virus that causes COVID-19, isolated from a patient in the United States, emerging from the surface of cells (pink) cultured in the lab. Credit: NIAID-RML

NIAID STRATEGIC PLAN FOR COVID-19 RESEARCH

FY2020 – FY2024

April 22, 2020

National Institute of Allergy and Infectious Diseases

Table of Contents

Executive Summary

The National Institute of Allergy and Infectious Diseases (NIAID) at the United States (U.S.) National Institutes of Health (NIH) is committed to safeguarding the health of Americans and people around the world by accelerating research efforts to prevent, diagnose, and treat COVID-19 and characterize the causative agent of this disease, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This *NIAID Strategic Plan for COVID-19 Research* builds on current trans-NIAID efforts to better understand SARS-CoV-2 pathogenesis, transmission, and mechanisms of protective immunity by expanding resources and activities that support rapid development of biomedical tools to more effectively combat this disease and pandemic. Given the urgency of the public health response, studies that inform efforts to control virus spread and mitigate morbidity and mortality, including therapeutics and vaccine development, are the priority. In addition, it is essential to develop rapid, accurate, point-of-care diagnostics—a critical asset to mitigating the spread of COVID-19.

Box 1
NIAID Strategic Plan for COVID-19 Research Mission

Conduct and support research on SARS-CoV-2 and COVID-19 to accelerate the development of safe and effective medical countermeasures that decrease disease incidence, mitigate morbidity and prevent mortality.

The *NIAID Strategic Plan for COVID-19 Research* aligns with the priorities set by U.S. Government–wide task forces for the development of medical countermeasures. NIAID actively participates in COVID-19 task forces to identify opportunities, ensure open communication, encourage resource sharing, and avoid duplication of effort. The plan is structured around four strategic research priorities:

1. **Improve fundamental knowledge of SARS-CoV-2 and COVID-19,** including studies to characterize the virus and how it is transmitted and understand the natural history, epidemiology, host immunity, disease immunopathogenesis, and the genetic, immunologic, and clinical associations with more severe disease outcomes. This includes accelerating the development of small and large animal models that replicate human disease.

2. **Support the development of diagnostics and assays,** including point-of-care molecular and antigen-based diagnostics for identifying and isolating COVID-19 cases and serologic assays to better understand disease prevalence in the population. Diagnostics also will be essential for evaluating the effectiveness of candidate countermeasures.

3. **Characterize and test therapeutics,** including identifying and evaluating repurposed drugs and novel broad-spectrum antivirals, virus-targeted antibody-based therapies (including plasma-derived intravenous immunoglobulin (IVIG) and monoclonal antibodies), and host-directed strategies to combat COVID-19.

4. **Develop safe and effective vaccines against SARS-CoV-2,** including support of clinical trial testing.

To accelerate research, NIAID will leverage current resources and global collaborations, including existing research programs and clinical trials networks. NIAID's research response to COVID-19 will build on experience with diseases caused by other zoonotic coronaviruses (CoVs), including severe acute

respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). NIAID will pursue public-private partnerships to facilitate the translation of research outcomes into life-saving public health interventions. Working with pharmaceutical companies, NIAID has already initiated Phase 1 clinical trials for candidate COVID-19 vaccines and therapeutics. A concerted effort will be made to include minority populations, as well as at-risk and vulnerable populations, in all aspects of NIAID-sponsored research to address health disparities between diverse groups. Characterization of the fundamental virology of SARS-CoV-2 and the immunological response to infection will inform future studies and facilitate the development of effective medical countermeasures. With collaboration from all agencies within the U.S. government and other key U.S. and global partners, NIAID will rapidly disseminate these results so that the information can be translated into clinical practice and public health interventions to combat the pandemic. As such, NIAID has already implemented open sharing of scientific data through publicly available websites and will continue to promote the prompt disclosure of SARS-CoV-2 and COVID-19 research data by the scientific community.

Research Plan

Priority 1: Improve fundamental knowledge of SARS-CoV-2 and COVID-19

Developing effective medical and public health countermeasures against a newly emergent virus like SARS-CoV-2 will require a better understanding of the complex molecular and immune mechanisms underlying infection and disease. Studies that delineate the viral lifecycle and host immune responses to infection can lead to the identification of novel targets for intervention against SARS-CoV-2 infection and COVID-19. Early studies suggest that the clinical manifestations of COVID-19 can vary significantly, and disease severity can range from mild to critical. Thus, a detailed understanding of the clinical course of disease, as well as the clinical, virologic, immunological, and genetic predictors of disease severity, are needed. Gaps also exist in our understanding of the dynamics of disease transmission in different populations over time, including the role of pediatric and elderly populations in viral spread, and the potential seasonality of viral circulation.

Objective 1.1: Characterize fundamental SARS-CoV-2 virology and immunological host response to infection

- **Support the development and distribution of reagents and viral isolates to researchers.** NIAID will continue to support both intramural and extramural researchers by developing reagents and assays for virus characterization and immunological analyses. NIAID will continue to accelerate SARS-CoV-2 research by sourcing viral isolates and clinical specimens for the research community and placing them in repositories to help advance research and countermeasure development. In addition, NIAID will place other critical reagents needed for assay development (e.g. pseudovirions and antigens) in publicly available repositories for distribution.
- **Characterize virus biology and immunological responses to disease.** A comprehensive understanding of the

Box 2 **Priority 1: Improve fundamental knowledge of SARS-CoV-2 and COVID-19**
Objective 1.1: Characterize fundamental SARS-CoV-2 virology and immunological host response to infection *Objective 1.2: Evaluate disease dynamics through natural history, transmission, and surveillance studies* *Objective 1.3: Develop animal models that recapitulate human disease*

biological processes involved in SARS-CoV-2 infection and the pathogenesis of COVID-19 are paramount to developing new medical countermeasures to fight the spread of disease. Building on prior research related to MERS and SARS coronaviruses, early studies confirmed several critical features of SARS-CoV-2 infection, including the primary host receptor, angiotensin converting enzyme 2 (ACE-2), and the structure of the virus receptor-binding domain. Studies that delineate the viral lifecycle and host immune responses to infection can lead to the identification of novel targets for intervention against SARS-CoV-2 infection and COVID-19. Understanding the function of essential viral proteins will be necessary for improving diagnostic and immunological assays, *in vitro* and *in vivo* models, and other resources needed to advance safe and effective medical countermeasure development. In addition, evaluating the dynamics of host-pathogen interactions at the molecular and cellular levels will be critical to advancing our understanding of viral pathogenesis and immune responses that contribute to SARS-CoV-2 infection.

- **Determine viral evolution and molecular epidemiology.** With a newly emergent virus like SARS-CoV-2, studies to characterize genetic diversity, including those that assess the potential for the virus to evolve and escape host immunity, are pivotal for understanding disease progression and transmission dynamics and may have implications for countermeasure development. Viral genomic analysis matched with patient clinical data will be important to identify biomarkers of virulence and establish paradigms of sequence diversity. In addition, evaluating viral sequence associations with disease outcomes, immune status, and viral replication will provide crucial data to accelerate the development of effective medical countermeasures.

- **Develop low-containment assays to study virus neutralization.** Studies using non-infectious pseudovirions can be conducted in labs without BSL-3 capacity, making them an important tool to enhance understanding of SARS-CoV-2 infection. This capability would enable researchers without high-containment infrastructure to study the dynamics of virus neutralization *in vitro*.

- **Research into optimal public health prevention and mitigation modalities**. Clinical trials including family members of a COVID-19 positive individual can be devised to evaluate transmission, prevention, and other mitigation measures within the household.

Objective 1.2: Evaluate disease dynamics through natural history, transmission, and surveillance studies

- **Characterize disease incidence through surveillance studies.** Clinical manifestations of COVID-19 can vary greatly, ranging from asymptomatic or mildly symptomatic to the development of pneumonia, acute respiratory distress syndrome, and even death.[1] The variation in clinical presentation of COVID-19, combined with the challenges in diagnostic capacity, have made accurate initial assessments of disease incidence a formidable challenge. However, rapid point-of-care and point-of-need molecular tests, which became available in March 2020, will enable hospitals and other healthcare facilities to make informed decisions regarding patient isolation and care. Studies that leverage existing high-throughput diagnostic capacity along with these rapid tests will advance our understanding of disease incidence across the nation and will be a critical component of strategies to implement effective medical countermeasures. Combining these studies with broad serosurveillance studies across existing surveillance networks, including blood bank studies, would

[1] Wu Z and McGoogan JM. *JAMA* 2020 Feb 24. Epub. PMID 32091533.

provide a more complete picture of the scope of disease and the dynamics of infection. Detailed knowledge of host genetics and the human responses to infection across the lifespan will not only provide insights into new approaches for diagnosis, treatment, and prevention, but also may elucidate why individuals respond to SARS-CoV-2 in different ways. Reports to date suggest that COVID-19 resolves in most cases,[2] implying that the immune system can keep the infection from progressing to severe disease in many individuals. However, additional research is needed to better understand why some people progress to severe disease, which will lend critical insights to medical countermeasure development.

- **Assess the dynamics of disease transmission.** Our current understanding of COVID-19 transmission is limited. While recent studies have suggested timeframes for virus survival in aerosols and on surfaces,[3] the contributions of different routes of transmission and the dynamics of animal-to-human and human-to-human transmission remain unclear. The diverse clinical presentations of COVID-19, including a high prevalence of asymptomatic cases, add further complexity to understanding transmission dynamics. Providing a clearer picture of the natural history of viral shedding is a priority, both in acute cases and in asymptomatic infection. Given the challenges of accurately diagnosing asymptomatic individuals because they do not present for treatment, determining the role they play in transmission would provide valuable insights. Elucidating the role of pediatric cases in the spread of SARS-CoV-2 is particularly important. Although pediatric COVID-19 cases are generally asymptomatic or have less severe clinical manifestations than those of adults, the role that children play in spreading the virus is unknown. Additionally, studies to identify potential animal reservoirs and better understand transmission from animals to humans are a research priority, as these reservoirs may lead to future virus introductions and re-emergence of disease in humans. Virus transmission depends on a complex interplay of host, viral, and environmental factors that contribute to disease incidence and spread. Identifying the factors that maintain the disease transmission cycle is critical to developing effective medical countermeasures and public health interventions that will prevent future pandemics.

- **Determine disease progression through natural history studies.** Delineating the natural history of COVID-19 will inform immunopathogenesis, viral tropisms and length of shedding, immune phenotypes, and both protective immunity and host susceptibility. Disease assessment using longitudinal cohort studies, including among high-risk populations such as healthcare workers and the elderly, are important to better understand disease pathogenesis and immune responses to infection. Biomarkers identified from these studies may provide valuable insights into predictors of disease severity.

Objective 1.3: Develop animal models that recapitulate human disease

- **Develop small and large animal models that replicate SARS-CoV-2 pathogenesis.** Developing animal models that recapitulate human disease is a vital early step toward understanding disease pathogenesis and testing the efficacy of medical countermeasures. Small animal models enable rapid, scalable analyses that are particularly valuable for screening countermeasure candidates for efficacy and addressing issues concerning vaccine-induced immune enhancement. Among the small animal models being tested, transgenic mice expressing the human ACE-2 receptor are a promising candidate. In parallel, development and characterization of large animal models, including non-human primates (NHPs) that mimic human COVID-19, are a pivotal step to advance promising

[2] Ibid.
[3] van Doremalen *N et al. N Engl J Med* 2020 Mar 17. Epub. PMID 32182409.

countermeasure candidates. Previous experience with related coronavirus diseases such as MERS and SARS suggests that replicating human disease, particularly its more severe manifestations, in an animal model may be challenging. Fundamental research assessing animal models ranging from mice to NHPs is already underway. NIAID will continue to support the development of small and large animal model candidates to better understand this emerging infection and investigate optimal ways to treat and prevent COVID-19. NIAID also will ensure that validated animal models are made available to the scientific community for evaluating priority countermeasures.

Priority 2: Support the development of diagnostics and assays

Availability of rapid, accurate Food and Drug Administration (FDA)-cleared or authorized diagnostics will increase testing capacity and are critical for identifying and rapidly isolating cases, tracking spread of the virus, managing patient care, and supporting clinical trials. Molecular tests specifically designed to detect SARS-Cov-2 RNA in clinical samples are able to detect low levels of pathogen in clinical samples and offer robust specificity in differentiating SARS-CoV-2 from other related viruses. Continuing to improve the speed and accuracy of molecular and antigen-based diagnostics and making them available at point- of-care will be paramount to accelerating the ability to mitigate disease spread in the current outbreak and any future outbreaks. The development of serologic assays would further bolster surveillance efforts, including the ability to identify individuals who may have resolved prior infection with SARS-CoV-2.

Objective 2.1: Accelerate the development and evaluation of diagnostic platforms

- **Support the development, characterization and availability of reagents for diagnostic validation.** NIAID will support this effort through the development and testing of reagents for diagnostic validation that will be made available through NIAID-sponsored repositories.

Box 3 **Priority 2: Support the development of diagnostics and assays**
Objective 2.1: Accelerate the development and evaluation of diagnostic platforms *Objective 2.2: Develop assays to increase understanding of infection and disease incidence*

- **Support the development of new rapid diagnostics.** NIAID will provide funding to support the development of new rapid diagnostics, including molecular tests and novel antigen detection tests with improved sensitivity, if deemed feasible based on natural history studies.

- **Support the evaluation of promising diagnostics.** In some cases, stakeholders that develop potential diagnostic tests do not have the infrastructure needed to rigorously validate those tests against clinical samples. NIAID will support the testing of promising diagnostics and provide the capacity for evaluating them with live virus samples using our biocontainment laboratories.

Objective 2.2: Develop assays to increase understanding of infection and disease incidence

- **Develop and validate SARS-CoV-2 serological assays.** Serological tests, which detect host antibodies to infectious agents, do not detect the presence of a pathogen directly but can be used as a surrogate marker of infection. Developing more effective serologic tests would help provide information on the extent of asymptomatic infections and cumulative disease incidence, for example through serosurveillance studies. NIAID, with the Centers for Disease Control and

Prevention and the FDA, is developing tests that identify antibodies to SARS-CoV-2 proteins to determine seroprevalence rates and potentially help distinguish antibody responses in individuals receiving vaccines. NIAID will support the development and validation of additional serological assays for serosurveillance studies and as tools for testing the efficacy of promising vaccine or therapeutic candidates.

Priority 3: Characterize and test therapeutics

Currently, there are no FDA-approved or licensed therapeutics specific for coronaviruses. While traditional development pathways for therapeutics can take years, the urgency of the current outbreak underscores the need for rapid development and testing of promising therapeutics. Possible avenues for developing therapeutics include the evaluation of broad-spectrum antiviral agents (antivirals) that have shown promise for other coronaviruses and the identification of novel monoclonal antibodies (mAbs). For broad-spectrum antivirals, Phase 2/2b testing of the RNA polymerase inhibitor developed by Gilead, remdesivir, is already underway. Additional studies will be critical to identify promising therapeutic candidates and to advance them through clinical trial testing. To optimize findings during the pandemic, multiple clinical trials will be conducted in parallel among various populations, including both inpatient and outpatient studies.

Objective 3.1: Identify promising candidates with activity against SARS-CoV-2

- **Screen protease inhibitor and nucleotide analogue class agents and other small molecules with documented activity against other coronaviruses SARS-CoV-2.** Screening drugs that are already licensed by the FDA for other indications and might be efficacious against SARS-CoV-2 infection may provide a route to identifying a therapeutic for use in the current pandemic. Broad-spectrum antivirals that are already FDA approved or in clinical development for other indications—including those previously targeting SARS-CoV-1 and MERS CoV—can be evaluated for their potential activity against SARS-CoV-2 infections. Approved therapeutics for other infectious diseases also are being evaluated as possible treatments for COVID-19. By leveraging their existing efficacy, safety, and manufacturability data, the time to development and production can be reduced. NIAID also will continue working with partners to screen compound libraries for potential activity against SARS-CoV-2. For these studies, priority will be given to compounds based on *in vitro* screening data and the existence of human safety data.

Box 4
Priority 3: Characterize and test therapeutics

Objective 3.1: Identify promising candidates with activity against SARS-CoV-2
Objective 3.2: Conduct treatment studies to advance high-priority therapeutic candidates

- **Identify viral targets for therapeutic development.** Advances in structural biology technology enable researchers to map key viral structures at an unprecedented level. The Structural Genomics Centers for Infectious Diseases (SGCID) apply state-of-the-art, high-throughput technologies and methodologies, including computational modeling, x-ray crystallography, nuclear magnetic resonance imaging, and cryogenic electron microscopy, to experimentally characterize the three dimensional atomic structure of proteins that play an important biological role in human pathogens and infectious diseases. NIAID will continue to support use of this powerful technology to identify viral targets of SARS-CoV-2 for therapeutics or vaccines.

- **Identify novel mAbs for use as therapy or prophylaxis.** Data from early studies indicate that well-characterized convalescent plasma may provide a treatment benefit in COVID-19.[4] Therefore, IVIG derived from convalescent plasma may also hold promise for treatment. Moreover, peripheral blood mononuclear cells and plasma are being used to identify novel neutralizing antibodies. Through collaborations with structural biologists, binding properties can be quickly assessed. Paired with assessment of neutralization activity, the most promising mAbs will be identified for further characterization in animal models and human trials.

Objective 3.2: Conduct treatment studies to advance high-priority therapeutic candidates

- **Characterize and evaluate host-directed strategies for treatment of disease.** Experience with other coronaviruses indicates that infection of the respiratory tract is rapid and damage is primarily mediated by the host inflammatory response.[5] These conditions may make it difficult to modify COVID-19 with pathogen-directed therapeutics. Instead, host-directed strategies that target the immune response may exert a beneficial therapeutic effect. Host-directed strategies, including immune-modulating agents, will be investigated as potential therapeutic candidates.

- **Conduct clinical trials to demonstrate safety and efficacy of lead therapeutic candidates.** Many potential therapeutic candidates have been identified and are being tested in clinical trials.
  - In March 2020, NIAID launched a multicenter, adaptive, randomized controlled clinical trial to evaluate the safety and efficacy of the investigational antiviral drug remdesivir (GS-5734) for the treatment of COVID-19 in hospitalized adults with laboratory-confirmed SARS-CoV-2 infection and evidence of lung involvement. The trial builds on recent studies by NIAID scientists showing that remdesivir can improve the disease course in rhesus macaques when administered promptly after viral challenge with the MERS CoV.[6] The trial is also adaptive, allowing for additional arms should other therapeutics warrant assessment for efficacy.
  - NIAID is finalizing the protocol for the Big Effect Trial (BET), in which putative therapeutics that have existing human data and are readily available will be tested in patients hospitalized with lower respiratory tract disease. Each potential intervention will be given to approximately 75 patients and evaluated for mitigating disease symptoms. Candidate therapeutics that meet the criteria in this initial study will be further evaluated in larger clinical trials for which the infrastructure is already in place.
  - As mentioned above, identification of novel mAbs for therapy or prophylaxis is another strategic priority. These mAbs should be safe, highly effective, amenable to fast manufacturing, and easy to administer. They will be tested in clinical trials to develop immunotherapies for the prevention and early treatment of COVID-19, potentially in high-risk populations including healthcare workers.

- **Conduct outpatient studies for mild COVID-19 cases**. In cases of mild COVID-19 that do not require hospitalization, outpatient studies could be extremely valuable for testing promising, orally administered FDA-approved drugs that have existing safety data. The antiviral activity of hydroxychloroquine and azithromycin against SARS-CoV-2 has been the focus of many early

[4] Roback JD and Guarner J. *JAMA* 2020 Mar 27. Epub. 32219429.
[5] Newton AH et al. *Semin Immunopathol.* 2016;38(4):471-82. PMID 26965109.
[6] de Wit E et al. *Proc Natl Acad Sci USA* 2020;117(12):6771-6. PMID 32054787.

therapeutic studies.[7,8,9] Testing of these and other candidates, including protease inhibitors and other molecules, in outpatient studies may provide critical efficacy data and could identify an existing drug or drug combination that is safe and effective against COVID-19.

- **Conduct outpatient studies in high-risk populations.** High-risk populations, including health care workers, the elderly or individuals with chronic conditions, are a critical target for the development of therapeutics. Conducting studies in patients with mild cases of COVID-19 among these high-risk groups would be of interest for identifying the benefits of early treatment strategies to mitigate the impact of infection. Therapeutic candidates that have once a day dosing could also be considered for pre-exposure prophylaxis (PrEP) in some of these populations.

Priority 4: Develop safe and effective vaccines against SARS-CoV-2

Developing a safe and effective SARS-CoV-2 vaccine is a priority for preventing future outbreaks of the virus. As vaccine candidates for MERS-CoV, SARS-CoV-1 and other coronaviruses have previously been developed, NIAID investigators and the scientific community are well poised to use similar approaches in the current pandemic. NIAID will leverage its broad intramural and extramural infrastructure to advance vaccine candidates through Phase 1 safety and dosing clinical trials, with considerations for Phase 2/2b clinical trials for the most promising candidates.

Objective 4.1: Advance promising vaccine candidates through clinical trial testing

- **Conduct a Phase 1 clinical trial of (mRNA) platform candidate mRNA-1273.** Given the urgency of the response effort to develop a safe and effective vaccine, NIAID is prioritizing promising vaccine candidates that can be rapidly produced and tested. NIAID, in collaboration with the biotechnology company Moderna, is conducting a Phase 1 clinical trial of a vaccine candidate that uses a messenger RNA (mRNA) vaccine platform expressing a NIAID-designed recombinant spike protein of SARS-CoV-2. The trial is being conducted at NIAID-funded clinical research sites, with the first enrolled individual receiving the vaccine on March 16, 2020.

- **Prepare for a pivotal Phase 2/2b clinical trial of candidate mRNA-1273. Preparing for the likelihood of a seasonal recurrence of SARS-CoV-2 is imperative to the public health response.** Given the theoretical risk of vaccine-enhanced respiratory disease, large Phase 2 trials are unlikely to launch until this possibility is evaluated in animal models. Planning for those animal studies is underway, and, assuming favorable results, a Phase 2/2b study could be launched later in 2020. This represents a historically fast timeline for the development and testing of a vaccine candidate. Additionally, these studies will provide information on correlates of immunity that will help accelerate the advancement of other vaccine candidates. If the mRNA-1273 vaccine candidate shows protection against SARS-CoV-2 infection in a Phase 2/2b trial, NIAID will work with government partners to ensure that the vaccine is manufactured in sufficient quantities to allow prompt distribution to those at highest risk of acquiring disease.

---

[7] Gautret P et al. *Int J Antimicrob Agents*. 2020 Mar 20:105949. Epub. PMID 32205204.

[8] Molina JM et al. 2020 Med Mal Infect. 2020 Mar 30. pii:S0399-077X(20)30085-8. Epub. PMID 32240719.

[9] Chen Z et al. medRxiv 2020:2020.03.22.20040758. https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2

Box 5. Priority 4: Develop safe and effective vaccines against SARS-CoV-2
Objective 4.1: Advance promising vaccine candidates through clinical trial testing *Objective 4.2: Advance vaccine development through assay and reagent development* *Objective 4.3: Advance vaccine development through adjuvant characterization and development*

- **Investigate additional candidates through NIAID vaccine programs.** Although promising candidates may show efficacy in preclinical studies, many do not translate into effective vaccines in clinical trials. Therefore, it is crucial to support multiple promising preclinical candidates in the research and development pipeline. To that end, NIAID is advancing multiple additional SARS-CoV-2 vaccine candidates through its Rocky Mountain Laboratories (RML), including approaches that have shown promise against coronaviruses that cause SARS and MERS. Building on previous research to develop a MERS-CoV vaccine, scientists at RML are collaborating with Oxford University investigators to develop a SARS-CoV-2 vaccine that uses a chimpanzee adenovirus vector. RML investigators also are partnering with the biopharmaceutical company CureVac on an mRNA vaccine candidate and collaborating with the University of Washington on a universal coronavirus vaccine development. By leveraging its extensive expertise and research infrastructure, NIAID will continue working with partners and collaborators to advance promising SARS-CoV-2 vaccine candidates.

- **Leverage existing vaccine approaches to target SARS-CoV-2.** NIAID is pursuing multiple strategies to develop a COVID-19 vaccine. Building on past research on emerging pathogens, especially MERS-CoV and SARS-CoV-1 (the virus that causes SARS), NIAID is using previously developed vaccine platforms to rapidly assess the potential of SARS-CoV-2 vaccine candidates. This approach has already resulted in several promising strategies that may be leveraged for SARS-CoV-2, including vaccination using recombinant spike protein, chimpanzee adenovirus vaccine vector, virus-like particles, and live attenuated virus. In addition, NIAID is funding the development of novel vaccine candidates that will be efficacious across the lifespan, including in the elderly.

Objective 4.2: Advance vaccine development through assay and reagent development

- **Develop critical reagents to support vaccine development.** Appropriate tools are needed to identify the most promising vaccine candidates and advance the development of lead candidates as rapidly as possible. To accelerate the vaccine pipeline, NIAID is generating master and working SARS-CoV-2 virus stocks and other reagents critical for developing SARS-CoV-2 immune assays, developing quantitative tests for characterizing SARS-CoV2 assay material, developing a quantitative SARS-CoV-2-specific ELISA, developing virus-specific neutralization assays, and developing quantitative assays for assessing SARS-CoV-2 viral load.

Objective 4.3: Advance vaccine development through adjuvant characterization and development

- **Provide adjuvants to support vaccine development.** Adjuvants are vaccine components that improve vaccine efficacy by inducing long-lived protective immunity. Selection of appropriate adjuvants is crucial for developing safe and effective vaccines. NIAID is working with multiple collaborators to provide adjuvants to the research community for use in SARS-CoV-2 vaccine candidates. These adjuvants are at various stages of development and include compounds that

specifically improve vaccine efficacy in elderly individuals or modulate host immunity toward protective responses while limiting or preventing harmful inflammatory responses.

Conclusion

The sudden emergence and rapid global spread of the novel coronavirus SARS-CoV-2 has created a daunting public health challenge. To address this challenge, NIAID is focusing its considerable expertise and emerging infectious disease resources to facilitate the development of medical countermeasures including diagnostics, therapeutics, and vaccines. The resulting discoveries will not only help mitigate the current pandemic, but also inform prevention, diagnosis, and treatment of future emerging infectious diseases.

A comprehensive strategy requires a coordinated effort among governmental, academic, private, and community-based organizations. The *NIAID Strategic Plan for COVID-19 Research* defines the areas of COVID-19 research within the NIAID mission and outlines the institute's research priorities and goals. This strategic plan builds on many other national efforts and represents a commitment from multiple U.S. government agencies to improve coordination of COVID-19 research and discovery efforts and the development of medical countermeasures.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

cc: Dr. Erik Stemmy
Ms. Emily Linde

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

23 July 2021

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: R01AI110964, U01AI151797, U01AI153420

Dear Drs. Chmura and Daszak:

Thank you for your correspondence of April 11, 2021 and April 23, 2021 regarding R01AI110964. We are in the process of conducting detailed analyses of your answers to our questions and well as of the documents you sent, and we have the following additional requests:

1. Records

For us to continue our analyses, we will need to receive and review WIV's records validating expenditures specific to R01AI110964 as well as any and all monitoring, safety, and financial reports specific to R01AI110964 that WIV submitted to you. As a reminder, subawardees are required to have a financial management system that includes records that identify adequately the source and application of funds for federally-funded activities. These records must contain information pertaining to Federal awards, authorizations, obligations, unobligated balances, assets, expenditures, income and interest and be supported by source documentation. 45 C.F.R. §§ 75.101 and 75.302.

As a term and condition of award, NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. 75.364). This right of access applies not only to awardee records, but also to subawardee records. Awardees indicate their acceptance of an NIH award and its associated terms and conditions as they draw down the NIH grant funds to support the scientific project (see NIHGPS Section 5).

We will also need to see subaward agreements, subawardee audit reports, subawardee safety monitoring documents, subawardee progress reports submitted to you, and subawardee financial and accounting records for two other NIH EcoHealth Alliance grants. Specifically, please send us all responsive documents for:

- U01AI151797 (Daszak): subawardees Chulalongkorn Hospital, Chulalongkorn University, Duke-National Singapore University, and University of North Carolina at Chapel Hill
- U01AI153420 (Epstein): subawardees International Center for Diarrhoeal Disease Research of Bangladesh, Institute of Epidemiology Disease Control and Research of Bangladesh.

We remind you that the Notice of Award for U01AI151797 already contains the following specific award conditions that must still be satisfied by 30 days from establishment.

> Subaward Agreement Requirements: The ECOHEALTH ALLIANCE, INC. must provide NIAID with copies of all (existing and newly established) subaward agreements established under this award, including descriptions of the biosafety monitoring plans, within 30 days of establishment.
>
> Federal Funding Accountability and Transparency Subaward Reporting System (FSRS) Requirements: This award is subject to the Transparency Act subaward reporting requirement of 2 CFR Part 170, which must be reported through the Federal Funding Accountability and Transparency Subaward Reporting System (FSRS). The ECOHEALTH ALLIANCE, INC. must provide NIAID with proof of documentation of timely entries of subaward information into the FSRS within 30 days of submitting to FSRS.

2. Reports

We are also writing to notify you that a review of our records for R01AI110964 indicates that EcoHealth Alliance, Inc. is out of compliance with requirements to submit the following reports that are outlined in the NIHGPS: the Federal Financial Report (FFR, see 8.4.1.2.3 Modified Financial Reporting Requirements) and the Interim Research Performance Progress Report (I-RPPR, see NIHGPS 8.4.1.4 Final Research Performance Progress Report).

R01AI110964 was issued under the Streamlined Noncompeting Award Process (SNAP). For awards under SNAP, an FFR must be submitted within 120 days after the end of the competitive segment and must report on the cumulative support awarded for the entire segment.

Additionally, NIH requires that organizations submit an Interim-RPPR while their Type 2 application is under consideration. In the event that the Type 2 is funded, NIH treats the Interim-RPPR as the annual performance report for the final year of the previous competitive segment.

The FFR and I-RPPR for R01AI110964 were due within 120 days after the end of the project period. In this case, the competitive segment ended on May 31, 2019, and reports were due September 30, 2019. To date, NIH has still not received these reports. Compliance with Section 8, Administrative Requirements within the NIH Grants Policy Statement (NIHGPS) is a standard term and condition of award that applies to all NIH recipients.

A recipient's failure to comply with the terms and conditions of award may cause NIH to take one or more actions on the award, depending on the severity and duration of the non-compliance. Additionally, a history of non-compliance related to R01AI110964, including reporting non-compliance, may impact other projects where EcoHealth serves as the primary grant recipient. When a recipient has a history of failure to comply with the general or specific terms and conditions of a previous Federal award, NIH may impose specific award conditions on other awards of the recipient, including withholding authority to proceed to the next phase of a project until receipt of evidence of acceptable performance (see NIHGPS Section 8.5, Remedies for Noncompliance or Enforcement Actions: Suspension, Termination, and Withholding of Support).

In closing, please be advised that EcoHealth Alliance, Inc. must satisfy the existing specific award condition for U01AI151797 by 30 days from establishment and must provide the remaining documents and reports requested herein for all three grants (R01AI110964, U01AI151797, U01AI153420) no later than August 27, 2021.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research

[redacted]

cc: Ms. Emily Linde
Dr. Erik Stemmy

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

20 October 2021

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: R01AI110964, U01AI151797, U01AI153420

Dear Drs. Chmura and Daszak:

Thank you for your correspondence (including supporting materials) of August 27, 2021, regarding R01AI110964, U01AI151797, U01AI153420. We also note that you submitted on August 3, 2021, an interim RPPR for the R01AI110964 budget period of June 1, 2018 to May 31, 2019.

For us to continue our analyses, as required by the NIH Grants Policy Statement, 4.1.1.2, NIH requires verification of IACUC approval; therefore, please provide us documentation from the WIV IACUC regarding approval for field work (e.g. work in caves to collect materials from live bats) supported by R01AI110964. We also need to see all remaining unpublished data supported by this same grant that you have not already reported in your RPPRs. If all such data supported by this grant has been reported (either through peer-reviewed publication or through RPPRs), please indicate.

We look forward to receiving these materials by no later than close-of-business on Wednesday, October 27, 2021.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research

[redacted]

cc: Ms. Emily Linde
Dr. Erik Stemmy

EcoHealth Alliance

October 26th 2021

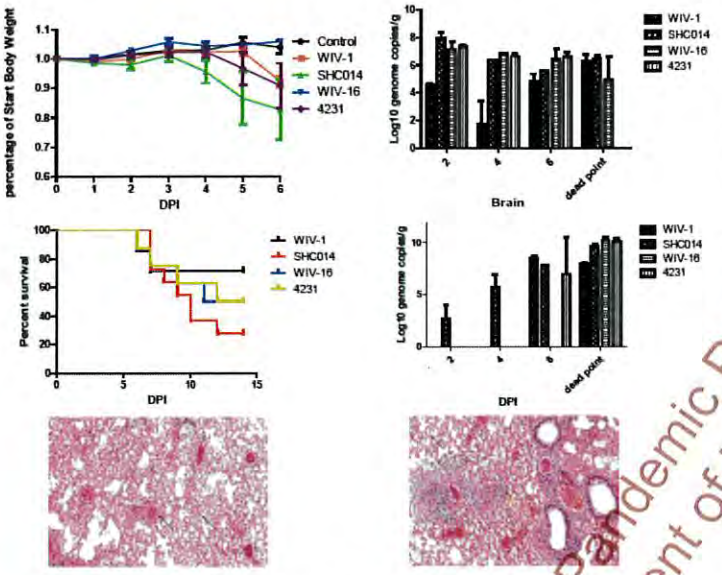
Dear Dr Lauer (cc'ing Dr. Tabak),

I am responding to your letter requesting IACUC information and unpublished data from our original R01. As I read your letter, I realized that this request is likely related to a letter from Dr. Tabak to Congressional member Comer released publicly on the 20th October *(PDF attachment #1)*. In his letter Dr. Tabak referred to a mouse infection experiment in our FoIA'd year 5 report, and stated that *"EcoHealth failed to report this finding right away, as was required by the terms of the grant"*. The experiment referred to is, in fact, the same one we reported in our Year 4 Report on April 13, 2018. There was just the one experiment conducted, with results from follow-up analyses included in the Year 5 Report. **Thus, EcoHealth did in fact comply with all reporting requirements**. We respectfully would like to clarify this below:

Firstly, Dr. Tabak's letter appears to refer to our year 5 report, and we note that in your email accompanying you also refer to a *Figure 13* from that year 5 report. However, as is visible in the pattern of viral genome measurements, this figure closely resembles *Figure 35* from our year 4 report, but with follow-up histopathological and survival data added (both are inserted, below). The reason for this is that **both figures *are from the same experiment* – conducted in 2018 and, as noted above, reported rapidly to NIH on 13th April 2018 in our Year 4 report.** Proof of submission on that date is attached *(PDF attachment #2)*. It is very important that these facts be acknowledged, as they clearly show that EcoHealth Alliance is *not* out of compliance with our oversight and reporting obligations, and in fact reported this experiment over 3 years and 6 months ago.

In our modified NoA, we were instructed to *"provide the NIAID Program Officer and Grants Management Specialist, and Wuhan Institute of Virology Institutional Biosafety Committee with the relevant data and information related to these unanticipated outcomes"*. The Year 4 report was filed in the NIH system on April 13th 2018 and a copy emailed to our Program Officer at NIAID on April 25th 2018 *(PDF attachment #3)*. At no time did program staff indicate to us that this work required further clarification or secondary review. In fact, our report was deemed sufficient for the Year 5 to be awarded without delay. Our relationship with NIH has always been that if we are asked for information, we respond and follow up in a timely manner. If NIH had indicated to us at any point that any issues needed further clarification, we would of course have complied immediately with any request, as we have always done. On June 8th 2016, we wrote to NIH to explain the rationale for these planned experiments and suggested alternative approaches involving non-infectious virus-like particles *(PDF attachment #4)*. Had NIH reviewed our 2018 report and found a need to change the nature of this work, we could have simply shifted to that alternative strategy. No such review or request was reported or made to us.

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org



Year 4 report Figure 35 (Top 2 graphs). *In vivo infection of SARSr-CoVs in hACE2-expressing mice. Left: Body weight change; Right: Viral genome copies per gram in lung tissue.*

Year 5 report Figure 13 (Below): *In vivo infection of SARSr-CoV in hACE2-expressing mice. Survival rate, viral genome copies/gram, histopathology WIV-1, histopathology rWIV1-SHC014 S.*

Secondly, the direction in our revised Year 3 NoA, was that we should report experiments in which *"the MERS-like or SARS-like chimeras generated under this grant show evidence of enhanced virus growth greater than 1 log over the parental backbone strain"*. In virological terms, "virus growth" normally refers to viral titer measuring the concentration of infectious viruses by plaque assay. The experiment we reported to NIH actually shows genome copies per gram *not* viral titer. We have been advised by senior virologists that data on genome copies per gram usually do not accurately equate to viral titer, since genomic material from inactivated, incompletely formed, or dead virus are also measured. Viral titers were not conducted in this experiment. We also note that the genome copy data for SHC014 are only enhanced relative to the WIV1 backbone at the earliest part of the experiment and by day 6-8, there was no discernably significant difference among the different viral types. This suggests that differences, if real, were transient. Given the small number of mice, it is also uncertain whether the survival and weight loss data were statistically relevant, and as no further replications of this experiment were performed, we are unable to corroborate these initial results. We assume that these were the rationale NIH used at the time for *not* highlighting this work as requiring further clarification or secondary review.

Thirdly, regarding the timing of our year 5 (final) report. As we informed you previously, and as is documented by the NIH receipt system itself *(PDF attachment #5)*, we first uploaded this report on time, in July 2019 (the final allowable date for submission would have been September 30th 2019). However, by the time we tried to officially submit, our R01 grant had been renewed (July 24th 2019) and the system locked us out from submitting a normal annual final Year 5 report at that point. On July 30th 2019, we requested further information about the submission of the Year 5 report from the NIH Grants Management Specialist who had been dealing with our renewal, but we did not receive a response to

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

our questions (*PDF attachment #6)*. NIH also did not send any subsequent request to us for the Year 5 report, despite the reality that we were in frequent communication with staff during that period. Because the new award had been made and the work was permitted to commence we had no indication there was anything missing, and assumed that the Year 1 report for the renewal grant would provide all of the relevant information. It is standard NIH policy to contact a grant recipient if additional information of reporting is required. We heard nothing further from NIH in the period subsequent to this until your letter in April 2020 requesting that we not fund work at WIV, which we complied with, and then the termination notice you sent a few days later. We presumed at that point that no further reporting was required of us, however when we received a request from your office on July 23rd 2021 for the year 5 report, we immediately took steps to file the report. We were finally able to get the system to accept our report within 11 days, but only after considerable efforts from NIH staff to circumvent the system's lockout. Note also that, even though the grant was terminated and then suspended, and funding is not available to us to work on this, we have continued to comply with NIH reporting requests, and submitted reporting for Years 6 and 7 of this grant.

We take our compliance oversight role very seriously at EcoHealth Alliance, and hope you understand our need to correct these misinterpretations. We have cc'd Dr. Tabak so that he is aware, and we hope he understands that we are making these comments respectfully, and that we acknowledge these are complex technical issues that can be easily misinterpreted. We would like to point out that these types of mistakes about the timing or nature of our reporting can be better addressed by contacting us to request clarification prior to responding to any congressional inquiry. This will help ensure factually correct responses and will save our organization and staff from undue disparagement and unjustified accusation of inappropriate behavior that have now ensued in the press. We believe it is very important that the impressions the Congressional inquiry may take away from the incorrect information provided them be addressed quickly and clearly. We remain, of course, ready to respond to any future questions you or Dr. Tabak may have. We are also available to work with program staff at NIAID on any future technical questions – as would be normal procedure for a grantee.

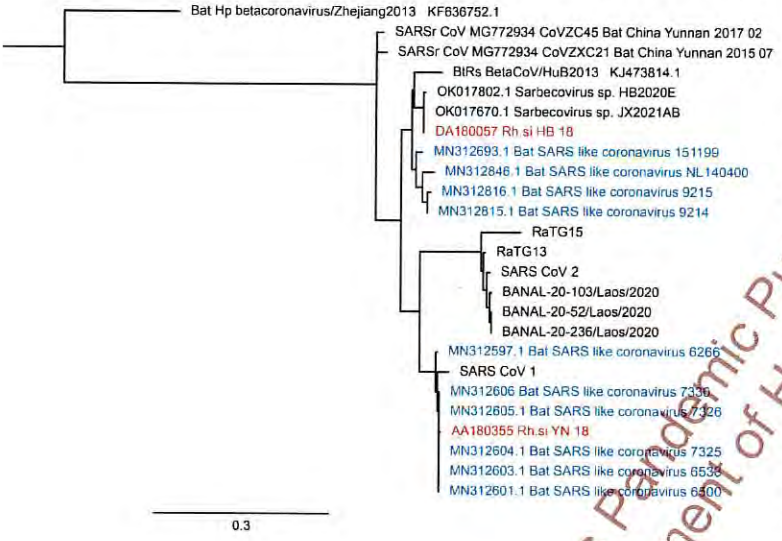
Request for IACUC information and unpublished data.

As requested in your letter, we have provided unpublished data below and in pdf attachments. We would like to respectfully point out that our NIH grant funding for this work was terminated in a letter from you in April 24th 2020. The grant was then suspended and the funds remain unavailable to us due to the logistically near-impossible conditions that NIH has placed on us, and that we have addressed in previous correspondence. In your letter of April 24th 2020, you instructed us to discontinue all of our contractual work with WIV. Both the lack of funding, and the instruction to cease contractual work with WIV have led to significant disruption of the normal interactions and dialog among collaborating scientists. Despite these challenges, we have continued to comply with all requests from your office. We have also made significant efforts to analyze data we have access to, and to draft papers and publish our work in international peer-reviewed journals, and to upload sequence data to Genbank. We strongly believe doing whatever we can to collate, analyze, and publish data we have from our prior efforts is critical to advancing science and protecting US citizens and people of all nations from future pandemic threats. However, because of the limitations placed on us by NIH our progress has been substantially

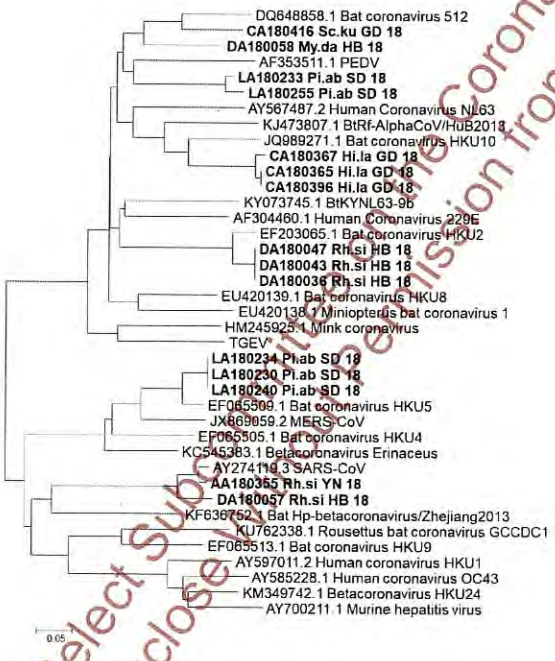
EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

slowed. What we have provided below within the 5-day time limit given to us by Dr. Tabak and yourself, is a good-faith attempt to supply available data as quickly as we are able. These include:

1. A phylogenetic tree of two new SARSr-CoV RdRp sequences reported in ***Figure 5*** *from our 5 year report.* These are from *Rhinolophus sinicus* bats sampled in Hubei and Yunnan provinces, respectively, in 2018. The tree below clearly demonstrates they these viruses (shown in red) are not related closely to SARS-CoV-2, and that the recently-described BANAL coronaviruses are the closest relatives of the pandemic strain. The RdRp sequences for these two viruses are now going through approval process by Chinese authorities so that they can be uploaded to Genbank at the earliest possible opportunity.



2. We have requested that the 13 other novel RdRp sequences (in bold) included in Figure 5 of our year 5 report to be uploaded to Genbank. These are now going through the approval process by the Chinese authorities so that that they can be uploaded to Genbank at the earliest possible opportunity.



Year 5 report Fig. 1 (left): Phylogenetic analysis of partial RdRp gene of CoV (440-nt partial sequence)

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

3. We supply new analyses of our work on SADSr-CoVs and HKU2-CoVs *(PDF attachment #7)* that was referred to in our Year 5 report. These viruses are alpha-coronaviruses, not the beta-coronavirus group that contains the viruses responsible for SARS or COVID-19. We are currently drafting a paper on this work for submission to an international peer-reviewed scientific journal. All SADSr-CoV and HKU2 sequences have been uploaded to Genbank, and following widely-accepted scientific standards and norms, will be released publicly once the paper is accepted for publication. Considering that none of these viruses are related to either SARS-CoV or SARS-CoV-2, we believe this is an appropriate balance between public health interests and the need to maintain integrity of the scientific process of discovery, analysis, peer-review, and publication.

4. We supply a manuscript submitted for review that cites our R01 grant *(PDF attachment #8)*. This paper analyzes hotspots for SARSr-CoV spillover in China, Southeast Asia and South Asia. It identifies a large geographic area that acts as an interface for bat-to-human spillover of CoVs, with spillover hostspots in southern China, Myanmar, Laos, Vietnam, and further potential for viral emergence across the whole region. It also estimates the number of people infected annually with novel bat-SARSr-CoVs as a median of 50,000 and a mean of 400,000. This highlights a substantial public health risk, further consolidates our underlying assumption that viruses like SARS-CoV-2 are far more likely to have emerged via a so-called 'natural' pathway than a so-called 'lab-leak', and provides a much-needed road-map for targeting sample collection and surveillance for future spillover events. The analyses are new, but based on already-published data.

5. We provide our DHHS/NIH Office of Laboratory Animal Welfare Interinstitutional Agreement for the WIV animal work on this grant *(PDF attachment #9)*. As required by DHHS/NIH and NIH Grants Policy, the Interinstitutional Agreement document for R01AI110964 was approved and signed by the NIH/OLAW Assured Institution (WIV) IACUC chairperson, the WIV Director, and the NIH Office of Laboratory Animal Welfare Division of Assurances Director. The effective date of our Interinstitutional Agreement is 07 May 2014 for our award (R01AI110964) that started on the 1st of June 2014. Both the Interinstitutional Agreement and the confirmatory email from NIH copying our NIH/NIAID program grants management specialist are included here.

Please let me know if you have additional questions or if it would be helpful to schedule a meeting to review the information submitted with this letter.

Yours sincerely,

[redacted]

Dr. Peter Daszak, President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

A. COVER PAGE

Project Title: Understanding the Risk of Bat Coronavirus Emergence	
Grant Number: 5R01AI110964-05	**Project/Grant Period:** 06/01/2014 - 05/31/2019
Reporting Period: 06/01/2017 - 05/31/2018	**Requested Budget Period:** 06/01/2018 - 05/31/2019
Report Term Frequency: Annual	**Date Submitted:** 09/16/2020
Program Director/Principal Investigator Information: PETER DASZAK , PHD BS **Phone number:** [redacted] **Email:** [redacted]	**Recipient Organization:** ECOHEALTH ALLIANCE, INC. ECOHEALTH ALLIANCE, INC. 460 W 34TH ST 17TH FLOOR NEW YORK, NY 100012320 **DUNS:** 077090066 **EIN:** 1311726494A1 **RECIPIENT ID:** NIAID Coronavirus
Change of Contact PD/PI: N/A	
Administrative Official: ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** [redacted] **Email:** [redacted]	**Signing Official:** ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** [redacted] **Email:** [redacted]
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Zoonotic coronaviruses are a significant threat to global health, as demonstrated with the emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, and the recent emergence Middle East Respiratory Syndrome (MERS-CoV). The wildlife reservoirs of SARS-CoV were identified by our group as bat species, and since then hundreds of novel bat-CoVs have been discovered (including >260 by our group). These, and other wildlife species, are hunted, traded, butchered and consumed across Asia, creating a largescale human-wildlife interface, and high risk of future emergence of novel CoVs.
To understand the risk of zoonotic CoV emergence, we propose to examine 1) the transmission dynamics of bat-CoVs across the human-wildlife interface, and 2) how this process is affected by CoV evolutionary potential, and how it might force CoV evolution. We will assess the nature and frequency of contact among animals and people in two critical human-animal interfaces: live animal markets in China and people who are highly exposed to bats in rural China. In the markets we hypothesize that viral emergence may be accelerated by heightened mixing of host species leading to viral evolution, and high potential for contact with humans. In this study, we propose three specific aims and will screen free ranging and captive bats in China for known and novel coronaviruses; screen people who have high occupational exposure to bats and other wildlife; and examine the genetics and receptor binding properties of novel bat-CoVs we have already identified and those we will discover. We will then use ecological and evolutionary analyses and predictive mathematical models to examine the risk of future bat-CoV spillover to humans. This work will follow 3 specific aims:

Specific Aim 1: Assessment of CoV spillover potential at high risk human-wildlife interfaces. We will examine if: 1) wildlife markets in China provide enhanced capacity for bat-CoVs to infect other hosts, either via evolutionary adaptation or recombination; 2) the import of animals from throughout Southeast Asia introduces a higher genetic diversity of mammalian CoVs in market systems compared to within intact ecosystems of China and Southeast Asia; We will interview people about the nature and frequency of contact with bats and other wildlife; collect blood samples from people highly exposed to wildlife; and collect a full range of clinical samples from bats and other mammals in the wild and in wetmarkets; and screen these for CoVs using serological and molecular assays.

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk. We propose two competing hypotheses: 1) CoV host-range in bats and other mammals is limited by the phylogenetic relatedness of bats and evolutionary conservation of CoV receptors; 2) CoV host-range is limited by geographic and ecological opportunity for contact between species so that the wildlife trade disrupts the 'natural' co-phylogeny, facilitates spillover and promotes viral evolution. We will develop CoV phylogenies from sequence data collected previously by our group, and in the proposed study, as well as from Genbank. We will examine co-evolutionary congruence of bat-CoVs and their hosts using both functional (receptor) and neutral genes. We will predict host-range in unsampled species using a generalizable model of host and viral ecological and phylogenetic traits to explain patterns of viral sharing between species. We will test for positive selection in market vs. wild-sampled viruses, and use data to parameterize mathematical models that predict CoV evolutionary and transmission dynamics. We will then examine scenarios of how CoVs with different transmissibility would likely emerge in wildlife markets.

Specific Aim 3: Testing predictions of CoV inter-species transmission. We will test our models of host range (i.e. emergence potential) experimentally using reverse genetics, pseudovirus and receptor binding assays, and virus infection experiments in cell culture and humanized mice. With bat-CoVs that we've isolated or sequenced, and using live virus or pseudovirus infection in cells of different origin or expressing different receptor molecules, we will assess potential for each isolated virus and those with receptor binding site sequence, to spill over. We will do this by sequencing the spike (or other receptor binding/fusion) protein genes from all our bat-CoVs, creating mutants to identify how significantly each would need to evolve to use ACE2, CD26/DPP4 (MERS-CoV receptor) or other potential CoV receptors. We will then use receptor-mutant pseudovirus binding assays, in vitro studies in bat, primate, human and other species' cell lines, and with humanized mice where particularly interesting viruses are identified phylogenetically, or isolated. These tests will provide public health-relevant data, and also iteratively improve our predictive model to better target bat species and CoVs during our field studies to obtain bat-CoV strains of the greatest interest for understanding the mechanisms of cross-species transmission.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Year 4 NIAID CoV Report_Final for eRA Commons.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: Year 4 NIAID CoV Training and Prof Devlp.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

1.Conference and University Lectures: PI Daszak, and Co-investigators Shi, Epstein, Olival, and Zhang gave invited University and Conference lectures including Harvard Univ. Columbia Univ., Tufts Univ., Mt. Sinai, the 2nd International Symposium on Emerging Viral Disease in China, the 2nd International Symposium on the Infectious Diseases of Bats in Colorado, Cell Symposia: Emerging and Re-emerging Viruses 2017 in Virginia, The International Union of Microbiological Societies 2017 National Academy of Sciences in Singapore, 2018 Borneo Quality of Life Conference in Malaysia, 2017 Chemical and Biological Defense Science and Technology (CBD S&T) in California, Prince Mahidol Award Conference in Bangkok, Collaboration for Environmental Evidence Meeting in Paris, US-China NSF Ecology and Evolution of Infectious Disease (EEID) Meeting, and others that included specific discussion of the current project and results.

2.Agency and other briefings: PI Daszak and Co-investigator Shi introduced this project and discussed new opportunities about predicting and preventing zoonoses within National Institute of Allergy and Infectious Disease Office, Defense Advanced Research Projects Agency, National Natural Science Foundation of China, Chinese Center for Disease Control and Prevention, US NASEM Forum on Microbial Threats, Chinese Academy of Sciences, and the Health Working Group at the US Embassy in Beijing.

3.Public outreach: PI Daszak and Co-investigator Shi, Epstein, Olival, have presented this work to the general public in a series of meetings over Year 4 including at Cosmos Club briefings that EcoHealth Alliances hosts in Washington DC, over 10 meetings on the China National Virome Project and the Global Virome Project in China, Europe, Australia, Southeast Asia and Latin America. Co-investigator Olival presented this work at a public event on Disease Transmission and Technologies in New York, co-investigator Ross presented this work at EcoHealth Webinar on wildlife trade network research. Zhu broadly introduced this work to the conservation and ecological research community in China through field training workshops.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Specific Aim 1: Assessment of CoV spillover potential at high risk human-wildlife interfaces.

•To commence an in-depth analysis of data collected from the integrated biological behavioral surveillance from Yunnan, Guangxi, and Guangdong provinces, incorporating questionnaires and serological testing results.
•To initiate lab analysis of human samples collected from the passive hospital surveillance from four hospitals in Yunnan province: 1) Dali College Affiliated Hospital; 2) Dali Prefecture Hospital; 3) Kunming No. 3 People's Hospital, and 4) Chuxiong Prefecture Hospital. The goal will be to identify examples of CoV spillover events in China that may lead to illness.

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk

•To repeat and continue in vivo experiments of SARSr-CoVs with spike variants on hACE-expressing transgenic mice (survival rate, histopathological analysis, etc) to evaluate the risk of cross-species infection of different SARSr-CoVs to humans;
•Continue searching for the receptor of SARSr-CoVs with deletions in the homologous region of SARS-CoV RBD (i.e. Rp3, Rs672), and SARSr-CoVs that are unable to utilize bat ACE2 (e.g. Rs4231).
•Continue the phylogeographic study of bat-CoV with newly collected samples to better understand the geographic distribution and evolution of bat-CoV genetic diversity in south China and SE Asia.

Specific Aim 3: Testing predictions of CoV inter-species transmission.

•Using the full-length infectious cDNA clone of MERS-CoV, chimeric viruses with the spikes of newly identified MERSr-CoVs will be constructed. The pathogenesis of these MERSr-CoVs will be tested on the human DPP4-expressing mouse model that has already been developed and validated in Y4.
•To conduct a population genetics study of Rhinolophus sinicus ACE2s, including the amplification of ACE2 genes from R. sinicus samples of different origin, test of the usage efficiency of R. sinicus ACE2s of different origins by SL-CoVs and kinetics study on the binding of SL-CoV RBD to different R. sinicus ACE2s.
•In collaboration with South China Agricultural University, gather data on the spatial structure and barn-level mortality records to parameterize our mathematical model of virus spread that incorporates a meta-population structure in individual and use this to fit the model on a training set of farms and validate it on a hold-out set.
•Using the intra-farm transmission model, we will (a) determine the characteristics of a farm that determine the likelihood and size of an outbreak given a spillover event, and (b) determine whether SADS and PEDV outbreaks on farms can be distinguished by differing dynamics, as measured by transmission parameters in our intra-farm transmission model.

Year 4 Report: Understanding the Risk of Bat Coronavirus Emergence

Award Number: R01AI110964-03

Reporting Period: 06/01/2017 – 05/31/2018

****

B.2 What was accomplished under these goals?

Summary

The results of the 4th year of our R01 work are detailed below. They include:

- Completed behavioral risk survey questionnaires and biological sample data collection for 1,585 people in Yunnan, Guangxi, and Guangdong provinces.
- Preliminary analysis of behavioral survey responses exploring key risk factors relating to potential viral zoonotic disease spillover in China, indicating notable differences among the respondents in Guangdong, Guangxi, and Yunnan.
- Completed serologic testing of collected human samples for MERS-CoV, SARSr-CoV, HKU9 CoV and HKU10 CoV, showing the serologic evidence of spillover of bat SARS-related CoVs (7 people in Yunnan province) and HKU9 CoV (2 people in Guangxi province).
- Testing of samples from 671 individual bats to identify diverse alpha- and beta-coronaviruses.
- Genetic diversity and genomic characterization of beta-coronaviruses in fruit bats and characterization of the full-length genome sequence of a novel HKU9-related CoV.
- Analysis of host-virus phylogeography for all bat CoV RdRp sequences collected by our group in China from 2008-2015 (Alpha-CoVs: n = 491; Beta-CoVs: n = 326) to identify the geographic areas that are likely sources of origin/diversity for this important group of viruses.
- Identification of two novel MERS-related CoVs that use DPP4 receptor.
- *In vivo* infection of SARSr-CoVs with variants of S protein in human ACE2 (hACE2) expressing mice.
- Identification of a novel bat-origin CoV (swine acute diarrhea syndrome coronavirus, SADS-CoV) causing a multi-farm outbreak of fatal acute diarrhea in piglets in Guangdong (published in *Nature* in April 2018).
- Development of an intra-farm transmission model to understand SADS-CoV spread and help predict and prevent future outbreaks.

Specific Aim 1: Assessment of CoV spillover potential at high-risk human-wildlife interfaces

During Year 4 we completed behavioral risk surveys and biological sample collection from people at selected sites in three provinces in southern China (Guangdong, Guangxi, and Yunnan) and began analyzing the results.

Behavioral Survey

We administered 1,585 surveys in Guangdong, Guangxi, and Yunnan provinces. Questions explored respondent health-seeking behavior, experiences with unusual illnesses, contact with wildlife and livestock, and general background information. Blood samples were collected from respondents and tested for SAS-related CoVs (SARSr-CoVs) and HKU10-CoV using serological assays. Survey data was analyzed by province to examine patterns among respondent characteristics and behavioral risk factors across provinces.

Respondent General Background Information

Of the 1,585 respondents who completed the survey, 420 were from Guangdong, 412 were from Guangxi, and 753 were from Yunnan. More females than males completed the survey in all provinces. The mean age of the overall survey sample was 52 years **(Figs. 1, 2)**.

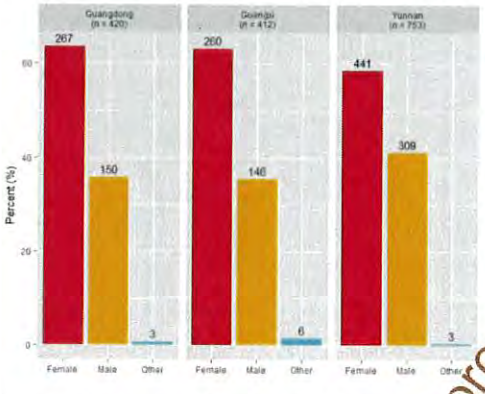


Figure 1: *Gender of respondents*

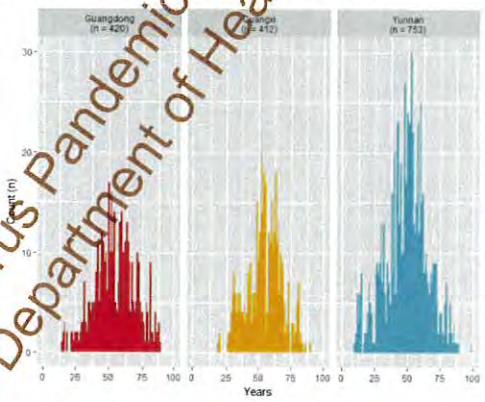


Figure 2: *Age distribution of respondents.*

Across all provinces, most respondents had lived in their respective locales for more than 5 years (96.3%) **(Fig. 3)** and earned less than 10,000 renminbi (RMB) annually (84.6%) **(Fig. 4)**. In 2016, the updated poverty standard in China was 3,000 RMB as defined by Poverty Alleviation Office of State Council. More families in Guangxi (61.8%) lived at or below the poverty level as compared to those in Guangdong (36.9%) and Yunnan (43.3%).

Figure 3: *Duration of residency.*

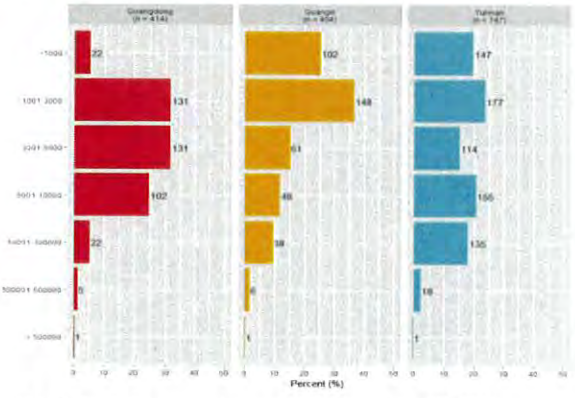


Figure 4: *Family annual per capita income (RMB).*

In Guangdong, Guangxi, and Yunnan, 73.9%, 57.0% and 69.6% of respondents, respectively, had a primary school-level education or less **(Fig. 5)**. Across all provinces the most common livelihood was crop production. In Yunnan, 699 out of 753 (92.8%) individuals from the province identified crop production as a livelihood activity. In comparison, 237 out of 420 (56.4%) individuals from Guangdong, and 260 out of 412 (63.1%) individuals from Guangxi **(Fig. 6)** named crop production as a livelihood in the last year. Respondents, however, where not restricted to defining a single livelihood, many indicated engaging in multiple types of livelihoods.

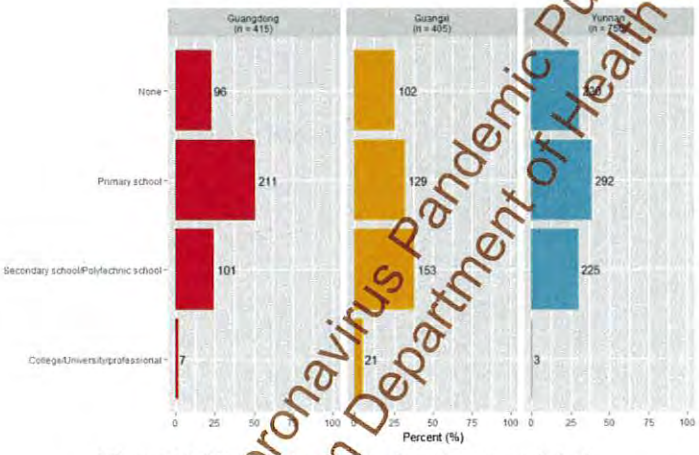


Figure 5: *Highest level of education completed*

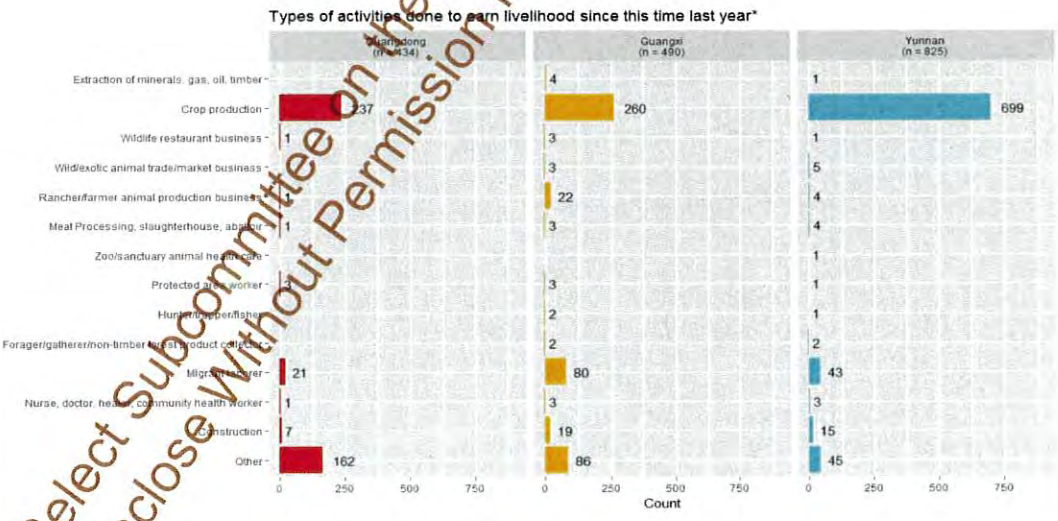


Figure 6: *Types of activities conducted to earn a livelihood since this time last year (above)*

In Guangdong, Guangxi, and Yunnan, 41.7%, 50.7% and 59.6% of respondents, respectively, indicated that they traveled outside of their village town or city in the past year. Among those who traveled, the average number of trips was 5 in Guangdong and Guangxi, and 6 in Yunnan. The average distance traveled by respondents in Guangdong and Yunnan were 113 Km and 118 Km, respectively, compared to 66 Km by respondents in Guangxi.

Health-Seeking Behavior and Experiences with Unusual Illnesses

When asked where they usually get treatment for illness or infection, the top 3 responses across all provinces in aggregate were hospitals, clinics, and pharmacies/dispensaries in descending order **(Fig. 7)**. However, within Yunnan, most respondents went to hospitals, followed by pharmacies, then clinics.

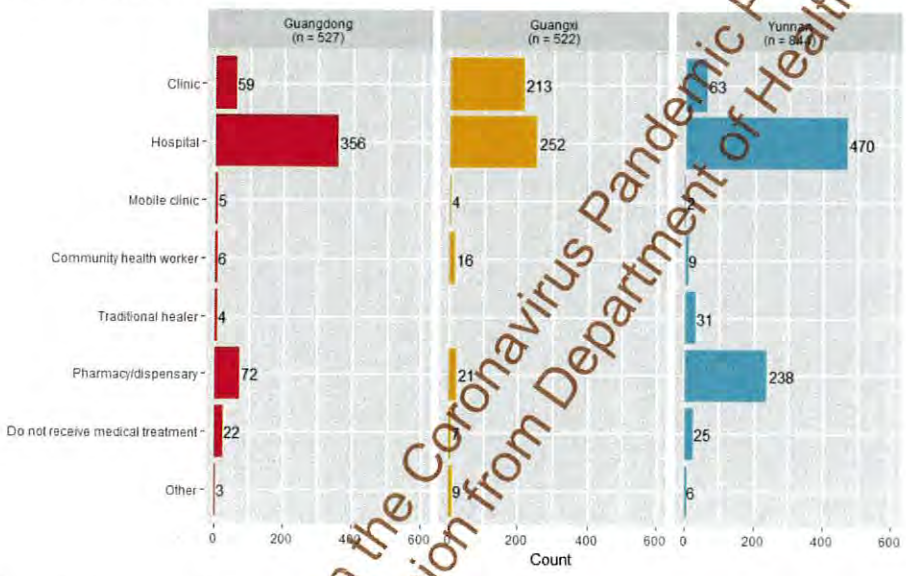
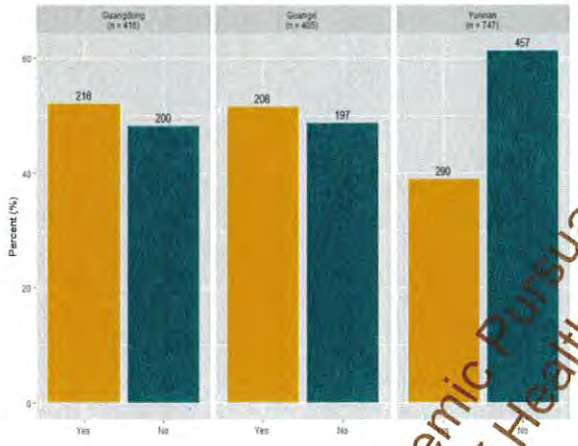


Figure 7: *Location where care was usually received for illness or infection.*

All survey respondents were asked whether they had experienced an unusual illness in their lifetime and in the past year, defined by a series of the most common symptoms associated with encephalitis, hemorrhagic fever (HF), severe acute respiratory infection (SARI), and influenza-like illness (ILI). Additional symptoms that were asked about included: fever with diarrhea or vomiting; fever with rash; and, persistent rash or sores on skin. Respondents were not restricted to selecting one illness and could provide multiple responses.

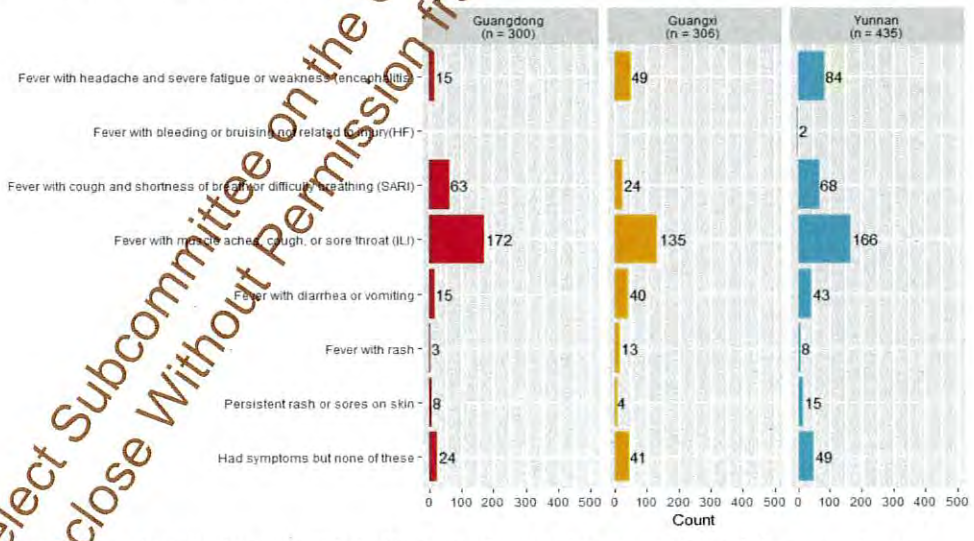
The proportion of respondents who had an unusual illness with any of the above-mentioned symptoms in their lifetime varied slightly by province. Between the three provinces, Yunnan had the fewest number of respondents who reported experiencing the symptoms provided (38.8%), compared to Guangdong and Guangxi (51.9% and 51.3%, respectively). Yunnan was also the only province where less than half of the respondents reported experiencing the symptoms provided **(Fig. 8)**.

Figure 8: *Respondent's experience of unusual illnesses.*



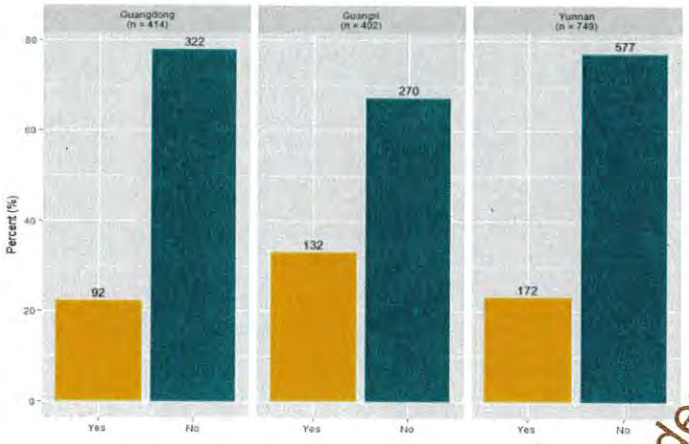
Across all three provinces, among those who had experienced any symptoms of unusual illness in their lifetimes, those associated with ILI were the most commonly reported. In Guangdong province, this was followed by symptoms associated with SARI, then by other symptoms not mentioned in the survey. In Guangxi province, the second most reported symptoms were ones associated with encephalitis, followed by other symptoms not mentioned in the survey. Similarly, in Yunnan, symptoms associated with encephalitis were the second most commonly reported, but this was followed by symptoms associated with SARI **(Fig. 9)**.

Figure 9: *Symptoms reported by people who had experienced unusual illness in their lifetime.*



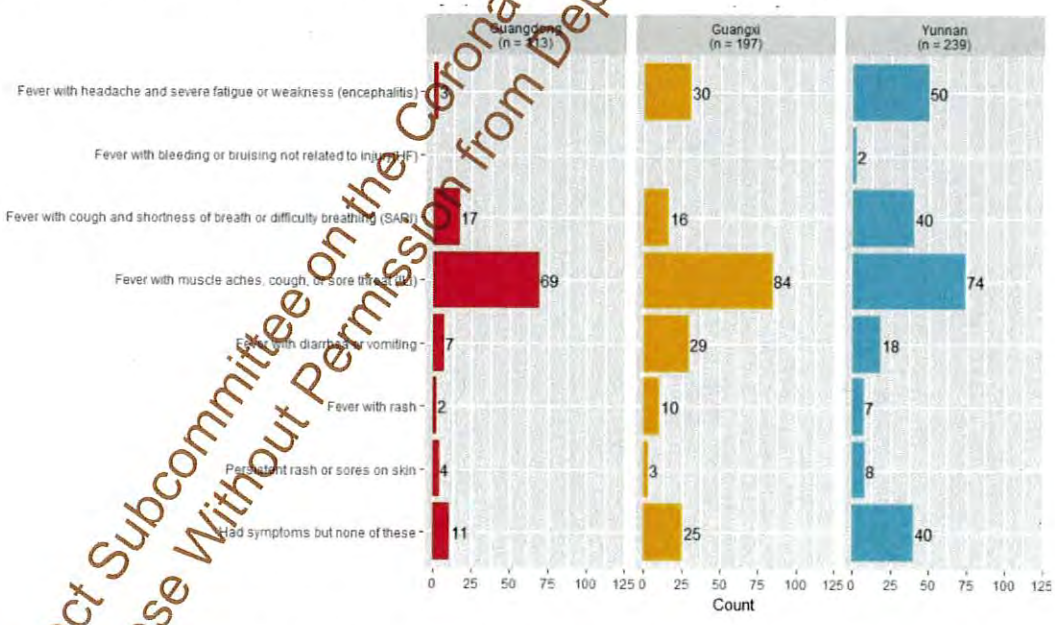
In each province, just under one-third of respondents who experienced the symptoms associated with an unusual illness in their lifetime indicated experiencing any of the symptoms in the past year – 22.2% in Guangdong, 32.8% in Guangxi and 23.0% in Yunnan **(Fig. 10)**.

Figure 10: *Whether respondents had experienced symptoms associated with an unusual illness in the past year.*



Of the respondents who reported having symptoms of unusual illness in the past year, across all three provinces, symptoms associated ILI were the most commonly reported. In Guangdong province, this was followed by symptoms associated with SARI then by other symptoms not provided in the survey. In Guangxi, symptoms associated with ILI were followed by symptoms associated with encephalitis, then by fever with diarrhea or vomiting. In Yunnan, symptoms associated with ILI were followed by symptoms associated with encephalitis, then by both SARI and other symptoms not provided in survey **(Fig. 11)**.

Figure 11: *Symptoms experienced by those reporting unusual illness in the past year.*



When respondents were asked what caused the symptoms associated with unusual illness experienced in the past year, 64.4% in Guangxi (85 of 132 respondents), and 50.0% in both Guangdong and Yunnan (46 of 92 respondents and 86 of 172, respectively), said they did not know the cause **(Fig. 12)**. Only one respondent in Guangxi said their symptoms were due to

contact with animals (wild animals, specifically). Two respondents in Guangdong and one respondent in Guangxi said their symptoms were due to contact with animals (non-wild animals, specifically), whereas none of the respondents in Yunnan attributed their cause to contact with animals.

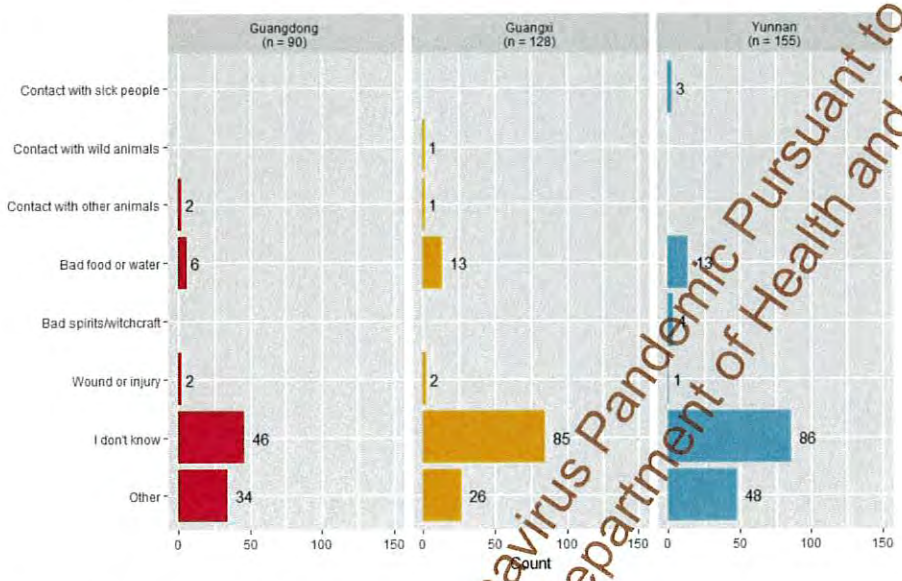
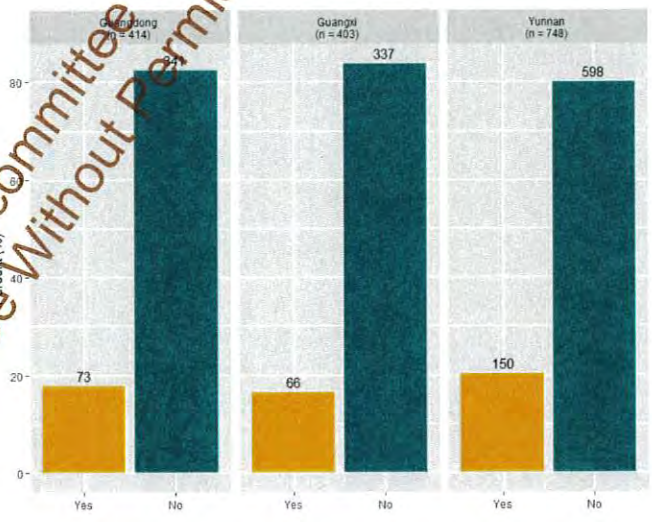


Figure 12: *Reported cause of sickness in the past year*

Respondents reporting an unusual illness in the past year were asked if any of the people they lived with in the past year had symptoms similar to theirs, to assess possibilities of transmission among household members. Most respondents did not, across all three provinces: 82.4% in Guangdong, 83.6% in Guangxi and 79.9% in Yunnan **(Fig. 13)**.

Figure 13: *Whether household members had similar symptoms of unusual illness, in the past year*



Of the household members who experienced symptoms of unusual illness in the past year, the most commonly reported symptoms were those associated with ILI **(Fig. 14)**.

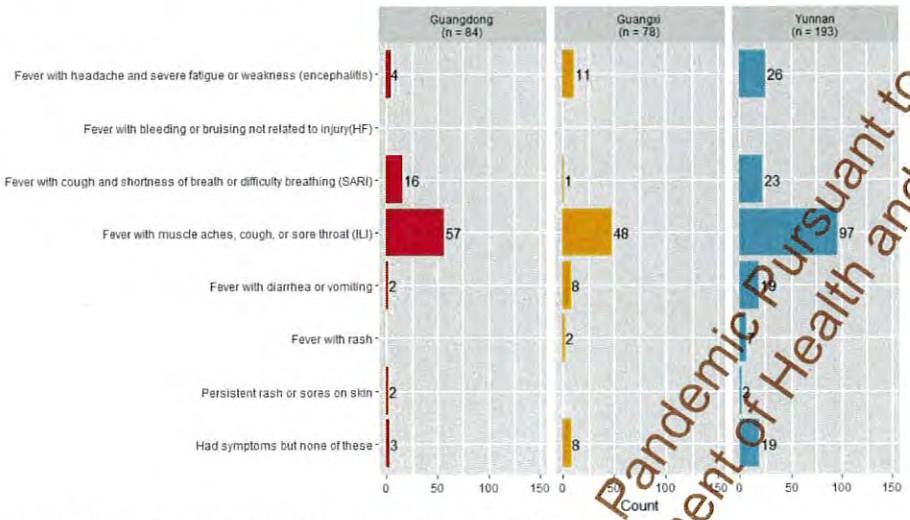


Figure 14: *Symptoms of household members who were ill, in past year.*

Respondents were also asked if any members of their household who experienced symptoms of unusual illness died as a result of their illness in the past year. Across all the three provinces, almost none had died from these illnesses **(Fig. 15)**.

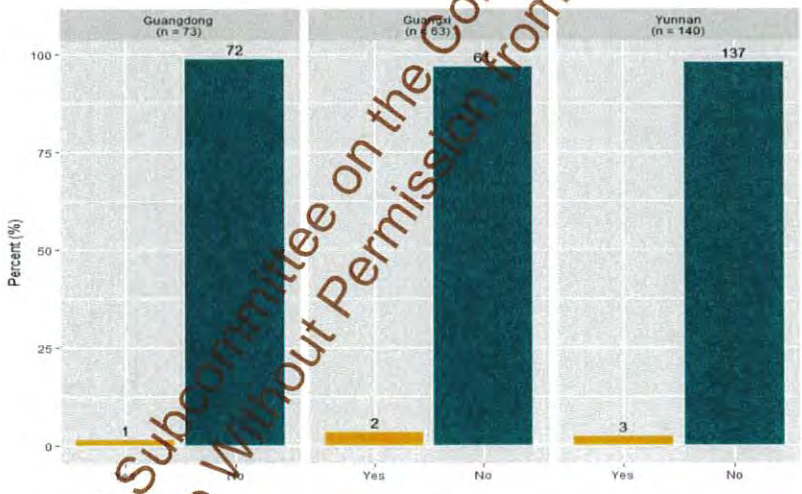


Figure 15: *Whether household members died from illness, in the past year.*

Contact with Animals

All respondents were asked about various types of animal contacts in their lifetime and in the past year. More than two-thirds of the respondents across all provinces, as well as in each of the provinces, reported raising an animal within their lifetime (71.2% in Guangdong, 77.7% in Guangxi, and 97.7% in Yunnan). More than half of the respondents in each province reported having animals come inside their dwellings (83.1 % in Guangdong, 60.2% in Guangxi, and 92.5% in Yunnan). More than half of respondents in each province reported handling live animals (51.5 % in Guangdong, 56.9% in Guangxi, and 62.9% in Yunnan) **(Table 1)**. Respondents from Yunnan had more types of contact with animals in their lifetime than those from Guangdong and Guangxi. With the exception of cooking or handling meat, organs, or blood from a recently killed animal and being scratched or bitten by an animal, the proportion of respondents from Yunnan who engaged in all types of animal activities was higher than the other provinces.

Type of animal contact (past year)	Guangdong		Guangxi		Yunnan	
	(n)	(%)	(n)	(%)	(n)	(%)
Lived with an animal as a pet	43	100 %	72	98.6 %	335	100 %
Handled live animals	212	100 %	226	98.3 %	332	99.7 %
Raised a live animal	296	100 %	312	99.4 %	518	99.8 %
Shared water source with animals for washing	47	100 %	19	95.0 %	97	100 %
Seen animal feces in or near food before you have eaten it	18	100 %	15	93.8 %	43	100 %
Eaten food after an animal has touched or damaged it	6	100 %	6	100 %	29	100 %
Animals come inside the dwelling where you live	345	100 %	239	98.0 %	493	100 %
Cooked or handled meat, organs, or blood from a recently killed animal	333	100 %	144	97.3 %	412	100 %
Eaten raw or undercooked meat or organs or blood	2	100 %	25	89.3 %	65	98.5 %
Eaten an animal that was not well/sick	--	--	1	100 %	6	100 %
Found a dead animal and collected it to eat, share, or sell	--	--	3	100 %	10	100 %
Been scratched or bitten by an animal	1	100 %	31	100 %	28	96.6 %
Slaughtered an animal	145	100 %	69	98.6 %	303	100 %
Hunted or trapped an animal	9	100 %	4	100 %	22	95.7%

Table 1: *Types of animal contact within a respondent's lifetime.*

Respondents who reported having animal contact in their lifetime were also asked to indicate if they had the same type of animal contact in the past year **(Table 2)**. In the past year, across all three provinces and in each province, almost all respondents engaged in all contact types with the exception of eating an animal that was not well/sick, and finding a dead animal and collecting it to eat, share, or sell (0% for both in Guangdong).

Type of animal contact (lifetime)	Guangdong		Guangxi		Yunnan	
	(n)	(%)	(n)	(%)	(n)	(%)
Lived with an animal as a pet	43	10.4 %	73	18.1 %	335	62.9 %
Handled live animals	212	51.5 %	230	56.9 %	334	62.8 %
Raised a live animal	296	71.2 %	314	77.7 %	521	97.7 %
Shared water source with animals for washing	47	11.5 %	21	5.2 %	97	18.2 %
Seen animal feces in or near food before you have eaten it	18	4.4 %	16	3.9 %	43	8.1 %
Eaten food after an animal has touched or damaged it	6	1.5 %	6	1.5 %	29.0	5.4 %
Animals come inside the dwelling where you live	345	83.1 %	244	60.2 %	493	92.5 %
Cooked or handled meat, organs, or blood from a recently killed animal	333	80.4 %	148	36.7 %	413	77.5 %
Eaten raw or undercooked meat or organs or blood	2	0.5 %	28	6.9 %	68	12.8 %
Eaten an animal that was not well/sick	--	--	1	0.3 %	6	1.1 %
Found a dead animal and collected it to eat, share, or sell	--	--	3	0.7 %	10	1.9 %

Table 2: *Types of animal contact, in past year.*

Respondents who had animal contact in the past year were asked to identify the animals involved in the interaction. *(Figs. 16-26, below: the first two figures are enlarged to show row labels, which are identical for all)*. Cats and dogs were the most common pets reported across all provinces and in each province **(Fig. 16b)**.

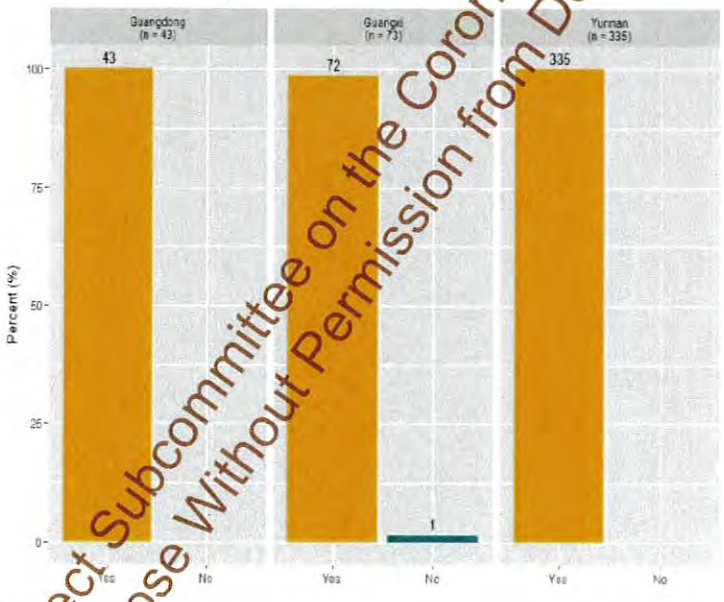
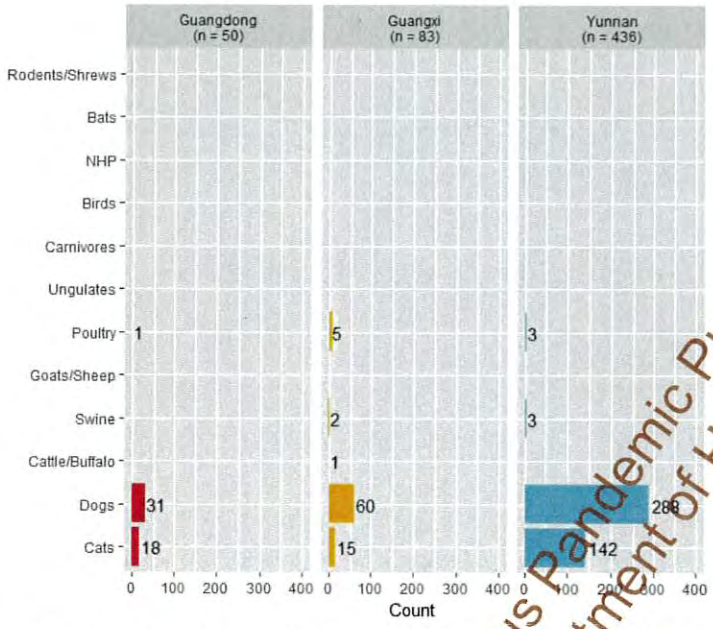


Figure 16a (top) & b (below): *(a) Whether respondents had lived with an animal as a pet, in the past year, and (b) among those who had, types of animal kept as pets.*



Poultry was the most common type of animal handled across all provinces as well as in each province, with 96.2%, 90.3%, and 92.8% of respondents handling animals in Guangdong, Guangxi and Yunnan, respectively **(Fig. 17b)**.

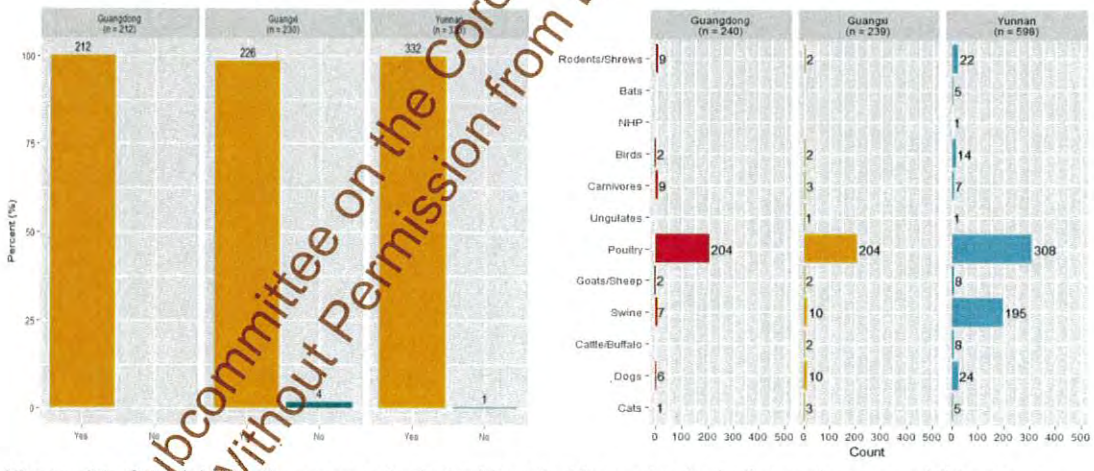
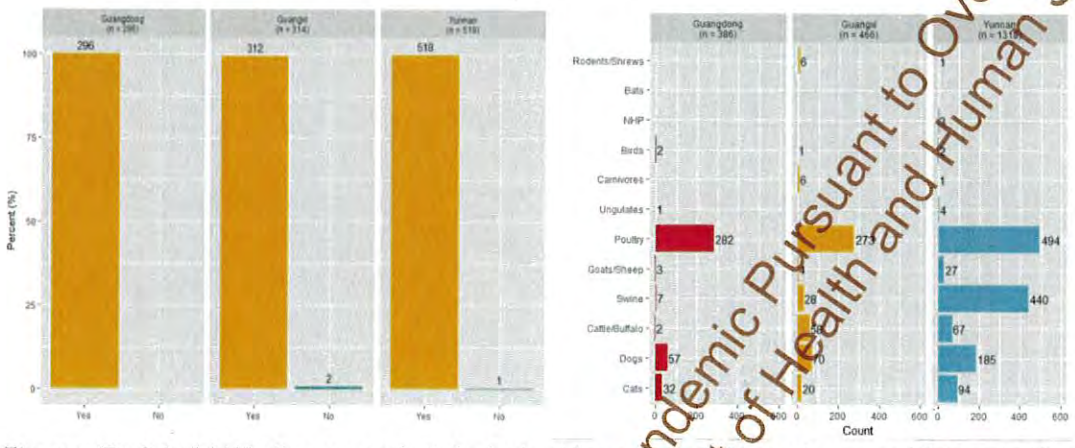


Figure 17a & b: *(a) Whether respondents had handled live animals, in the past year, and (b) among those who had, types of live animals handled.*

Poultry was also the most commonly raised animal in each of the three provinces; 95.3%, 87.5%, 95.4% in Guangdong, Guangxi, and Yunnan, respectively **(Fig. 18b)**.



Figures 18a & b: *(a) Whether respondents had raised live animals in the past year, and (b) among those who had, types of animals raised.*

In all three of the provinces, the most common type of animals found in respondent dwellings were rodents or shrews. In Guangdong and Yunnan, birds were the second most common animal type found in dwellings. In Guangxi province, birds along with poultry were the second most common animal type. Respondents in Guangdong and Yunnan reported that all 12 animal taxa had come inside their dwellings in the past year. Taxa seen in the dwellings of respondents from Guangdong and Yunnan and not Guangxi were non-human primates, ungulates, goats or sheep, swine, and cattle or buffalo **(Fig. 20b)**.

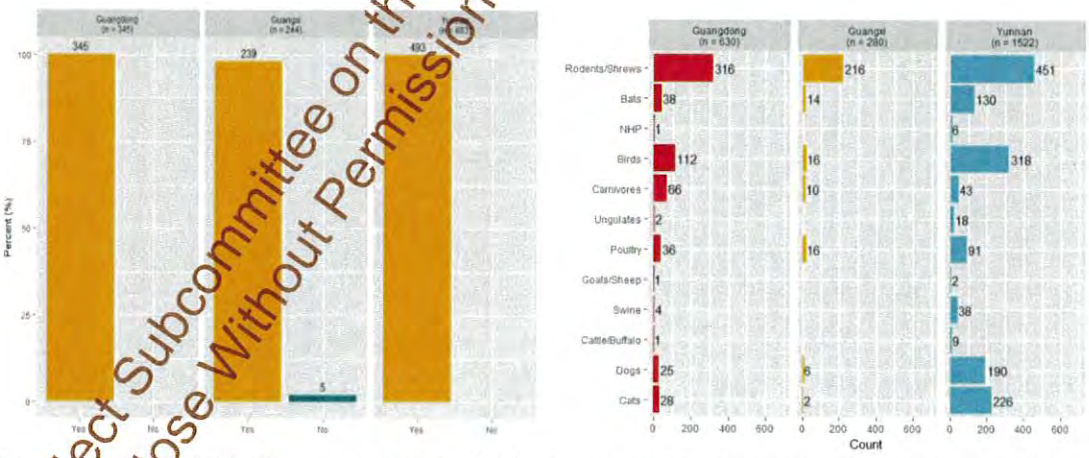


Figure 19a & b: *(a) Whether respondents had animals come inside dwelling, in the past year, and (b) among those who had, types of animals in dwelling.*

Almost all of the respondents who said they have cooked or handled meat, organs, or blood in their lifetime reported doing so in the past year. Common animal types that were cooked/handled included poultry and swine in all three provinces **(Fig. 20)**.

Figure 20a & b: *(a) Whether respondents had cooked or handled meat, organs or blood from a recently killed animal, in the past year, and (b) among those who had, types of animals whose meat, organs or blood was cooked or handled.*

More respondents in Yunnan reported eating raw or undercooked meat compared to respondents in Guangdong and Guangxi **(Fig. 21)**. In Yunnan, 96% of respondents who ate raw or undercooked meat in their lifetime did so in the past year. The types of animal products that were eaten raw or undercooked by respondents in Yunnan were mostly from swine. In Guangxi, the most commonly reported type of animal meat that had been eaten raw or undercooked was that of carnivores.

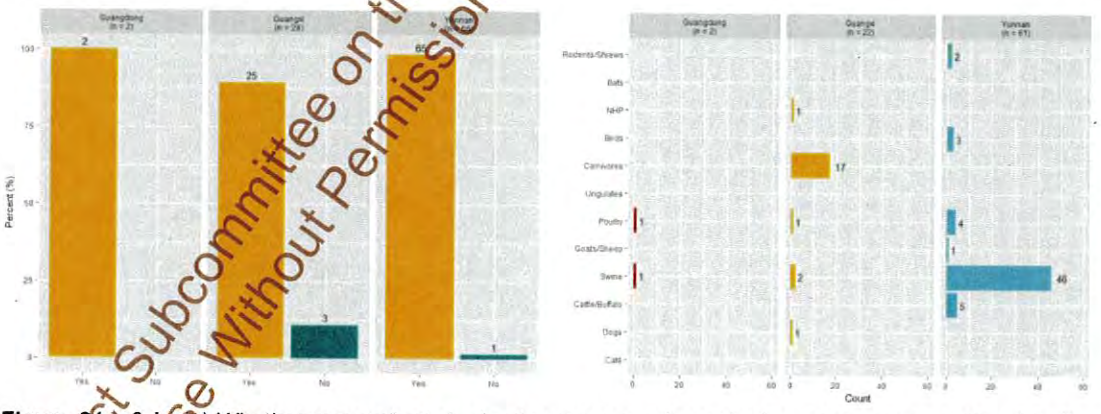


Figure 21 a & b: *(a) Whether respondents had eaten raw or undercooked meat or organs or blood, in the past year, and (b) among those who had, types of animals whose meat, organs or blood were eaten raw or undercooked.*

Across all provinces, a total of 13 respondents in Guangxi and Yunnan indicated that they collected an animal that was found dead to eat, share or sell. In Guandong, no respondents reported finding a dead animal and collecting it to eat, share, or sell. The most common type of animal collected across all provinces in aggregate was poultry. In Yunnan, poultry was the most common type of animal found dead and collected to eat, share or sell (80.0%), whereas dogs were the most common type in Guangxi (66.7%) **(Fig. 22)**.

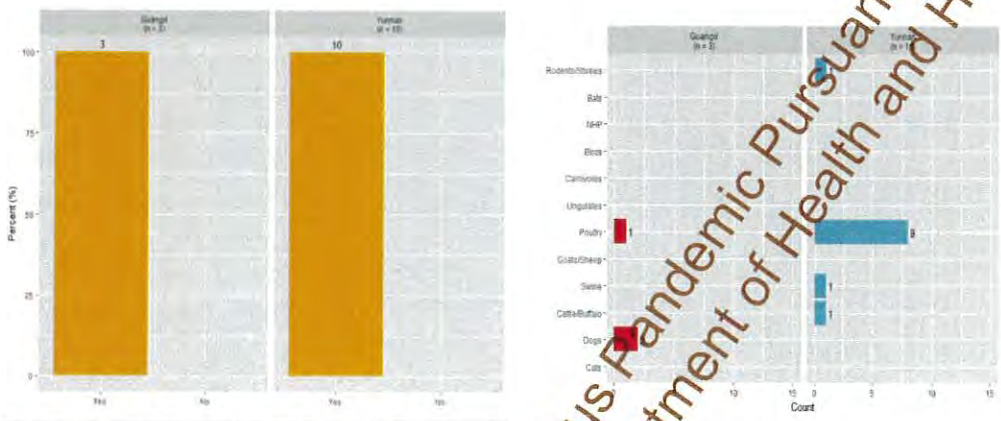


Figure 22 a & b: *(a) Whether respondents had found a dead animal and collected it to eat, share, or sell, in the past year, and (b) among those who had, types of animals that were found dead and collected to eat, share, or sell.*

In each province, almost all of the respondents who indicated being scratched or bitten by an animal in their lifetime said it occurred in the past year (100% in Guangdong, 98.6% in Guangxi, and 100% in Yunnan). In both Guangxi and Yunnan, dogs were the common type of animal that respondents said they were scratched or bitten by (64.5% in Guangxi and 50.0% in Yunnan). Cats were the second most common in Guangxi and Yunnan (9.6% in Guangxi, and 28.5% in Yunnan). Across all three provinces, only one respondent from Yunnan said that they were scratched or bitten by a bat **(Fig. 23)**.

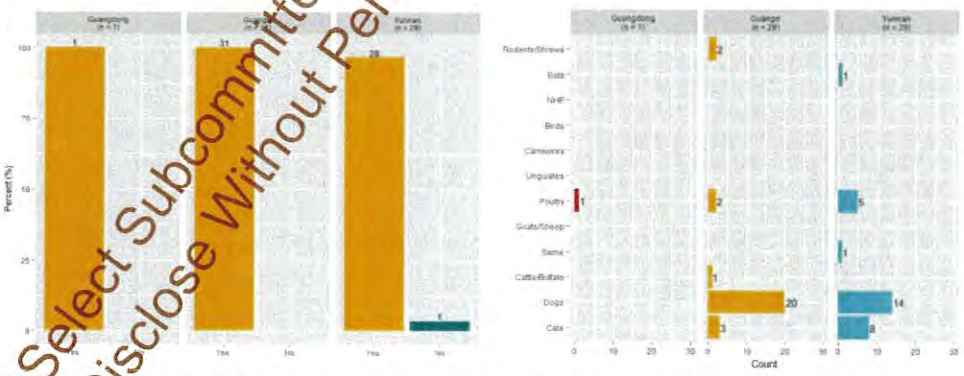


Figure 23 a & b: *(a) Whether respondents had been scratched or bitten by an animal, in the past year, and (b) among those who had, types of animals that scratched or bit respondents.*

Poultry was the most common type of animal slaughtered during the past year across all provinces as well as in each province (95.8% in Guangdong, 79.7% in Guangxi, and 94.1% in Yunnan). In addition to poultry, respondents in Yunnan also commonly only slaughtered swine (43.9%), compared to 1.4% in Guangdong and 7.3% in Guangxi **(Fig. 24)**.

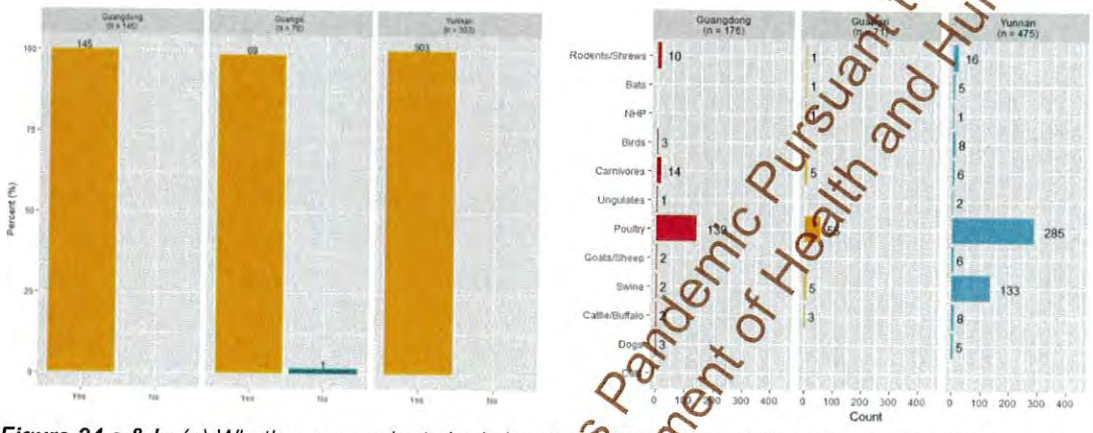


Figure 24 a & b: *(a) Whether respondents had slaughtered an animal, in the past year, and (b) among those who had, types of animals slaughtered.*

Carnivores were the most common taxa of animals hunted or trapped in the past year, in Guangdong and Guangxi. In Yunnan, rodents or shrews and birds were reported as the most common. Bats, non-human primates and dogs were animal types hunted by respondents in Yunnan but not by respondents in Guangdong and Guangxi **(Fig. 25)**.

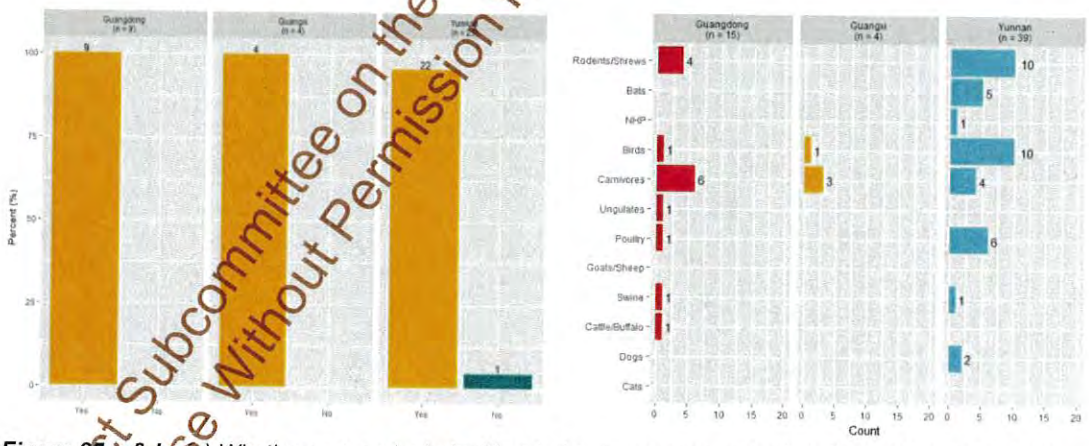


Figure 25 a & b: *(a) Whether respondents had hunted or trapped an animal, in the past year, and (b) among those who had, types of animals hunted or trapped.*

In examining bat-specific contact, across all provinces and within each province, the most common interaction with bats was finding them inside their houses. Respondents in Yunnan also hunted/trapped and handled bats, and were scratched/bitten by bats, whereas these did not occur in Guangdong or Guangxi **(Fig. 26)**.

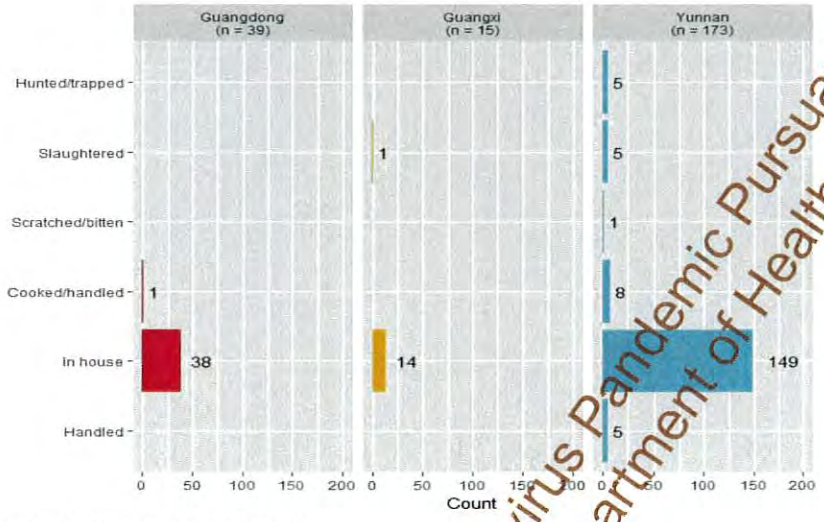


Figure 26: *Types of bat contact.*

After respondents were asked about their contact with wildlife and livestock, they were asked about their knowledge of whether animals can spread diseases and whether they were worried about diseases and disease outbreaks at wet markets. The proportion of respondents who thought that animals can spread disease was highest in Guangdong province (72.3%). In Guangxi and Yunnan, the proportion of those who thought animals could spread disease compared to those who thought that they did not were roughly equivalent – 47.5% versus 50.7% in Guangxi and 49.2% versus 49.3% in Yunnan **(Fig. 27)**.

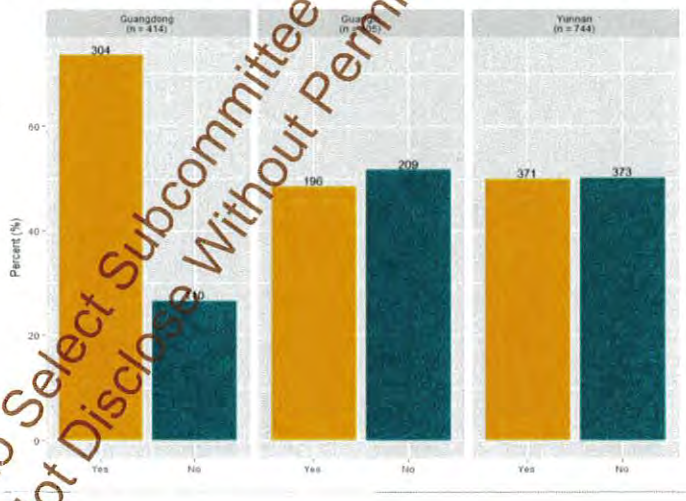


Figure 27: *Whether respondents thought that animals can spread disease.*

Similarly, when respondents were asked about whether they were worried about diseases or disease outbreaks in animals at wet markets, Guangdong had the highest proportion of respondents who said they were worried (67.3%). In both Guangxi and Yunnan, the proportion of respondents that was not worried (57.5% and 51.5%, respectively) was higher than the proportion that was worried **(Fig. 28)**

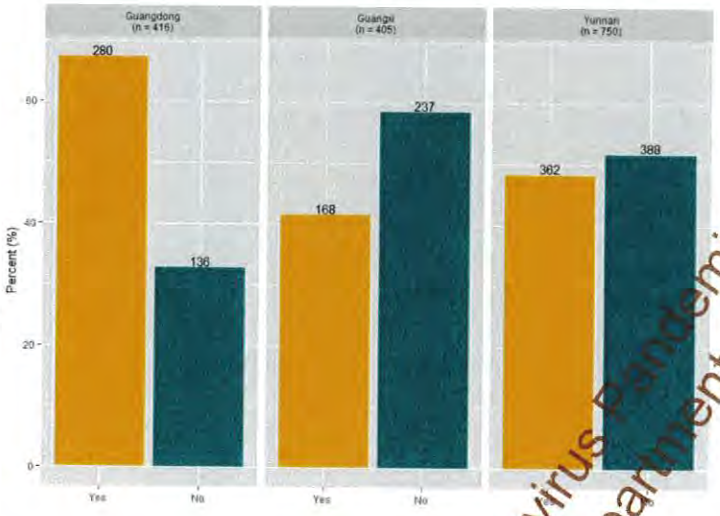


Figure 28: *Whether respondents were worried about diseases or disease outbreaks in animals at wet markets.*

Serological Evidence of Bat SARS-related CoV Infection in Humans

Respondents were asked to provide a biological sample to assess whether SARS-CoV spillover had occurred at the high-risk location where the survey has been implemented. A total of 1,530 serum samples were collected from 2016 to 2017 from individual residents in villages close to bat caves where coronaviruses were previously detected.

We developed an ELISA serology test using the purified NP protein of MERS-CoV, SARSr-CoV, HKU9 CoV and HKU10 CoV as coating antigen respectively and using Anti-Human IgG Monoclonal antibody as secondary antibody. All sera were screened for antibodies against these 4 bat-origin coronaviruses. Anti-SARSr-CoV NP IgG was detected in 10 samples, and 6 samples were positive for IgG against HKU10 NP. The 16 ELISA positive samples were further tested by confirmatory western blot, 7 samples from Yunnan province were confirmed positive for anti-SARSr-CoV, two samples (one from Guangdong province and one Guangxi province) were confirmed positive for anti-HKU10 **(Table 3)**.

Locations		Sample No.	NP Antibody Positive No.			
			HKU9 CoV	MERS CoV	SARSr-CoV	HKU10 CoV
Yunnan (2016)	Jinning	209			*6	
	Mengla	168			2 (*1)	
	Jinghong	212				2
	Lufeng	144				
Guangdong (2016)	Zengcheng	234			1	2
	Ruyuan	179				
Guangxi (2017)	Mashan	160			1	
	Guilin	224				*2
Total		1,530	0	0	*7	*2

Table 3 *Results of ELISA testing of human sera for antibodies to 4 different bat CoV species (*confirmed with western blot).*

Links Between ELISA Results and Behavior

Only one out of the seven SARS-related CoV seropositive respondents said that they had an unusual illness in their lifetime with reported symptoms similar to encephalitis or neural involvement. Two of the respondents said they had experienced symptoms in the past year with only one respondent specifying that they experienced epigastric pain and dizziness. The seven seropositive SARSr-CoV respondents reported various types of animal contacts in the past year. Three had lived with an animal as a pet, four handled a live animal, four raised a live animal, five saw animals inside their dwellings, five had cooked or handled meat, organs, or blood from a recently killed animals, one ate an animal that they knew was not well or sick, one was scratched or bitten by an animal, and four had slaughtered an animal. The only bat contact reported was by one respondent who saw a bat in their dwelling.

Both of the respondents who tested positive for HKU10-CoV antibodies said they had experienced an unusual illness in their lifetime, with symptoms associated with encephalitis and SARI. Neither respondent had experienced any symptoms of unusual illness in the past year. Both had reported handling and raising animals, with one indicating they saw animals come inside their dwelling, and one indicating cooking or handling meat, organs, or blood from a recently killed animal. No bat contact was reported by either of the respondents. Overall, five of the total nine SARS-related CoV and HKU10-CoV seropositive respondents reported being worried about disease or disease outbreaks at wet markets. Seven of the nine reported purchasing live animals from a wet market.

Specific Aim 1: Summary of Key Findings

Our analysis of the key risk factors relating to potential viral zoonotic disease spillover in China indicated some notable differences among the respondents in Guangdong, Guangxi, and Yunnan. With respect to demographic factors, Guangxi fared the lowest on key socio-economic

status indicators when compared to Guangdong and Yunnan provinces as reflected by the higher proportion of respondents in Guangxi living under the poverty level.

When assessing the type of animal contact and the associated animal taxa over the course of a respondent's lifetime, the results show that respondents in Yunnan engaged in greater contact with animals then those from Guangdong and Guangxi. For example, for 12 of the 14 animal contact types, a higher proportion of Yunnan respondents engaged in these respective activities than in Guangdong and Guangxi. Respondents in Yunnan also reported hunting bats, dogs, and non-human primates which were not reported to being hunted in Guangdong and Guangxi. Swine contact was higher in Yunnan for handling, raising, and slaughtering activities. When examining the various types of animal contact associated with bats only, our results also show that Yunnan respondents reported more varied types of contact with bats. Respondents in Yunnan indicated handling, being scratched by, slaughtering, and hunting bats, but these interactions did not occur in Guangdong or Guangxi. Additional analyses that examine predictors of animal contact in each province will be the focus of human behavioral analyses in Year 5 of the study.

Even though our sample population lives in areas that have dense and diverse bat populations, our results show an overall low proportion of respondents reporting hunting and trapping bats in all three provinces. The low proportion of hunting practice could be attributed to the success of conservation enforcement efforts undertaken by the government. These efforts may have effectively reduced the illegal practice of hunting wildlife or, as a consequence, moved the activity underground which made respondents less forthcoming about revealing their engagement in such practices. Further investigation into the potential causes is also warranted.

Our analyses also reveal differences in perceptions associated with zoonotic disease spillover between Guangdong, and Guangxi and Yunnan. For example, the proportion of respondents who thought that animals can spread disease was highest in Guangdong province at 72.3%, as compared to Guangxi (48.3%) and Yunnan (49.9%). Moreover, about two-thirds of respondents in Guangdong were worried about diseases and disease outbreaks in wet markets. These differences in perception observed in Guangdong compared to Guangxi and Yunnan could potentially be attributable to a heightened awareness of zoonotic disease emergence due to the 2001 SARS outbreak.

Finally, our serological testing results provide the first evidence ever of a bat SARSr-CoV spilling over into people in the wild. All of the SARSr-CoV positive individuals were from Yunnan province, which is the site of a cave in which we have identified a large diversity of SARSr-CoVs within the virome of which every genetic element of SARS-CoV can be identified. These findings warrant further investigations into the type of exposures that may have contributed to bat SARS-related CoVs to infect humans in this particular region. **They also highlight this region as a hotspot for SARSr-CoV future spillover risk.**

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk

Bat CoV PCR Detection and Sequencing from Live-Sampled Bat Populations

We collected rectal swab and oral swab samples from 671 individual bats from 20 species in Guangdong and Guangxi provinces in southern China in Year 4 **(Table 4)**. 671 rectal swab samples were tested for CoV RNA and 154 (23.0%) were positive **(Table 5)**.

Date of Sampling	Sampling Locations	Rectal swabs	Oral swabs
May 10th 2017	Hezhou, Guangxi	6	6
May 11-12th 2017	Chongzuo, Guangxi	67	67
May 13th 2017	Nanning, Guangxi	66	66
May 17th, 2017	Beihai, Guangxi	23	23
May 19th 2017	Chongzuo, Guangxi	36	36
May 21st 2017	Yangshan, Qingyuan, Guangdong	46	46
May 22nd, June 7 h 2017	Huidong, Huizhou, Guangdong	103	103
June 9th 2017	Nanning, Guangxi	71	71
June 9th 2017	Ningming, Chongzuo, Guangxi	63	63
September 10th 2017	Huidong, Huizhou, Guangdong	100	100
September 11th 2017	Yingde, Guangdong	90	90
Total		671	671

Table 4. *Bat samples collected for CoV surveillance in Year 4*

Species	Guangdong	Guangxi	Total
Rhinolophus sinicus	**9**/27	6	**9**/33
Rhinolphus rex		4	4
Rhinolophus pusilus	1	2	3
Rhinolophus pearsoni	5		5
Hipposideros armiger	24	8	32
Hipposideros larvatus	9	9	18
Hipposideros pomona		20	20
Hipposideros pratti	26		26
Aselliscus stoliczkanus		1	1
Miniopterus fuliginosus	1		1
Miniopterus pusillus	**29**/39		**29**/39
Myotis chinensis	**2**/27		**2**/27
Myotis daubentonii	2		2
Myotis ricketti	**86**/178		**86**/178
Pipistrellus abramus		2	2
Pipistrellus pipistrellus		2	2
Scotophilus kuhli		**24**/137	24/137
Tylonycteris pachypus		**4**/115	**4**/115
Tylonycteris robustula		3	3
Cynopterus sphinx		23	23
Total	126/339	28/332	154/671

Table 5*. Number of bat specimens tested and positive (bold) in Year 4*

A high prevalence of HKU6-related coronaviruses (48.3%), Scotophilus coronavirus 512 (17.5%), and coronavirus 1B (71.8%) was detected in *Myotis ricketii*, *Schotophilus khulii* and *Miniopterus pusillus*, respectively. SARS-related coronaviruses and HKU2-related coronaviruses were discovered in 4 and 5 *Rhinolophus sinicus* samples respectively from Guangdong. HKU4 coronaviruses were identified in 4 *Tylonycteris pachypus* from Guangxi **(Fig. 29)**.

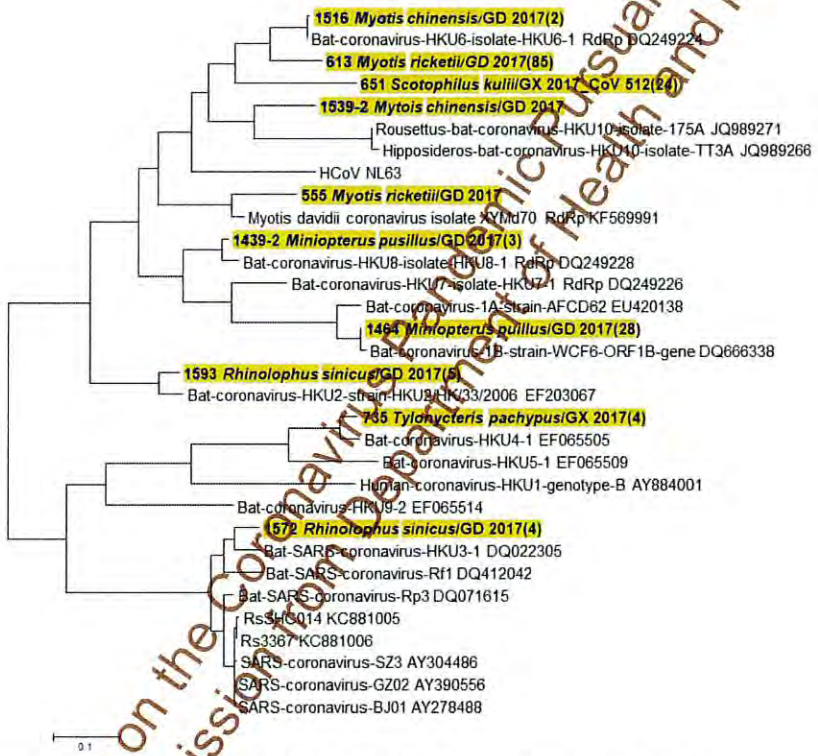


Figure 29: *Phylogenetic analysis of partial RdRp gene of CoV (440-nt partial sequence)*

Genetic Diversity and Genomic Characterization of Betacoronaviruses in Fruit Bats

In Year 4, we analyzed the genetic diversity of betacoronaviruses we have detected since 2009 in different species of fruit bats in Yunnan province, including *Eonycteris spelaea*, *Rousettus leschenaultia* and an unclassified *Rousettus* species. These viruses are classified into two betacoronavirus species, HKU9-CoV and GCCDC1-CoV. All HKU9-related viruses (n=46) were found in *Rousettus* spp. bats while GCCDC1-related viruses (n=13) from *E. spelaea*. Phylogenetic analysis of the full-length N gene suggests that HKU9-related CoVs are highly diverse and divided into 5 lineages with previously reported strains, and the GCCDC1-related CoVs were more similar between each other **(Fig. 30)**.

The full-length genome sequence of a novel HKU9-related CoV termed 2202 was determined. It shares 83% nt identity with other HKU9 strains, with the most divergent regions located in the S

protein, but shares only 68% aa identity with those of other HKU9 strains. Virus quantification revealed that intestine was the primary infected organ for HKU9-related CoVs while kidney and lungs could also be target tissues, suggesting potential for spillover through oral-fecal, respiratory, or uro-genitary routes.

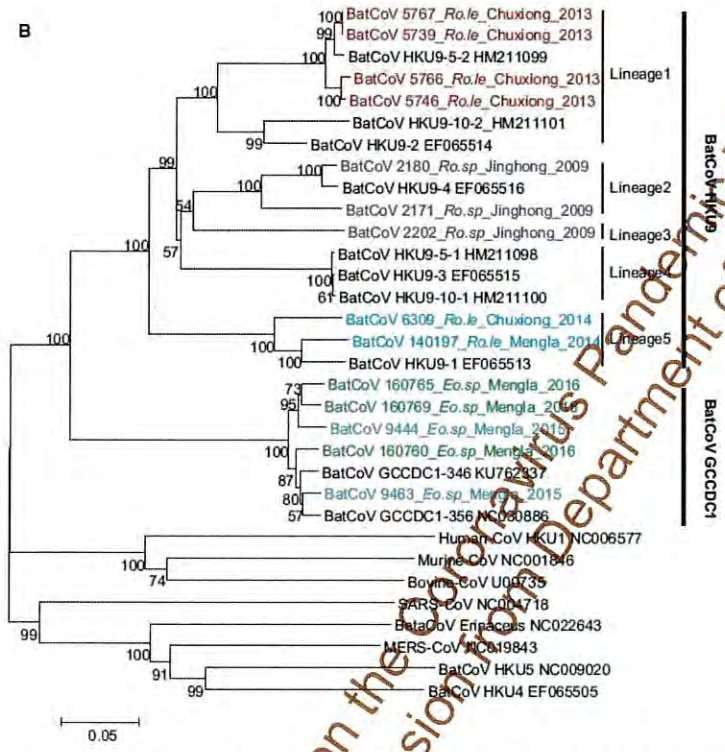


Figure 30. *Phylogenetic analysis of full-length N gene of HKU9 and GCCDC1 CoVs*

Bat Coronavirus Host-Virus Phylogeography in China

We used discrete ancestral character state reconstruction to estimate viral history and reconstructed the inferred bat host genus for each node within the phylogenetic tree **(Figs. 31, 32)**. The color of tree branches indicates the inferred ancestral host bat genus for the reconstructed phylogeny. *Rhinolophus* is the inferred ancestral host of lineages B and C (SARS-like CoVs and MERS-like CoVs, respectively). This genus played an important role in the diversification of Beta-CoVs. A larger host diversity is observed for Alpha-CoVs. Our dataset for this analysis includes all CoV RdRp sequences isolated from bat specimens collected by our team from 2008-2015 (Alpha-CoVs: n = 491 – Beta-CoVs: n = 326), including those collected under prior NIAID funding (1 R01 AI079231), funding from Chinese Federal Agencies, and a large majority from our current NIAID project. All Chinese bat CoV RdRp sequences available in GenBank were also added to our dataset (Alpha-CoVs: n = 226 – Beta-CoVs: n = 206).

Phylogenetic trees were reconstructed for Alpha- and Beta-CoVs separately using Bayesian inference (BEAST 1.8).

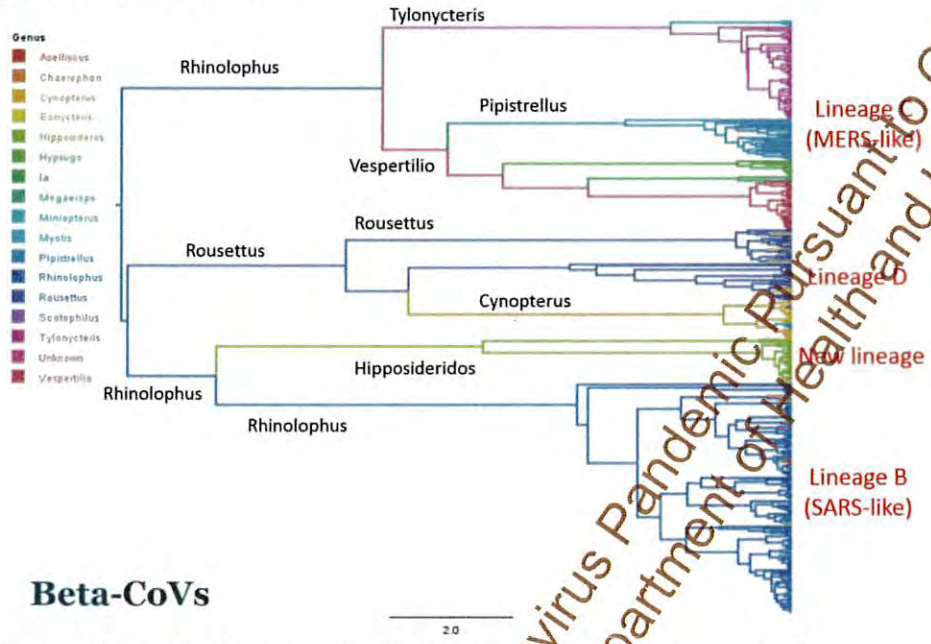


Figure 31. *Ancestral host reconstruction for Beta-CoVs, at a host genus level.*

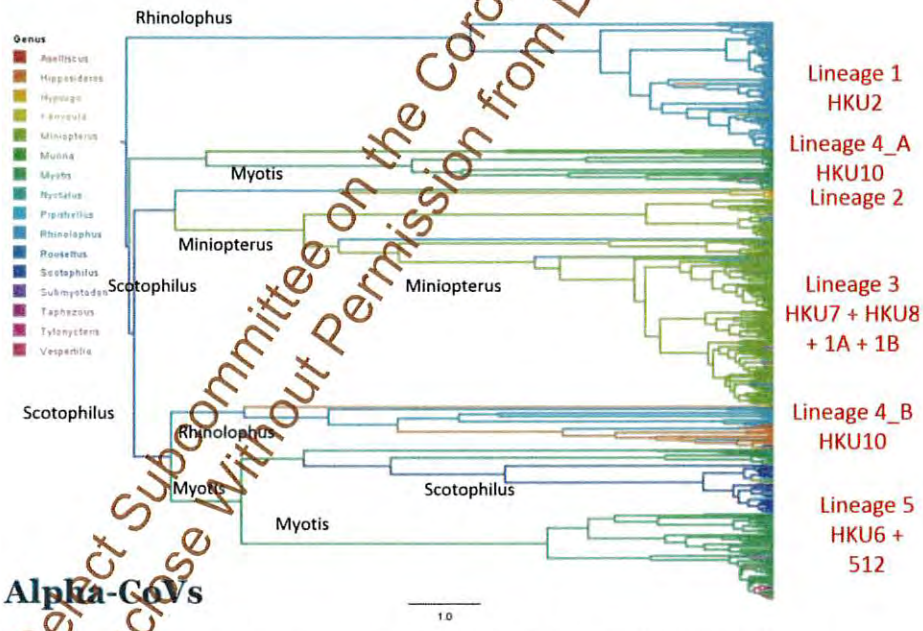


Figure 32. *Ancestral host reconstruction for Alpha-CoVs, at a host genus level.*

To better understand the geographic origins and extent of specific CoV clades, we also used discrete ancestral character state reconstruction in BEAST to reconstruct the ancestral location of each branch of the tree. We used SPREAD to visualize the tree in its geographic context and infer CoV spatial spread in China **(Fig. 33)**. These analyses allow us to identify the geographic areas that are likely sources of origin/diversity for this important group of viruses. The common ancestor of most Beta-CoVs lineages is located in Hong Kong and Guangdong. The common ancestor of most Alpha-CoV lineages was located in Yunnan province, and our results suggest they spread to other provinces from Yunnan.

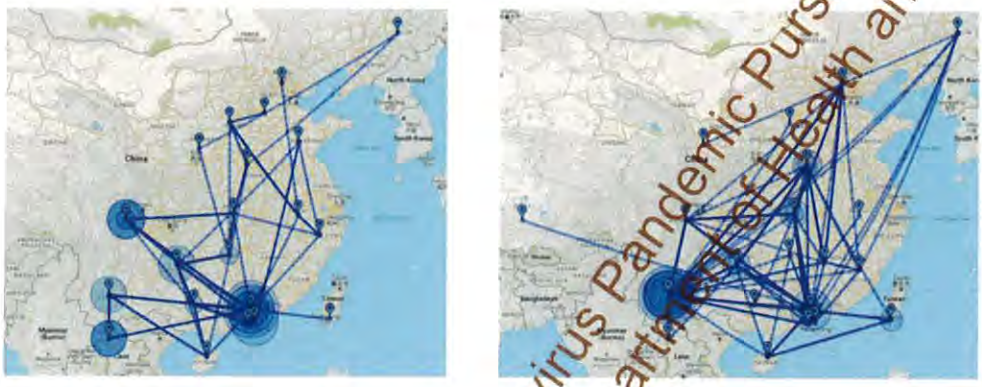


Figure 33. *Ancestral location reconstruction for Beta- and Alpha-CoVs. The bigger the circle is, the more ancestral the corresponding node is.*

Specific Aim 3: Testing Predictions of CoV Inter-Species Transmission

Identification of two novel MERS-related CoVs that use DPP4 receptor

Two novel MERSr-CoVs, BtCoV/li/GD/2013-845 and BtCoV/li/GD/2014-422, were identified from great evening bats (*Ia io*) in Guangdong province. Phylogenetic analysis of polyprotein 1 and the E, M, and N proteins suggests that the two novel strains are more closely related to MERS-CoV than to other lineage C Beta-CoVs. Their RdRp sequences are closely related to those of MERS-CoV and other MERSr-CoVs, with 94.4–97.0% aa identities. In contrast, they are divergent from MERS-CoV and other MERSr-CoVs in the spike protein, with only 58.9–64.7% aa identities. However, in the receptor-binding domain (RBD) of the spike protein, the two novel MERSr-CoVs are identical to MERS-CoV at six out of the 13 residues that directly interact with human DPP4 receptor, making them more similar to MERS-CoV than any other known lineage C BetaCoVs **(Fig. 34a)**. Protein–protein interaction assays demonstrated that the spike proteins of the novel MERSr-CoVs bind to both human and bat DPP4 **(Fig. 34b)**. Moreover, bat cells exogenously expressing human DPP4 support the entry of the retrovirus pseudotyped with BtCoV/li/GD/2014-422 spike, while the pseudovirus fails to enter cells that do not express DPP4. The results demonstrate that the spike protein of the newly identified MERSr-CoV recognizes the human DPP4 receptor.

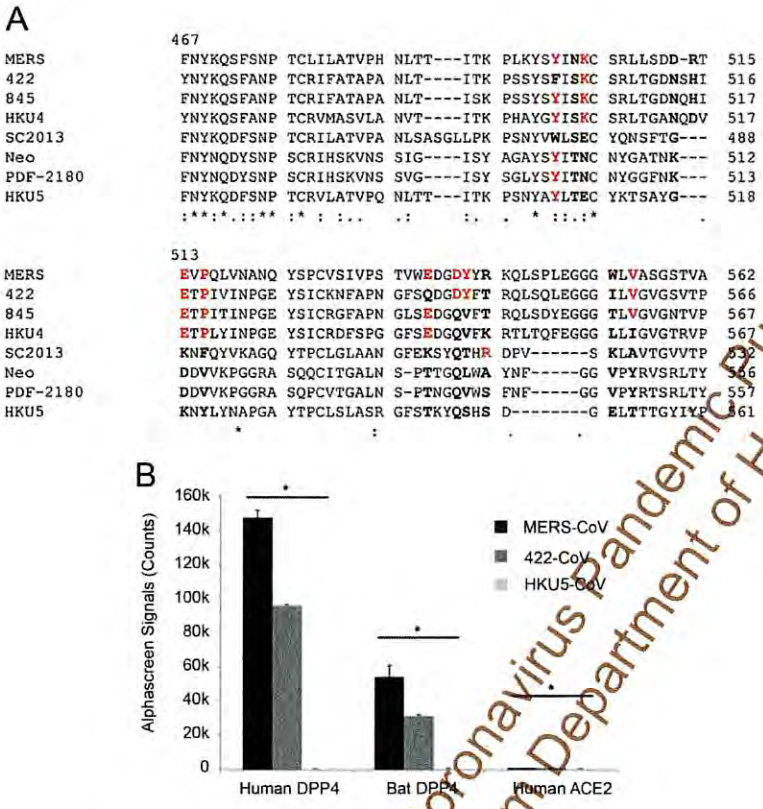


Figure 34. *BtCoV/li/GD/2014-422 RBD analysis (a) and DPP4-binding assay (b)*

In Vivo Infection of Human ACE2 (hACE2) Expressing Mice with SARSr-CoV S Protein variants

Using the reverse genetic methods we previously developed, infectious clones with the WIV1 backbone and the spike protein of SHC014, WIV16 and Rs4231, respectively, were constructed and recombinant viruses were successfully rescued. In Year 4, we performed preliminary *in vivo* infection of SARSr-CoVs on transgenic mice that express hACE2. Mice were infected with 10^5 pfu of full-length recombinant virus of WIV1 (rWIV1) and the three chimeric viruses with different spikes. Pathogenesis of the 4 SARSr-CoVs was then determined in a 2-week course. Mice challenged with rWIV1-SHC014S have experienced about 20% body weight loss by the 6th day post infection, while rWIV1 and rWIV-4231S produced less body weight loss. In the mice infected with rWIV1-WIV16S, no body weight loss was observed **(Fig. 35a)**. 2 and 4 days post infection, the viral load in lung tissues of mice challenged with rWIV1-SHC014S, rWIV1-WIV16S and rWIV1-Rs4231S reached more than 10^6 genome copies/g and were significantly higher than that in rWIV1-infected mice **(Fig. 35b)**. These results demonstrate varying pathogenicity of SARSr-CoVs with different spike proteins in humanized mice.

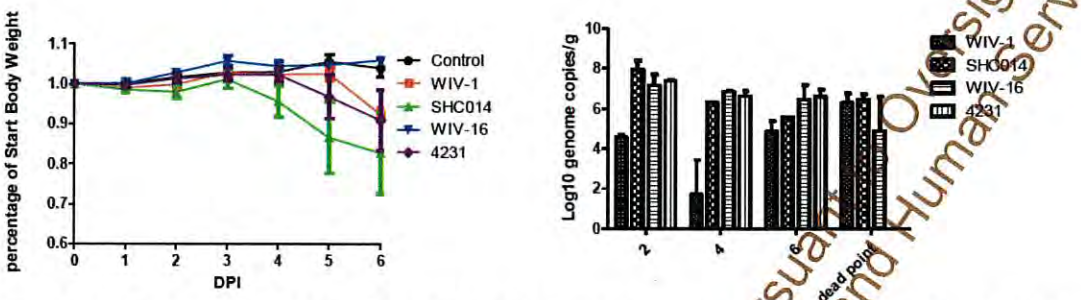


Figure 35. *In vivo infection of SARSr-CoVs in hACE2-expressing mice. (a, left) Body weight change after infection; (b, right) Viral load in lung tissues*

Additional Year 4 Results for Specific Aim 3:

Identification of a HKU2-related Coronavirus of Bat Origin that Caused Fatal Acute Diarrhea in Piglets

From October 2016, a series of fatal swine diarrhea disease outbreaks occurred in Guangdong province. By May 2017, it had resulted in death of 24,693 piglets across four farms. We identified a novel coronavirus as the etiological agent of the disease by metagenomic analysis, viral isolation and experimental infection, and named this "Swine Acute Diarrhea Syndrome coronavirus (SADS-CoV). During Year 4, we submitted and published a paper on this finding to *Nature* (Zhou *et al.*, 2018). The full-length genome of SADS-CoV shares 95% sequence identity to bat CoV HKU2. However, the S gene sequence identity is only 86%, suggesting that the previously reported HKU2-CoV is not the direct progenitor of SADS-CoV, but that they may have originated from a common ancestor.

Using a SADS-CoV specific qPCR assay based on its RdRp gene, SADS-related coronaviruses (SADSr-CoVs) were detected in rectal swabs of *Rhinolophus* bats collected from 2013 to 2016 in Guangdong. Full-length genome sequencing of 4 bat SADSr-CoVs revealed 96% to 98% overall genome sequence identity between SADSr-CoVs and SADS-CoV. Most importantly, the S protein of SADS-CoV shared more than 98% sequence identity with those of the two SADSr-CoVs (162149 and 141388), compared to 86% with HKU2-CoV **(Fig. *36a*)**. The phylogeny of S1 protein sequence showed strong co-evolutionary relationships with bat alphacoronavirus and their hosts, with swine SADS-CoV more closely related to SADSr-CoVs from *Rhinolophus affinis* than strains from *Rhinolophus sinicus* in which HKU2-CoV was found **(Fig. 36b)**. Analysis of the 33 SADS-CoV full genome sequences we were able to characterize from pigs suggests that viruses from the four farms may have been transmitted from their reservoir hosts independently. These findings highlight the importance of identifying coronavirus diversity and distribution in bats to mitigate future outbreaks that threaten livestock and public health.

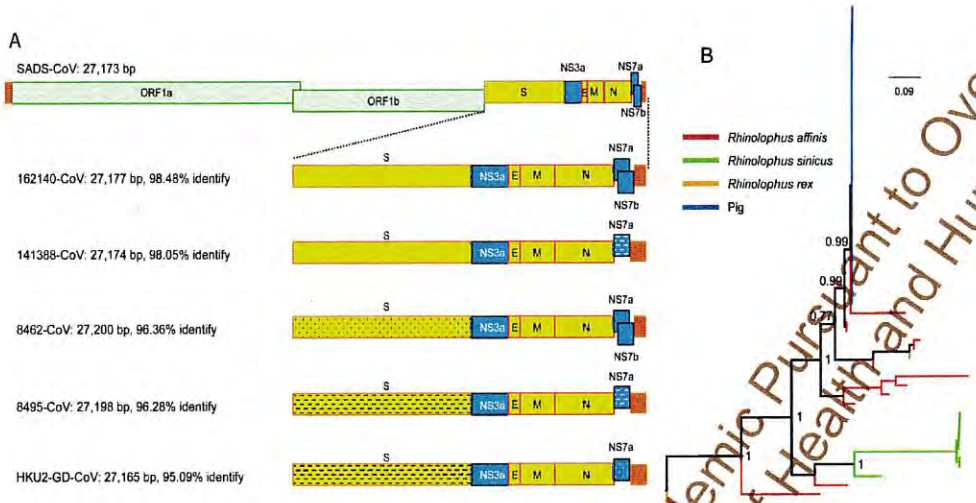


Figure 36. *Genome organization and comparison (a) and Phylogenetic analysis of S1 protein (b) of SADS-CoV and bat SADSr-CoVs*

Intra-Farm Transmission Model to Understand to Predict Future Transmission and Outbreak

To better understand amplification dynamics and assess the potential for future transmission resulting in large outbreaks, we developed an intra-farm, age-structured, stochastic transmission model for SADS-CoV **(Fig. 37)**. We developed multiple versions of this model to represent different hypotheses of disease transmission mechanisms and fit them to time-series data of reported deaths on multiple SADS-infected farms.

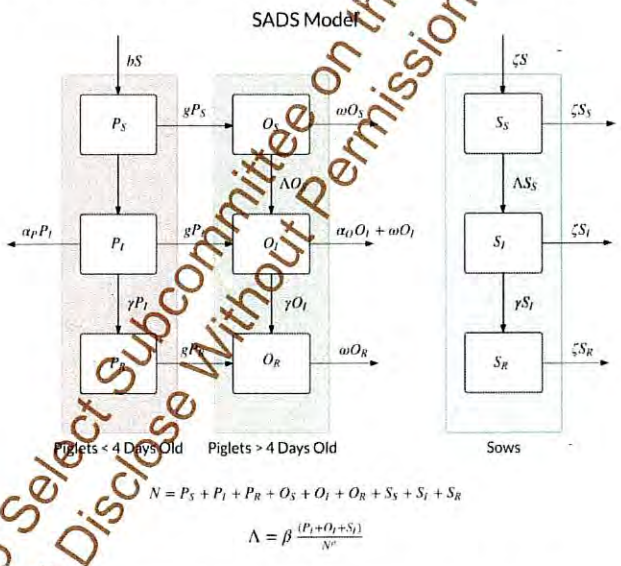


Figure 37: *Schematic of intra-farm transmission mode.*

Our first model structure, which assumed equal mixing of animals across farms **(Fig. 38)** showed that age structure alone was insufficient to generate the temporal pattern of reported deaths on SADS-infected farms. Our second model structure **(Fig. 39)** represented individual barns on a farm as a series of pig-virus meta-populations. This structure was sufficient to re-create the dynamics of the series of rapid "mini-epidemics" that progressed in SADS-infected farms.

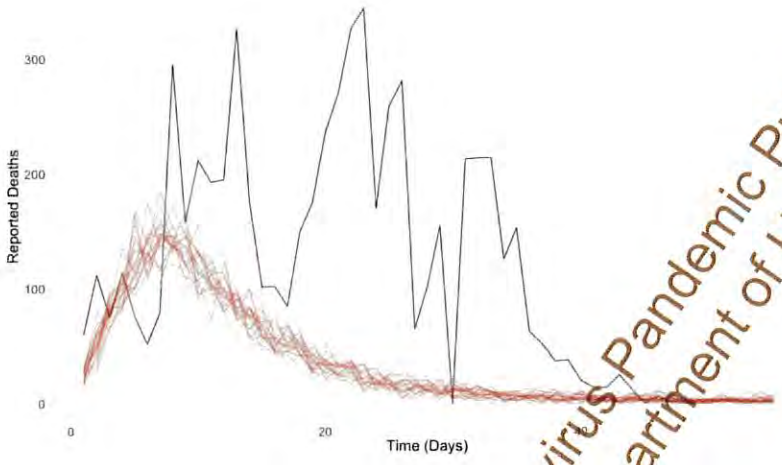


Figure 38: *Best-fit simulations (red) from an equal-mixing transmission model and actual reported death time series (black) on a SADS-infected farm.*

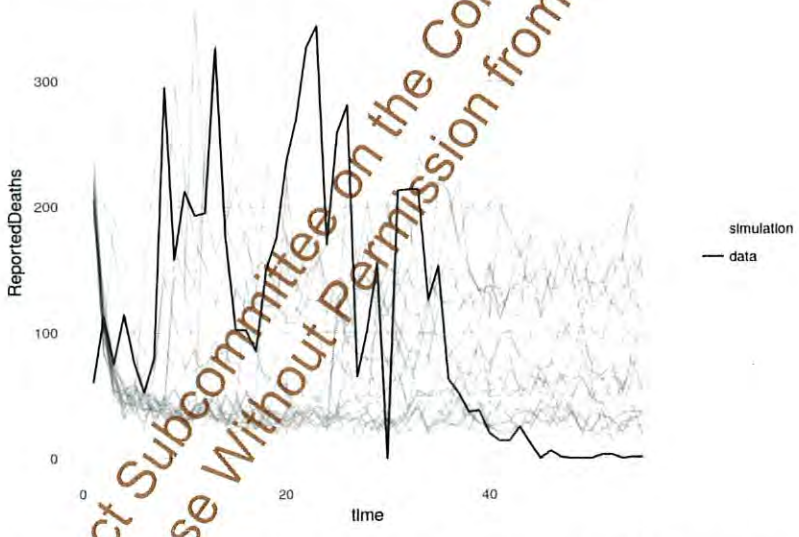


Figure 39: *Best-fit simulations (grey) from an metapopulation transmission model and actual reported death time series (black) on a SADS-infected farm.*

Specific Goals Not Meet

- The wild animal farm survey was piloted in early Y4, with data collected from seven wild animal farms, it was postponed due to the emergence of SADS-CoV where our group had focused on instead in Y4, but will be resumed in Y5 to continue collecting and analyzing data.
- The passive hospital surveillance has been piloted will continue in Year 4 to collect and test for CoVs.

B. 4 What opportunities for training and professional development has the project provided?

1. Conference and University lectures: We provided human subject research trainings to chief physicians and nurses at local clinics, staff from Yunnan Institute of Endemic Diseases Control and Prevention, students from Dali College and Wuhan University for both qualitative and quantitative research.

2. Agency and other briefing: Dr. Guangjian Zhu was invited by the Guangdong Institute of Applied Nature Resources, Guangdong Academy of Sciences to provide training to 8 field team members regarding biosafety and PPE use, bats and rodents sampling. Dr. Zhengli Shi participated in the US National Science Foundation-funded EcoHealthNet (grant to EcoHealth Alliance – Epstein PI) that provides research exchange opportunities to undergraduate and graduate-level students.

3. Public outreach: PI Daszak, and Co-investigators Shi, Epstein, and Olival presented the results of this project to the public via interviews with national central and local television, social media, newspaper and journals in China and the US.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Luo CM, Wang N, Yang XL, Liu HZ, Zhang W, Li B, Hu B, Peng C, Geng QB, Zhu GJ, Li F, Shi ZL. Discovery of Novel Bat Coronaviruses in South China That Use the Same Receptor as Middle East Respiratory Syndrome Coronavirus. Journal of virology. 2018 July 1;92(13). PubMed PMID: 29669833; PubMed Central PMCID: PMC6002729; DOI: 10.1128/JVI.00116-18.
Complete	Field HE. Evidence of Australian bat lyssavirus infection in diverse Australian bat taxa. Zoonoses and public health. 2018 September;65(6):742-748. PubMed PMID: 29785730; PubMed Central PMCID: PMC6249124; DOI: 10.1111/zph.12480.
Complete	Eskew EA, Olival KJ. De-urbanization and Zoonotic Disease Risk. EcoHealth. 2018 December;15(4):707-712. PubMed PMID: 30120670; PubMed Central PMCID: PMC6265062; DOI: 10.1007/s10393-018-1359-9.
Complete	Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nature reviews. Microbiology. 2019 March;17(3):181-192. PubMed PMID: 30531947; PubMed Central PMCID: PMC7097006; DOI: 10.1038/s41579-018-0118-9.
Complete	Li HY, Zhu GJ, Zhang YZ, Zhang LB, Hagan EA, Martinez S, Chmura AA, Francisco L, Tai H, Miller M, Daszak P. A qualitative study of zoonotic risk factors among rural communities in southern China. International health. 2020 February 12;12(2):77-85. PubMed PMID: 32040190; PubMed Central PMCID: PMC7017878; DOI: 10.1093/inthealth/ihaa001.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
[redacted]	Y	DASZAK, PETER	BS,PHD	PD/PI	[redacted] (6)	[redacted] (6)	[redacted] (6)			NA
[redacted]	N	Chmura, Aleksei	BS,PHD	Non-Student Research Assistant	[redacted] (6)	[redacted] (6)	[redacted] (6)			NA
[redacted]	N	Ross, Noam Martin	PhD	Co-Investigator	[redacted]	[redacted]	[redacted]			NA
[redacted]	Y	Olival, Kevin J.	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]			NA
[redacted]	Y	Zhang, Shu-yi	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	East China Normal University	CHINA	NA
	N	ZHU, GUANGJIAN	PHD	Co-Investigator	[redacted] (6)	[redacted] (6)	[redacted] (6)	East China Normal University	CHINA	NA
	N	GE, XINGYI	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	Wuhan Institute of Virology	CHINA	NA
	N	KE, CHANGWEN	PHD	Co-Investigator	[redacted] (6)	[redacted] (6)	[redacted] (6)	Center for Disease Control and Prevention of Guangdong Province	CHINA	NA
	Y	ZHANG, YUNZHI	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	Yunnan Provincial Institute of Endemic Diseases Control & Prevention	CHINA	NA
[redacted]	N	EPSTEIN, JONATHAN H	MPH,DVM ,BA,PHD	Co-Investigator	[redacted] (6)	[redacted] (6)	[redacted] (6)			NA
[redacted]	N	SHI, ZHENGLI	PhD	Co-Investigator	[redacted]	[redacted]	[redacted]	Wuhan Institute of Virology	CHINA	NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth)
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award? No
D.2.b New Senior/Key Personnel Are there, or will there be, new senior/key personnel? No
D.2.c Changes in Other Support Has there been a change in the active other support of senior/key personnel since the last reporting period? No
D.2.d New Other Significant Contributors Are there, or will there be, new other significant contributors? No
D.2.e Multi-PI (MPI) Leadership Plan Will there be a change in the MPI Leadership Plan for the next budget period? NA

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Dollar Amount	Country
$201,422	CHINA

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Sub-Project ID:	Study ID	Study Title:	Delayed Onset	Clinical Trial	NCT	NIH-Defined Phase 3	ACT
	58010	Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001	NO	NO		NO	

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: EcoHealth Alliance, Inc.	077090066	NY-010	460 West 34th Street 17th Floor New York NY 100012317
Wuhan Institute of Virology	529027474		Xiao Hong Shan, No. 44 Wuchang District Wuhan NONE
East China Normal University	420945495		3663 Zhongshan Beilu Shanghai NONE
ECOHEALTH ALLIANCE	077090066		ECOHEALTH ALLIANCE, INC. 460 W 34TH ST

			NEW YORK NY 100012320

G.9 FOREIGN COMPONENT

Organization Name: Wuhan Institute of Virology
Country: CHINA
Description of Foreign Component:
Principal Laboratory for all Research in China as per section G8 (above) and detailed in our Specific Aims

Organization Name: Wuhan School of Public Health
Country: CHINA
Description of Foreign Component:
Principal Coordinating Team for all project field work as per section G8 (above) and detailed in our Specific Aims

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Section 1 - Basic Information (Study 58010)

OMB Number: 0925-0001 and 0925-0002
Expiration Date: 03/31/2020

1.1. Study Title *

Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001

1.2. Is this study exempt from Federal Regulations * ○ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	○ Yes	● No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	○ Yes	● No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	○ Yes	● No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 58010)

2.1. Conditions or Focus of Study		
2.2. Eligibility Criteria		
2.3. Age Limits	Min Age:	Max Age:
2.4. Inclusion of Women, Minorities, and Children		
2.5. Recruitment and Retention Plan		
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline		

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
IER 58010	Foreign	

Inclusion Enrollment Report 58010

Using an Existing Dataset or Resource* : ○ Yes ● No

Enrollment Location Type* : ○ Domestic ● Foreign

Enrollment Country(ies): CHN: CHINA

Enrollment Location(s):

Comments:

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	1230	1230	0	0	2460
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More than One Race	0	0	0	0	0
Total	1230	1230	0	0	2460

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	980	616	0	0	0	0	0	0	0	1596
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	980	616	0	0	0	0	0	0	0	1596

Section 3 - Protection and Monitoring Plans (Study 58010)

3.1. Protection of Human Subjects

3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site? ○ Yes ○ No ○ N/A

If yes, describe the single IRB plan

3.3. Data and Safety Monitoring Plan

3.4. Will a Data and Safety Monitoring Board be appointed for this study? ○ Yes ○ No

3.5. Overall structure of the study team

Section 4 - Protocol Synopsis (Study 58010)

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

Type	Name	Description

4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ○ Yes ● No

4.2.e. Intervention Model

4.2.f. Masking ○ Yes ○ No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

4.4. Statistical Design and Power

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? ○ Yes ○ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan

A. COVER PAGE

Project Title: Understanding the Risk of Bat Coronavirus Emergence	
Grant Number: 5R01AI110964-05	**Project/Grant Period:** 06/01/2014 - 05/31/2019
Reporting Period: 06/01/2018 - 05/31/2019	**Requested Budget Period:** 06/01/2018 - 05/31/2019
Report Term Frequency: Annual	**Date Submitted:** 08/03/2021
Program Director/Principal Investigator Information: PETER DASZAK , PHD BS **Phone Number:** [redacted] **Email:** [redacted]	**Recipient Organization:** ECOHEALTH ALLIANCE, INC. ECOHEALTH ALLIANCE, INC. 520 EIGHTH AVENUE NEW YORK, NY 100181620 **DUNS:** 077090066 **EIN:** 1311726494A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** [redacted] **Email:** [redacted]	**Signing Official:** ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** [redacted] **Email:** [redacted]
Human Subjects: Yes **HS Exempt:** NA **Exemption Number:** **Phase III Clinical Trial:** NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Zoonotic coronaviruses are a significant threat to global health, as demonstrated with the emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, and the recent emergence Middle East Respiratory Syndrome (MERS-CoV). The wildlife reservoirs of SARS-CoV were identified by our group as bat species, and since then hundreds of novel bat-CoVs have been discovered (including >260 by our group). These, and other wildlife species, are hunted, traded, butchered and consumed across Asia, creating a largescale human-wildlife interface, and high risk of future emergence of novel CoVs. To understand the risk of zoonotic CoV emergence, we propose to examine 1) the transmission dynamics of bat-CoVs across the human-wildlife interface, and 2) how this process is affected by CoV evolutionary potential, and how it might force CoV evolution. We will assess the nature and frequency of contact among animals and people in two critical human-animal interfaces: live animal markets in China and people who are highly exposed to bats in rural China. In the markets we hypothesize that viral emergence may be accelerated by heightened mixing of host species leading to viral evolution, and high potential for contact with humans. In this study, we propose three specific aims and will screen free ranging and captive bats in China for known and novel coronaviruses; screen people who have high occupational exposure to bats and other wildlife; and examine the genetics and receptor binding properties of novel bat-CoVs we have already identified and those we will discover. We will then use ecological and evolutionary analyses and predictive mathematical models to examine the risk of future bat-CoV spillover to humans. This work will follow 3 specific aims:

Specific Aim 1: Assessment of CoV spillover potential at high risk human-wildlife interfaces. We will examine if: 1) wildlife markets in China provide enhanced capacity for bat-CoVs to infect other hosts, either via evolutionary adaptation or recombination; 2) the import of animals from throughout Southeast Asia introduces a higher genetic diversity of mammalian CoVs in market systems compared to within intact ecosystems of China and Southeast Asia; We will interview people about the nature and frequency of contact with bats and other wildlife; collect blood samples from people highly exposed to wildlife; and collect a full range of clinical samples from bats and other mammals in the wild and in wetmarkets; and screen these for CoVs using serological and molecular assays.

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk. We propose two competing hypotheses: 1) CoV host-range in bats and other mammals is limited by the phylogenetic relatedness of bats and evolutionary conservation of CoV receptors; 2) CoV host-range is limited by geographic and ecological opportunity for contact between species so that the wildlife trade disrupts the 'natural' co-phylogeny, facilitates spillover and promotes viral evolution. We will develop CoV phylogenies from sequence data collected previously by our group, and in the proposed study, as well as from Genbank. We will examine co-evolutionary congruence of bat-CoVs and their hosts using both functional (receptor) and neutral genes. We will predict host-range in unsampled species using a generalizable model of host and viral ecological and phylogenetic traits to explain patterns of viral sharing between species. We will test for positive selection in market vs. wild-sampled viruses, and use data to parameterize mathematical models that predict CoV evolutionary and transmission dynamics. We will then examine scenarios of how CoVs with different transmissibility would likely emerge in wildlife markets.

Specific Aim 3: Testing predictions of CoV inter-species transmission. We will test our models of host range (i.e. emergence potential) experimentally using reverse genetics, pseudovirus and receptor binding assays, and virus infection experiments in cell culture and humanized mice. With bat-CoVs that we've isolated or sequenced, and using live virus or pseudovirus infection in cells of different origin or expressing different receptor molecules, we will assess potential for each isolated virus and those with receptor binding site sequence, to spill over. We will do this by sequencing the spike (or other receptor binding/fusion) protein genes from all our bat-CoVs, creating mutants to identify how significantly each would need to evolve to use ACE2, CD26/DPP4 (MERS-CoV receptor) or other potential CoV receptors. We will then use receptor-mutant pseudovirus binding assays, in vitro studies in bat, primate, human and other species' cell lines, and with humanized mice where particularly interesting viruses are identified phylogenetically, or isolated. These tests will provide public health-relevant data, and also iteratively improve our predictive model to better target bat species and CoVs during our field studies to obtain bat-CoV strains of the greatest interest for understanding the mechanisms of cross-species transmission.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : Year 5 NIAID CoV Report Accomplishments Final.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File Uploaded : B4 Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

1. Conference and University Lectures: PI Daszak and Co-investigators Shi, Epstein, Olival, and Zhang gave invited conference and university lectures at The US-China Dialogue on the Challenges of Emerging Infections, Laboratory Safety and Global Health Security in Galveston, US; the US-China Workshop on Frontiers in Ecology and Evolution of Infectious Diseases in Berkeley, US and Shenzhen, China; the Sino-Germany symposium "Globalization-Challenge and Response for Infectious Diseases" in Hamburg, Germany; the 8th International Symposium on Emerging Viral Diseases in Wuhan, China; the Global Virome Project meeting, Bangkok, Thailand; the Western Asia Bat Research Network (WAB-Net) workshop, Tbilisi, Georgia; the International Conference on Emerging Infectious Diseases (ICEID), Atlanta, US; the North American Society for Bat Research (NASBR) Conference, Puerta Vallerta, Mexico; and the 3rd Symposium of Biodiversity and Health in Southeast Asia, Chiayi, Taiwan

2. Agency and other briefing: PI Daszak and Co-investigators Shi, Olival presented this project at the Cary Institute for Ecosystem Studies, New York, US; the National Institute for Viral Disease Control and Prevention, China CDC; the Chinese Academy of Sciences; and the Chinese Academy of Medical Sciences

3. Public outreach: PI Daszak and Co-investigator Shi, Epstein, Olival, have presented this work to the general public in a series of meetings over Year 5 including at a Cosmos Club briefing that EcoHealth Alliances hosts in Washington DC, multiple meetings of the China National Virome Project and the Global Virome Project in China, Europe, Australia, Southeast Asia and Latin America. As in Year 4, Co-Investigator Zhu introduced this work to the conservation and ecological research community in China through field training workshops.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

The results of the 5th year of our R01 work are detailed below. They include:

Specific Aim 1: Assessment of CoV spillover potential at high-risk human-wildlife interfaces

During Year 5, we finalized the analysis of both quantitative and qualitative data from human surveillance in three provinces in Southern China: Yunnan, Guangxi, and Guangdong provinces.

1.1 High-risk human-animal interaction increase bat coronavirus spillover potential among rural residents in southern China

We conducted a cross-sectional biological behavioral surveillance in Yunnan, Guangxi, and Guangdong provinces from 2015 to 2017. From 8 study sites, a total of 1,596 residents were enrolled, of these, 1,585 participants completed the questionnaires and 11 participants withdrew from the questionnaire interview due to personal schedule reasons. After the interviews, 1,497 participants provided biological samples for lab analysis **(Fig. 1)**.

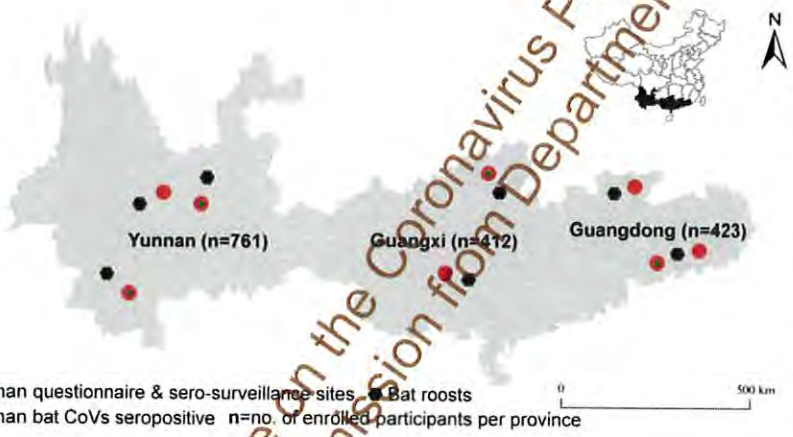


Fig. 1: Eight field surveillance sites for human questionnaire & sero-surveillance with concurrent bat sampling in Yunnan, Guangxi, Guangdong provinces in Southern China. Bat coronavirus sero-positivity were detected in human population in four sites in this study

1.1.1 Demographics

There were more female (62%) than male (38%) from the communities participated in this study. Most participants were adults over 45 years old (69%) and had been living in the community for more than 5 years (97%) with their family members (95%). A majority relied on a comparatively low family annual per capita income less than 10,000 RMB (86%), which is below the national level of per capita disposable income of rural households from 2015 to 2017. Most participants (98%) had not received a higher education from college and were making a living on crop production (76%). 9% of the participants frequently traveled outside the county as migrant laborers.Some participants were working in sectors where frequent human-animal contacts occur, such as the animal production business (1.7%), wild animal trade (0.5%), slaughterhouses or abattoirs (0.5%), protected nature reserve rangers (0.4%) or in wildlife restaurants (0.3%). It was common for participants to have multiple part-time jobs as income sources **(Table 1)**.

Variable	Total	
	N	Valid %
Gender (n= 1,574)		
Fema e	968	61.5
Ma e	605	38.4
Other	1	0.1
Age (n=1,582)		
Under 18 years	71	4.5
18 to 44 years	420	26.5
45 to 64 years	780	49.3
Age 65 or o der	311	19.7
Province (n=1,585)		
Guang Dong	420	26.5
Guang X	412	26.0
Yun Nan	753	47.5
Time of residence (n=1,568)		
< 1 month	4	0.3
1 month – 1 year	12	0.8
1 year – 5 years	26	1.7
> 5 years	1,526	97.3
Family annual per capita income (RMB) (n=1,565)		
<1000	271	17.3
1001-10000	1067	68.2
>10000	227	14.5
Activities to earn livelihood since last year		
Extract on of m nera s, gas, o , t mber (n=1,566)	5	0.3
Crop product on (n=1,569)	1,196	76.2
W d fe restaurant bus ness (n=1,564)	5	0.3
W d/exot c an ma trade/market bus ness (n=1,566)	8	0.5
Rancher/farmer an ma product on bus ness (n=1,566)	27	1.7
Meat process ng, s aughterhouse, abatto r (n=1,567)	8	0.5
Zoo/sanctuary an ma hea th care (n=1,565)	1	0.1
Protected area worker (n=1,567)	7	0.4
Hunter/trapper/f sher (n=1,565)	3	0.2
Forager/gatherer/non-t mber forest product co ector (n=1,566)	4	0.3
M grant aborer (n=1,567)	144	9.2
Nurse, doctor, hea er, commun ty hea th worker (n=1567)	7	0.4
Construct on (n=1,564)	41	2.6
Other (n=1,568)	293	18.7
Highest level of education you completed (n=1,570)		
None	428	27.3
Pr mary Schoo	632	40.3
Secondary schoo /Po ytechn c schoo	479	30.5
Co ege/un vers ty/profess ona	31	2.0
Live with family (n=1,564)		
No	73	4.7
Yes	1491	95.3

Table 1: Demographics of study participants. Total counts differ due to missing responses.

1.1.2 Animal contact and exposure to bat coronaviruses

Serological testing of serum samples from 1,497 local residents revealed 9 individuals (0.6%) were positive for bat coronavirus, indicating exposure at any point in their life to bat-born SARS-related Coronavirus (n=7, Yunnan) and HKU10 Coronavirus (n=2, Guangxi), or other coronaviruses that are phylogenetically closely related to these two coronaviruses (Table 2). All individuals who tested positive (male=6, female=3) were over 45 years old, and most (n=8)

were making a living from crop production.None of those participants reported any symptoms in the preceding 12 months in the interview.

Site	# tested	Bat CoV + (%)	SARSr-CoV Rp3 + (%)	HKU10 + (%)	HKU9 + (%)	MERS-CoV+ (%)
J nn ng, Yunnan	209	6 (2.87)	6 (2.87)	-	-	-
Meng a, Yunnan	168	1 (0.6)	1 (0.6)	-	-	-
J nghong, Yunnan	212	-	-	-	-	-
Lufeng, Yunnan	144	-	-	-	-	-
Guangdong	420	-	-	-	-	-
Guangx	412	2 (0.48)	-	2 (0.48)	-	-

Table 2: ELISA testing of human sera for 4 bat CoVs

Due to the low rate of sero-positivity, we did not conduct statistical comparisons of animal-contact behavior by coronavirus outcome. Figure 2 shows animal contact rates among the survey population (n= 1,585) and among sero-positive individuals (n=9).Participants reported common contact with poultry and rodents/shrews, and most animal contact occurred in domestic settings through raising animal or food preparation activities.

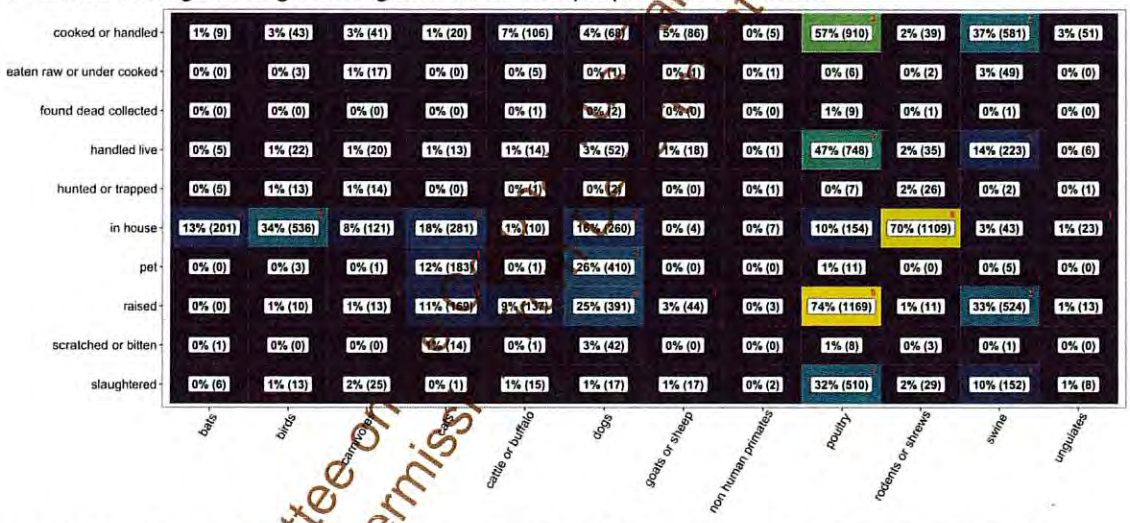


Fig. 2: Animal contact by taxa and activities. Values and shading represent survey population; red numbers in upper-right corners of cells indicate the number of sero-positive individuals with the given contact.

1.1.3 Self-report SARI/ILI symptoms and animal contact

Among the 1,585 participants who responded, 17% (n=265) had experienced fever with cough and shortness of breath or difficulty breathing (38, 14%), indicative of severe acute respiratory infection (SARI), or fever with muscle aches; cough, or sore throat (192, 72%), indicative of influenza like illness (ILI), or both symptoms (35, 13%) in the past 12 months.

LASSO analyses of the associations between animal contact and self-report SARI or ILI symptoms showed that eating raw or undercooked carnivores (OR = 1.6; bootstrap support = 0.67) was the most salient predictor of experiencing SARI or ILI symptoms, followed by slaughtering poultry as a resident of Guangxi province (OR = 1.4; support = 0.68); having an income below 10,000 as a resident of Guangxi province (OR = 1.3; support = 0.84); domestic

contact with bats (OR = 1.3 ; support = 0.63) and domestic contact with rodents or shrews as a resident of Guangdong province (OR = 1.2; support = 0.63) **(Fig. 3)**.

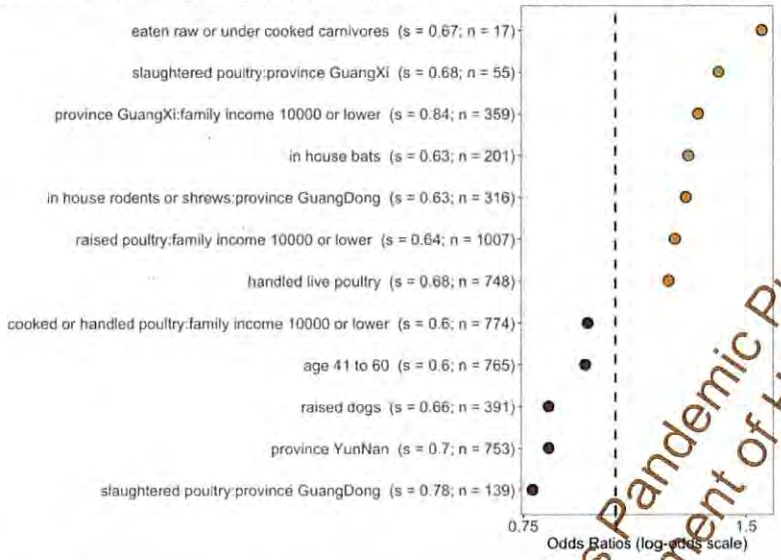


Fig. 3: Most salient predictors of self-reported ILI and/or SARI symptoms in the last year (s = bootstrap support; n = count positive out of 1585 respondents). Bootstrap support values = 0.6 are demonstrated here meaning they were identified as associated with the outcome for 60% or more of the bootstrap iterations. Odds ratios > 1 (orange) are positively associated with the outcome, and odds ratios <1 (purple) are negatively associated with the outcome.

This study provides serological evidence of subclinical or asymptomatic bat-born SARS-related Coronavirus and HKU10 Coronavirus spillover event(s) in rural communities in Southern China, highlights the associations between human-animal interaction and zoonotic spillover risk. The rate of seropositivity observed in this study is clearly lower than would be seen for established human infections. However it has important implications for predicting and preventing pandemics:

1. It indicates that spillover of novel bat-CoVs is detectable if populations that live within areas inhabited by likely bats hosts are targeted. **This provides a pathway to identify spillover events rapidly, perhaps even before a SARS-like disease can become established in people**;
2. It allows us to calculate the likely number of people infected by novel bat SARSr-CoVs annually in this region. Our preliminary analyses suggest that if similar seroprevalence occurs in human populations across the region bat SARSr-CoV hosts inhabit, **there may be as many as the low hundreds of thousands to over a million people infected each year in South China and Southeast Asia.** We aim to conduct a detailed analysis of this in the future.
3. It highlights ways to refine surveillance that could help prevent pandemics, by targeting populations where seroprevalence suggests that they are **at higher risk due to behavioral preferences (e.g. wildlife hunting, farming, or trading)** or where **early-stage SARS-like illnesses could be identified using syndromic surveillance of clinics**.

Contact with poultry and rodents/shrews were commonly reported among participants and associated with self-reported ILI and/or SARI symptoms, which suggests that domestic animals, in addition to wildlife, are an important link in understanding the coronavirus transmission from bat to human populations, indirect exposure might occur through contact with live domestic animals in house or market when the animals had prior exposure to bat coronavirus.

When clinical evidence is limited, undiagnosed or subclinical symptoms similar to SARI and ILI in a population should be brought to our attention as indicators in monitoring zoonotic pathogen spillover events, and considered for prevention strategies. This is particularly important in rural community settings, where people have a higher level of exposure to both domestic and wild animals, but may not seek diagnosis or treatment in a timely fashion, thus slowing the processes of early detection and response.

1.2 Qualitative Approach to Developing Zoonotic Risk Mitigation Strategies in Southern China

To explore the potential drivers of zoonotic exposure and the opportunities for intervention, we conducted field observation and semi-structured ethnographic interviews among 88 community members who have frequent exposure to wildlife and domestic animals and/or have extensive local knowledge in 9 sites in Yunnan, Guangdong, and Guangxi provinces.

The majority of participants in this study were adults between 31 to 50 years of age, residing in rural or suburban areas. Most earned their livelihoods from multiple sources, primarily in crop production, subsistence animal farming, small business, and other temporary jobs as migrant workers. Risk and protective factors were identified at the individual, community, and policy levels regarding potential zoonosis exposures, recommending risk-mitigation strategies with the strengthened policy enforcement and multi-sectoral collaboration among human, animal, and environment health programs **(Fig. 4).**

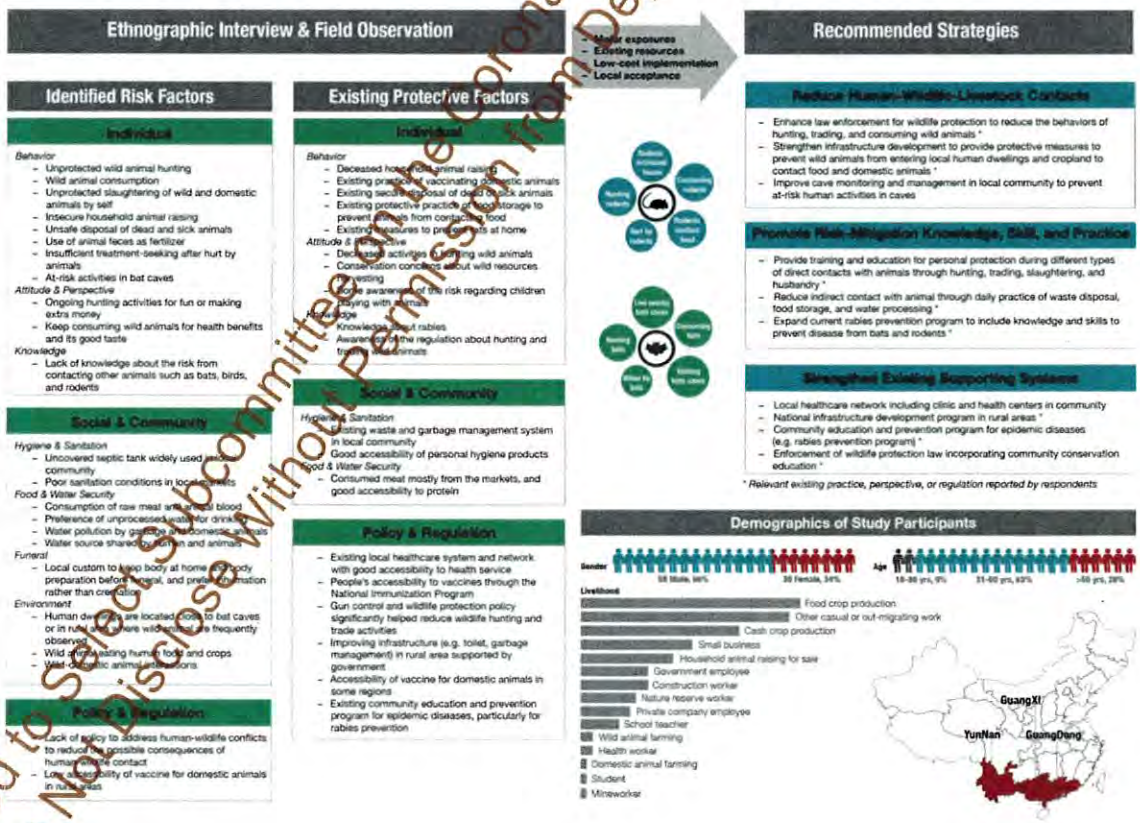


Fig. 1: Community Zoonosis Exposure Risk Mitigation Strategy Development Process. Leveraging ethnographic interview and observational research data to identify risk and protective factors and develop risk-mitigation recommendations

This demonstrated a qualitative approach to understand the zoonotic risks in community, and provided guidance for future research and interventions with focused potential zoonotic risks for disease control and prevention in southern China and a broader area with similar ecological, culture, and demographic contexts.

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk

2.1 Bat CoV PCR detection and sequencing from live-sampled bat populations

From May to October 2018, we collected 1,697 rectal swabs, oral swabs, and feces specimens from 26 bat species in Hubei, Shandong, Yunnan and Guangdong Provinces across southern, central and northern China in Year 5, all specimen were tested for CoV RNA and 109 (6.4%) were positive. SARS-related coronaviruses were discovered in *Rhinolophus sinicus* samples from Yunnan and Hubei provinces while HKU2-related coronaviruses were detected in *R.sinicus* from Hubei. HKU5-related and HKU10-related coronaviruses were identified in *Pipistrellus abramus* from Shandong and *Hipposideros larvatus* from Guangdong, respetively. *Scotophilus* coronavirus 512 was detected in Guangdong. Addtionally, two novel *Pipistrellus* alphacoronaviruses were found in Shandong province in northern China **(Fig. 5)**.

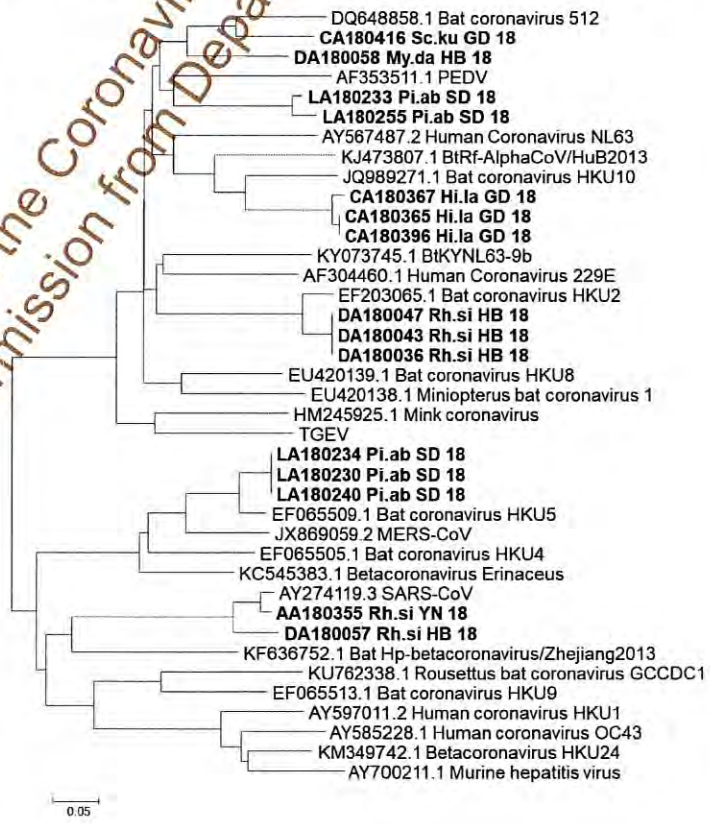


Fig. 2: Phylogenetic analysis of partial RdRp gene of CoV (440-nt partial sequence)

2.2 Bat coronavirus host-virus phylogeography in China

Our dataset includes all CoV RdRp sequences isolated from bat specimens collected by our team from 2008-2015 (Alpha-CoVs: n = 491 – Beta-CoVs: n = 326), including those collected under prior NIAID funding (1 R01 AI079231), and funding from Chinese Federal Agencies. All Chinese bat CoV RdRp sequences available in GenBank were also added to

our dataset (Alpha-CoVs: n = 226 – Beta-CoVs: n = 206). Phylogenetic trees were reconstructed for Alpha- and Beta-CoVs separately using Bayesian inference (BEAST 1.8).

2.2.1 Ancestral hosts and cross-species transmission

We used ancestral character state reconstruction and a Bayesian stochastic search variable selection (BSSVS) to identify host switches between bat families **(Fig. 6)** and genera **(Fig. 7)** that occurred along the branches of the phylogenetic tree and calculated BF to estimate the significance of these non-zero transition rates. We identified nine and three highly supported (BF > 10) **inter-family** host transition rates for alpha- and beta-CoVs, respectively **(Figs. 6A and 6B)**. To quantify the intensity of these host switches, we estimated the number of state changes (Markov jumps) along the significant inter-family transition rates **(Figs. 6C and 6D)**. The total estimated number of inter-family host jump events was more than eight times higher in the evolutionary history of alpha- (n = 90) than beta-CoVs (n = 11) in China. Host transition events from Rhinolophidae and Miniopteridae were greater than from other families for alpha-CoVs while Rhinolophidae were the highest donor family for beta-CoVs. Rhinolophidae and Hipposideridae were the families receiving the highest numbers of transition events for alpha- and beta-CoVs, respectively **(Figs. 6C and 6D)**.

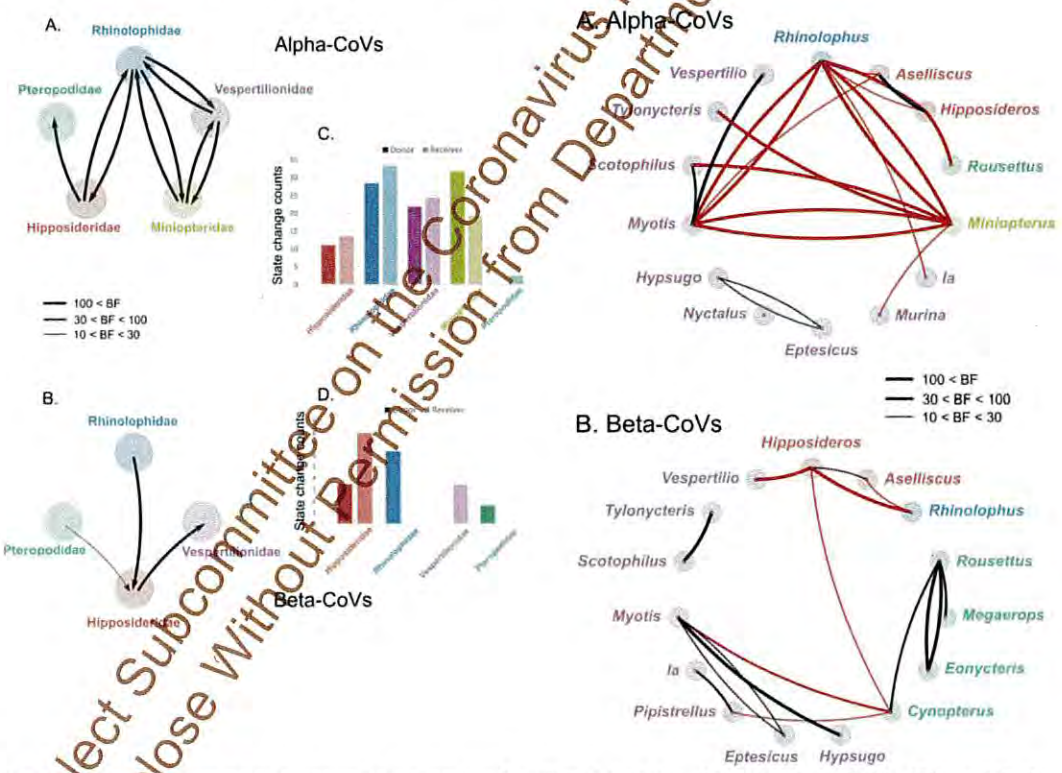


Figure 3: Non-zero transition rates between bat families for alpha- **(A)** and beta-CoVs **(B)** and their significance level (Bayes factor, BF), BF < 10 are considered as non-significant. Arrows indicate the direction of the transition; arrow thickness is proportional to the transition significance level. Histograms show total number of state changes (Markov jumps) from/to each bat family along the significant inter-family transition rates for alpha- **(C)** and beta-CoVs **(D)**.

Figure 4: Non-zero transition rates between bat genera for alpha- **(A)** and beta-CoVs **(B)** and their significance level (Bayes factor, BF), BF < 10 are considered as non-significant. Lines with a rightward curvature depict transitions from that bat genus, while lines with leftward curvature depict transition to that bat genus. Inter-family transitions are highlighted in red.

At the genus level, we identified 20 highly supported inter-genus host transition rates for alpha-CoVs **(Fig. 7A)**. *Rhinolophus* and *Myotis* were the donor genera in four of these transitions while *Miniopterus* and *Rhinolophus* were each the recipients of four of these transitions **(Fig. 7A)**. Sixteen highly supported inter-genus transition rates were identified for beta-CoVs **(Fig.7B)**. Four of these 16 host switches originated in *Cynopterus* while three of them ended in *Myotis* **(Fig. 7B)**. Fifteen out of the 20 significant pairwise host transitions (75%) for alpha-CoVs involved two genera belonging to different bat families, while this proportion is only 6/16 (37.5%) for beta-CoVs. This confirmed the highest number of inter-family host transitions for alpha-CoVs. The estimated total number of inter-genus host switches was almost two times higher for alpha- (n = 123) than beta-CoVs (n = 70).

These findings indicate that alpha-CoVs were able to switch hosts more frequently and between more distantly related taxa during their evolution and suggest that phylogenetic distance among hosts represents higher constraint on host switches for beta- than alpha-CoVs.

2.2.2 CoV spatiotemporal dispersal in China

We also used our Bayesian discrete phylogeographic model using zoogeographic regions as character states to reconstruct the spatiotemporal dynamics of CoV dispersal in China. Eleven and seven highly significant (BF > 10) dispersal routes within China were identified for alpha- and beta-CoVs, respectively **(Fig. 8A and 8B)**. The Rhinacovirus lineage that includes HKU2 and SADS-CoV likely originated in SO region while all other alpha-CoV lineages likely arose in SW China and spread to other regions before several dispersal events occurred from SO and NO in all directions **(Fig. 8A)**.

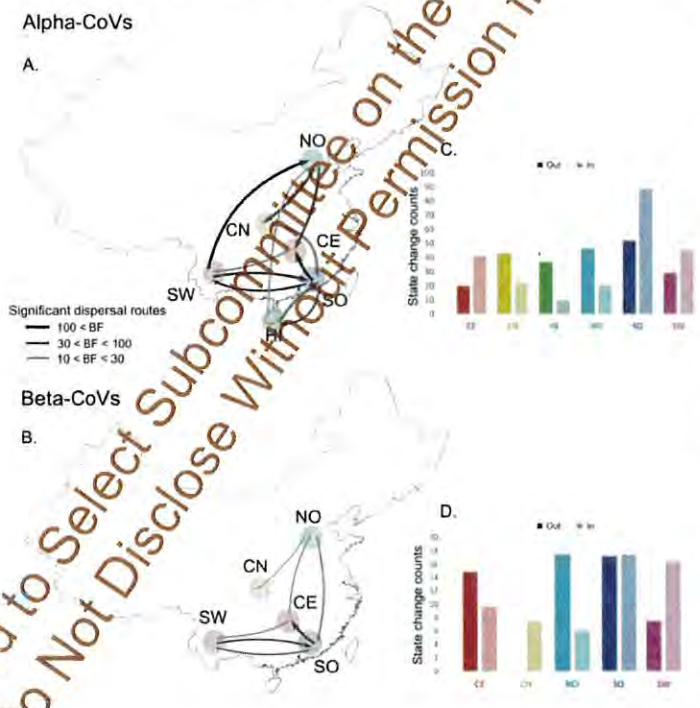


Fig. 8: Significant dispersal routes among China zoogeographic regions for alpha- **(A)** and beta-CoVs **(B)**. Arrows indicate the direction of the transition; arrow thickness is proportional to the transition significance level. Darker arrow colors indicate older dispersal events. **Fig. 8 (C & D)** Histograms of total number of state changes (Markov jumps) from/to each region along the significant dispersal routes for alpha- **(C)** and beta-CoVs **(D)**. NO, Northern region; CN, Central northern region; SW, South western region; CE, Central region; SO, Southern region; HI, Hainan island.

The oldest inferred dispersal movements among beta-CoVs occurred among SO and SW regions **(Fig. 8B)**. SO region is the likely origin of Merbecovirus (Lineage C, including HKU4 and

HKU5) and Sarbecovirus subgenera (Lineage B, including HKU 3 and SARS-related CoVs) while Nobecovirus (lineage D) and Hibecovirus (lineage E) subgenera originated in SW-China. Then several dispersal movements likely originated from SO and CE **(Fig. 8B)**. More recent southward dispersal from NO was observed.

The estimated total number of migration events along these significant dispersal routes is four times higher for alpha- (n = 227) than beta-CoVs (n = 57). SO has the highest number of outbound and inbound migration events for alpha-CoVs **(Fig. 8C)**. For beta-CoVs, the highest numbers of outbound migration events have been estimated from NO and SO while SO and SW have the highest numbers of inbound migration events **(Fig. 8D)**.

Our Bayesian ancestral reconstructions revealed the high importance of South western and Southern China as centers of diversification for both alpha- and beta-CoVs. These two regions are clearly hotspots of CoV phylo-diversity, harboring evolutionary old and phylogenetically diverse lineages of alpha- and beta- CoVs.

2.2.3 Phylogenetic diversity

In order to quantitatively evaluate the diversity and the clustering process in our phylogenies, the Mean Phylogenetic Distance (MPD) and the Mean Nearest Taxon Distance (MNTD) statistics and their standardized effect size (SES) were calculated for each zoogeographic region, bat family and genus. The SES corresponds to the difference between the phylogenetic distances in the observed communities versus null communities built by randomly reshuffling tip labels 1000 times along the entire phylogeny. Low and negative SES values denote phylogenetic clustering, high and positive values indicate phylogenetic over-dispersion while values close to 0 show random dispersion.

Significant negative SES MPD values ($p < 0.05$), indicating basal phylogenetic clustering, were observed within all bat families and genera for both alpha- and beta-CoVs, except within *Aselliscus* and *Tylonycteris* for alpha-CoVs **(Figs. 9A & B)**. Negative and mostly significant SES MNTD values, reflecting phylogenetic structure closer to the tips, were also observed within most bat families and genera for alpha- and beta-CoVs but we found non-significant positive SES MNTD value for Vespertilionidae and *Pipistrellus* for beta-CoVs (Fig. 4A and 4B). In general, we observed lower phylogenetic diversity for beta- than alpha-CoVs within all bat families and most genera when looking at SES MPD, while similar level of diversity are observed when looking at SES MNTD **(Figs. 9A & B)**. These results suggest stronger basal clustering (at the deeper nodes) for beta-CoVs than alpha-CoVs.

Chinese zoogeographic regions don't harbor a random set of CoVs as alpha- and beta-CoV strains within most regions are more closely related than expected by chance as denoted by negative and mostly significant values of MPD and MNTD **(Fig. 9C)**. However, positive SES MPD value for alpha-CoVs in SW indicate wider evolutionary diversity in that region **(Fig. 9C)**.

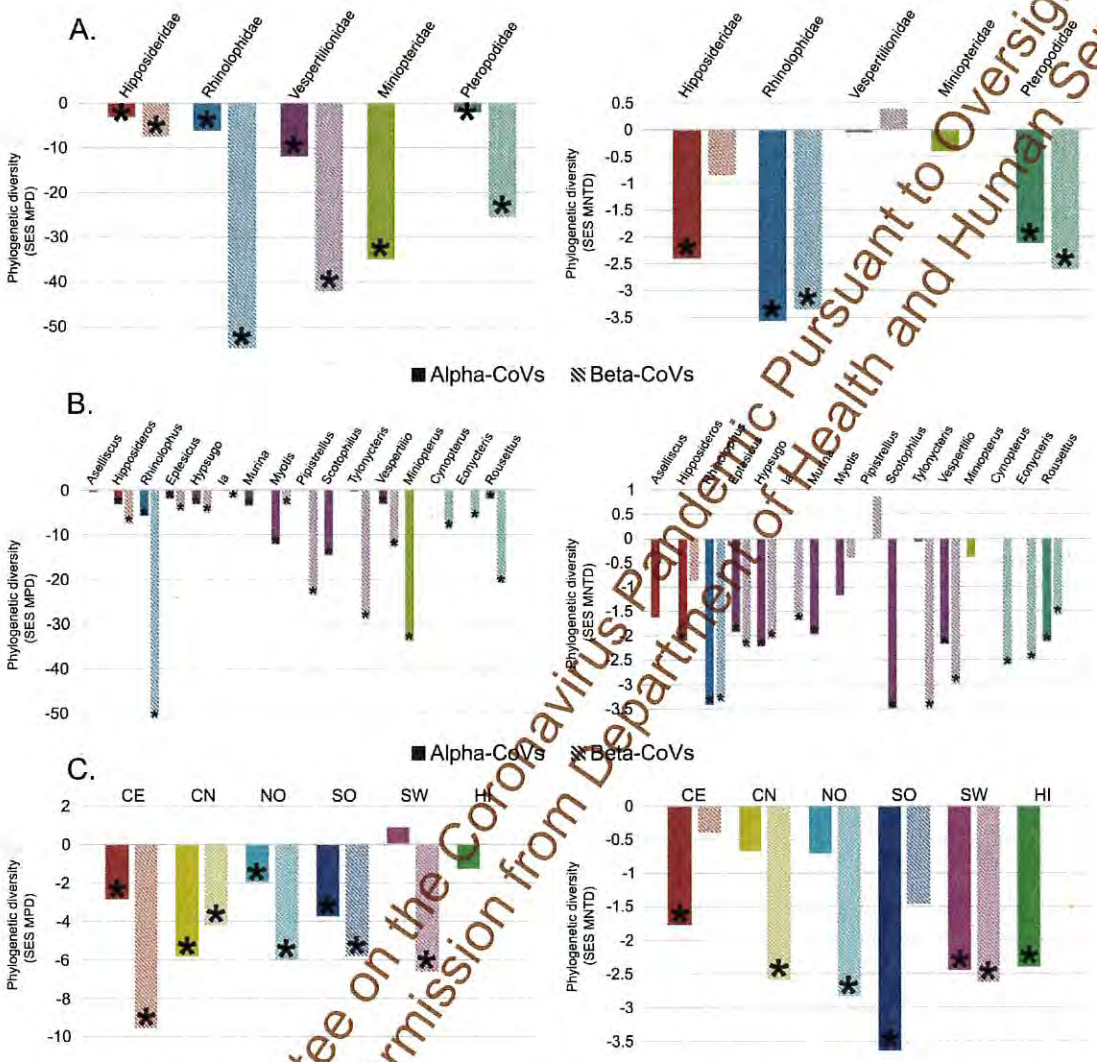


Fig. 9: CoV phylogenetic diversity bat families **(A),** genera **(B),** and zoogeographic regions **(C)**: SES MPD, standardized effect size of Mean Phylogenetic Distance **(Left)**; and SES MNTD, standardized effect size of Mean Nearest Taxon Distance **(Right)**. Values departing significantly from null model (p-value < 0.05) indicated with an asterisk. NO, Northern region; CN, Central northern region; SW, South western region; CE, Central region; SO, Southern region; HI, Hainan island.

2.3 Characterization of SADSr-CoV coronaviruses diversity and distributions

In previous project years, our team identified and characterized Swine Acute Diarrheal Syndrome coronavirus (SADS-CoV), a novel swine virus causing outbreaks in farms in multiple Chinese provinces.In this year, we were able to identify SADS-related CoVs in bats from our wild bat sampling.In >17,000 bat and other mammals at 47 sites across southern China, we found 78 new SADSr-CoVs[11], all in 9 bat species, with mean prevalence of 0.1 to 37.5%.

Our phylogenetic analysis suggests that pig SADS-CoV recently spilled over from *R. sinicus* or *R. affinis* bats **(Fig. 10 Left)** However, analysis of full pig viral genomes from 4 initially infected

farms suggests that either the virus evolved as it circulated or that multiple spillover events occurred **(Fig. 10 Right)**.

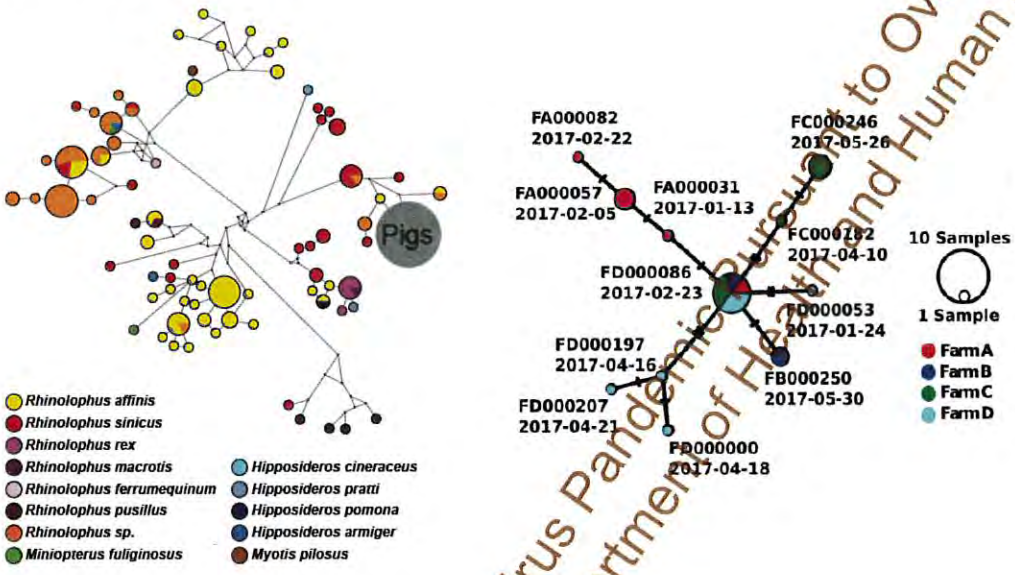


Fig. 10: Left: Median joining network of conserved RdRp gene fragment of 198 unique SADSr-CoV sequences discovered in China under our previous funding. Size of circle proportional to the number specimens with identical viral sequences. **Right:** Median joining network of SADS-CoV full genome sequence data from 4 infected pigs farms in S. China.

We built species distribution models of the major bat species hosts of SADSr-CoVs across southeast Asia to determine the areas where their ranges intersect with large swine operations similar to those of the original outbreak. We found that these are Southern China (including Taiwan), throughout Vietnam, the Philippines, and Thailand. Compared to other countries, China had the largest area of bat-pig overlap with 329,847 km2 (3.4% of total country area) and 2,127,006 pigs located within predicted bat distributions. By Chinese province, the largest area of overlap was found in Jiangsu (35,226 km2 amounting to 34.3% of the province's area and 242,299 pigs within this area). Sichuan had the largest pig population at risk (the pig population within an area that intersects with predicted bat occurrence), at 274,353 heads over 26,015 km2 (5.4% of the total area of the province) **(Figs. 11 & 12)**.

Fig. 5: Areas of bat-pig overlap where probability of SADS-CoV Rhinolophus spp. reservoir occurrence is high (>75%) and pig densities are indicative of intensive pig farming (>100 heads per km2).

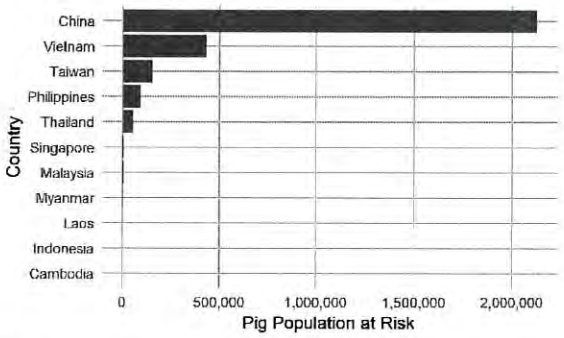


Fig. 6: Top: Country-level, and **Bottom:** province-level estimate of swine populations at-risk based on overlap between modeled populations of bat species known to be SADSr-CoV hosts and large swine operations.

Specific Aim 3: Testing Predictions of CoV Inter-Species Transmission

3.1 *In vivo* infection of Human ACE2 (hACE2) expressing mice with SARSr-CoV S protein variants

In Year 5, we continued with *in vivo* infection experiments of diverse bat SARSr-CoVs on transgenic mice expressing human ACE2. Mice were infected with 4 strains of SARSr-CoVs with different S protein, including the full-length recombinant virus of SARSr-CoV WIV1 and three chimeric viruses with the backbone of WIV1 and S proteins of SHC014, WIV16 and Rs4231, respectively. Pathogenicity of the 4 SARSr-CoVs was evaluated by recording the survival rate of challenged mice in a 2-week course. All of the 4 SARSr-CoVs caused lethal infection in hACE2 transgenic mice, but the mortality rate vary among 4 groups of infected mice **(Fig. 13a)**. 14 days post infection, 5 out of 7 mice infected with WIV1 remained alive (71.4%), while only 2 of 8 mice infected with rWIV1-SHC014 S survived (25%). The survival rate of mice infected with rWIV1-WIV16S and rWIV1-4231S were 50%. Viral replication was confirmed by quantitative PCR in spleen, lung, intestine and brain of infected mice. In brain, rWIV1, rWIV1-WIV16S and rWIV1-4231S cannot be detected 2 days or 4 days post infection. However, rWIV1-SHC014 was detected at all time points and showed an increasing viral titer after infection. The viral load reached more than 10^9 genome copies/g at the dead point **(Fig. 13b)**. We also conducted histopathological section examination in infected mice. Tissue lesion and lymphocytes infiltration can be observed in lung, which is more significant in mice infected with rWIV1-SHC014 S **(Fig. 13d)** than those infected with rWIV1 **(Fig. 13c)**. These results suggest that the pathogenicity of SHC014 is higher than other tested bat SARSr-CoVs in transgenic mice that express hACE2.

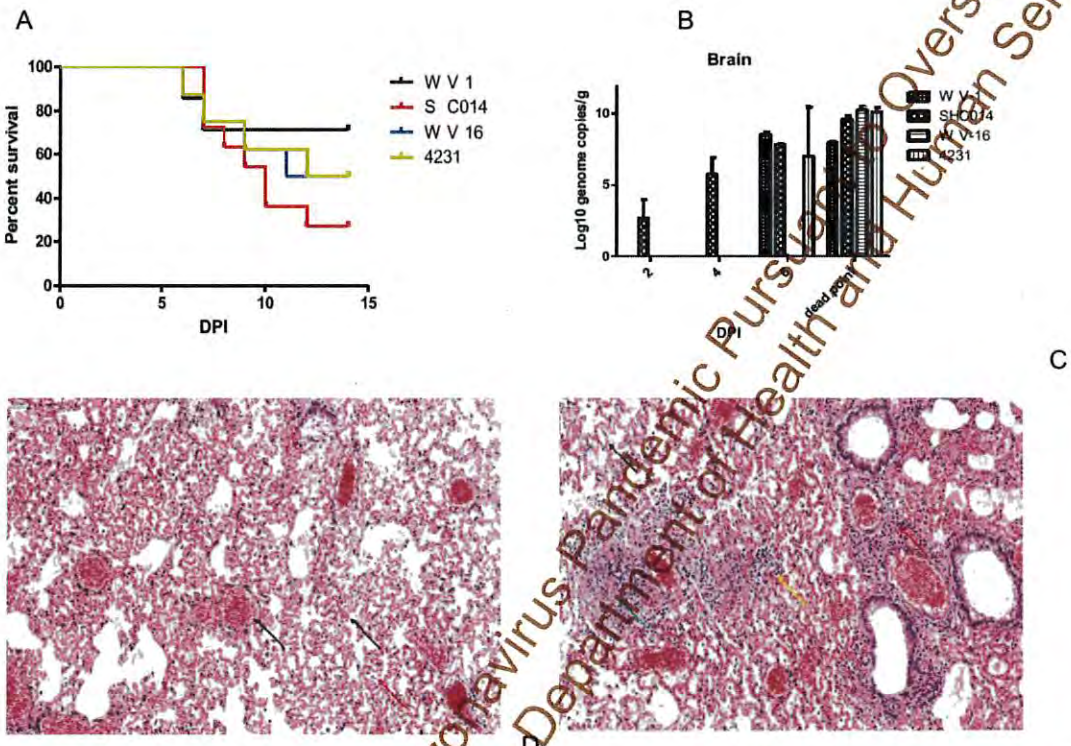


Fig. 13: *In vivo* infection of SARSr-CoV in hACE2-expressing mice. **(A)** Survival rate of hACE2_mice after infection **(B)** Viral load in brains of infected hACE2-expressing mice. **(C)** Histopathological section of lung tissue of mice infected with rWIV1. **(D)** Histopathological section of lung tissue of mice infected with rWIV1-SHC014 S.

3.2 Assessment of interspecies transmission risk of bat HKU4-related coronaviruses

Taking a similar reverse genetics strategy that we used in SARSr-CoV studies, we constructed the full-length infectious clone of MERS-CoV, and replaced the RBD of MERS-CoV with the RBDs of various strains of HKU4-related coronaviruses previously identified in bats from different provinces in southern China. The full-length MERS-CoV and chimeric viruses with RBDs of HKU4r-CoVs were then rescued. Immunofluorescence assay showed that these chimeric MERS-HKU4rRBD coronaviruses were able to infect human cells from different tissues including lung, liver, intestine and kidney **(Fig. 14 Left)**. Moreover, efficient replication of the chimeric HKU4r-CoVs were detected by real-time PCR in HeLa cells that expressed human DPP4 receptor **(Fig. 14 Right)**. The results suggest potential risk of the bat HKU4r-CoVs for cross-species infection in humans.

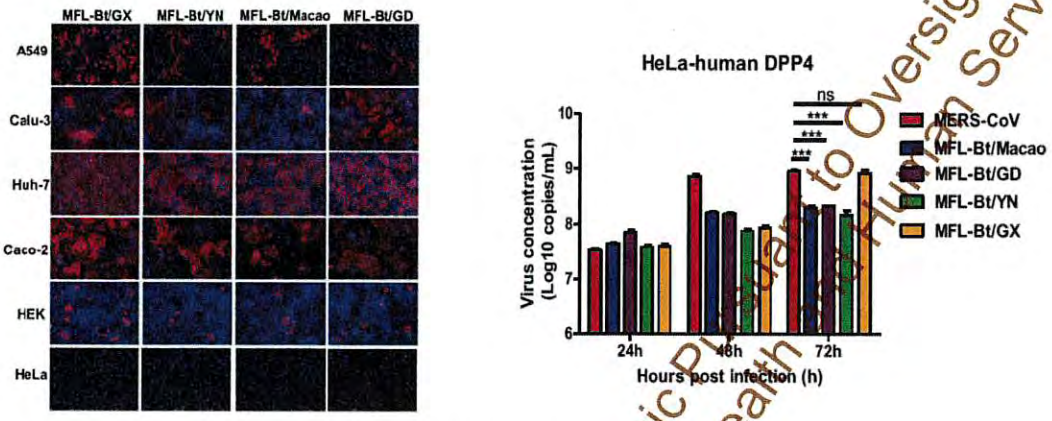


Fig. 7: Left: Immunofluorescence assay confirms Infection of 4 chimeric viruses with the backbone of MERS-CoV and RBD of bat HKU4r-CoVs in different cell lines derived from human tissues. **Right:** Replication of MERS-HKU4rRBD CoVs in HeLa cells expressing human DPP4 was determined by real-time PCR.

B.4 (B4 Training.pdf)

1. Conference and University lectures: We continued to provide human subject research trainings to chief physicians and nurses at local clinics, staff from Yunnan Institute of Endemic Diseases Control and Prevention, students from Dali College and Wuhan University for both qualitative and quantitative research.
2. Agency and other briefing: Dr. Guangjian Zhu provided training to 18 field team members from the Dali College and 4 Wuhan Insitute of Virology laboratory team members regarding biosafety and PPE use, bats and rodents sampling.
3. Public outreach: PI Daszak, and Co-investigators Shi, Epstein, and Olival presented the Year 5 results of this project to the public via interviews with national central and local television, social media, newspaper and journals in China and the US.

C. PRODUCTS

C.1 PUBLICATIONS Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award? No
C.2 WEBSITE(S) OR OTHER INTERNET SITE(S) NOTHING TO REPORT
C.3 TECHNOLOGIES OR TECHNIQUES NOTHING TO REPORT
C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No
C.5 OTHER PRODUCTS AND RESOURCE SHARING NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
[redacted]	Y	DASZAK, PETER	BS,PHD	PD/PI	[redacted]	[redacted]	[redacted]			NA
	N	KE, CHANGWEN	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	Center for Disease Control and Prevention of Guangdon g Province	CHINA	NA
	N	ZHANG, YUNZHI	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	Yunnan Provincial Institute of Endemic Diseases Control & Prevention	CHINA	NA
	N	ZHU, GUANGJIAN	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	East China Normal University	CHINA	NA
[redacted]	N	Chmura, Aleksei	BS,PHD	Non-Student Research Assistant	[redacted]	[redacted]	[redacted]			NA
[redacted]	N	Ross, Noam Martin	PhD	Co-Investigator	[redacted]	[redacted]	[redacted]			NA
[redacted]	N	Olival, Kevin J.	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]			NA
[redacted]	N	Zhang, Shu-yi	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	East China Normal University	CHINA	NA
[redacted]	N	SHI, ZHENGLI	PhD	Co-Investigator	[redacted]	[redacted]	[redacted]	Wuhan Institute of Virology	CHINA	NA
	N	GE, XINGYI	PHD	Co-Investigator	[redacted]	[redacted]	[redacted]	Wuhan Institute of Virology	CHINA	NA
[redacted]	N	EPSTEIN, JONATHAN H	MPH,DVM,BA,PHD	Co-Investigator	[redacted]	[redacted]	[redacted]			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable
D.2.b New Senior/Key Personnel Not Applicable
D.2.c Changes in Other Support Not Applicable
D.2.d New Other Significant Contributors Not Applicable
D.2.e Multi-PI (MPI) Leadership Plan Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Dollar Amount	Country
$66,500	CHINA

G. SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Sub-Project ID	Study ID	Study Title	Delayed Onset	Clinical Trial	NCT	NIH-Defined Phase 3	ACT
	58010	Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001	NO	NO		NO	

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Organization Name: Wuhan Institute of Virology
Country: CHINA

Description of Foreign Component: Principal Laboratory for all Research in China and detailed in our Specific Aims
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

Section 1 - Basic Information (Study 58010)

OMB Number: 0925-0001
Expiration Date: 02/28/2023

1.1. Study Title *

Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001

1.2. Is this study exempt from Federal Regulations *	○ Yes	● No						
1.3. Exemption Number	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	❑ 6	❑ 7	❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	○ Yes	● No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	○ Yes	● No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	○ Yes	● No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 58010)

2.1. Conditions or Focus of Study		
2.2. Eligibility Criteria		
2.3. Age Limits	Min Age:	Max Age:
2.3.a. Inclusion of Individuals Across the Lifespan		
2.4. Inclusion of Women and Minorities		
2.5. Recruitment and Retention Plan		
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline		
2.8. Enrollment of First Participant (SEE SECTION 6.3)		

2.9. Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
IER 58010	Foreign	

Inclusion Enrollment Report 58010

1. Inclusion Enrollment Report Title* : China Study Report

2. Using an Existing Dataset or Resource* : ○ Yes ● No

3. Enrollment Location Type* : ○ Domestic ● Foreign

4. Enrollment Country(ies): CHN: CHINA

5. Enrollment Location(s):

6. Comments:

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	1230	1230	0	0	2460
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More than One Race	0	0	0	0	0
Total	1230	1230	0	0	2460

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	980	616	0	0	0	0	0	0	0	1596
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	980	616	0	0	0	0	0	0	0	1596

Section 3 - Protection and Monitoring Plans (Study 58010)

3.1. Protection of Human Subjects

3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site? ○ Yes ○ No ○ N/A

If yes, describe the single IRB plan

3.3. Data and Safety Monitoring Plan

3.4. Will a Data and Safety Monitoring Board be appointed for this study? ○ Yes ○ No

3.5. Overall structure of the study team

Section 4 - Protocol Synopsis (Study 58010)

4.1. Study Design

4.1.a. Detailed Description

4.1.b. Primary Purpose

4.1.c. Interventions

Type	Name	Description

4.1.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ○ Yes ● No

4.1.e. Intervention Model

4.1.f. Masking ○ Yes ○ No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.1.g. Allocation

4.2. Outcome Measures

Type	Name	Time Frame	Brief Description

4.3. Statistical Design and Power

4.4. Subject Participation Duration

4.5. Will the study use an FDA-regulated intervention? ○ Yes ○ No

4.5.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND), Investigational Device Exemption (IDE) status

4.6. Is this an applicable clinical trial under FDAAA? (SEE SECTION 6.6)

4.7. Dissemination Plan

I. OUTCOMES

I.1 What were the outcomes of the award?

The aims of our grant (R01AI110964) were to: 1) Analyze the risk that there could be a repeat of the SARS outbreak, due to bat coronaviruses still circulating in China; 2) Work out how we can predict which bat viruses would be most likely to emerge, so that we can prevent new outbreaks; 3) Using lab tests, find out if any of the coronaviruses still present in bat populations in China have the potential to infect people. The overall goal of this work is to help design vaccines and therapeutics against future potentially emerging viruses, work out which communities are on the frontline of a new potential outbreak, and reduce the risk of them being infected by analyzing their risk behavior. During this 5-year period of work, we made significant discoveries leading to 18 peer-reviewed scientific papers, including in some of the world's foremost scientific journals.

Overall, our work shows that bats in China harbor a high number and diversity of coronaviruses, some closely related to SARS-CoV (the virus that caused the SARS pandemic in 2003). We sampled over 16,000 individual bats and found evidence of hundreds of different SARS-related coronavirus genetic sequences. We found out that bats across China harbor these viruses, and that they are common, with 6.7% of bats sampled being positive. Many of these bats are found across China, Southeast Asia, South Asia and beyond, suggesting viruses with zoonotic potential may exist in those regions also. Many of these bats are abundant, and roost and feed close to people and livestock, suggesting high potential for future viral spillover. We also dentified one cave system in Yunnan Province with horseshoe bats that had diverse SARSr-CoVs, including some with S proteins able to use human ACE2 as entry receptors. Bats in this cave carried SARSr-CoVs with all unique genetic elements of the SARS-CoV outbreak virus, suggesting that this site may be a potential public health risk.

To analyze which viruses were a potential public health risk, we managed to culture three strains of SARSr-CoVs from bat feces: WIV1, WIV16 and Rs4874. We used the genetic codes of some of the other viruses we found in bats and inserted the spike protein genes of those viruses (the proteins that attach to cells) into the cultured viruses. By doing this experiment we showed that other viruses may also be able to infect human cells, and were able to do this safely without the need to culture large amounts of virus. We also showed that some of these viruses cause SARS-like illness in mice that are adapted to have similar cell surface receptors to people. This work proves that there is a clear and present danger for future emergence of novel SARS-like viruses in people. We also demonstrated that outbreaks can happen in livestock. In 2016-17, we analyzed fecal samples from pigs at 5 farms in South China affected by a fatal diarrheal disease. We discovered a new coronavirus, Swine Acute Diarrheal Syndrome coronavirus (SADS-CoV), and showed that it originates in bats, caused the death of more than 20,000 pigs, but also is able to infect human cells in the lab.

Our work has produced predictive algorithms to map hotspots of viral risk so that public health measures can be taken to protect communities at the frontline of potentially the next SARS pandemic. We have produced new reagents and viral cultures that can be used by labs across the world to design novel vaccines and therapeutics against SARS-CoV and other related viruses that might emerge in the future. Finally, our work has been used directly by the WHO to list SARS-related coronaviruses as one of the highest priority group of pathogens with pandemic potential, so that efforts can be taken to stop a future pandemic before it happens.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

5 November 2021

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: R01AI110964

Dear Drs. Chmura and Daszak:

Thank you for your correspondence (including supporting materials) of October 26, 2021. We are requesting additional materials regarding Institutional Animal Care and Use Committee (IACUC) approval for the field work, and the experiments reported in the Year 4 Research Performance Progress Report (RPPR) and Year 5 interim-RPPR (I-RPPR).

IACUC Approval

As we noted before and as required by the NIH Grants Policy Statement (GPS), 4.1.1.2, NIH requires verification of IACUC approval of those sections of the grant application that involve use of vertebrate animals. As noted by the NIH Office of Laboratory Animal Welfare (OLAW) cover letter accompanying your Interinstitutional Agreement for the WIV animal work, "under your approved Assurance with the Wuhan Institute of Virology, their Institutional Animal Care and Use Committee (IACUC) is authorized to carry out subsequent reviews of this project." In the final Vertebrate Animal Section of your Just-in-Time materials submitted on May 16, 2014 for 1 R01 AI110964-01, you stated that "all animal work to be done at Wuhan has been approved by the Wuhan IRB (IACUC) #WIVA05201402. Animals will be housed in a BSL-3 facility and will be under the care of a full-time veterinarian." Thus, it appears that the WIV IACUC approved "all animal work to be done at Wuhan."

In my October 20, 2021 letter, I requested documentation from the *WIV IACUC* regarding approval for *field work* (e.g., work in caves to collect materials from live bats) supported by R01AI110964. You responded by sending us OLAW documentation, not WIV IACUC documentation. This is not documentation demonstrating that the WIV IACUC explicitly approved the field work, the work done outside the BSL-3 facility that involved free-ranging bats and rodents. Therefore, we again ask for you to provide us with *WIV IACUC* documentation of approval for *field work* involving free-ranging bats and wild rodents; or to confirm that no such approval was obtained.

Experiments Described in Year 4 RPPR and Year 5 I-RPPR

In the text description of your Year 5 RPPR Figure 13, you stated, "In Year 5, we continued with in vivo infection experiments of diverse bat SARSr-CoVs on transgenic mice expressing human ACE2. Mice were infected with 4 strains of SARSr-CoVs with different S protein…" In your October 26, 2021 correspondence, you stated that Figure 13 of your Year 5 I-RPPR and Figure 35 of your Year 4 RPPR are taken from the same experiment. You ask that "these facts be acknowledged."

For us to further understand the details of these experiments, please send us complete and dated copies of the original laboratory notebook entries and of the original electronic files that led to the generation of the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13, along with all their accompanying texts (e.g., the Year 5 I-RPPR text in which you stated that "rWIV1-SHC014 was detected at all time points and showed an increasing viral titer after infection…")

Our document requests – for documentation of WIV IACUC approval for field work, the original laboratory notebook entries, and the original electronic files underlying the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13 – are consistent with the term and condition of award that NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. 75.364). This right of access applies not only to awardee records, but also to subawardee records. Awardees indicate their acceptance of an NIH award and its associated terms and conditions as they draw down the NIH grant funds to support the scientific project (see NIHGPS Section 5).

We look forward to receiving these materials by no later than close-of-business on Friday, November 19, 2021.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research

[redacted]

cc: Ms. Emily Linde
Dr. Erik Stemmy

EcoHealth Alliance

November 18th 2021

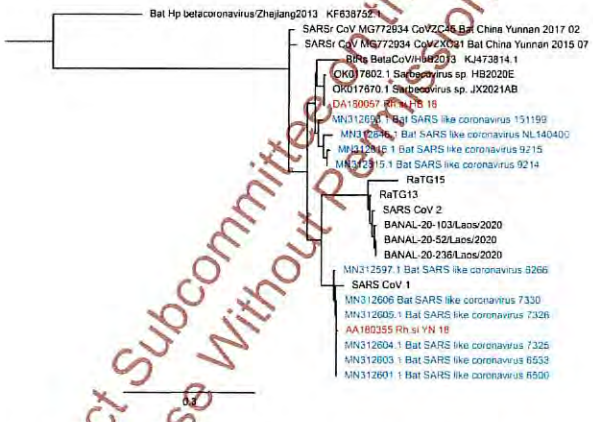
Dear Dr Lauer,

I am responding to your letter requesting further IACUC information and more details on the SARSr-CoV experiments in our Year 4 and 5 reports from R01AI110964.

As I respectfully pointed out just over two weeks ago, on April 24th 2020 you instructed EcoHealth Alliance, Inc. ("EHA") to discontinue all of our contractual work with WIV. We agreed, and informed you that EHA did not have an active contract with WIV at that time. Notwithstanding our compliance, you then informed us that the grant covering this work was terminated. The grant was subsequently reinstated and instantly suspended by NIH and the funds remain unavailable to us due to the proliferating, and logistically near-impossible conditions that NIH has placed on us. The lack of funding and your instructions to cease contractual work with WIV have led to significant disruption of the normal interactions and dialogue among staff at EHA and at the WIV. Despite these challenges, we have continued to comply with all requests from your office, promptly.

I would therefore like to first provide further details on the work in our Year 5 report, and inform you that the RdRp gene sequences of the two SARSr-CoVs we reported then (figure below, highlighted in red), have now been uploaded to the open-access publicly-available, NIH-managed database Genbank (NCBI) by scientists at WIV. Their accession numbers are:

- AA180355: GenBank Accession No. OK663614
- DA180057: GenBank Accession No. OK663615



This will allow scientists from around the world to conduct their own analyses to compare the genetic information from these viruses with others we have reported previously, and with SARS-CoV and SARS-

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

CoV-2. As we reported in our letter of October 26th 2021, the genetic sequences demonstrate that these viruses are, like all other SARS-related CoVs we have discovered in our work under NIH funding, unrelated to the SARS-CoV-2 virus that causes COVID-19.

In response to your specific request for "*WIV IACUC* documentation of approval for field work involving free-ranging bats and wild rodents". As we stated previously, like many other countries, China does not require IACUC approval for *fieldwork* involving wild bats and rodents. The regulations in China that may be relevant to the type of fieldwork in our grant are:

1) Regulation for the collection of genetic resources. This took effect on 1/1/12 and is still in force: https://www.mee.gov.cn/ywgz/fgbz/bz/bzwb/stzl/201109/t20110919_217418.shtml
2) List of State Protected Species. Any animal that is listed as protected requires specific permits to collect or sample. Neither bats nor the other species we worked with under our NIH funding were covered by this rule. The list was revised on 2/5/21: http://www.gov.cn/xinwen/2021-02/09/content_5586227.htm

Even though IACUCs are not required by China, the fieldwork in China that we conducted under our R01 is covered by the Inter-institutional agreement we cited in our letter of October 26th, and by our relevant US institutional IACUC approval.

In response to your request for "complete and dated copies of the original laboratory notebook entries and of the original electronic files that led to the generation of the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13, along with all their accompanying texts". We do not have copies of these, which were created by and retained by the WIV. Nonetheless, I have forwarded your letter to the WIV, and will let you know their response as soon as WIV replies to our request.

Finally, I would like to comment that we strongly believe it is in the interests of the American public, and people of all nations, to continue doing our best to keep communication open with collaborators in China, so that we can analyze and publish data from our work, advance the science of pandemic prevention, and protect the public from pandemic threats. In this spirit, we look forward to filing our next annual report for R01AI110964, despite this grant being suspended and funding not available to us, as we did in June of 2021. In our next report, we will include any further analyses of the work conducted previously, and advance copies of publications we aim to submit. We will do this in the normal way, through the NIH RPRR reporting system, with copies sent to our NIAID Program Officer, Dr. Erik Stemmy.

Yours sincerely,

[redacted]

Dr. Peter Daszak, President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

January 6, 2022

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St.
Suite 1701
New York, NY 10001

Re: U01AI151797 and U01AI153420

Dear Drs. Chmura and Daszak:

I am writing to inform you of the actions that the National Institutes of Health (NIH) is taking with respect to grants administration at EcoHealth Alliance (EcoHealth). Pursuant to 45 C.F.R. § 75.207 and the NIH Grants Policy Statement Chapter 8.5, NIH is imposing specific award conditions on EcoHealth's active awards, U01AI151797 and U01AI153420. EcoHealth has demonstrated a history of failure to comply with several elements of the terms and conditions of grant awards not only for these active awards, but also for the suspended award, R01AI110964. Specifically, we have identified deficiencies in the timely submission of financial and Research Performance Progress Reports (RPPR), compliance with the Federal Funding Accountability and Transparency Act (FFATA) via FFATA Subaward Reporting System (FSRS), and other monitoring requirements.

NIH has reviewed the materials you provided in prior correspondence and determined that EcoHealth's subaward agreements do not contain required components, as outlined in 45 C.F.R. § 75.352 and the NIH GPS 15.2.1, and are out of compliance. Specifically:

Written Agreement Requirements	Compliance - Status
All requirements imposed by the pass-through entity on the subrecipient so that the Federal award is used in accordance with Federal statutes, regulations and the terms and conditions of the Federal award. ("The terms and conditions of Federal-awards (including [45 CFR 75]) flow down to subawards to subrecipients" 45 CFR 75.101(b))	Non-compliant: Not provided.
Any additional requirements that the pass-through entity imposes on the subrecipient in order for the pass-through entity to meet its own responsibility to the HHS awarding agency including identification of any required financial and performance reports.	Non-compliant: The agreements lacked clear requirements for when financial and performance reports are due, and what must be included in them. In addition, the recipient failed to submit the reports, when requested.
A requirement that the subrecipient permit EcoHealth and auditors to have access to the subrecipient's records and financial statements as necessary for EcoHealth to meet the requirements under 45 CFR part 75.	Non-compliant: Not provided.
Procedures for directing and monitoring the research effort.	Non-compliant: Not provided.

If the subrecipient's Investigators must comply with the subrecipient's Financial Conflict of Interest policy, the subrecipient shall certify as part of the written agreement that its policy complies with the 2011 revised FCOI regulation (42 CFR 50 Subpart F). If the subrecipient cannot provide such certification, the agreement shall state that the subrecipient's Investigators are subject to the Financial Conflict of Interest policy of the awardee Institution for disclosing Significant Financial Interests that are directly related to the subrecipient's work for the awardee Institution.	Non-compliant: Subrecipient FCOI policy not provided, nor was there a certification as part of the written agreement demonstrating compliance with the 2011 revised FCOI regulation (42 CFR 50 Subpart F).
A provision addressing ownership and disposition of data produced under the consortium agreement. This includes whether cell lines, samples or other resources will be freely available to other investigators in the scientific community or will be provided to particular investigators only.	Non-compliant: Not provided.
A provision making the NIH data sharing and inventions and patent policy, including a requirement to report inventions to the recipient (see Administrative Requirements-Availability of Research Results: Publications, Intellectual Property Rights, and Sharing Research Resources), applicable to each consortium participant and its employees in order to ensure that the rights of the parties to the consortium agreement are protected and that the recipient can fulfill its responsibilities to NIH.	Non-compliant: Not provided.
Incorporation of applicable public policy requirements and provisions indicating the intent of each consortium participant to comply, including submission of applicable assurances and certifications (see Public Policy Requirements, Objectives, and Other Appropriation Mandates).	Non-compliant: The agreement does not incorporate applicable public policy requirements.

NIH further identified non-compliance within EcoHealth's subaward agreement and invoices with the Wuhan Institute of Virology on grant R01AI110964, where it showed that EcoHealth did not charge the correct Facilities and Administrative (F&A) rate of 8 percent for the cost of compliance (see NIH GPS 16.6) which is required for all foreign awards. NIH identified that an inappropriate F&A was charged at a rate of 11 percent for years 2-5 of the subaward agreement.

When NIH identifies a recipient's history of non-compliance with the general or specific terms and conditions of NIH grant awards, NIH may take proactive actions to protect the Federal government's interests and may impose additional specific award conditions as needed (see 45 CFR 75.207 and NIH GPS 8.5). Given the non-compliance in the aforementioned areas, NIH is implementing specific award conditions (SAC) on all active awards to EcoHealth (U01AI151797 and U01AI153420), as follows.

- The expanded authority for automatic no-cost extensions is withdrawn. This will require that EcoHealth request and receive written prior approval from the appropriate NIH awarding Institute or Center (IC) before any extensions of the final budget period.

- Automatic carryover authorities are withdrawn. This will require EcoHealth to request and receive written approval to carry over any unobligated balances on all awards prior carrying over unobligated balances from one budget period to any subsequent budget period.
- EcoHealth is required to submit semi-annual RPPRs and Federal Financial Reports to the awarding IC.

EcoHealth must develop and successfully implement a Corrective Action Plan (CAP) for these awards with milestones to address and correct the deficiencies noted in this letter. The Corrective Action Plan, at a minimum, must include the following:

- Show proof of written policies and procedures for the development and issuance of subaward agreements, and a plan for revising the policies to address any deficiencies. The policy must include procedures for ensuring the appropriate F & A rate is applied to all subawards.
- Provide NIH with copies of updated subaward agreements for all active awards that correct the deficiencies noted above and demonstrate compliance with the NIH GPS 15.2.1 Written Agreement. The subaward agreements must state the correct F&A rate which, for foreign subrecipients is 8% (see NIH GPS 16.6).
- Show proof of written policies and procedures for timely submission of financial and progress reporting, and a plan for revising the policies to address any deficiencies.
- Show proof of written policies and procedures for subaward reporting as required by FFATA (see NIH GPS 8.4.1.5.5), and a plan for revising the policies to address any deficiencies.
- Provide NIH with copies of FSRS reporting for all subawards.

Once NIH reviews the CAP and determines that EcoHealth has successfully implemented it and has corrected the deficiencies noted in this letter, we will remove the SACs on the active awards without additional action on the part of EcoHealth. If we determine that additional information and actions are required, we will notify EcoHealth so that we can ensure compliance and, ultimately, remove the SACs.

Please provide the CAP to me within 30 days of receipt of this letter. If you have questions or would like to request reconsideration of the specific award conditions on the active awards, please feel free to contact me via email.

Sincerely,

[redacted]

Michael S. Lauer, M.D.
NIH Deputy Director for Extramural Research

[redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

6 January 2022

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: R01AI110964

Dear Drs. Chmura and Daszak:

Thank you for your correspondence of November 18, 2021. We are following up on your response to our request for Institutional Animal Care and Use Committee (IACUC) approval for the field work, and your response to our request for laboratory notebook entries and electronic files related to the experiments described in the Year 4 RPPR and Year 5 I-RPPR.

IACUC Approval

As we noted before and as required by the NIH Grants Policy Statement (GPS), 4.1.1.2, NIH requires verification of IACUC approval of those sections of the grant application that involve use of vertebrate animals. As noted by the NIH Office of Laboratory Animal Welfare (OLAW) cover letter accompanying your Interinstitutional Agreement for the WIV animal work, "under your approved Assurance with the Wuhan Institute of Virology, their Institutional Animal Care and Use Committee (IACUC) is authorized to carry out subsequent reviews of this project." In the final Vertebrate Animal Section of EcoHealth's Just-in-Time materials submitted on May 16, 2014 for 1 R01 AI110964-01, you stated that "all animal work to be done at Wuhan has been approved by the Wuhan IRB (IACUC) #WIVA05201402. Animals will be housed in a BSL-3 facility and will be under the care of a full-time veterinarian."

In my November 5, 2021, letter I requested documentation from the *WIV IACUC* regarding approval for *field work* (e.g., work in caves to collect materials from live bats) supported by R01AI110964. In your November 18, 2021, letter you indicated that no such *WIV IACUC* documentation exists. You stated, "the fieldwork in China that we conducted under our R01 is covered by the Inter-institutional agreement we cited in our letter of October 26th, and by our relevant US institutional IACUC approval."

Through our own search, we have confirmed that the field work was indeed approved by an IACUC. We understand that one of your co-investigators, Dr. Jonathan Epstein, submitted the field work proposal to the Tufts University IACUC; the Tufts University IACUC provided approval; and NIAID accepted the use of the Tufts University IACUC. However, in response to our requests for documentation of IACUC approval, you did not identify who the US institutional IACUC was, nor did you provide us with the Tufts University IACUC approval documentation. We had to obtain the documentation directly from Tufts University. While we are satisfied that the field work was approved by an IACUC, EcoHealth's inability or unwillingness to

provide the Tufts University IACUC documentation to us upon request raises questions about the quality and rigor of EcoHealth's record-keeping.

Laboratory Notebooks and Electronic Files

In my letter of November 5, 2021, I asked you to send us by no later than Friday, November 19, 2021, complete and dated copies of the original laboratory notebook entries and of the original electronic files that led to the generation of the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13, along with all their accompanying texts (e.g., the Year 5 I-RPPR text in which you stated that "rWIV1_SHC014 was detected at all time points and showed an increasing viral titer after infection…"). On November 18, 2021, you responded: "We do not have copies of these, which were created by and retained by the WIV. Nonetheless, I have forwarded your letter to the WIV, and will let you know their response as soon as WIV replies to our request." We are following up to confirm whether you received a response from WIV and whether the materials are forthcoming.

As a reminder, it is critical to note that our request for the original laboratory notebook entries and the original electronic files underlying the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13 is consistent with the term and condition of award which provides that NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. 75.364). It is also consistent with the term and condition of award that "The Federal Government has the right to obtain the data produced under a Federal award." (45 C.F.R. 75.322(d)). Moreover, as a term and condition of award, unless extended by the Federal awarding agency, all "records pertinent to a Federal award must be retained for a period of three years from the date of submission of the final expenditure report or, for Federal awards that are renewed quarterly or annually, from the date of the submission of the quarterly or annual financial report, respectively, as reported to the HHS awarding agency or pass-through entity in the case of a subrecipient." (45 C.F.R. 75.361). NIH's rights of access "are not limited to the required retention period but last as long as the records are retained." (45 C.F.R. 75.364(c)). These rights and requirements apply not only to EcoHealth's records and data, but also to WIV's records and data, regardless of whether WIV is an active subawardee of EcoHealth at this time. Awardees indicate their acceptance of an NIH award and its associated terms and conditions as they draw down the NIH grant funds to support the scientific project (see NIHGPS Section 5). If an awardee fails to comply with the terms and conditions of award, and NIH determines that noncompliance cannot be remedied with specific award conditions, the NIH may take one or more enforcement actions, including terminating the award in whole or in part, disallowing all or part of the cost of the activity or action not in compliance, and withholding further federal awards for the project. (45 C.F.R. 75.371).

Upon receipt of this letter, please confirm whether you have received a response from WIV and whether the materials are forthcoming. If the materials are forthcoming, we request that they be provided to us no later than close-of-business on January 14, 2022.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research

[redacted]

cc: Ms. Emily Linde
Dr. Erik Stemmy

EcoHealth Alliance

January 21st 2022

Dear Dr Lauer,

I am responding to your letter of 1.6.2022 commenting on the IACUC information related to fieldwork in China under R01AI110964, and requesting an update from WIV, should one be available.

1) **Regarding the IACUC information.** Thank you for informing us that you are satisfied with the IACUC information pertaining to our award. In our previous letter we informed you that EcoHealth Alliance's own IACUC approval was granted via our inter-institutional assurance with a US university. This is standard procedure for organizations that do not have an in-house IACUC committee and is an arrangement that we had informed NIH about in 2014 (see attached excerpt from a letter sent by EHA to Dr. Laura Pone of NIH on 2/11/2014). In fact, details of our inter-institutional assurance have been known to NIH since at least 2007 when IACUC approval was granted via this mechanism for 2R01TW005869 (Daszak PI) funded through the NIH Fogarty International Center. Had details of the inter-institutional assurance and IACUC proposal been requested clearly in previous communication from your office, we would have provided them. As previously stated, at all relevant times, on all proposals and reports, and in response to all letters from NIH, EcoHealth Alliance has responded to requests for information in a timely manner, and with full compliance.

2) **Regarding your request for WIV lab notes etc.** As requested by NIH, we passed on your request to WIV, but have not received any further information from them. We will inform you if and when we receive a response.

Yours sincerely,

[redacted]

Dr. Peter Daszak, President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
[redacted]
EcoHealthAlliance.org

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

August 19, 2022

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St.
Suite 1701
New York, NY 10001

Re: R01AI110964

Dear Drs. Chmura and Daszak:

Thank you for your response dated, January 21, 2022, and all of your prior correspondence on the above-mentioned grant. In am writing to inform you that the National Institutes of Health (NIH) is taking the following actions with respect to grant R01AI110964, as more fully described in this letter:

(1) NIH is terminating the subaward from EcoHealth Alliance (EHA) to the Wuhan Institute of Virology (WIV) due to material non-compliance with terms and conditions of award that cannot be remedied by specific award conditions. This will be accomplished as a partial termination of the award to EHA under 45 CFR 75.371(c).
(2) NIAID will work with EHA to explore renegotiating the remainder of the award to proceed without involvement from WIV, if the award can be renegotiated without representing a significant scientific departure from the original, peer reviewed project. If the award is not able to be renegotiated without such a departure, then NIH will request a bilateral termination, and EHA may submit a new competitive (Type 1) application for funding of the revised project.
(3) If the remaining award can be renegotiated successfully, then NIAID will issue a revised award, subject to specific award conditions outlined below, which include that EHA must conduct or arrange for the conduct of onsite subrecipient facility inspections every 6 months to ensure that subaward activities are being properly executed.

Termination in Part

In my previous correspondence, dated November 5, 2021, and again on January 6, 2022, NIH requested from EHA complete and dated copies of the original laboratory notebook entries and of the original electronic files from the Wuhan Institute of Virology (WIV), that led to the generation of the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13, along with all their accompanying texts (e.g., the Year 5 I-RPPR text in in which you stated that "rWIV1-SHC014 was detected at all time points and showed an increasing viral titer after infection…"). You responded that EHA relayed the request to WIV, but that EHA has not received a response from WIV and will inform NIH once the response is received. To date, NIH has not received the requested items.

We have also examined the subaward agreement from EHA to WIV, and we found that the agreement did not include "a requirement that the subrecipient [WIV] permit the pass-through entity [EHA] and auditors to have access to the subrecipient's records and financial statements as necessary for the pass-through

entity to meet the requirements of this part" as required under 45 C.F.R. 75.352. The agreement also did not include "all requirements imposed by the pass-through entity on the subrecipient so that the Federal award is used in accordance with Federal statutes, regulations and the terms and conditions of the Federal award[.]" 45 CFR 75.352. One such term and condition is that "The HHS awarding agency, Inspectors General, the Comptroller General of the United States, and the pass-through entity, or any of their authorized representatives, must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts." 45 CFR 75.364. The terms and conditions of Federal awards, including 45 CFR 75.364, flow down to subawards to subrecipients. 45 CFR 75.101(b). The subaward agreement to WIV did not indicate that the NIH, Inspectors General, the Comptroller General of the United States, and the pass-through entity (EHA), or any of their authorized representatives, must have the right of access to any documents, papers, or other records of the non-Federal entity (WIV) which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts.

As provided under 45 CFR 75.371, "If a non-Federal entity fails to comply with Federal statutes, regulations, or the terms and conditions of a Federal award, the HHS awarding agency or pass-through entity may impose additional conditions, as described in § 75.207. If the HHS awarding agency or pass-through entity determines that noncompliance cannot be remedied by imposing additional conditions, the HHS awarding agency or pass-through entity may take one or more [enforcement] actions, as appropriate in the circumstances[.]" 45 CFR 75.371. Such actions may include partly terminating the Federal award. Id. at 75.371(c).

NIH has determined that WIV's refusal to provide the requested records, and EHA's failure to include the required terms in WIV's subaward agreement represent material failures to comply with the terms of award. NIH has further determined that in these circumstances, WIV's refusal to provide records cannot be remedied by imposing additional conditions, and that a partial termination of award (i.e., termination of the subaward to WIV) is the only appropriate action.

Renegotiation of Award

As a result of NIH's termination of the subaward to WIV, we ask that EHA outline, within 30 days of this letter, how EHA will accomplish the purpose of the grant that was originally awarded without the subaward arrangement with WIV. This will require EHA to provide us with a change in scope outlining how the scope of the work will be modified to save the overall project while removing that portion of the research that was supported by WIV. Any change of scope, however, may not represent a significant scientific departure from the original peer reviewed project. If the change represents a significant departure from the original peer reviewed project, then NIH will request a bilateral termination of the remaining award, and EHA may submit a new competitive (Type 1) application for funding of the revised project. NIAID will work directly with EHA on such negotiations, including in reviewing EHA's proposal and discussing any needed scientific and budgetary adjustments.

Specific Award Conditions

If the remaining award is able to be renegotiated successfully, then the revised award will be subject to specific award conditions pursuant to 45 CFR 75.371 and 45 CFR 75.207. As provided under 45 CFR 75.371, "If a non-Federal entity fails to comply with Federal statutes, regulations, or the terms and conditions of a Federal award, the HHS awarding agency or pass-through entity may impose additional conditions, as described in § 75.207."

NIH will be imposing these specific award conditions, because NIH has determined that for grant R01AI110964, apart from the WIV-related non-compliance noted above, EHA failed to comply with

requirements for the timely submission of financial and Research Performance Progress Reports (RPPR) and compliance other monitoring requirements. Additionally, EHA's subaward agreements for the R01AI110964 grant did not contain required components, as outlined in 45 C.F.R. § 75.352 and the NIH GPS 15.2.1, and were out of compliance. Specifically:

Written Agreement Requirements	Compliance - Status
All requirements imposed by the pass-through entity on the subrecipient so that the Federal award is used in accordance with Federal statutes, regulations and the terms and conditions of the Federal award. ("The terms and conditions of Federal-awards (including [45 CFR 75]) flow down to subawards to subrecipients" 45 CFR 75.101(b))	Non-compliant: Not provided.
Any additional requirements that the pass-through entity imposes on the subrecipient in order for the pass-through entity to meet its own responsibility to the HHS awarding agency including identification of any required financial and performance reports.	Non-compliant: The agreements lacked clear requirements for when financial and performance reports are due, and what must be included in them. In addition, the recipient failed to submit the reports, when requested.
A requirement that the subrecipient permit EcoHealth and auditors to have access to the subrecipient's records and financial statements as necessary for EcoHealth to meet the requirements under 45 CFR part 75.	Non-compliant: Not provided.
Procedures for directing and monitoring the research effort.	Non-compliant: Not provided.
If the subrecipient's Investigators must comply with the subrecipient's Financial Conflict of Interest policy, the subrecipient shall certify as part of the written agreement that its policy complies with the 2011 revised FCOI regulation (42 CFR 50 Subpart F). If the subrecipient cannot provide such certification, the agreement shall state that the subrecipient's Investigators are subject to the Financial Conflict of Interest policy of the awardee Institution for disclosing Significant Financial Interests that are directly related to the subrecipient's work for the awardee Institution.	Non-compliant: Subrecipient FCOI policy not provided, nor was there a certification as part of the written agreement demonstrating compliance with the 2011 revised FCOI regulation (42 CFR 50 Subpart F).
A provision addressing ownership and disposition of data produced under the consortium agreement. This includes whether cell lines, samples or other resources will be freely available to other investigators in the scientific community or will be provided to particular investigators only.	Non-compliant: Not provided.
A provision making the NIH data sharing and inventions and patent policy, including a requirement to report inventions to the recipient (see Administrative Requirements-Availability of	Non-compliant: Not provided.

Research Results: Publications, Intellectual Property Rights, and Sharing Research Resources), applicable to each consortium participant and its employees in order to ensure that the rights of the parties to the consortium agreement are protected and that the recipient can fulfill its responsibilities to NIH.	
Incorporation of applicable public policy requirements and provisions indicating the intent of each consortium participant to comply, including submission of applicable assurances and certifications (see Public Policy Requirements, Objectives, and Other Appropriation Mandates).	Non-compliant: The agreement does not incorporate applicable public policy requirements.

NIH further identified that EHA did not charge the correct Facilities and Administrative (F&A) rate of 8 percent (see NIH GPS 16.6) to the foreign subawards under R01AI110964.

NIH has determined that in these circumstances, these violations can be remedied by imposing additional conditions. 45 CFR 75.371. Accordingly, if the remaining award is able to be renegotiated successfully, then the revised award will include the following specific award conditions:

(1) EHA must conduct or arrange for the conduct of onsite subrecipient facility inspections every 6 months to ensure that subaward activities are being properly executed.

(2) EHA must provide NIH with copies of updated subaward agreements for R01AI110964 that correct the deficiencies noted in the table above and demonstrate compliance with the NIH GPS 15.2.1 Written Agreement. The subaward agreements must state the correct F&A rate which, for foreign subrecipients is 8% (see NIH GPS 16.6).

(3) The expanded authority for automatic no-cost extensions will be withdrawn. This will require that EHA request and receive written prior approval from NIAID before any extensions of the final budget period.

(4) Automatic carryover authorities will be withdrawn. This will require EHA to request and receive written approval to carry over any unobligated balances on all awards prior carrying over unobligated balances from one budget period to any subsequent budget period.

(5) EHA is required to submit semi-annual RPPRs and Federal Financial Reports to NIAID.

(6) Provide NIAID with copies of FSRS reporting for all subawards issued under the revised R01AI119064.

These specific award conditions will be in place for a period of at least 3 years from the date of the revised Notice of Award with an annual review to ensure proper compliance.

This letter represents the final decision of the Chief Grants Management Officer, NIAID, NIH. However, the NIH reserves the right to take additional compliance actions as needed, such as disallowing funds or imposing additional specific award conditions, if the HHS Office of Inspector General identifies other noncompliance and/or recommends such actions as a result of its audit of EcoHealth.

I note that the partial termination (i.e., termination of the subaward) is appealable. Accordingly, the partial termination shall be final and in effect unless within 30 days after receiving this decision, you deliver a written notice of appeal of the partial termination to:

Michelle G. Bulls
NIH Grant Appeals Officer
National Institutes of Health
[redacted]
6705 Rockledge Drive, Room 3534/MSC 7963
Bethesda, MD 20892-7963

Please include a copy of this decision, your appeal justification, and any material or documentation that will support your position. Finally, the appeal must be signed by the institutional official authorized to sign award applications and must be postmarked no later than 30 days after the postmarked date of this notice.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
[redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

October 20, 2021

The Honorable James Comer
Ranking Member, Committee on Oversight and Reform
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative Comer:

Thank you for your continued interest in the work of the National Institutes of Health (NIH). I am writing today to provide additional information and documents regarding NIH's grant to EcoHealth Alliance, Inc.

It is important to state at the outset that published genomic data demonstrate that the bat coronaviruses studied under the NIH grant to EcoHealth Alliance, Inc. and subaward to the Wuhan Institute of Virology (WIV) are not and could not have become SARS-CoV-2. Both the progress report and the analysis attached here again confirm that conclusion, as the sequences of the viruses are genetically very distant.

The fifth and final progress report for Grant R01AI110964, awarded to EcoHealth Alliance, Inc. is attached with redactions only for personally identifiable information. This progress report was submitted to NIH in August 2021 in response to NIH's compliance enforcement efforts. It includes data from a research project conducted during the 2018-19 grant period using bat coronavirus genome sequences already existing in nature.

The limited experiment described in the final progress report provided by EcoHealth Alliance was testing if spike proteins from naturally occurring bat coronaviruses circulating in China were capable of binding to the human ACE2 receptor in a mouse model. All other aspects of the mice, including the immune system, remained unchanged. In this limited experiment, laboratory mice infected with the SHC014 WIV1 bat coronavirus became sicker than those infected with the WIV1 bat coronavirus. As sometimes occurs in science, this was an unexpected result of the research, as opposed to something that the researchers set out to do. Regardless, the viruses being studied under this grant were genetically very distant from SARS-CoV-2.

The research plan was reviewed by NIH in advance of funding, and NIH determined that it did not to fit the definition of research involving enhanced pathogens of pandemic potential (ePPP) because these bat coronaviruses had not been shown to infect humans. As such, the research was not subject to departmental review under the HHS P3CO Framework. However, out of an abundance of caution and as an additional layer of oversight, language was included in the terms and conditions of the grant award to EcoHealth that outlined criteria for a secondary review, such as a requirement that the grantee report immediately a one log increase in growth. These

measures would prompt a secondary review to determine whether the research aims should be re-evaluated or new biosafety measures should be enacted.

EcoHealth failed to report this finding right away, as was required by the terms of the grant. EcoHealth is being notified that they have five days from today to submit to NIH any and all unpublished data from the experiments and work conducted under this award. Additional compliance efforts continue.

The second document is a genetic analysis demonstrating that the naturally occurring bat coronaviruses used in experiments under the NIH grant from 2014-2018 are decades removed from SARS-CoV-2 evolutionarily. The analysis compares the sequence relationships between:

- SARS-CoV-1, the cause of the SARS outbreak in 2003;
- SARS-CoV-2, the cause of COVID-19 pandemic;
- WIV-1, a naturally occurring bat coronavirus used in experiments funded by the NIH;
- RaTG13, one of the closest bat coronavirus relatives to SARS-CoV-2 collected by the Wuhan Institute of Virology; and
- BANAL-52, one of several bat coronaviruses recently identified from bats living in caves in Laos.

While it might appear that the similarity of RaTG13 and BANAL-52 bat coronaviruses to SARS-CoV-2 is close because it overlaps by 96-97%, experts agree that even these viruses are far too divergent to have been the progenitor of SARS-CoV-2. For comparison, today's human genome is 96% similar to our closest ancestor, the chimpanzee. Humans and chimpanzees are thought to have diverged approximately 6 million years ago.

The analysis attached confirms that the bat coronaviruses studied under the EcoHealth Alliance grant could not have been the source of SARS-CoV-2 and the COVID-19 pandemic.

If you or your staff have questions, NIH would be pleased to brief you on these documents.

Lawrence A. Tabak, D.D.S., Ph.D.
Principal Deputy Director

From:	Peter Daszak
To:	Stemmy, Erik (NIH/NIAID) [E]
Cc:	Pone, Laura (NIH/NIAID) [E]; Aleksei Chmura
Subject:	Year 1 Report for Bat CoV Emergence Award (1R01AI110964-01)
Date:	Friday, May 1, 2015 2:57:01 PM
Attachments:	NIAID CoV Year 1 report 1R01AI110964-01.pdf

Dear Erik,

We just uploaded our Y1 Report for our Understanding the Risk of Bat Coronavirus Emergence award (1R01AI110964-01). I wanted to send you a copy of the report as well.

We have already some exciting results and I look forward to talking with you more at the ATS Meeting in Colorado in a few weeks!

Cheers,

Peter Daszak
President
EcoHealth Alliance
460 West 34th Street – 17th Floor
New York, NY 10001
[redacted] (direct)
+1.212.380.4465 (fax)
www.ecohealthalliance.org
EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that promote conservation and prevent pandemics.

From: Peter Daszak
To: Stemmy, Erik (NIH/NIAID) [E]
Cc: Normil, Carine (NIH/NIAID) [C]; Pone, Laura (NIH/NIAID) [E]; Aleksei Chmura
Subject: Year 2 Report for 5R01AI110964 - 02 PI Name: DASZAK, PETER
Date: Friday, May 13, 2016 12:55:49 PM
Attachments: Year 2 NIAID CoV Report as submitted via eRA Commons.pdf
Importance: High

Dear Erik,
I just wanted to let you know that we submitted our Year 2 Report yesterday (attached as a pdf).

It's been a pretty productive year, and some of the highlights include: collecting samples from 15 bat genera in southern China with 280 (12%) testing positive for coronaviruses; SARS-like coronaviruses being detected in *Rhinolophus* spp. bats in both Yunnan and Guangdong provinces; 7 published papers from work under our award (including one in *J. Virol.* and one in press at *J. Virol*); 218 quantitative interviews with samples and 47 qualitative coded interviews conducted transcribed and translated.

In the report, I highlight the reduced amount of wildlife in the local markets within Southern China compared to that we've seen before, as well as the continued expansion of the Chinese wildlife trade within SE Asia so that it is now a largescale international activity. It means that SL-CoVs we find in the wildlife trade would likely have an origin in adjacent countries. Given that our collaborators and field team in China have great contacts in these countries, and EHA also has field teams in many of them, we would like to conduct short field trips to assess markets, identify wildlife in them, and sample species of bats and other high-risk hosts in countries that neighbor China (Myanmar, Vietnam, Cambodia, Lao PDR) and others that supply wildlife to the international trade to China (Thailand, Malaysia, Indonesia). All samples collected would still be tested at the Wuhan Institute of Virology in China. Is there a formal process to ask for permission for this, or is the report and this email appropriate?

I also wanted to let you know about a recent personnel change. Since [redacted] has moved to the [redacted] earlier this year, we hired another senior researcher Noam Ross to conduct data analysis and spatial mapping. Our Year 2 report includes his CV. Noam has great enthusiasm and I am eager to see his work on our data collected to date. He has already been out to China is hitting the ground running!

We have had great successes this past year and I'd be happy to discuss any of them with you, if you'd like.

Cheers,
Peter

Peter Daszak
President
EcoHealth Alliance
460 West 34th Street – 17th Floor
New York, NY 10001
[redacted] (direct)

+1.212.380.4465 (fax)
www.ecohealthalliance.org
EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that promote conservation and prevent pandemics.

From:	Peter Daszak
To:	Stemmy, Erik (NIH/NIAID) [E]
Cc:	Smith, Philip (NIH/NIAID) [E]; Aleksei Chmura; Hongying Li; Alison Andre
Subject:	RE: 5R01AI110964 Coronavirus Year 4 Report
Date:	Wednesday, April 25, 2018 9:26:36 PM
Attachments:	Year 4 NIAID CoV Report.pdf

....and here's the report attachment....
Cheers,
Peter

Peter Daszak
President
EcoHealth Alliance
460 West 34th Street – 17th Floor
New York, NY 10001
Tel. [redacted]
www.ecohealthalliance.org
@PeterDaszak
@EcoHealthNYC
EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that prevent pandemics and promote conservation.

From: Peter Daszak
Sent: Wednesday, April 25, 2018 9:16 PM
To: Stemmy, Erik (NIH/NIAID) [E]
Cc: [redacted]; Aleksei Chmura; Hongying Li; Alison Andre
Subject: 5R01AI110964 Coronavirus Year 4 Report
Dear Erik,

I just wanted to send you a pdf of our Year 4 Report which I submitted last week. We've had some fantastic results this past year and I've put these in the report summary, but also included the discovery of SADS-CoV as another key findings. As you'll see, we're on track to hit all the major goals of the project by the end of Yr5, including human questionnaires and sampling, risk modeling, more in-depth viral characterization and discovery.
I know you've likely not had chance to read the report yet, but I also wanted to check-in with you soon about submitting a new proposal/renewal to build on the work we've done. You suggested that this would be good timing when we met last summer, and right now I'm looking at the November 5th 2018 deadline (renewal). I have a couple of questions on this: First, I've not submitted a renewal before the end of a current R01, and just want to check that this is the standard procedure. Our R01 officially ends in May 31st 2019. Secondly, I wanted to check in which study section would be best for this. The original proposal went to CFRS-Clinical Research and Field Studies of Infectious Diseases. I've asked Alison to set up a time for us to have a quick chat sometime in the next few weeks if possible.
Cheers,
Peter

Peter Daszak
President

Message

From: Ralph Baric [redacted]
Sent: 5/27/2021 7:00:34 AM
To: Peter Daszak [redacted]
Subject: Re: BSL levels for viral culture in China, US, other countries

Sorry Peter. Your being told a bunch of BS. Bsl2 w negative pressure, give me a break. There last paper mentioned bsl2 w appropriate PPE. This last part was the first and only time this was ever mentioned, never in earlier papers, and in the latest paper never defined either. I have no doubt that they followed state determined rules and did the work under bsl2. Yes china has the right to set their own policy. You believe this was appropriate containment if you want but don't expect me to believe it. Moreover, don't insult my intelligence by trying to feed me this load of BS.
Ralph

On Thu, May 27, 2021, 1:08 AM Peter Daszak [redacted] wrote:

Hi Ralph,

Hope all's well, given this ridiculous week for politics around covid origins in the news!

Since we last spoke, I've checked on a bunch of rules governing culture of viruses in the US, China and other countries. Hope you don't take this the wrong way – I'm sending you this so you're aware, and in case you get questions from reporters, and other scientists, or the govt agencies etc., not to disagree with your opinion, which I respect.

In China, the rules allow for organizations to conduct culture of animal viruses at BSL-2, including chimeras. We checked with Zhengli, who let us know that she used "BSL-2 with negative pressure and appropriate PPE". I also know that they are stricter now on SADS-CoV (it's BSL-3 I believe) ever since you showed it was able to infect human airway epithelial cells, so that's evidence they do take these things more seriously than it would seem on the surface.

I also checked the rules on a bunch of viruses for the US and was surprised to find lethal human pathogens cultured at BSL-2 (e.g. Rabies, some vector borne viruses) as well as many wildlife viruses. I also spoke with Chris Broder who let me know that the bat paramyxovirus Cedar virus (close to Nipah/Hendra) is cultured at BSL-2, including the recombinants he has made with Nipah and Hendra elements. Reference here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5869790/

I've attached a list of some of the findings with refs. Hope it's useful in case there are questions about this. I'm sure there are reasons for all of the above classifications, and justifications that can be debated, but I just want you to know that I did the due diligence on this, and checked that they were following the rules, and that similar rules exist here. I'm sure it will be criticized, and maybe there will be tightening of biosafety levels given the hype around the lab leak hypothesis at the moment. However, I'm still very confident that nothing untoward happened there, and have good reasons for that based on the protocols they used, and the results they were sharing as we wrote a paper for Nat. Communications in the lead up to the outbreak.

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: [redacted]
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

From: Ralph Baric [redacted]
Sent: Monday, May 10, 2021 4:44 PM
To: Peter Daszak [redacted]
Subject: Re:

Hi Peter, it is true that this isn't definitive proof and I agree there is no evidence of a SARS2 like virus in their collection that is closer than RaTG13, which is still pretty distant. I also still agree that a natural origin from nature is the most likely scenario. Take care, Ralph

On Mon, May 10, 2021 at 1:57 PM Peter Daszak [redacted] wrote:

> Thanks Ralph – I'd seen those and I understand your rationale for signing the letter. I've already seen a copy – reporters are already lining up questions for me, to which I'm saying – you should contact WHO.
>
> The real issue that everyone seems to forget is whether they had a virus similar to SARS-CoV-2 in their collection. Given that we published ~650 novel RdRps (alpha and beta covs) in spring 2020, and that they were piling in every single positive they had, it just seems like a very implausible scenario. Yes, they cultured bat-CoVs at a safety level you don't, but there's no evidence anywhere that they had SARS2 or a progenitor. Journalists will write whatever they want I guess...
>
> Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: [redacted]
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

From: Ralph Baric [redacted]
Sent: Monday, May 10, 2021 12:21 PM
To: Peter Daszak [redacted]
Subject:

BSL2 noted in methods
J Virol. 2016 Jul 15; 90(14): 6573–6582.
Published online 2016 Jun 24. Prepublished online 2016 May 11. doi: 10.1128/JVI.03079-15
PMCID: PMC4936131; PMID: 27170748
Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 Encodes an Extra Accessory Protein, ORFX, Involved in Modulation of the Host Immune Response Lei-Ping Zeng,a Yu-Tao Gao,a Xing-Yi Ge,a Qian Zhang,a Cheng Peng,a Xing-Lou Yang,a Bing Tan,a Jing Chen,a Aleksei A. Chmura,b Peter Daszak,b and Zheng-Li Shicorresponding author

J Virol. 2020 Oct; 94(20): e00902-20.
Published online 2020 Sep 29. Prepublished online 2020 Jul 22. doi: 10.1128/JVI.00902-20
PMCID: PMC7527062
PMID: 32699095
Evolutionary Arms Race between Virus and Host Drives Genetic Diversity in Bat Severe Acute Respiratory Syndrome-Related Coronavirus Spike Genes Hua Guo,#a,b Bing-Jie Hu,#a Xing-Lou Yang,a Lei-Ping Zeng,a Bei Li,a Songying Ouyang,c and Zheng-Li Shicorresponding author

I think there are at least one more such paper. I'll forward letter to the editor shortly, but thought you should be informed this methodology continued into 2020.

Disclaimer

Disclaimer

The information contained in this communication from the sender is confidential. It is intended solely for use by the recipient and others authorized to receive it. If you are not the recipient, you are hereby notified that any disclosure, copying, distribution or taking action in relation of the contents of this information is strictly prohibited and may be unlawful.

This email has been scanned for viruses and malware, and may have been automatically archived by Mimecast, a leader in email security and cyber resilience. Mimecast integrates email defenses with brand protection, security awareness training, web security, compliance and other essential capabilities. Mimecast helps protect large and small organizations from malicious activity, human error and technology failure; and to lead the movement toward building a more resilient world. To find out more, visit our website.

Gain-of-Function Research Involving Potential Pandemic Pathogens

In this kit:

Potential Pandemic Pathogens

Potential pandemic pathogens (PPPs) are bacteria, viruses, and other microorganisms that are likely highly transmissible and capable of wide, uncontrollable spread in human populations *and* highly virulent, making them likely to cause significant morbidity and/or mortality in humans. Examples of pathogens that have the potential to cause human pandemics, or have caused a human pandemic, include the H5N1 or H7N9 influenza viruses, also referred to as bird or avian influenzas, SARS-CoV, which caused an epidemic in several countries in 2003, and SARS-CoV-2, also known as Severe Acute Respiratory Syndrome coronavirus 2, which causes COVID-19 disease. Genetic changes or mutations in pathogens, especially viruses that have ribonucleic acid as its genetic material, regularly occur in nature. Some mutations in nature can cause pathogens to gain new functions or enhance existing characteristics such as fitness or pathogenicity (ability to cause disease). We have seen many examples of that with SARS-CoV-2 since the beginning of the pandemic.

Gain-of-Function Research

The term gain-of-function (GOF) research describes a type of research that modifies a biological agent so that it confers new or enhanced activity to that agent. Some scientists use the term broadly to refer to *any* such modification. However, not all research described as GOF entails the same level of risk. For example, research that involves the modification of bacteria to allow production of human insulin, or the altering of the genetic program of immune cells in CAR-T cell therapy to treat cancer generally would be considered low risk. The subset of GOF research that is anticipated to enhance the *transmissibility* and/or *virulence* of potential pandemic pathogens, which are likely to make them more dangerous to humans, has been the subject of substantial scrutiny and deliberation. Such GOF approaches can sometimes be justified in laboratories with appropriate biosafety and biosecurity controls to help us understand the fundamental nature of human-pathogen interactions, assess the pandemic potential of emerging infectious agents, and inform public health and preparedness efforts, including surveillance and the development of vaccines and medical countermeasures. This research poses biosafety and biosecurity risks, and these risks must be carefully managed. When supported with NIH funds, this subset of GOF research may only be conducted in laboratories with stringent oversight and appropriate biosafety and biosecurity controls to help protect researchers from infection and prevent the release of microorganisms into the environment.

U.S. Government Funding Pause

In 2014, the White House Office of Science and Technology Policy (OSTP), in coordination with agencies across the U.S. Government (USG), including the Department of Health and Human Services (HHS) and the National Institutes of Health (NIH), initiated a funding pause pdf on GOF research that was reasonably anticipated to confer attributes to influenza, Middle East Respiratory Syndrome (MERS), or SARS viruses such that the virus would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route.

The pause allowed the USG, in partnership with the life sciences community and stakeholders, to conduct a public, deliberative process with the explicit goal of developing a new federal policy framework to guide future investments in this area of research. The deliberative process included multiple public meetings and two commissioned independent studies, including a comprehensive risk and benefit assessment of GOF research. As noted above, not all studies that may be considered GOF research pose the same level of risk. The deliberative process identified the subset of research that enhances a pathogen to make it likely highly transmissible and virulent in humans (enhanced PPP) as involving risks that warranted additional oversight.

HHS P3CO Framework

At the conclusion of the deliberative process, HHS issued its Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO Framework) pdf. This HHS P3CO Framework is responsive to and in accordance with the Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight pdf issued by OSTP. The Framework guides HHS funding decisions on proposed research that is reasonably anticipated to create, transfer, or use PPPs resulting from the enhancement of a pathogen's transmissibility and/or virulence in humans (enhanced PPP) and seeks to preserve the benefits of life sciences research involving enhanced PPPs while minimizing potential biosafety and biosecurity risks. Unlike the 2014 funding pause, the HHS P3CO Framework is not limited to certain pathogens. The HHS P3CO Review Group includes experts in scientific research, biosafety, biosecurity, medical countermeasures, law, ethics, public health preparedness and response, biodefense, select agent regulations, and public health policy. Research deemed acceptable under the HHS P3CO Framework must be conducted in an appropriate laboratory with stringent oversight and biosafety and biosecurity controls.

Once the HHS P3CO review and oversight process was in place, NIH announced in December 2017 that it was lifting the funding pause on NIH-supported research. Since that time, NIH has funded two projects involving enhanced PPP research subsequent to review by the HHS P3CO Review Group. Both projects involved influenza virus. The HHS P3CO Review Group determined that for both research proposals, there were no feasible, equally effective alternative methods to address the same question in a manner that poses less risk, and that the research was acceptable for HHS funding. NIH makes all funded research publicly available on NIH RePORTER. Pre-funding information about unfunded individual proposals is not made public to preserve confidentiality and protect sensitive information, preliminary data, and intellectual property.

Research Within P3CO Scope

As an example, the University of Wisconsin-Madison research experiment on influenza that was reviewed in accordance with the HHS P3CO Framework was considered acceptable for HHS funding. The research project focused on H5N1 (an avian influenza virus that represents a serious pandemic threat) and was designed to improve understanding of the features and mechanisms that would enable avian influenza viruses to transmit to mammals. The leap from birds to humans (or from birds to another species such as pigs, then to humans) has been an important way that spillover has occurred in the past with influenza A virus. In this project, mutations associated with adaptation in mammals would be introduced into H5 avian influenza viruses. The project proposed that resulting viruses would be tested for their ability to transmit between ferrets, a common animal model for studying influenza A transmission that might be relevant to humans. In the ferret experiments, additional mutations then would be introduced to see if those changes made the viruses more transmissible between ferrets. The information generated from these ferret experiments provided a basis for assessing the potential risks to humans of circulating and emerging avian influenza viruses. Identification of specific mutations enables enhanced surveillance and response efforts, because finding these mutations in future avian influenza viruses could inform a public health response by identifying the need for development and use of protective vaccines and therapeutics.

Research Outside P3CO Scope

An example of a research project that some might describe as GOF research broadly but does not meet the criteria for review under the HHS P3CO Framework involves virus manipulation that results in the ability to generate higher vaccine yield. For background, egg-based influenza vaccine viruses are not always suitable for cell-cultured vaccine production due to potential issues with growth, protein yield, and antigenic stability (a substance that evokes an immune response). To increase cell-culture influenza vaccine production, a high-growth master influenza virus adapted to cells competent for vaccine production was needed. New mutations introduced in a mouse-adapted influenza virus (A/PR/8/1934) in cell culture resulted in a virus that had increased pathogenicity in mice and increased yield in cell culture which would advance vaccine development. Because the parental or primary virus was adapted in mice, it did not meet the definition of a PPP. This research is described in this *Nature* paper pdf.

Timeline

December 19, 2017: NIH announces that it is lifting the funding pause.

December 19, 2017: HHS issues Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens pdf.

January 9, 2017: U.S. Government issues Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO) pdf.

May 2016: National Science Advisory Board for Biosecurity issues Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research pdf.

March 10-11, 2016: National Academies of Sciences, Engineering, and Medicine hosts 2nd symposium on gain-of-function research (meeting summary).

December 15-16, 2014: National Academies of Sciences, Engineering, and Medicine hosts symposium on potential risks and benefits of gain-of-function research (meeting summary).

October 17, 2014: U.S. Government outlines the Gain-of-Function Deliberative Process and Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS, and SARS viruses pdf.

October 16, 2014: NIH issues statement on U.S. Government funding pause on certain types of gain-of-function research.

Related Resources

NIH Gain-of-Function Research

HHS P3CO

This page last reviewed on July 12, 2021

Research Involving Enhanced Potential Pandemic Pathogens

In this kit:

Potential Pandemic Pathogens

Potential pandemic pathogens (PPPs) are bacteria, viruses and other microorganisms that are likely highly transmissible and capable of wide, uncontrollable spread in human populations *and* highly virulent, making them likely to cause significant morbidity and/or mortality in humans. Examples of pathogens that have the potential to cause human pandemics, or have caused a human pandemic, include the H5N1 or H7N9 influenza viruses, also referred to as bird or avian influenzas, SARS-CoV, which caused an epidemic in several countries in 2003, and SARS-CoV-2, also known as Severe Acute Respiratory Syndrome Coronavirus 2, which causes COVID-19 disease. Genetic changes or mutations in pathogens, especially viruses that have ribonucleic acid as its genetic material, regularly occur in nature. Some mutations in nature can cause pathogens to gain new functions or enhance existing characteristics such as fitness or pathogenicity (ability to cause disease) as has been seen with the many variants of SARS-CoV-2 since the beginning of the pandemic.

ePPP Research

On limited occasions, when justified by compelling public health need and conducted in very high biosecurity laboratories, NIH has supported certain research that may be reasonably anticipated to create, transfer or use potential pandemic pathogens resulting from the enhancement of a pathogen's transmissibility and/or virulence in humans. The U.S. Government and the Department of Health and Human Services define such research as enhanced potential pandemic pathogen (ePPP) research. NIH-supported ePPP research requires strict oversight and may only be conducted with appropriate biosafety and biosecurity measures. This research can help us understand the fundamental nature of human-pathogen interactions, assess the pandemic potential of emerging infectious agents such as viruses and inform public health and preparedness efforts, including surveillance and the development of vaccines and medical countermeasures. While such research is inherently risky and requires strict oversight, the risk of not doing this type of research and not being prepared for the next pandemic is also high. While ePPP research is a type of so called "gain-of-function" (GOF) research, the vast majority of GOF research does not involve ePPP and falls outside the scope of oversight required for research involving ePPPs.

Oversight

The HHS Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO Framework) pdf was established in 2017 to guide funding decisions on proposed research that is reasonably anticipated to create, transfer or use potential pandemic pathogens resulting from the enhancement of a pathogen's transmissibility and/or virulence in humans, called ePPP research. The HHS P3CO Framework is responsive to and in accordance with the Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight pdf issued by the White House Office of Science and Technology Policy. These policies were developed after a three-year deliberative process during which the U.S. government initiated a funding pause from 2014-2017 for select research that was reasonably anticipated to enhance pathogenicity and/or transmissibility of influenza, MERS or SARS viruses in mammals via the respiratory route.

The Framework seeks to preserve the benefits of life sciences research involving ePPPs while minimizing potential biosafety and biosecurity risks. The HHS P3CO Review Group includes experts in scientific research, biosafety, biosecurity, medical countermeasures, law, ethics, public health preparedness and response, biodefense, select agent regulations and public health policy. Research deemed acceptable under the HHS P3CO Framework must be conducted in an appropriate laboratory with stringent oversight and biosafety and biosecurity controls.

To date, only three projects involving ePPP research were reviewed by the HHS P3CO Review Group and proposed for funding by NIH. The HHS P3CO Review Group determined that for two of the research proposals, focused on influenza, there were no feasible, equally effective alternative methods to address the same question in a

manner that poses less risk and that the research was acceptable for HHS funding. Those two projects have ended. For the third project, the HHS P3CO Review Group determined that a subset of the proposed research involving ePPPs was acceptable for funding with the implementation of additional risk mitigation measures. However, NIAID ultimately decided to redirect all funds under the award to support alternative approaches that do not involve ePPP research. NIH makes all funded research publicly available on NIH RePORTER. Pre-funding information about unfunded individual proposals is not made public to preserve confidentiality and protect sensitive information, preliminary data and intellectual property.

Related Resources

HHS P3CO

This page last reviewed on October 20, 2021

EcoHealth Alliance

Peter Daszak <[redacted]>

Letter from NIH

Peter Daszak <[redacted]> Mon, Nov 15, 2021 at 6:55 PM
To: Zhengli Shi <[redacted]>

Dear Zhengli,

Please see the attached letter. There are two questions that NIH have asked me to answer. The first one, on the permission to work with vertebrate animals (bats in caves etc.), I have the information for and will respond to NIH. The second issue, I will write to NIH and explain that I've forwarded it to WIV, because I don't have that information.

Cheers,

Peter

Peter Daszak

President

EcoHealth Alliance

520 Eighth Avenue, Suite 1200

New York, NY 10018-6507

USA

Tel.: +[redacted]

Website: www.ecohealthalliance.org

Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

---

To EcoHealth R01AI110964 11 5 21 clean.pdf
210K

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

5 November 2021

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: R01AI110964

Dear Drs. Chmura and Daszak:

Thank you for your correspondence (including supporting materials) of October 26, 2021. We are requesting additional materials regarding Institutional Animal Care and Use Committee (IACUC) approval for the field work, and the experiments reported in the Year 4 Research Performance Progress Report (RPPR) and Year 5 interim-RPPR (I-RPPR).

IACUC Approval

As we noted before and as required by the NIH Grants Policy Statement (GPS), 4.1.1.2, NIH requires verification of IACUC approval of those sections of the grant application that involve use of vertebrate animals. As noted by the NIH Office of Laboratory Animal Welfare (OLAW) cover letter aecompanying your Interinstitutional Agreement for the WIV animal work, "under your approved Assurance with the Wuhan Institute of Virology, their Institutional Animal Care and Use Committee (IACUC) is authorized to carry out subsequent reviews of this project." In the final Vertebrate Animal Section of your Just-in-Time materials submitted on May 16, 2014 for 1 R01 AI110964-01, you stated that "all animal work to be done at Wuhan has been approved by the Wuhan IRB (IACUC) #WIVA05201402. Animals will be housed in a BSL-3 facility and will be under the care of a full-time veterinarian." Thus, it appears that the WIV IACUC approved "all animal work to be done at Wuhan."

In my October 20, 2021 letter, I requested documentation from the *WIV IACUC* regarding approval for *field work* (e.g., work in caves to collect materials from live bats) supported by R01AI110964. You responded by sending us OLAW documentation, not WIV IACUC documentation. This is not documentation demonstrating that the WIV IACUC explicitly approved the field work, the work done outside the BSL-3 facility that involved free-ranging bats and rodents. Therefore, we again ask for you to provide us with *WIV IACUC* documentation of approval for *field work* involving free-ranging bats and wild rodents, or to confirm that no such approval was obtained.

Experiments Described in Year 4 RPPR and Year 5 I-RPPR

In the text description of your Year 5 RPPR Figure 13, you stated, "In Year 5, we continued with in vivo infection experiments of diverse bat SARSr-CoVs on transgenic mice expressing human ACE2. Mice were infected with 4 strains of SARSr-CoVs with different S protein…" In your October 26, 2021 correspondence, you stated that Figure 13 of your Year 5 I-RPPR and Figure 35 of your Year 4 RPPR are taken from the same experiment. You ask that "these facts be acknowledged."

For us to further understand the details of these experiments, please send us complete and dated copies of the original laboratory notebook entries and of the original electronic files that led to the generation of the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13, along with all their accompanying texts (e.g., the Year 5 I-RPPR text in which you stated that "rWIV1-SHC014 was detected at all time points and showed an increasing viral titer after infection…")

Our document requests – for documentation of WIV IACUC approval for field work, the original laboratory notebook entries, and the original electronic files underlying the Year 4 RPPR Figure 35 and the Year 5 I-RPPR Figure 13 – are consistent with the term and condition of award that NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. 75.364). This right of access applies not only to awardee records, but also to subawardee records. Awardees indicate their acceptance of an NIH award and its associated terms and conditions as they draw down the NIH grant funds to support the scientific project (see NIHGPS Section 5).

We look forward to receiving these materials by no later than close-of-business on Friday, November 19, 2021.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Michael.Lauer@nih.gov

cc: Ms. Emily Linde
Dr. Erik Stemmy

Tarter Krinsky & Drogin LLP
1350 Broadway
New York, NY 10018
P 212.216.8000
F 212.216.8001
www.tarterkrinsky.com

Andrew N. Krinsky, *Partner*
212-216-8080, *Direct Dial*
[redacted]

August 13, 2020

Via Email, Certified Mail, & FedEx
[redacted]

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research
National Institutes of Health
National Institute of Allergy and Infectious Diseases
1 Center Drive, Building 1, Room 144
Bethesda, Maryland 20892

Re: Suspension of NIH Grant 2R01 AI 110964-6

Dear Dr. Lauer:

This firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance"), in connection with the post-award decision by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institute of Health ("NIH"), under the Department of Health and Human Services ("HHS"), on July 8, 2020, to suspend grant 2R01 AI 110964-6 (the "Suspension:"), which funds the project *Understanding the Risk of Bat Coronavirus Emergence* (the "Project").

This letter constitutes EcoHealth Alliance's initial response to the Suspension, which was due to purported concerns regarding the safety of unspecified research being conducted at the Wuhan Institute of Virology ("WIV") and for EcoHealth Alliance's alleged failure to report certain subawards in connection with grant 2R01 AI 110964-6 (the "Grant").[1] As set forth in more detail below, the Suspension is unjustified as WIV has no connection to the Project or EcoHealth Alliance's current research and EcoHealth Alliance had not issued any subawards in connection with the Grant at the time of the Suspension. Moreover, NIAID is not authorized under 45 CFR §§ 75.371, 75.205, and 75.207, entitled *Specific Award Conditions*, to impose, *inter alia*, conditions that consist of demands for information regarding entities that are neither subrecipients of grant funds nor project affiliates.[2] Accordingly, EcoHealth Alliance hereby demands that the Suspension be withdrawn and all funding in the HHS Payment Management System be released immediately.

BACKGROUND

A. EcoHealth Alliance

EcoHealth Alliance is a prolific New York-based nonprofit institution dedicated to protecting the health of people, animals, and the environment from emerging zoonotic diseases. For more than a decade, EcoHealth Alliance has been conducting cutting edge scientific research

[1] A copy of my prior letter, dated May 22, 2020, regarding NIH's termination of the Grant, is attached hereto as Exhibit 1.

[2] Notwithstanding NIH's lack of authority to impose extraneous conditions on the Grant and Project, EcoHealth Alliance has made a good faith effort to respond to NIH's questions regarding WIV.

to identify hundreds of new coronaviruses ("CoVs") in bats and to study the capacity of these viruses to infect human cells. The purpose of this research is to identify high risk populations so international actors can leverage their resources to address potential pandemics. In cooperation with a global network of over seventy partners, including academic institutions, intergovernmental and governmental agencies, infectious disease surveillance laboratories, and other international and national organizations in over thirty countries, EcoHealth Alliance's work has led to numerous scientific papers published in high impact journals. These publications have been critical in raising awareness of the threat that CoVs pose to global health, the global economy, and U.S. National Security.

EcoHealth Alliance has a long history of successful cooperation with NIH including multiple Research Project Grant R01 awards. In particular, Peter Daszak, EcoHealth Alliance's President and Chief Scientist, has been the Principal Investigator on more than five multidisciplinary R01s. As demonstrated by Dr. Daszak's research, which produced the first ever global emerging disease "hotspots" map that identified locations in the world where viruses with pandemic potential are most likely to emerge, EcoHealth Alliance is uniquely qualified to assist in both identifying the origins of severe acute respiratory syndrome coronavirus 2 ("SARS-CoV-2") and developing and implementing strategies to combat coronavirus disease 2019 ("COVID-19").

Significantly, at this time, EcoHealth Alliance is working with several countries including, *inter alia*, Bangladesh, Côte d'Ivoire, Indonesia, Liberia, Malaysia, Republic of Congo, and Thailand to distribute PPE and provide critical reagents to test for and contain COVID-19. Notably, this effort is being supported by both the United States Department of State and the United States Agency for International Development. EcoHealth Alliance is also assisting the U.S. Geological Survey, the U.S. Fish & Wildlife Service, the International Union for Conservation of Nature, the World Health Organization, the World Organization for Animal Health, and the World Bank Group to place the COVID-19 pandemic in historical context, assess the risk of COVID-19 resurgence and spillover impacts, and determine best practices and cost-effective solutions to combat the virus. In sum, EcoHealth Alliance's research agenda is more consequential than ever.

B. NIH Issues EcoHealth Alliance A Five-Year Research Grant To Continue The Project

NIH issued EcoHealth Alliance an initial five-year research award for the Project in 2014. In 2019, EcoHealth Alliance submitted a renewal application to NIH through NIAID that contained a revised scope of work, research goals, and proposed collaborators and sought to extend the Project for an additional five years. Upon filing of its renewal application, the Project was ranked as an "extremely high priority" (in the top 3%) by NIAID during its external review process. In light of its success, the absence of any allegation that EcoHealth Alliance had violated the terms and conditions of its prior awards, and the importance of EcoHealth Alliance's continued research, on July 24, 2019, NIH reauthorized grant R01 AI 110964 and issued EcoHealth Alliance a notice of award in the amount of $733,750.00 funded under grant 2R01 AI 110964-6.[3]

[3] A copy of the notice of award, dated July 24, 2019, is attached hereto as Exhibit 1-A.

C. EcoHealth Alliance Informs HHS That WIV Is Not A Subrecipient Of Grant Funds And Agrees Not To Collaborate With WIV In Connection With The Project

On April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH regarding WIV. The letter stated that, given allegations that COVID-19 "was precipitated by the release from WIV of the coronavirus responsible for COVID-19", NIH was pursuing suspension of WIV from participating in Federal programs. However, Dr. Lauer assured EcoHealth Alliance that "[t]his suspension of the sub-recipient does not affect the remainder of [EcoHealth Alliance's] grant, assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension." [4]

On April 21, 2020, Dr. Daszak of EcoHealth Alliance responded by email to Dr. Lauer stating that he could "categorically state that no funds from [sic] 2R01 AI 110964-6 have been sent to Wuhan Institute of Virology, nor has any contract been signed." Dr. Daszak further represented that EcoHealth Alliance would comply with all NIAID requirements. Dr. Lauer acknowledged (1) that no monies from grant 2R01 AI 110964-6 had gone to WIV and no contract between EcoHealth Alliance and WIV had been signed and (2) EcoHealth Alliance's agreement that it would not provide any funds to WIV until and unless directed otherwise by NIH.[5]

D. NIH Unlawfully Terminates The Grant "For Convenience"

Notwithstanding NIH's representation that suspension of WIV would not affect EcoHealth Alliance's ongoing research, the Grant, or the Project, on April 24, 2020, NIH notified EcoHealth Alliance by letter that, effective immediately, the Grant and Project had been terminated (the "Termination"). The purported grounds for the Termination were: (1) convenience; (2) NIH's discretion not to award a grant, or to award a grant at a particular funding level; and (3) NIH's belief that the Project outcomes did not align with the program goals and agency priorities.[6] As a result of the Termination, EcoHealth Alliance was notified by HHS that it was required to submit a Final Research Performance Progress Report for the Project.

E. EcoHealth Alliance Files A First-Level Appeal Of The Termination

On May 22, 2020, by letter, EcoHealth Alliance filed a first-level appeal of the Termination on NIH, pursuant to NIH Grants Policy Statement Section 8.7 and 42 CFR 50, Subpart D (the "Appeal"). (Ex. 1). In its Appeal, EcoHealth Alliance argued, *inter alia*, that: (1) NIH research grants are not subject to termination for convenience; (2) NIH's discretion to award a grant at a particular funding level did not authorize NIH to issue a post-award decision to terminate a duly awarded grant during the budget period; (3) the research goals of the Project and the NIAID are substantially identical; and (4) there was no rational basis to terminate the Grant for cause.

[4] A copy of the NIAID's letter regarding WIV, dated April 19, 2020, is attached hereto as Exhibit 1-B.
[5] A copy of the email correspondence between NIH and EcoHealth Alliance is attached hereto as Exhibit 1-C.
[6] A copy of the NIAID's letter regarding the Termination, dated April 24, 2020, is attached hereto as Exhibit 1-D.

F. NIAID Withdraws The Termination But Suspends The Grant Due To Alleged Safety Concerns At WIV And For EcoHealth's Purported Failure To Report Subawards

Lacking a rational basis for its decision to terminate the Grant, on July 8, 2020, Dr. Lauer notified EcoHealth Alliance by letter that NIAID had withdrawn its termination of the Grant supporting the Project.[7] However, citing "bio-safety concerns" at WIV and EcoHealth Alliance's purported failure to report unspecified subawards, NIAID proceeded to immediately suspend the Grant and the Project, pursuant to 45 CFR § 75.371 and NIH Grants Policy Statement Section 8.5.2, leaving the status of the Project effectively unchanged. In addition, the Suspension seeks to impose on EcoHealth Alliance the outrageous obligation to provide NIH with information and materials in the custody and control of WIV and to somehow facilitate access by an USFG "inspection team" to WIV, as a condition for lifting the Suspension.[8]

ARGUMENT

In the Suspension, NIAID identifies two and only two grounds for its decision to suspend the Grant and the Project: (1) purported safety concerns regarding WIV; and (2) EcoHealth Alliance's purported failure to report unspecified subawards. As set forth in detail herein, EcoHealth Alliance is not conducting any research or otherwise collaborating with WIV in connection with the Project. Moreover, EcoHealth Alliance had not issued any subawards in connection with the Grant at the time of the Suspension. Accordingly, the Suspension should be withdrawn immediately.[9]

A. NIH's Purported Concern That WIV Poses A Threat To Public Health And Welfare Is Not A Basis To Suspend The Grant Or The Project As WIV Is Not A Current Subrecipient Of Grant Funds And Has No Connection To The Project

Under 45 CFR §§ 75.207, 75.205, and 75.371 and NIH Grants Policy Statement Section 8.5.2, NIAID may take one or more enforcement actions where a grant recipient has failed to materially comply with the terms and conditions of the award. Under 45 CFR 75.374, the HHS awarding agency must provide the non-Federal entity an opportunity to object and provide information challenging any suspension or termination action. Given the exclusion of WIV from the Project, and NIH's failure to identify any other safety concerns, there is no basis for NIAID to suspend the Grant or to impose additional conditions.

At all relevant times, EcoHealth Alliance has duly monitored the activities of its subrecipients as necessary to ensure that any subawards were used for authorized purposes, in compliance with federal statutes, regulations, and the terms and conditions of the subaward. Moreover, EcoHealth Alliance is not aware of any allegation that any subrecipient of grant 1R01 AI 110964 funds has ever used such funds for unauthorized purposes, or in violation of any Federal

[7] Please confirm that, due to the withdrawal of the Termination, EcoHealth Alliance is not required to submit a final Project Report at this time.
[8] A copy of the NIAID's letter regarding the Suspension, dated July 8, 2020, is attached hereto as Exhibit 2.
[9] EcoHealth Alliance notes that the Suspension did not state any specific deadline for EcoHealth Alliance to respond to the Suspension or proposed additional conditions. Accordingly, this response is timely.

statutes, regulations, or the terms and conditions of the subject subaward. Furthermore, NIH has never accused EcoHealth Alliance of any act that posed a risk to public welfare and safety.

Significantly, WIV is the only organization identified in the Suspension as posing a risk to public welfare and safety. As stated in my prior letter on May 22, 2020, regarding the now admittedly unlawful termination of the Grant, at NIH's express request, no Grant funds have been distributed to WIV and no contract has been signed between EcoHealth Alliance and WIV in connection with the Project. Thus, the allegation that WIV's independent research at its facility poses unspecified bio-safety concerns should have no bearing on the Project, which was in strict compliance with NIH Grants Policy Statement §§ 4 and 4.1.24, and the terms and conditions of the Notice of Award (Ex. 1-A), at the time of the Suspension.

To reiterate, WIV is not a subrecipient of any Grant funds and will not be involved in the Project in any capacity. (*see* Ex. 1-C-7). Significantly, NIAID explicitly told EcoHealth Alliance that it could exclude WIV and continue the Project without jeopardizing the Grant so long as "no grant funds [were] provided to WIV." (Ex. 1-B).

B. EcoHealth Alliance Has Duly Reported All Issued Subawards And Was In Compliance With The Transparency Act At The Time Of The Suspension

Contrary to NIAID's assertion that EcoHealth Alliance failed to report unspecified subawards, EcoHealth Alliance did not issue or sign any subawards in connection with the 2019 Grant or before July 8, 2020. Accordingly, the reporting requirements of the Federal Funding Accountability and Transparency Act (the "FFATA") did not apply at the time of the Suspension.

Regarding the Project period between 2014 and 2019, EcoHealth Alliance duly complied with all NIAID-system-only financial reporting requirements. While EcoHealth Alliance had not entered the FFATA reporting information in the Federal Subaward Reporting System ("the FSRS"), all subawards issued in connection with the 2014 Project and the 2019 Project are now fully reported in the FSRS. Notably, no one at NIAID or NIH ever contacted or otherwise notified EcoHealth Alliance that it was not in compliance. As EcoHealth Alliance has taken appropriate corrective action that fully resolves its alleged non-compliance with the FFATA, pursuant to NIH Grants Policy Statement Section 8.5.2, the Suspension should be withdrawn.

C. HHS Has No Authority To Impose New Conditions That Are Wholly Unrelated To The Project And EcoHealth Alliance's Ongoing Research

Under 45 CFR § 75.207, NIAID may impose additional specific award conditions under the following circumstances: when the applicant or recipient has a history of failure to comply with the general or specific terms and conditions of a Federal award; when an applicant or recipients fails to meet expected performance goals; and when an applicant or recipient is not otherwise responsible. Allowed conditions include: (1) requiring payments as reimbursements rather than advance payments; (2) withholding authority to proceed to the next phase until receipt of evidence of acceptable performance within a given period of performance; (3) requiring additional, more detailed financial reports; (4) requiring additional project monitoring (5) requiring the non-Federal entity to obtain technical or management assistance; or (6) establishing additional

prior approvals. (45 CFR § 75.207[b]). The purpose of these additional conditions are to encourage the award recipients to comply with the original terms and conditions of the award, applicable statutes, and regulations.

There is no statute or NIH Grants Policy Statement provision that authorizes NIAID to impose additional conditions that consist of demands for information and materials regarding entities that are neither current subrecipients of grant funds nor connected to the research project funded by the subject grant. This makes sense, given that the purpose of imposing additional conditions is to ensure that research funded under a particular grant is conducted safely and in compliance with applicable laws.

Here, NIH's First, Second, Third, Fourth, Fifth, and Sixth proposed conditions, which require that EcoHealth Alliance, *inter alia*, provide information and materials regarding WIV, are wholly unrelated to the safety and efficacy of Project and EcoHealth Alliance's ongoing research as WIV is not a subrecipient of Grant funds (*see* Ex. 1-C-6, 7 and 8). Moreover, certain conditions, including the Sixth condition that "EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019" seek to impose impossible obligations. EcoHealth Alliance has no authority to grant NIAID access to the WIV lab facilities and is not conducting any research with WIV in connection with the Project. Whether or not EcoHealth Alliance is able to provide responses to the proposed conditions regarding WIV will not affect the safety of EcoHealth Alliance's current research, which will not involve WIV.

Without waiving any objections, in the interest of cooperation, EcoHealth Alliance has made a good faith effort to provide responses to the additional conditions (the "Requests") based on information now known to Peter Daszak, EcoHealth Alliance's President and Chief Scientist.[10]

CONCLUSION

Every single outbreak of a novel virus has been accompanied by the allegation that the subject virus was created in a lab including, *inter alia*, HIV, Ebola, and now SARS-CoV-2. There is no credible evidence to support these theories. By comparison, we know that seventy-five percent of new emerging diseases originate in wildlife. Every species of wildlife carry these viruses, an estimated 1.7 million of which are still unknown. While many of these viruses are benign, occasionally a lethal virus will emerge that can directly infect humans. EcoHealth Alliance is a valuable resource. The instant request to resume the Project funded by the Grant presents HHS with the opportunity to support proven research regarding the threat of zoonotic disease emergence and to support scientists who are working to determine whether certain vaccines and drugs can kill the SARS-CoV-2 virus to save our lives.

At this time, EcoHealth Alliance is in compliance with all of the terms and conditions of the award including the FFATA, there is no public health concern posed by EcoHealth Alliance's

[10] A copy of EcoHealth Alliance's Objections and Responses to the Requests is attached hereto as Exhibit 3.

resumption of the Project, which will not involve WIV in any capacity (*see* NIH Grants Policy Sections 4 and 4.1.24), and EcoHealth Alliance has hereby provided, to the best of its ability, the information and materials requested by NIH in the Suspension. Accordingly, the Suspension should be withdrawn and all funding in the HHS Payment Management System should be released immediately.

Please note that this letter is not intended to provide an exhaustive list of all possible grounds for vacating the Suspension and may not reflect all arguments and claims that EcoHealth Alliance will assert in the event that it is required to file a first-level appeal or other action or proceeding concerning any future adverse determination by NIAID affecting the Grant or the Project. All of EcoHealth Alliance's rights and remedies to seek review of any adverse determination are expressly reserved.

Should you wish to present evidence in an effort to refute any of the factual assertions made in this letter, and/or to engage in good faith negotiations regarding appropriate terms and conditions for the resumption of funding for grant 2R01 AI110964-6, we are prepared to review such evidence and to participate in such negotiations.

We await your response to this letter.

Very truly yours,

[redacted]

Andrew K. Krinsky

cc: (*by email*)

Dr. Erik Stemmy [redacted]
Ms. Emily Linde [redacted]

Exhibit 1

Tarter Krinsky & Drogin LLP
1350 Broadway
New York, NY 10018
P 212.216.8000
F 212.216.8001
www.tarterkrinsky.com

Andrew N. Krinsky, *Partner*
212-216-8080, *Direct Dial*
[redacted]

May 22, 2020

Via Email, Certified Mail, & FedEx
[redacted]

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research
National Institutes of Health
National Institute of Allergy and Infectious Diseases
1 Center Drive, Building 1, Room 144
Bethesda, Maryland 20892

Re: Termination of NIH Grant 2R01 AI 110964-6

Dear Dr. Lauer:

This firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance") with regard to the post-award decision by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institute of Health ("NIH"), under the Department of Health and Human Services ("HHS"), to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI 110964, on April 24, 2020 (the "Termination").

This letter, pursuant to NIH Grants Policy Statement Section 8.7 and 42 CFR 50, Subpart D, constitutes EcoHealth Alliance's first-level appeal of the Termination, which was "for convenience." As set forth in more detail below, the Termination is not authorized under the NIH Grants Policy Statement, arbitrary and capricious and an indefensible attack on public health and welfare given that it undermines a pivotal 10-year research project involving the origins, spread and threat of emerging bat coronaviruses during the peak of an unprecedented worldwide coronavirus pandemic. Accordingly, EcoHealth Alliance hereby demands that grant 2R01 AI 110964-6 be reinstated immediately.

BACKGROUND

A. EcoHealth Alliance

EcoHealth Alliance is a prominent New York-based nonprofit institution dedicated to protecting the health of people, animals, and the environment from emerging zoonotic diseases. For more than a decade, EcoHealth Alliance has been conducting cutting edge scientific research to identify hundreds of new coronaviruses ("CoVs") in bats and to study the capacity of these viruses to infect human cells. The purpose of this research is to identify high risk populations so international actors can leverage their resources to address potential pandemics. In cooperation with a global network of over seventy partners, including academic institutions, intergovernmental

and governmental agencies, infectious disease surveillance laboratories, and other international and national organizations in over thirty countries, EcoHealth Alliance's work has led to numerous scientific papers published in high impact journals. These publications have been critical in raising awareness of the threat that CoVs pose to global health, the global economy, and U.S. National Security.

EcoHealth Alliance has a long history of successful cooperation with NIH including multiple Research Project Grant R01 awards. In particular, Peter Daszak, EcoHealth Alliance's President and Chief Scientist, has been the Principal Investigator on five multidisciplinary R01s. All of these projects used modeling, epidemiology, laboratory, and field science to test hypotheses on the emergence of wildlife-origin viral zoonoses, including SARS-CoV, the Nipah and Hendra viruses, Avian influenza, and other bat-origin viruses. EcoHealth Alliance, a 501(c)(3) organization, is unique in that it goes one step further by leveraging its research goals to create an alliance of international collaborators that can advocate for real-world changes to protect high risk populations.

Notably, in collaboration with virologists in China, EcoHealth Alliance isolated and characterized SARSr-CoVs from bats that use the same human host cell receptor (ACE2) as SARS-CoV. This work provided critical reagents and resources that have advanced scientific understanding of virus-host binding and contributed to vaccine development. For example, the genetic sequences of the bat viruses that EcoHealth Alliance discovered under its NIH research funding, which were published online (Genbank & GISAID), have been used to test the effectiveness of the drug Remdesivir against not only SARS-CoV, but also MERS, and other potentially zoonotic or pre-pandemic bat CoVs. Significantly, this type of testing can be performed without the need for viral cultures or shipping viruses internationally.

B. <u>NIH Awards And Extends EcoHealth Alliance Research Grant R01 AI 110964</u>

In 2014, NIH issued EcoHealth Alliance a five-year research award for the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI 110964 (the "Project"). EcoHealth Alliance received additional awards for the Project each year between 2015 and 2018. Between 2015 and 2019, the Project resulted in the publication of more than twenty papers.

In 2019, EcoHealth Alliance submitted a renewal application to NIH through NIAID to extend the Project period for an additional five years. Upon filing of its renewal application, the Project was ranked as in "extremely high priority" (in the top 3%) by NIAID during its external review process. In light of its success and the importance of EcoHealth Alliance's work, on July 24, 2019, NIH authorized grant R01 AI 110964 and increased EcoHealth Alliance's funding. EcoHealth Alliance was issued a notice of award in the amount of $733,750.00 (the "2019 Award"). The notice of award also extended the Project period for an additional five years to 2024. A copy of the notice of award is attached hereto as Exhibit A.

<u>EcoHealth Alliance Agrees Not To Fund The Wuhan Institute Of Virology</u>

During the pendency of the Project, in December of 2019, China reported a cluster of cases of pneumonia in Wuhan, Hubei Province. It was later determined that the cause of this pneumonia

was a novel CoV, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease (COVID-19). Thereafter, SARS-CoV-2 spread to nearly every country throughout the world. In response, EcoHealth Alliance has prioritized its efforts in conducting research that will be integral to developing an effective strategy to combat SARS-CoV-2.

On April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH regarding a laboratory in China, the Wuhan Institute of Virology ("WIV"). WIV was a prior sub-recipient of a small portion of the R01 AI 110964 grant funds. The letter stated that, given allegations that COVID-19 "was precipitated by the release from WIV of the coronavirus responsible for COVID-19", NIH was pursuing suspension of WIV from participating in Federal programs. However, Mr. Lauer assured EcoHealth Alliance that "[t]his suspension of the sub-recipient does not affect the remainder of [EcoHealth Alliance's] grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension." A copy of the letter is attached hereto as Exhibit B.

On April 21, 2020, Dr. Daszak of EcoHealth Alliance responded by email to Dr. Lauer stating that he could "categorically state that no funds from [sic] 2R01 AI 110964-6 have been sent to Wuhan Institute of Virology, nor has any contract been signed." Dr. Daszak further represented that EcoHealth Alliance would comply with all NIAID requirements. Dr. Lauer acknowledged (1) that no monies from grant 2R01 AI 110964-6 had gone to WIV and no contract between EcoHealth Alliance and WIV had been signed and (2) EcoHealth Alliance's agreement that it would not provide any funds to WIV until and unless directed otherwise by NIH. A copy of the email correspondence between NIH and EcoHealth Alliance is attached hereto as Exhibit C.

D. NIH Abruptly Terminates Research Grant 2R01 AI 110964-6 "For Convenience"

Notwithstanding NIH's representation that suspension of WIV would not affect the remainder of EcoHealth Alliance's 2019 Award, on April 24, 2020, NIH notified EcoHealth Alliance by letter that, effective immediately, the 2019 Award had been terminated by NIAID. The stated grounds for the Termination were: (1) convenience; (2) NIH's discretion not to award a grant, or to award a grant at a particular funding level; and (3) NIH's belief that the Project outcomes did not align with the program goals and agency priorities. A copy of the Termination is attached hereto as Exhibit D.

ARGUMENT

A. NIH Research Grants Are Not Subject To Termination For Convenience

"Termination for convenience" refers to the exercise of the government's right to bring to an end the performance of all or part of the work provided for under a contract prior to the expiration of the contract "when it is in the Government's interest" to do so. Federal agencies typically incorporate clauses in their procurement contracts which give them the right to terminate for convenience. Here, there is no clause in the terms and conditions applicable to the 2019 Award, or in the NIH Grants Policy Statement, that permits NIAID or NIH to issue a post-award decision to terminate a NIH research grant award "for convenience."

Moreover, the unprecedented assertion by NIH that active research grants can be terminated "for convenience" during the subject budget period renders Section 8.5.2 of the NIH Grants Policy Statement meaningless. *See, e.g., Li v. Eddy*, 324 F.3d 1109, 1110 (9th Cir. 2003) (rejecting suggested statutory interpretation on the grounds that the interpretation ran squarely against the canon of construction that courts interpret statutes so as not to render any section meaningless). Section 8.5.2 of the NIH Grants Policy Statement governs, *inter alia*, modification or termination of an award for misconduct. If NIH grants were terminable for convenience, NIH could always choose to terminate for convenience to avoid (1) the "for cause" restriction on grant terminations and (2) the labor intensive task of enforcing compliance through disallowing costs, withholding further awards, or wholly suspending the grant, pending corrective action.

B. NIH's Discretion Not To Award A Grant, Or To Award a Grant At A Particular Funding Level, Does Not Authorize A Post-Award Decision To Terminate

NIH's discretion regarding the "decision not to award a grant, or to award a grant at a particular funding level" does not give NIH the authority to issue a post-award decision terminating a duly awarded grant during the budget period. This purported discretion, which is based on language in the last paragraph of NIH Grants Policy Statement Section 2.4.4, entitled *Disposition of Applications*, concerns NIH's authority to reject incomplete or otherwise undesirable grant applications in the first instance only. The provisions of Section 2, generally, have no bearing on post-award decisions affecting duly approved grants for which specified funds have already been allocated. As the 2019 Grant in the amount of $733,750.00 was awarded to EcoHealth Alliance on July 24, 2019, NIH's authority to deny initial grant applications does not allow NIH to terminate the 2019 Grant.

C. The Research Goals Of EcoHealth Alliance And NIAID Are Virtually Identical

NIH's contention that the Project's outcomes do not align with the agency's priorities is demonstrably false. First, the Project was ranked as "extremely high priority" on external review by NIAID less than nine months ago, before the discovery of SARS-CoV-2. Since this discovery, NIH has promulgated new grants seeking applicants to conduct research on the same issues covered by the Project and the 2019 Award.

In addition, there is substantial overlap between the four strategic research priorities on page 1 of NIAID's Strategic Plan for COVID-19 Research, published April 22, 2020, and the three Specific Aims of the Project. Both NIAID and EcoHealth Alliance seek to: (1) improve fundamental knowledge of SARS-Cov-2; (2) develop methods to assess the rate of infection and disease incidence; (3) contribute to the development of an effective vaccine; and (4) increase public health preparedness. Copies of the Project's Specific Aims and the NIAID Strategic Plan's four strategic research priorities for COVID-19 research are attached hereto as Exhibit E.

D. There Is No Rational Basis To Terminate The 2019 Award For Cause

The grounds and procedures for suspension and termination of awards are specified in NIH Grants Policy Statement Section 8.5.2 and 45 CFR Parts 75.371 through 75.373. Notably, Section

8.5.2 provides, *inter alia*, that NIH will generally suspend (rather than immediately terminate) a grant and allow the recipient an opportunity to take appropriate corrective action before NIH makes a termination decision. Through this lens, 45 CFR 75.372 provides that NIH may terminate a Federal award, in whole or in part, if: (1) the non-Federal entity fails to comply with the terms and conditions of the award; (2) for cause; (3) by the HHS awarding agency or pass-through entity with the consent of the non-Federal entity; or (4) by the non-Federal entity upon written notice to the HHS awarding agency setting forth the reasons for such termination, and other information. None of the foregoing predicate conditions exist here.

As of the date of the Termination, EcoHealth Alliance had not received any notice from NIH, NIAID, or HHS that it either failed to comply with any of the terms or conditions of the 2019 Award, or committed any misconduct in connection with the award. To the contrary, in email correspondence following EcoHealth Alliance's representation that it had not and would not give any funds from the 2019 Award to WIV, Aleksei Chmura, EcoHealth Alliance's Chief of Staff, memorialized the mutual agreement between NIH and EcoHealth Alliance that EcoHealth Alliance was in compliance with all requests. (Ex. C, p. 1). To be clear, EcoHealth Alliance clearly and unequivocally stated that it had not and will not distribute any funds from the 2019 Award to WIV.

In sum, there is no statutory, regulatory, or contractual basis for NIAID's termination of the Project, *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant 2R01 AI 110964-6. However, please note that this letter is not intended to provide an exhaustive list of all possible grounds for reversal of the Termination and may not reflect all arguments and claims that EcoHealth Alliance will assert in the event that a formal second-level appeal of the Termination is required.

Should you wish to present evidence in an effort to refute any of the factual assertions made in this letter and/or to engage in good faith negotiations regarding appropriate terms and conditions for the resumption of funding for grant 2R01 AI 110964-6, we are prepared to review such evidence and to participate in such negotiations.

We await your response to this letter.

Sincerely yours,

[redacted]

Andrew N. Krimsky

cc: (*by email*)

Dr. Erik Stemmy ([redacted])
Ms. Emily Linde ([redacted])

Exhibit A

Notice of Award

RESEARCH **Federal Award Date:** 07/24/2019

Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 2R01AI110964-06
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Dr. Daszak, Peter
PD/PI
460 West 34th Street
Suite 1701
New York, NY 100012320

Award e-mailed to: [redacted]

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2020
Project Period: 06/01/2014 – 06/30/2024

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $733,750 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Tseday G Girma
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

[redacted]

[redacted]

Approved Budget	$733,750
Total Amount of Federal Funds Obligated (Federal Share)	$733,750
TOTAL FEDERAL AWARD AMOUNT	$733,750
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$733,750

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
6	$733,750	$733,750
7	$709,750	$709,750
8	$709,750	$709,750
9	$709,750	$709,750
10	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021	2022	2023
AI	8472364	$733,750	$709,750	$709,750	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 41B / **Released**: GIRMATG 07/18/2019
Award Processed: 07/24/2019 12:03:26 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01AI110964-06

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 2R01AI110964-06

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.

c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 2R01AI110964-06

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

[redacted]

****

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

[redacted]

****

This award reflects current Federal policies regarding Facilities & Administrative (F&A) Costs for foreign grantees including foreign sub-awardees and domestic awards with foreign sub-awardees. Please see: Chapter 16 Grants to Foreign Organizations, International Organizations, and Domestic Grants with Foreign Components, Section 16.6 "Allowable and Unallowable Cost" of the NIH Grants Policy.

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

The budget period anniversary start date for future year(s) will be **July 1**.

****

Dissemination of study data will be in accord with the Recipient's accepted genomic data sharing plan as stated in the page(s) **203** of the application. Failure to adhere to the sharing plan as mutually agreed upon by the Recipient and the NIAID may result in Enforcement Actions as described in the NIH Grants Policy Statement.

****

This award is subject to the Clinical Terms of Award referenced in the NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032. These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

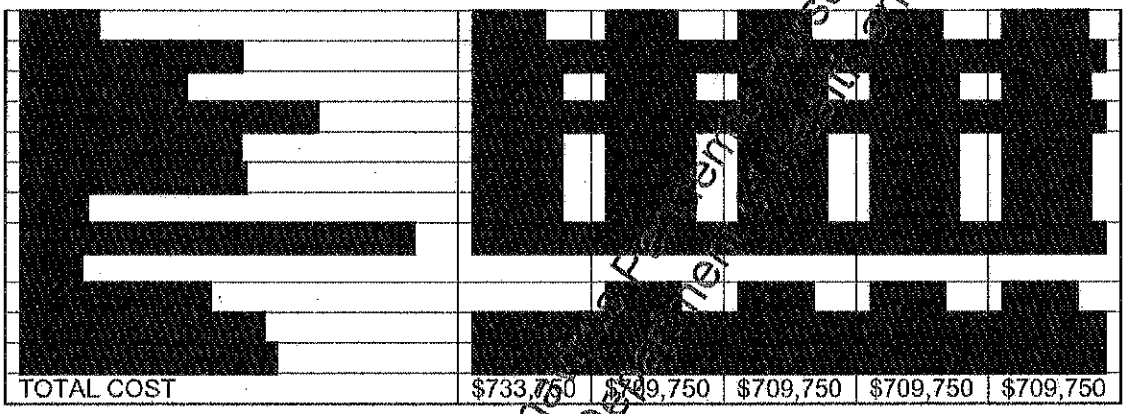
The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Tseday G Girma
Email: [redacted] **Phone:** 240-747-7388 **Fax:** 301-493-0597

Program Official: Erik J. Stemmy
Email [redacted] **Phone:** 240-627-3380

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01AI110964-06

INSTITUTION: ECOHEALTH ALLIANCE, INC.



TOTAL COST	$733,750	$709,750	$709,750	$709,750	$709,750

Facilities and Administrative Costs	Year 6	Year 7	Year 8	Year 9	Year 10
F&A Cost Rate 1	32%	32%	32%	32%	32%
F&A Cost Base 1	$438,711	$363,711	$363,711	$363,711	$363,711
F&A Costs 1	$140,388	$116,388	$116,388	$116,388	$116,388

Exhibit B

Date: April 19, 2020

From: Michael S Lauer, MD
NIH Deputy Director for Extramural Research

Lauer, Michael (NIH/OD) [E] Digitally signed by Lauer, Michael (NIH/OD) [E] Date: 2020.04.19 10:47:40 -04'00'

To: Kevin Olival, PhD
Vice-President for Research
EcoHealth Alliance
[redacted]

Naomi Schrag, JD
Vice-President for Research Compliance, Training, and Policy
Columbia University
[redacted]

Subject: Project Number 2R01AI110964-06

Dear Dr. Olival and Ms. Schrag:

EcoHealth Alliance, Inc. is the recipient, as grantee, of an NIH grant entitled "Understanding the Risk of Bat Coronavirus Emergence." It is our understanding that one of the sub-recipients of the grant funds is the Wuhan Institute of Virology (WIV). It is our understanding that WIV studies the interaction between corona viruses and bats. The scientific community believes that the coronavirus causing COVID-19 jumped from bats to humans likely in Wuhan where the COVID-19 pandemic began. There are now allegations that the current crisis was precipitated by the release from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs.

While we review these allegations during the period of suspension, you are instructed to cease providing any funds from the above noted grant to the WIV. This temporary action is authorized by 45 C.F.R. § 75.371(d) ("Initiate suspension or debarment proceedings as authorized under 2 C.F.R. part 180"). The incorporated OMB provision provides that the funding agency may, through suspension, immediately and temporarily exclude from Federal programs persons who are not presently responsible where "immediate action is necessary to protect the public interest." 2 C.F.R. § 180.700(c). It is in the public interest that NIH ensure that a sub-recipient has taken all appropriate precautions to prevent the release of pathogens that it is studying. This suspension of the sub-recipient does not affect the remainder of your grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension.

Exhibit C

From: Lauer, Michael (NIH/OD) [E] <[redacted]>
Sent: Sunday, April 19, 2020 11:00 AM
To: [redacted]; Naomi Schrag <[redacted]>
Cc: Black, Jodi (NIH/OD) [E] <[redacted]>
Subject: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Importance: High

Dear Dr. Olival and Ms. Schrag

Please see attached.

Many thanks, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: 301-496-1098
Email: [redacted]

2 Kevin Olival email on 20 April 2020

From: Kevin Olival <[redacted]>
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 20, 2020 at 4:12:28 PM EDT
To: "Lauer, Michael (NIH/OD) [E]" <[redacted]>
Cc: Naomi Schrag <[redacted]>, "Black, Jodi (NIH/OD) [E]" <[redacted]>

Dear Mike,

I received the attached letter, however please note:

1. I am not the PI on this award. You should contact Dr. Peter Daszak [redacted] who is the PI and leading this project for EcoHealth Alliance.
2. Columbia University is not involved in this NIH project, and it is not clear to me why Naomi and Columbia University were included.

Thank you,
Kevin

Kevin J. Olival, PhD
Vice President for Research

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

1.212.380.4478 (direct)
[redacted](mobile)
1.212.380.4465 (fax)
www.ecohealthalliance.org

Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

Lauer, Michael (NIH/OD) [E] <[redacted]>

Mon 4/20/2020 4:31 PM

To:Kevin Olival <[redacted]>; Peter Daszak <[redacted]>;

Cc:Naomi Schrag <[redacted]>; Black, Jodi (NIH/OD) [E] <[redacted]>; Lauer, Michael (NIH/OD) [E] <[redacted]>;

Importance: High

2 attachments

Screen Shot 2020-04-20 at 4.23.38 PM.png; EcoHealth Alliance re AI grant 4-19-20.docx;

Thank you Kevin

- We need to work with a senior responsible business official – usually PI's and senior business officials are different people.
- When I looked you up on the web, I see the Columbia logo (see attached screenshot). Specifically, it appears to be Columbia University > Ecology, Evolution, and Environmental Biology > EcoHealth Alliance (labeled as an "Affiliation/Department"). Thus the web profile makes it look to me as if EcoHealth Alliance is linked to Columbia University.
- In any case, I'm looping in Dr. Daszak
- We need to know all sites in China that have been in any way linked to this award (Type 1 and Type 2). We have data in NIH, but we want to make absolutely sure that we're of the same understanding.

We greatly appreciate your prompt attention to this matter.

Best, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: 301-496-1096
Email: [redacted]

Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

4 Michael Lauer email on 20 April 2020

Lauer, Michael (NIH/OD) [E] <[redacted]>

Mon 4/20/2020 6:34 PM

To:Naomi Schrag <[redacted]>; Kevin Olival <[redacted]>; Peter Daszak <[redacted]>;

Cc:Black, Jodi (NIH/OD) [E] <[redacted]>; Lauer, Michael (NIH/OD) [E] [redacted]

1 attachment

Screen Shot 2020-04-20 at 4.23.38 PM.png;

Thanks Naomi -- not the impression an observer would get looking at the website (see screen shot), but we understand about the grant.

If they "are entirely separate entities" then why does Columbia identify EcoHealth Alliance as an "Affiliation/Department" on its website.

Maybe with the label "Affiliation/Department" you would have a clearly visible disclaimer that says, "EcoHealth Alliance is not affiliated with nor a department of Columbia"? -- although even that is internally contradictory.

Best, Mike

From: Naomi Schrag <[redacted]>
Date: Monday, April 20, 2020 at 5:19 PM
To: "Lauer, Michael (NIH/OD) [E]" <[redacted]>, Kevin Olival <[redacted]>, "[redacted]" <[redacted]>
Cc: Naomi Schrag <[redacted]>, "Black, Jodi (NIH/OD) [E]" <[redacted]>
Subject: RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

Dear Dr. Lauer,
Columbia and EcoHealth Alliance are entirely separate entities. Some individuals affiliated with EcoHealth Alliance do have adjunct appointments in Columbia's Ecology, Evolution, and Environmental Biology ("E3B") department, but we are not aware of any Columbia involvement with the referenced grant, and have found no agreement or record in our grants system to the contrary.

We would be happy to answer any additional questions. Thank you.
Sincerely,
Naomi Schrag

Naomi J. Schrag

Vice President for Research Compliance, Training and Policy
Office of Research Compliance and Training
475 Riverside Drive, Suite 840
New York, New York 10115
212-854-8123
www.researchcompliance.columbia.edu

RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

5 Peter Daszak email on 21 April 2020

Peter Daszak

Tue 4/21/2020 1:32 AM

To:Lauer, Michael (NIH/OD) [E] [redacted]; Naomi Schrag [redacted]; Kevin Olival [redacted];

Cc:Black, Jodi (NIH/OD) [E] [redacted];

Dear Michael Lauer & Jodi Black – I now have your email and will deal with it directly with you and your staff. Naomi is correct that there is no involvement of Columbia University in this grant. I'm sure NIH has records to confirm that.

From this moment on, I will not cc any staff at Columbia as part of this discussion, and I hope you will also honor that. Respectfully, the discussion of whether or not EHA is an affiliate of CU is entirely irrelevant to the request that you contacted us about, and should remain a private matter between EcoHealth Alliance and Columbia University.

I'll look over your email and respond tomorrow.

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: +1-212-380-0474
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

6 Peter Daszak email on 21 April 2020

Peter Daszak

Tue 4/21/2020 7:03 PM

To:Lauer, Michael (NIH/OD) [E] <[redacted]>;

Cc:Black, Jodi (NIH/OD) [E] <[redacted]>; Aleksei Chmura <[redacted]>; Stemmy, Erik (NIH/NIAID) [E] <[redacted]>; <[redacted]>; <[redacted]>;

Importance: High

1 attachment

EcoHealth Alliance re AI grant 4 19 20.pdf;

Dear Michael – Confirming receipt of your email. I'm also cc'ing the following people so they're aware of this request:

1. Our AOR – Dr. Aleksei Chmura, who has access to all our records
2. My Program Officer for this award, Dr. Erik Stemmy & the Division Director (DMID), Dr. Emily Erberding, so they are informed and aware of the request and our response.

That said we need some time to go through the request for information and will provide this as quickly as we can.

However, **I can categorically state that no funds form 2R01AI110964-06 have been sent to Wuhan Institute of Virology, nor has any contract been signed.** Furthermore, we will comply with NIAID requirements, of course.

Concerning the request for information on all of the sites linked to this award in China, you should be aware that these are documented in our progress reports over the course of the grant. As you can understand we are under enormous pressure to generate data related to the current pandemic, and we do not want to divert staff to this effort. We are hoping the previously filed reports will satisfy this request.

We are well aware of the political concerns over the origins of this outbreak. Our collaboration with Wuhan Institute of Virology has been scientific and we have been consistently impressed with the scientific capabilities of that laboratory and its research staff. Our joint work has led to a series of critical papers published in high impact journals that served to raise awareness of the future threat coronaviruses pose for global health and therefore US national security. Scientific insights with epidemiological significance have been jointly published and our relationship has always been open and transparent and with one concern only, scientific validity. We are concerned that current actions may jeopardize 15 years of fruitful collaboration with colleagues in Wuhan, who are working at the leading edge to design vaccines and drugs that could help us fight this new threat in future years. It is quite remarkable that of the 5 vaccine candidates listed by WHO that are already in human trials, 3 have been developed in China. That said, we of course will

do all we can to make sure any further questions from NIH or any Federal agency are addressed to our fullest knowledge.

Yours sincerely,

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: +1-212-380-4474
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

From: Lauer, Michael (NIH/OD) [E] [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 21, 2020 at 19:28
To: Peter Daszak [redacted]
Cc: Black, Jodi (NIH/OD) [E] [redacted], Aleksei Chmura [redacted], Stemmy, Erik (NIH/NIAID) [E] [redacted], Erbelding, Emily (NIH/NIAID) [E] [redacted], Lauer, Michael (NIH/OD) [E] [redacted]

Many thanks Peter for your response.

We note that:

- No monies have gone to WIV on the Type 2 award and no contract has been signed.
- You agree that you will not provide any funds to WIV until and unless directed otherwise by NIH.
- All foreign sites for the Type 1 and Type 2 awards have been documented in the progress reports submitted to NIH.

We appreciate your working with us.

Best, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: 301-496-1096
Email: [redacted]

8 Aleksei Chmura email on 21 April 2020

From: Aleksei Chmura [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 23, 2020 at 13:50
To: Lauer, Michael (NIH/OD) [E] [redacted]
Cc: Peter Daszak [redacted] Black, Jodi (NIH/OD) [E] [redacted] Erik Stemmy [redacted] Erbelding, Emily (NIH/NIAID) [E] [redacted]

Dear Mike,

I read that we are in agreement and in compliance with all requests. Please let us know if anything further is required. We will continue in our usual close communication with our Program Officer Erik Stemmy.

Sincerely,

-Aleksei

Aleksei Chmura
Chief of Staff &
Authorized Organizational Representative

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

+1.212.380.4473 (office)
[redacted] (mobile)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

From: Lauer, Michael (NIH/OD) [E] [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 23, 2020 at 13:59
To: Aleksei Chmura [redacted]
Cc: Peter Daszak [redacted] Black, Jodi (NIH/OD) [E] [redacted] Stemmy, Erik (NIH/NIAID) [E] [redacted] Erbelding, Emily (NIH/NIAID) [E] [redacted] Lauer, Michael (NIH/OD) [E] [redacted] Compliance Review [redacted]

Many thanks Aleksei.

9 Michael Lauer email on 21 April 2020

Best, Mike

From: Lauer, Michael (NIH/OD) [E] [redacted]
Subject: PLEASE READ -- Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 24, 2020 at 16:47
To: Aleksei Chmura [redacted] Peter Daszak [redacted]
Cc: Black, Jodi (NIH/OD) [E] [redacted] Stemmy, Erik (NIH/NIAID) [E] [redacted]
Erbelding, Emily (NIH/NIAID) [E] [redacted] Linde, Emily (NIH/NIAID) [E] [redacted]
Lauer, Michael (NIH/OD) [E] [redacted] Bulls, Michelle G. (NIH/OD) [E] [redacted]

Dear Dr. Chmura and Dr. Daszak

Please see attached.

10 Michael Lauer email on 24 April 2020

Sincerely,
Michael S Lauer, MD

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: 301-496-1096
Email: [redacted]

From: Aleksei Chmura [redacted]
Subject: Re: PLEASE READ -- Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 27, 2020 at 23:57
To: Lauer, Michael (NIH/OD) [E] [redacted]
Cc: Peter Daszak [redacted] Black, Jodi (NIH/OD) [E] [redacted] Erik Stemmy [redacted]
Emily Erbelding [redacted] Linde, Emily (NIH/NIAID) [E] [redacted] Bulls, Michelle G. (NIH/OD) [E]
[redacted], Alison Andre [redacted]

Dear Michael,

Could Peter and I have a quick chat with you sometime tomorrow (Tuesday) about your email, below?

Sincerely,

11 Aleksei Chmura email on 27 April 2020

-Aleksei

Aleksei Chmura, PhD
Chief of Staff

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

+1.212.380.4473 (office)
[redacted] mobile)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

Exhibit D

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

24 April 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: Termination of NIH Grant R01 AI 110964

Dear Drs. Chmura and Daszak:

I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS) has elected to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI110964, for convenience. This grant project was issued under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284). This grant was funded as a discretionary grant as outlined in the NIH Grants Policy Statement, which states that the decision not to award a grant, or to award a grant at a particular funding level, is at the discretion of the agency, in accordance with NIH's dual review system.

At this time, NIH does not believe that the current project outcomes align with the program goals and agency priorities. NIAID has determined there are no animal and human ethical considerations, as this project is not a clinical trial, but rather an observational study.

As a result of this termination, a total of $369,819.56 will be remitted to NIAID and additional drawdowns will not be supported. The remaining funds have been restricted in the HHS Payment Management System, effective immediately.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

Lauer, Michael (NIH/OD) [E] Digitally signed by Lauer, Michael (NIH/OD) [E]
Date: 2020.04.24 16:41:16 -04'00'

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

cc: Dr. Dirk Stemmy
Ms. Emily Linde

Exhibit E

SPECIFIC AIMS

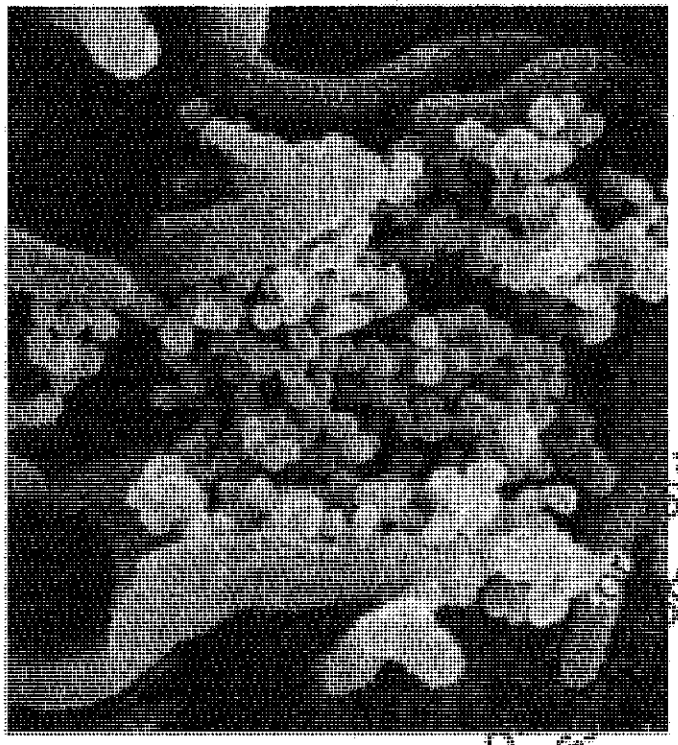
Zoonotic coronaviruses are a significant threat to global health, as demonstrated with the emergence of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) in 2002, and the continuing spread of Middle East Respiratory Syndrome (MERS-CoV). The wildlife reservoirs of SARS-CoV were identified by our group as bat species, and since then we have sequenced dozens of novel SARS-related-CoV (SARSr-CoV) strains. Our previous R01 work demonstrates that bats in southern China harbor an extraordinary diversity of SARSr-CoVs, some of which are able to use human ACE2 to enter into human cells, can infect humanized mouse models to cause SARS-like illness, and evade available therapies or vaccines. We found that the bat hosts of SARSr-CoVs appear to no longer be traded in wildlife markets, and that people living close to bat habitats are the primary risk groups for spillover. At one of these sites, we found diverse SARSr-CoVs containing every genetic element of the wild-type SARS-CoV genome, and serological evidence of human exposure among people living nearby. Thus, there is significant potential for future spillover of SARSr-CoVs, and of public health impacts. *Yet salient questions remain: Are there specific bat communities and sites that harbor CoV strains with higher risk for bat-to-human spillover? Which human behaviors drive risk of bat SARSr-CoV exposure that could lead to infection? Does human exposure to these viruses cause SARS-like or other illness? Can we characterize viral strain diversity, bat traits and human behaviors to assess risk of potential future CoV spillover?* **The proposed work in this renewal R01 builds on these findings** to address these issues by conducting: **1)** focused sampling of bats in southern China to **identify viral strains with high predicted risk of spillover**; **2)** community-based, and clinic-based syndromic, sampling of people to **identify spillover, and assess behavioral risk factors and evidence of illness**; and **3)** conduct *in vitro* and *in vivo* viral characterization and analyze epidemiological data **to identify hotspots of future CoV spillover risk.** This work will follow 3 specific aims:

Aim 1: Characterize the diversity and distribution of high spillover-risk SARSr-CoVs in bats in southern China. We will conduct targeted bat sampling at sites where we predict that undiscovered high risk SARSr-CoV strains exist. Bat sampling will be targeted geographically and by host species to test predictions about evolutionary diversity of SARSr-CoV. We will analyze RdRp and S protein sequences to test their capacity for spillover to people in Aim 3.

Aim 2: Community- and clinic-based surveillance to capture SARSr-CoV spillover, routes of exposure and potential public health consequences. We will conduct focused, targeted human surveys and sampling to identify key risk factors for SARSr-CoV spillover and evidence of illness. To maximize our opportunity of capturing human exposure to bat CoVs, we will conduct community-based surveillance in regions with high SARSr-CoV prevalence and diversity, and individuals having contact with bats. We will assess bat-CoV seropositive status against a small number of questions about human-wildlife contact and exposure. We will conduct clinic-based syndromic surveillance close to these sites to identify patients presenting with influenza-like illness and severe acute respiratory illness, assess their exposure to bats via a questionnaire, and test samples for PCR- and serological evidence of SARSr-CoV infection. We will conduct follow-up sampling to capture patients who had not yet seroconverted at the time of clinic visit.

Aim 3: ***In vitro* and *in vivo* characterization of SARSr-CoV spillover risk, coupled with spatial and phylogenetic analyses to identify the regions and viruses of public health concern.** We will characterize the propensity of novel SARSr-CoVs to infect people *in vitro* using primary human airway epithelial cells and *in vivo* using the transgenic hACE2 mouse model. We will use mAb and vaccine treatments to test our hypothesis that SARSr-CoVs with ~40-25% divergence in S protein sequences from SARS-CoV are likely able to infect human cells, and to evade mAb therapeutics and vaccines. We will then map the geographic distribution of their bat hosts and other ecological risk factors to identify the key 'hotspots' of risk for future spillover.

Overall, our SARSr-CoV program serves as a model platform to integrate virologic, molecular and ecologic factors contributing to CoV emergence while informing high impact strategies to intervene and prevent future pandemics. This includes providing critical reagents, therapeutic interventions and recombinant viruses for future SARSr-CoV pandemic and public health preparedness.



This scanning electron micrograph shows SARS-CoV-2 particles, the virus that causes COVID-19, isolated from a patient in the United States, emerging from the surface of cells grown in the lab. Credit: NIAID-RML

NIAID STRATEGIC PLAN FOR COVID-19 RESEARCH

FY2020 – FY2024

April 22, 2020

National Institute of Allergy and Infectious Diseases

Table of Contents

Executive Summary

The National Institute of Allergy and Infectious Diseases (NIAID) at the United States (U.S.) National Institutes of Health (NIH) is committed to safeguarding the health of Americans and people around the world by accelerating research efforts to prevent, diagnose, and treat COVID-19 and characterize the causative agent of this disease, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This *NIAID Strategic Plan for COVID-19 Research* builds on current trans-NIAID efforts to better understand SARS-CoV-2 pathogenesis, transmission, and mechanisms of protective immunity by expanding resources and activities that support rapid development of biomedical tools to more effectively combat this disease and pandemic. Given the urgency of the public health response, studies that inform efforts to control virus spread and mitigate morbidity and mortality, including therapeutic and vaccine development, are the priority. In addition, it is essential to develop rapid, accurate point-of-care diagnostics—a critical asset to mitigating the spread of COVID-19.

Box 1. NIAID Strategic Plan for COVID-19 Research Mission

Conduct and support research on SARS-CoV-2 and COVID-19 to accelerate the development of safe and effective medical countermeasures that decrease disease incidence, mitigate morbidity and prevent mortality.

The *NIAID Strategic Plan for COVID-19 Research* aligns with the priorities set by U.S. Government–wide task forces for the development of medical countermeasures. NIAID actively participates in COVID-19 task forces to identify opportunities, ensure open communication, encourage resource sharing, and avoid duplication of effort. The plan is structured around four strategic research priorities:

1. **Improve fundamental knowledge of SARS-CoV-2 and COVID-19,** including studies to characterize the virus and how it is transmitted and understand the natural history, epidemiology, host immunity, disease immunopathogenesis, and the genetic, immunologic, and clinical associations with more severe disease outcomes. This includes accelerating the development of small and large animal models that replicate human disease.

2. **Support the development of diagnostics and assays**, including point-of-care molecular and antigen-based diagnostics for identifying and isolating COVID-19 cases and serologic assays to better understand disease prevalence in the population. Diagnostics also will be essential for evaluating the effectiveness of candidate countermeasures.

3. **Characterize and test therapeutics,** including identifying and evaluating repurposed drugs and novel broad-spectrum antivirals, virus-targeted antibody-based therapies (including plasma-derived intravenous immunoglobulin (IVIG) and monoclonal antibodies), and host-directed strategies to combat COVID-19.

4. **Develop safe and effective vaccines against SARS-CoV-2,** including support of clinical trial testing.

To accelerate research, NIAID will leverage current resources and global collaborations, including existing research programs and clinical trials networks. NIAID's research response to COVID-19 will build on experience with diseases caused by other zoonotic coronaviruses (CoVs), including severe acute

respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). NIAID will pursue public-private partnerships to facilitate the translation of research outcomes into life-saving public health interventions. Working with pharmaceutical companies, NIAID has already initiated Phase 1 clinical trials for candidate COVID-19 vaccines and therapeutics. A concerted effort will be made to include minority populations, as well as at-risk and vulnerable populations, in all aspects of NIAID-sponsored research to address health disparities between diverse groups. Characterization of the fundamental virology of SARS-CoV-2 and the immunological response to infection will inform future studies and facilitate the development of effective medical countermeasures. With collaboration from all agencies within the U.S. government and other key U.S. and global partners, NIAID will rapidly disseminate these results so that the information can be translated into clinical practice and public health interventions to combat the pandemic. As such, NIAID has already implemented open sharing of scientific data through publicly available websites and will continue to promote the prompt disclosure of SARS-CoV-2 and COVID-19 research data by the scientific community.

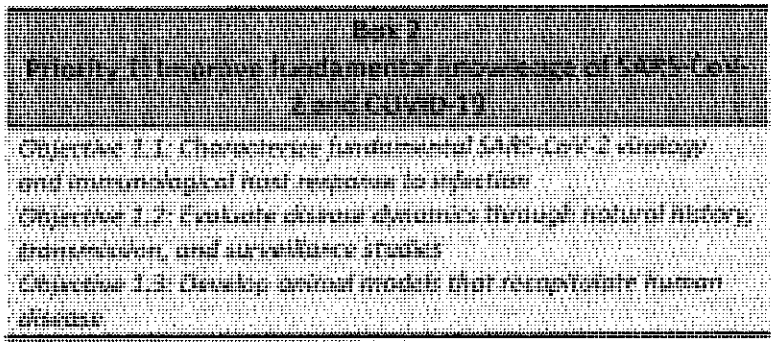
Research Plan

Priority 1: Improve fundamental knowledge of SARS-CoV-2 and COVID-19

Developing effective medical and public health countermeasures against a newly emergent virus like SARS-CoV-2 will require a better understanding of the complex molecular and immune mechanisms underlying infection and disease. Studies that delineate the viral lifecycle and host immune responses to infection can lead to the identification of novel targets for intervention against SARS-CoV-2 infection and COVID-19. Early studies suggest that the clinical manifestations of COVID-19 can vary significantly, and disease severity can range from mild to critical. Thus, a detailed understanding of the clinical course of disease, as well as the clinical, virologic, immunological, and genetic predictors of disease severity, are needed. Gaps also exist in our understanding of the dynamics of disease transmission in different populations over time, including the role of pediatric and elderly populations in viral spread, and the potential seasonality of viral circulation.

Objective 1.1: Characterize fundamental SARS-CoV-2 virology and immunological host response to infection

- **Support the development and distribution of reagents and viral isolates to researchers.** NIAID will continue to support both intramural and extramural researchers by developing reagents and assays for virus characterization and immunological analyses. NIAID will continue to accelerate SARS-CoV-2 research by sourcing viral isolates and clinical specimens for the research community and placing them in repositories to help advance research and countermeasure development. In addition, NIAID will place other critical reagents needed for assay development (e.g., pseudovirions and antigens) in publicly available repositories for distribution.



- **Characterize virus biology and immunological responses to disease.** A comprehensive understanding of the

biological processes involved in SARS-CoV-2 infection and the pathogenesis of COVID-19 are paramount to developing new medical countermeasures to fight the spread of disease. Building on prior research related to MERS and SARS coronaviruses, early studies confirmed several critical features of SARS-CoV-2 infection, including the primary host receptor, angiotensin converting enzyme 2 (ACE-2), and the structure of the virus receptor-binding domain. Studies that delineate the viral lifecycle and host immune responses to infection can lead to the identification of novel targets for intervention against SARS-CoV-2 infection and COVID-19. Understanding the function of essential viral proteins will be necessary for improving diagnostic and immunological assays *in vitro* and *in vivo* models, and other resources needed to advance safe and effective medical countermeasure development. In addition, evaluating the dynamics of host-pathogen interactions at the molecular and cellular levels will be critical to advancing our understanding of viral pathogenesis and immune responses that contribute to SARS-CoV-2 infection.

- **Determine viral evolution and molecular epidemiology.** With a newly emergent virus like SARS-CoV-2, studies to characterize genetic diversity, including those that assess the potential for the virus to evolve and escape host immunity, are pivotal for understanding disease progression and transmission dynamics and may have implications for countermeasure development. Viral genomic analysis matched with patient clinical data will be important to identify biomarkers of virulence and establish paradigms of sequence diversity. In addition, evaluating viral sequence associations with disease outcomes, immune status, and viral replication will provide crucial data to accelerate the development of effective medical countermeasures.

- **Develop low-containment assays to study virus neutralization.** Studies using non-infectious pseudovirions can be conducted in labs without BSL-3 capacity, making them an important tool to enhance understanding of SARS-CoV-2 infection. This capability would enable researchers without high-containment infrastructure to study the dynamics of virus neutralization *in vitro*.

- **Research into optimal public health prevention and mitigation modalities.** Clinical trials including family members of a COVID-19 positive individual can be devised to evaluate transmission, prevention, and other mitigation measures within the household.

Objective 1.2: Evaluate disease dynamics through natural history, transmission, and surveillance studies

- **Characterize disease incidence through surveillance studies.** Clinical manifestations of COVID-19 can vary greatly, ranging from asymptomatic or mildly symptomatic to the development of pneumonia, acute respiratory distress syndrome, and even death.[1] The variation in clinical presentation of COVID-19, combined with the challenges in diagnostic capacity, have made accurate initial assessments of disease incidence a formidable challenge. However, rapid point-of-care and point-of-need molecular tests, which became available in March 2020, will enable hospitals and other healthcare facilities to make informed decisions regarding patient isolation and care. Studies that leverage existing high-throughput diagnostic capacity along with these rapid tests will advance our understanding of disease incidence across the nation and will be a critical component of strategies to implement effective medical countermeasures. Combining these studies with broad serosurveillance studies across existing surveillance networks, including blood bank studies, would

[1] Wu Z and McGoogan JM. *JAMA* 2020 Feb 24. Epub. PMID 32091533.

provide a more complete picture of the scope of disease and the dynamics of infection. Detailed knowledge of host genetics and the human responses to infection across the lifespan will not only provide insights into new approaches for diagnosis, treatment, and prevention, but also may elucidate why individuals respond to SARS-CoV-2 in different ways. Reports to date suggest that COVID-19 resolves in most cases,[2] implying that the immune system can keep the infection from progressing to severe disease in many individuals. However, additional research is needed to better understand why some people progress to severe disease, which will lend critical insights to medical countermeasure development.

- **Assess the dynamics of disease transmission.** Our current understanding of COVID-19 transmission is limited. While recent studies have suggested timeframes for virus survival in aerosols and on surfaces,[3] the contributions of different routes of transmission and the dynamics of animal-to-human and human-to-human transmission remain unclear. The diverse clinical presentations of COVID-19, including a high prevalence of asymptomatic cases, add further complexity to understanding transmission dynamics. Providing a clearer picture of the natural history of viral shedding is a priority, both in acute cases and in asymptomatic infection. Given the challenges of accurately diagnosing asymptomatic individuals because they do not present for treatment, determining the role they play in transmission would provide valuable insights. Elucidating the role of pediatric cases in the spread of SARS-CoV-2 is particularly important. Although pediatric COVID-19 cases are generally asymptomatic or have less severe clinical manifestations than those of adults, the role that children play in spreading the virus is unknown. Additionally, studies to identify potential animal reservoirs and better understand transmission from animals to humans are a research priority, as these reservoirs may lead to future virus introductions and re-emergence of disease in humans. Virus transmission depends on a complex interplay of host, viral, and environmental factors that contribute to disease incidence and spread. Identifying the factors that maintain the disease transmission cycle is critical to developing effective medical countermeasures and public health interventions that will prevent future pandemics.

- **Determine disease progression through natural history studies.** Delineating the natural history of COVID-19 will inform immunopathogenesis, viral tropisms and length of shedding, immune phenotypes, and both protective immunity and host susceptibility. Disease assessment using longitudinal cohort studies, including among high-risk populations such as healthcare workers and the elderly, are important to better understand disease pathogenesis and immune responses to infection. Biomarkers identified from these studies may provide valuable insights into predictors of disease severity.

Objective 1.3: Develop animal models that recapitulate human disease

- **Develop small and large animal models that replicate SARS-CoV-2 pathogenesis.** Developing animal models that recapitulate human disease is a vital early step toward understanding disease pathogenesis and testing the efficacy of medical countermeasures. Small animal models enable rapid, scalable analyses that are particularly valuable for screening countermeasure candidates for efficacy and addressing issues concerning vaccine-induced immune enhancement. Among the small animal models being tested, transgenic mice expressing the human ACE-2 receptor are a promising candidate. In parallel, development and characterization of large animal models, including non-human primates (NHPs) that mimic human COVID-19, are a pivotal step to advance promising

[2] Ibid.
[3] van Doremalen *N et al. N Engl J Med* 2020 Mar 17. Epub. PMID 32182409.

countermeasure candidates. Previous experience with related coronavirus diseases such as MERS and SARS suggests that replicating human disease, particularly its more severe manifestations, in an animal model may be challenging. Fundamental research assessing animal models ranging from mice to NHPs is already underway. NIAID will continue to support the development of small and large animal model candidates to better understand this emerging infection and investigate optimal ways to treat and prevent COVID-19. NIAID also will ensure that validated animal models are made available to the scientific community for evaluating priority countermeasures.

Priority 2: Support the development of diagnostics and assays

Availability of rapid, accurate Food and Drug Administration (FDA)-cleared or authorized diagnostics will increase testing capacity and are critical for identifying and rapidly isolating cases, tracking spread of the virus, managing patient care, and supporting clinical trials. Molecular tests specifically designed to detect SARS-Cov-2 RNA in clinical samples are able to detect low levels of pathogen in clinical samples and offer robust specificity in differentiating SARS-CoV-2 from other related viruses. Continuing to improve the speed and accuracy of molecular and antigen-based diagnostics and making them available at point- of-care will be paramount to accelerating the ability to mitigate disease spread in the current outbreak and any future outbreaks. The development of serologic assays would further bolster surveillance efforts, including the ability to identify individuals who may have resolved prior infection with SARS-CoV-2.

Objective 2.1: Accelerate the development and evaluation of diagnostic platforms

- **Support the development, characterization and availability of reagents for diagnostic validation.** NIAID will support this effort through the development and testing of reagents for diagnostic validation that will be made available through NIAID-sponsored repositories.

Box 3

Priority 2: Support the development of diagnostics and assays

Objective 2.1: Accelerate the development and evaluation of diagnostic platforms

Objective 2.2: Develop assays to increase understanding of infection and disease incidence

- **Support the development of new rapid diagnostics.** NIAID will provide funding to support the development of new rapid diagnostics, including molecular tests and novel antigen detection tests with improved sensitivity, if deemed feasible based on natural history studies.

- **Support the evaluation of promising diagnostics.** In some cases, stakeholders that develop potential diagnostic tests do not have the infrastructure needed to rigorously validate those tests against clinical samples. NIAID will support the testing of promising diagnostics and provide the capacity for evaluating them with live virus samples using our biocontainment laboratories.

Objective 2.2: Develop assays to increase understanding of infection and disease incidence

- **Develop and validate SARS-CoV-2 serological assays.** Serological tests, which detect host antibodies to infectious agents, do not detect the presence of a pathogen directly but can be used as a surrogate marker of infection. Developing more effective serologic tests would help provide information on the extent of asymptomatic infections and cumulative disease incidence, for example through serosurveillance studies. NIAID, with the Centers for Disease Control and

Prevention and the FDA, is developing tests that identify antibodies to SARS-CoV-2 proteins to determine seroprevalence rates and potentially help distinguish antibody responses in individuals receiving vaccines. NIAID will support the development and validation of additional serological assays for serosurveillance studies and as tools for testing the efficacy of promising vaccine or therapeutic candidates.

Priority 3: Characterize and test therapeutics

Currently, there are no FDA-approved or licensed therapeutics specific for coronaviruses. While traditional development pathways for therapeutics can take years, the urgency of the current outbreak underscores the need for rapid development and testing of promising therapeutics. Possible avenues for developing therapeutics include the evaluation of broad-spectrum antiviral agents (antivirals) that have shown promise for other coronaviruses and the identification of novel monoclonal antibodies (mAbs). For broad-spectrum antivirals, Phase 2/2b testing of the RNA polymerase inhibitor developed by Gilead, remdesivir, is already underway. Additional studies will be critical to identify promising therapeutic candidates and to advance them through clinical trial testing. To optimize findings during the pandemic, multiple clinical trials will be conducted in parallel among various populations, including both inpatient and outpatient studies.

Objective 3.1: Identify promising candidates with activity against SARS-CoV-2

- **Screen protease inhibitor and nucleotide analogue class agents and other small molecules with documented activity against other coronaviruses SARS-CoV-2.** Screening drugs that are already licensed by the FDA for other indications and might be efficacious against SARS-CoV-2 infection may provide a route to identifying a therapeutic for use in the current pandemic. Broad-spectrum antivirals that are already FDA approved or in clinical development for other indications—including those previously targeting SARS-CoV-1 and MERS CoV—can be evaluated for their potential activity against SARS-CoV-2 infections. Approved therapeutics for other infectious diseases also are being evaluated as possible treatments for COVID-19. By leveraging their existing efficacy, safety, and manufacturability data, the time to development and production can be reduced. NIAID also will continue working with partners to screen compound libraries for potential activity against SARS-CoV-2. For these studies, priority will be given to compounds based on *in vitro* screening data and the existence of human safety data.

Box 4
Priority 3: Characterize and test therapeutics
Objective 3.1: Identify promising candidates with activity against SARS-CoV-2
Objective 3.2: Conduct treatment studies to advance high-priority therapeutic candidates

- **Identify viral targets for therapeutic development.** Advances in structural biology technology enable researchers to map key viral structures at an unprecedented level. The Structural Genomics Centers for Infectious Diseases (SGCID) apply state-of-the-art high throughput technologies and methodologies, including computational modeling, x-ray crystallography, nuclear magnetic resonance imaging, and cryogenic electron microscopy, to experimentally characterize the three dimensional atomic structure of proteins that play an important biological role in human pathogens and infectious diseases. NIAID will continue to support use of this powerful technology to identify viral targets of SARS-CoV-2 for therapeutics or vaccines.

- **Identify novel mAbs for use as therapy or prophylaxis.** Data from early studies indicate that well-characterized convalescent plasma may provide a treatment benefit in COVID-19.[4] Therefore, IVIG derived from convalescent plasma may also hold promise for treatment. Moreover, peripheral blood mononuclear cells and plasma are being used to identify novel neutralizing antibodies. Through collaborations with structural biologists, binding properties can be quickly assessed. Paired with assessment of neutralization activity, the most promising mAbs will be identified for further characterization in animal models and human trials.

Objective 3.2: Conduct treatment studies to advance high-priority therapeutic candidates

- **Characterize and evaluate host-directed strategies for treatment of disease.** Experience with other coronaviruses indicates that infection of the respiratory tract is rapid and damage is primarily mediated by the host inflammatory response.[5] These conditions may make it difficult to modify COVID-19 with pathogen-directed therapeutics. Instead, host-directed strategies that target the immune response may exert a beneficial therapeutic effect. Host-directed strategies, including immune-modulating agents, will be investigated as potential therapeutic candidates.

- **Conduct clinical trials to demonstrate safety and efficacy of lead therapeutic candidates.** Many potential therapeutic candidates have been identified and are being tested in clinical trials.
  - In March 2020, NIAID launched a multicenter, adaptive, randomized controlled clinical trial to evaluate the safety and efficacy of the investigational antiviral drug remdesivir (GS-5734) for the treatment of COVID-19 in hospitalized adults with laboratory-confirmed SARS-CoV-2 infection and evidence of lung involvement. The trial builds on recent studies by NIAID scientists showing that remdesivir can improve the disease course in rhesus macaques when administered promptly after viral challenge with the MERS CoV.[6] The trial is also adaptive, allowing for additional arms should other therapeutics warrant assessment for efficacy.
  - NIAID is finalizing the protocol for the Big Effect Trial (BET), in which putative therapeutics that have existing human data and are readily available will be tested in patients hospitalized with lower respiratory tract disease. Each potential intervention will be given to approximately 75 patients and evaluated for mitigating disease symptoms. Candidate therapeutics that meet the criteria in this initial study will be further evaluated in larger clinical trials for which the infrastructure is already in place.
  - As mentioned above, identification of novel mAbs for therapy or prophylaxis is another strategic priority. These mAbs should be safe, highly effective, amenable to fast manufacturing, and easy to administer. They will be tested in clinical trials to develop immunotherapies for the prevention and early treatment of COVID-19, potentially in high-risk populations including healthcare workers.

- **Conduct outpatient studies for mild COVID-19 cases.** In cases of mild COVID-19 that do not require hospitalization, outpatient studies could be extremely valuable for testing promising, orally administered FDA-approved drugs that have existing safety data. The antiviral activity of hydroxychloroquine and azithromycin against SARS-CoV-2 has been the focus of many early

[4] Robak JD and Guarner J. *JAMA* 2020 Mar 27. Epub. 32219429.
[5] Newton AH et al. *Semin Immunopathol.* 2016;38(4):471-82. PMID 26965109.
[6] de Wit E et al. *Proc Natl Acad Sci USA* 2020;117(12):6771-6. PMID 32054787.

therapeutic studies.[7,8,9] Testing of these and other candidates, including protease inhibitors and other molecules, in outpatient studies may provide critical efficacy data and could identify an existing drug or drug combination that is safe and effective against COVID-19.

- **Conduct outpatient studies in high-risk populations.** High-risk populations, including health care workers, the elderly or individuals with chronic conditions, are a critical target for the development of therapeutics. Conducting studies in patients with mild cases of COVID-19 among these high-risk groups would be of interest for identifying the benefits of early treatment strategies to mitigate the impact of infection. Therapeutic candidates that have once a day dosing could also be considered for pre-exposure prophylaxis (PrEP) in some of these populations.

Priority 4: Develop safe and effective vaccines against SARS-CoV-2

Developing a safe and effective SARS-CoV-2 vaccine is a priority for preventing future outbreaks of the virus. As vaccine candidates for MERS-CoV, SARS-CoV-1 and other coronaviruses have previously been developed, NIAID investigators and the scientific community are well-poised to use similar approaches in the current pandemic. NIAID will leverage its broad intramural and extramural infrastructure to advance vaccine candidates through Phase 1 safety and dosing clinical trials, with considerations for Phase 2/2b clinical trials for the most promising candidates.

Objective 4.1: Advance promising vaccine candidates through clinical trial testing

- **Conduct a Phase 1 clinical trial of (mRNA) platform candidate mRNA-1273.** Given the urgency of the response effort to develop a safe and effective vaccine, NIAID is prioritizing promising vaccine candidates that can be rapidly produced and tested. NIAID, in collaboration with the biotechnology company Moderna, is conducting a Phase 1 clinical trial of a vaccine candidate that uses a messenger RNA (mRNA) vaccine platform expressing a NIAID-designed recombinant spike protein of SARS-CoV-2. The trial is being conducted at NIAID-funded clinical research sites, with the first enrolled individual receiving the vaccine on March 16, 2020.

- **Prepare for a pivotal Phase 2/2b clinical trial of candidate mRNA-1273. Preparing for the likelihood of a seasonal recurrence of SARS-CoV-2 is imperative to the public health response.** Given the theoretical risk of vaccine-enhanced respiratory disease, large Phase 2 trials are unlikely to launch until this possibility is evaluated in animal models. Planning for those animal studies is underway, and, assuming favorable results, a Phase 2/2b study could be launched later in 2020. This represents a historically fast timeline for the development and testing of a vaccine candidate. Additionally, these studies will provide information on correlates of immunity that will help accelerate the advancement of other vaccine candidates. If the mRNA-1273 vaccine candidate shows protection against SARS-CoV-2 infection in a Phase 2/2b trial, NIAID will work with government partners to ensure that the vaccine is manufactured in sufficient quantities to allow prompt distribution to those at highest risk of acquiring disease.

---

[7] Gautret P et al. *Int J Antimicrob Agents*. 2020 Mar 20:105949. Epub. PMID 32205204.

[8] Molina JM et al. 2020 Med Mal Infect. 2020 Mar 30. pii:S0399-077X(20)30085-8. Epub. PMID 32240719.

[9] Chen Z et al. medRxiv 2020:2020.03.22.20040758. https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2

Box 5
Priority 4: Develop safe and effective vaccines against SARS-CoV-2

Objective 4.1: Advance promising vaccine candidates through clinical trial testing
Objective 4.2: Advance vaccine development through assay and reagent development
Objective 4.3: Advance vaccine development through adjuvant characterization and development

- **Investigate additional candidates through NIAID vaccine programs.** Although promising candidates may show efficacy in preclinical studies, many do not translate into effective vaccines in clinical trials. Therefore, it is crucial to support multiple promising preclinical candidates in the research and development pipeline. To that end, NIAID is advancing multiple additional SARS-CoV-2 vaccine candidates through its Rocky Mountain Laboratories (RML), including approaches that have shown promise against coronaviruses that cause SARS and MERS. Building on previous research to develop a MERS-CoV vaccine, scientists at RML are collaborating with Oxford University investigators to develop a SARS-CoV-2 vaccine that uses a chimpanzee adenovirus vector. RML investigators also are partnering with the biopharmaceutical company CureVac on an mRNA vaccine candidate and collaborating with the University of Washington on a universal coronavirus vaccine development. By leveraging its extensive expertise and research infrastructure, NIAID will continue working with partners and collaborators to advance promising SARS-CoV-2 vaccine candidates.

- **Leverage existing vaccine approaches to target SARS-CoV-2.** NIAID is pursuing multiple strategies to develop a COVID-19 vaccine. Building on past research on emerging pathogens, especially MERS-CoV and SARS-CoV-1 (the virus that causes SARS), NIAID is using previously developed vaccine platforms to rapidly assess the potential of SARS-CoV-2 vaccine candidates. This approach has already resulted in several promising strategies that may be leveraged for SARS-CoV-2, including vaccination using recombinant spike protein, chimpanzee adenovirus vaccine vector, virus-like particles, and live attenuated virus. In addition, NIAID is funding the development of novel vaccine candidates that will be efficacious across the lifespan, including in the elderly.

Objective 4.2: Advance vaccine development through assay and reagent development

- **Develop critical reagents to support vaccine development.** Appropriate tools are needed to identify the most promising vaccine candidates and advance the development of lead candidates as rapidly as possible. To accelerate the vaccine pipeline, NIAID is generating master and working SARS-CoV-2 virus stocks and other reagents critical for developing SARS-CoV-2 immune assays, developing quantitative tests for characterizing SARS-CoV2 assay material, developing a quantitative SARS-CoV-2-specific ELISA, developing virus-specific neutralization assays, and developing quantitative assays for assessing SARS-CoV-2 viral load.

Objective 4.3: Advance vaccine development through adjuvant characterization and development

- **Provide adjuvants to support vaccine development.** Adjuvants are vaccine components that improve vaccine efficacy by inducing long-lived protective immunity. Selection of appropriate adjuvants is crucial for developing safe and effective vaccines. NIAID is working with multiple collaborators to provide adjuvants to the research community for use in SARS-CoV-2 vaccine candidates. These adjuvants are at various stages of development and include compounds that

specifically improve vaccine efficacy in elderly individuals or modulate host immunity toward protective responses while limiting or preventing harmful inflammatory responses.

Conclusion

The sudden emergence and rapid global spread of the novel coronavirus SARS-CoV-2 has created a daunting public health challenge. To address this challenge, NIAID is focusing its considerable expertise and emerging infectious disease resources to facilitate the development of medical countermeasures including diagnostics, therapeutics, and vaccines. The resulting discoveries will not only help mitigate the current pandemic, but also inform prevention, diagnosis, and treatment of future emerging infectious diseases.

A comprehensive strategy requires a coordinated effort among governmental, academic, private, and community-based organizations. The *NIAID Strategic Plan for COVID-19 Research* defines the areas of COVID-19 research within the NIAID mission and outlines the institute's research priorities and goals. This strategic plan builds on many other national efforts and represents a commitment from multiple U.S. government agencies to improve coordination of COVID-19 research and discovery efforts and the development of medical countermeasures.

Exhibit 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious biosafety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

Sincerely,

Michael S. Lauer -S

Digitally signed by Michael S. Lauer -S
Date: 2020.07.08 21:43:41 -04'00'

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

cc: Dr. Erik Stemmy
Ms. Emily Linde

Exhibit 3

ECOHEALTH ALLIANCE'S OBJECTIONS AND RESPONSES TO NIH'S ADDITIONAL CONDITIONS ON GRANT 2R01 AI 110964-6

EcoHealth Alliance, Inc. ("EcoHealth Alliance"), by and through its attorneys, Tarter Krinsky & Drogin LLP, hereby responds and objects to the additional conditions (the "Requests") imposed on grant 2R01 AI 110964-6 on July 8, 2020, by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institutes of Health ("NIH"), under the Department of Health and Human Services ("HHS"), as follows:

GENERAL OBJECTIONS[1]

1. EcoHealth Alliance objects to the Requests to the extent they purport to impose obligations beyond those authorized by the NIH Grants Policy Statement and the applicable statutes and regulations.

2. EcoHealth Alliance objects to the Requests to the extent they seek information and documents that are neither relevant to the Project nor reasonably likely to affect the safety or efficacy of EcoHealth Alliance's continued research funded by grant 2R01 AI 110964-6.

3. EcoHealth Alliance objects to the Requests to the extent they seek the production of documents that are not in EcoHealth Alliance's possession, custody, or control.

4. EcoHealth Alliance objects to the Requests to the extent they are vague, ambiguous, or otherwise unclear as to the precise categories of documents and information sought.

5. EcoHealth Alliance objects to the Requests to the extent that they are overbroad, unduly burdensome or unreasonably cumulative and duplicative.

6. EcoHealth Alliance objects to the Requests to the extent they seek documents and information concerning personal information relating to individuals not affiliated with the Project or Grant on the ground that such requests may invade the rights of privacy of such individuals.

[1] Any capitalized terms not otherwise defined herein shall have the same meaning ascribed to them in EcoHealth Alliance's letter to NIAID, dated August 12, 2020.

7. EcoHealth Alliance objects to the Requests to the extent they seek documents and information regarding transactions or occurrences that took place on or before July 1, 2019, on the ground that such requests are overbroad, and that such documents and information are not relevant to EcoHealth Alliance's continued research funded by grant 2R01 AI 110964-6.

8. EcoHealth Alliance's Responses and Objections to the Requests (including each Request therein) shall not be interpreted as implying that: (i) responsive documents or information exist, (ii) EcoHealth Alliance acknowledges the proprietary of any Request; or (iii) that any Request propounded by NIH is either factually correct or legally binding upon EcoHealth Alliance.

9. EcoHealth Alliance specifically reserves its right to amend, modify, or supplement the objections and responses provided herein.

10. These general objections ("General Objections") are hereby incorporated by reference into each and every of EcoHealth Alliance's responses to the Requests, below.

RESPONSES AND OBJECTIONS TO THE REQUESTS

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.

Response to Request No. 1:

EcoHealth Alliance objects to the Request to the extent it seeks documents and information that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project, which was granted prior to the discovery of SARS-CoV-2. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it has no knowledge or information regarding the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.

2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.

Response to Request No. 2:

See General Objections. EcoHealth Alliance objects to the Request to the extent it purports to seek information or documents that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project. EcoHealth Alliance further objects to the extent the Request seeks documents and information concerning personal information relating to individuals who are not affiliated with the Project. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it lacks knowledge or information regarding the alleged "disappearance of Huang Yanling" or the contention that her "lab web presence has been deleted."

3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.

Response to Request No. 3:

See General Objections. EcoHealth Alliance objects to the Request to the extent it purports to seek information or documents that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that, upon information and belief, it is not in possession, custody, or control of "WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns."

4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.

Response to Request No. 4:

See General Objections. EcoHealth Alliance objects to the Request in that it is vague, ambiguous, or otherwise unclear as to the precise categories of documents and information that are being sought and because the term "out-of-ordinary" is undefined. EcoHealth Alliance further objects to the Request to the extent it purports to seek documents or information that are not in EcoHealth Alliance's possession, custody, or control. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it lacks knowledge or information regarding "diminished cell-phone traffic in October 2019" and/or "roadblocks surrounding [WIV] from October 14-19, 2019."

5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.

Response to Request No. 5:

See General Objections. EcoHealth Alliance objects to the Request to the extent it purports to seek information or documents that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it lacks knowledge or information regarding the contention that "WIV failed to note that the RatG13 virus…was [] isolated from an abandoned mine where three men died in 2012" and why this was not followed up.

6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.

Response to Request No. 6:

See General Objections. EcoHealth Alliance objects to the Request to the extent it seeks to impose obligations on EcoHealth Alliance that are not authorized by the NIH Grants Policy Statement or any applicable statute or regulation. EcoHealth Alliance further objects to the Request to the extent it seeks to impose obligations that are wholly unrelated to the Project or EcoHealth Alliance's ongoing research funding by the Grant. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that, on April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH that stated that EcoHealth Alliance was not allowed to collaborate with WIV regarding the Project and that it should not remit any Grant funds to WIV. On April 21, 2020, Peter Daszak of EcoHealth Alliance sent an email to Dr. Lauer that confirmed (i) no funds from the Grant had been sent to WIV, (ii) no contract had been signed between EcoHealth Alliance regarding research funded under the Grant, and (iii) EcoHealth Alliance would not provide any funds to WIV. As a result, at this time, EcoHealth Alliance is not collaborating with WIV, is not

in possession, custody, or control of WIV, and has no authority to grant NIAID and the U.S. National Academy of Sciences access the facility to conduct an inspection.

7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System.

Response to Request No. 7:

See General Objections. Subject to and notwithstanding the General Objections and without prejudice thereto, EcoHealth Alliance responds that, upon information and belief, as of the date of these responses, all of EcoHealth Alliance's subawards are fully reported in the Federal Subaward Reporting System.

Dated: New York, New York
August 13, 2020

TARTER KRINSKY & DROGIN LLP
Attorneys for EcoHealth Alliance

By: [redacted]
Andrew N. Krinsky
1350 Broadway, 11th Floor
New York, New York 10018
Tel: 212-216-8000

TO: Dr. Michael S. Lauer [redacted]
Dr. Erik Stemmy [redacted]
Ms. Emily Linde [redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

April 26, 2023

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-4182

Dear Dr. Chmura,

I am writing to inform you of the additional actions the National Institutes of Health (NIH) is taking with respect to grants administration at EcoHealth Alliance (EHA). As you recall, NIH has implemented additional oversight measures regarding EHA awards to ensure EHA's documented efforts to strengthen administrative processes meet NIH's expectations. NIH previously imposed Specific Award Conditions (SACs) on awards to EHA. As reflected in Notices of Award, NIH placed the initial SACs on:

- U01 AI151797 on August 29, 2020, and again on February 2, 2022
- U01 AI153420 on February 2, 2022
- R01 AI163118 on September 22, 2022

The award R01 AI110964 beginning on April 19, 2020, remains suspended pending the renegotiation of specific aims for the award without the involvement of the Wuhan Institute of Virology.

Based on NIH's assessment, EHA is still undertaking corrective actions in terms of reaching compliance with several elements of the terms and conditions for the awards cited above. However, the NIH National Institute of Allergy and Infectious Diseases (NIAID) identified remaining challenges in terms of achieving timely submissions, providing sufficient quality and accuracy of budgets and budget justifications, implementation and corrections of prior administrative failures identified and communicated to EHA both verbally and in writing. Additionally, NIAID reviewed EHA's year 3 subaward agreements, provided to NIAID on November 21, 2022, for U01 AI151797, on December 15, 2022, and February 1, 2023, for U01 AI153420 and found that none of these formal written agreements met all the minimum requirements set forth in the NIH Grants Policy Statement, a term and condition of every NIH grant award, Section 15.2 Administrative and Other Requirements. See attached, subaward evaluation charts, for specific elements missing from each written agreement.

NIH acknowledges prior cooperation and substantial improvement in EHA processes and recognizes EHA is still working on implementing corrective actions. However, given the seriousness of these challenges, and in accordance with Federal regulations at Title 2 Code of Federal Regulations (C.F.R.), Part 200.208(b) and NIHGPS Section 8.5, Specific Award Conditions and remedies for noncompliance (specific award conditions and Enforcement Actions), NIH will provide additional oversight of EHA's management of its grant awards, while EHA addresses the material deficiencies related to financial reporting and subrecipient monitoring. Additional specific award conditions will enable NIH grants management

officials to provide additional oversight and monitoring of spending on the grant while permitting EHA to continue work on this grant project.

Therefore, NIH is immediately instituting four SACs on NIAID awards to EHA, including R01 AI110964, U01 AI151797, R01 AI163118, U01 AI153420, along with any future NIH awards to EHA until the corrective actions described below have been implemented by EHA and accepted by NIH.

The four SACs NIH is instituting, described in more detail below, are:

1. Prior approval of subaward written agreement required, prior to entering into consortium agreements
2. Removal of eligibility for unrestricted advance payment
3. Develop or improve written policies and procedures that comply with NIH requirements for:
    a. charging costs to NIH awards, and
    b. entering into written agreements and monitoring subrecipients
4. Independent third-party financial capability review

The conversion from an unrestricted advance payment method to a cash request method extends to any future awards to EHA inclusive of any subaward agreements where EHA serves as a subrecipient on an NIH award.

SAC #1 – Prior approval of subaward written agreement required, prior to entering into consortium agreements

This SAC requires that, prior to entering into consortium agreements, EHA must submit all draft subaward agreements to NIH for prior approval, in accordance with NIHGPS Section 8.1.3 Requests for Prior Approval. Written agreements must be submitted at the following times:

- For the four above-referenced active awards, EHA must renegotiate and resubmit any written agreements for subawards for which work is planned to continue the stated aims of the award beyond the date of this letter, prior to NIH allowing any work by that subrecipient organization.
- Once the written agreement is approved, EHA must submit any proposed amendments to written agreements to NIH for prior approval no later than 30 days before the proposed effective date of the amendment.
- For future subawards requested during a period of performance, and in accordance with NIHGPS Section 8.1.3 Requests for Prior Approval, EHA must submit the written agreement to NIH no later than 30 days before the proposed start of the subaward agreement.
- For future subawards identified in a competing grant application, NIH will require the written agreement as part of Just-in-Time (See NIHGPS Section 2.5.1 Just-in-Time Procedures).

NIH will only approve written agreements that include, at a minimum, the specific requirements set forth in NIHGPS Section 15.2 Administrative and Other Requirements.

SAC #2 – Removal of eligibility for unrestricted advance drawdown of funds

This SAC requires that payments received by EHA under this award be converted from an advance payment method to a reimbursement method, to ensure costs are appropriately charged to NIH awards in accordance with NIHGPS Section 7.2 The Cost Principles.

EHA is ineligible for an unrestricted advance of funds due to this SAC; therefore, cash reimbursement requests must be submitted. Cash reimbursement requests are used when a recipient's cash management must be closely monitored. A recipient may be converted from an unrestricted advance payment method to a cash request basis if, during post-award administration, the responsible GMO determines that a recipient is not complying with the cash management requirements or other requirements of the award. While requests for reimbursement may be submitted monthly, a request for reimbursement may be submitted more often, if additional information is required by the grants management official within NIH. For timely receipt of cash reimbursements, a recipient must submit the request through the awarding office (in this case, NIAID) early enough for it to be forwarded to the HHS Payment Management System (PMS) and at least 20 days prior to the anticipated drawdown. PMS will make payments to the recipient electronically through the Automated Clearing House (ACH) process upon receipt of the approved payment request from the awarding Institute or Center (in this case, NIAID). Please see NIHGPS Section 6.2 Cash Request for additional information.

To ensure that grant payments are received in a timely manner the recipient must adhere to the specific award condition as outlined below:

> This award is ineligible for an unrestricted advance of funds and is on a reimbursement only payment method. EHA is required to provide NIAID with a detailed listing of actual expenses incurred, along with supporting documentation, to support monthly drawdown requests for funds from PMS. The listing of actual monthly expenditures must be submitted via the provided unlocked spreadsheet, with expenses reported by budget category. Supporting documentation for each expense, including all products and services and subawards, must be included with the request. Acceptable documentation includes signed and approved timesheets with description of work performed for all personnel expenses; invoices for supplies, equipment, services or subawards, etc. with a description of the need and how it relates to the aims of the grant; a complete accounting of travel expenses (e.g., hotel, air, per diem) and an explanation of the reason for travel and how it relates to the aims of the grant, etc. All submitted invoices must align with and total the dollar amount submitted on the spreadsheet. If you have other categories of expenses, contact the NIAID grants management specialist to discuss documentation requirements. NIH must approve all drawdown requests before funds can be accessed in PMS. Please submit drawdown requests and supporting documentation to:
>
> Shaun Gratton
> Lead Grants Management Specialist
> National Institute of Allergy and Infectious
> Diseases

National Institute of Health, DHHS
5601 Fishers Lane, Room 4G48, MSC 9824
Bethesda, MD 20892-9824
Phone: (240) 627-3594
Fax: (301) 493-0597
Email: shaun.gratton@nih.gov

All requests must be received by NIAID at least 20 business days prior to anticipated drawdown by EHA to provide sufficient time for review and approval by the appropriate awarding Institute/Center (IC) and transmission to PMS to ensure timely drawdowns.

SAC #3 – Develop or improve written policies and procedures that comply with NIH requirements for charging costs to NIH awards and entering into written agreements and monitoring subrecipients

This SAC requires EHA to develop or improve written policies and procedures to comply with NIH requirements for the following:

a. Costs charged to NIH awards in accordance with NIHGPS Section 7.2 The Cost Principles. Policies should contain, at a minimum, information on roles and responsibilities; definitions; disclosure, review, and approval requirements and processes; timeliness of reporting, and consequences for noncompliance.
b. Policy and processes used to enter into and monitoring subawards agreements under NIHGPS Section 15 Consortium Agreements. Policies and procedures must contain, at a minimum, information on roles and responsibilities; definitions; internal review and approval requirements and processes; how to negotiate subaward agreements; how to monitor subaward agreements, and consequences for noncompliance.

These policies and procedures must be provided to NIH for review no later than September 15, 2023. Please submit the documentation to:

Kristin Ta
Deputy Director, Office of Policy for Extramural Administration
Office of Extramural Research, Office of the Director
Phone: (301) 435-1376
Email: kristin.ta@nih.gov

SAC #4 – Independent third-party auditor

This SAC requires EHA to obtain an independent third-party accounting system audit. This must be a comprehensive review to determine if:

- Accounting practices are aligned with 2 C.F.R. § 200.302 Financial Management.
- EHA is financially capable of managing NIH grant funds in accordance with 2 C.F.R. § 200.302 Financial Management and maintains sufficient internal controls as required by 2 C.F.R. § 200.303 Internal Controls.

- Financial records are properly maintained as required by 2 C.F.R. § 200.334 Retention requirements for records.
- Financial reports are submitted to NIH timely and accurately.
- The recipient has complied with applicable laws, regulations, and terms and conditions of award.

For the independent third-party audit, EHA must select an organization that has not previously conducted an audit for EHA. EHA must submit potential firms to NIH for review by May 26, 2023. NIH will determine and communicate to EHA whether the selection is acceptable. The costs for the independent third-party audit may not be charged to NIH grants.

The report from this review must be provided to NIAID for review by September 15, 2023. NIAID will review the report, in detail, and will make informed decisions on whether EHA has satisfied the CAP within 60 days after the report is submitted.

Time allowed for completing corrective actions, and the method for requesting reconsideration of the conditions:

Please refer to the times noted above for the time allowed for completing the corrective actions. These additional SACs will remain effective until NIH assesses and accepts the corrective actions taken by EHA, based on EHA's submission of acceptable written agreements and drawdown requests, and NIH review of the written policies and procedures. Upon acceptance of corrective actions, NIH will notify EHA and will promptly lift the SACs. These SACs are a remedy for non-compliance and do not constitute an enforcement action. Therefore, the SACs are not appealable under 42 C.F.R. 50, subpart D. However, while not appealable under 42 C.F.R. 50, subpart D, EHA may request that NIH reconsider these SACs by submitting a written request within 30 days of the date of this letter to: Joel Snyderman, Director, Division of Grants Compliance and Oversight at: Joel.Snyderman@nih.gov

Please note this action does not preclude NIH from imposing additional SACs, corrective actions, or other remedies for non-compliance pursuant to 2 C.F.R. § 200.208(b) Specific Conditions and NIHGPS Section 8.5, including but not limited to withholding of support. However, if EHA fails to comply with any of the four SACs that are outlined in this letter, NIH reserves the right to terminate all awards to EHA pursuant to 2 C.F.R. § 200.340(a) Termination and will issue an official letter to EHA providing termination provisions and appeals rights.

Please contact me with any questions concerning this letter.

Michelle G. Bulls -S
Digitally signed by Michelle G. Bulls -S
Date: 2023.04.26 13:23:37 -04'00'

Michelle G. Bulls
Director, Office of Policy for Extramural Research Administration
Office of Extramural Research, Office of the Director

cc:
Dr. Michael S. Lauer
Dr. Emily Erbelding
Dr. Erik Stemmy

Dr. Sara Woodson
Dr. Eun-Chung Park
Ms. Emily Linde

Attachments:
Review of Subrecipient Agreements – EcoHealth Cooperative
Agreements Cost Reimbursement Reporting Format 2-3-23
Subaward Agreements

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

April 26, 2023

The Honorable Brad Wenstrup
Chair, Select Subcommittee on the Coronavirus Pandemic
Committee on Oversight and Accountability
U.S. House of Representatives
Washington, DC 20515

Dear Representative Wenstrup:

Due to your interest in the work of the National Institutes of Health (NIH), I write to you today in a continuing effort to be responsive to your inquiries about NIH oversight of awards to EcoHealth Alliance (EHA).

NIH takes its stewardship over the Nation's investment in biomedical research very seriously and routinely considers processes and measures for strengthening our oversight of federal funds. As you recall, NIH has implemented additional oversight measures regarding EHA awards to ensure EHA's documented efforts to strengthen administrative processes meet the NIH's expectations. We continue to actively monitor EHA's progress and are taking further actions today to ensure we meet our collective goal of supporting rigorous science to improve human health.

As background, awards to EHA aimed to advance our understanding of how pathogens can emerge from wildlife and spillover to cause disease in people. This includes research important for understanding how bat coronaviruses evolve naturally in the environment to become transmissible to the human population. This type of research is critical for the U.S. to prepare for how to respond if these pathogens do enter the human population. All awards were reviewed through NIH's two-stage review process and were determined to be scientifically meritorious during external peer review. Prior to funding, all awards were rigorously assessed by NIH to determine if any additional biosafety or biosecurity measures would be necessary. After a detailed administrative review of EHA's management of these awards, NIH notified EHA of the need to implement a corrective action plan to ensure robust oversight and accountability to the NIH. A summary of these communications and actions are as follows:

- On January 6, 2022, NIH provided Congress with a status update regarding an ongoing NIH Office of Extramural Research (OER) administrative review of EHA. At that time, NIH determined that EHA needed to improve specific areas of its administrative policies and practices representing shortcomings identified by the OER administrative review. Therefore, NIH placed immediate specific award conditions (SACs) on EHA while the grantee worked on a requested Corrective Action Plan (CAP) to address the identified issues.
- On August 19, 2022, NIH provided Congress an update on EHA's implementation of the CAP. At that time, NIH determined that EHA had demonstrated it was working toward

correction of the administrative and financial problems with a full implementation plan laid out in the CAP.

- However, NIH also identified one non-compliance requirement under the grant R01AI110964 (R01) that could not be remedied with SACs. NIH had requested EHA provide NIH the laboratory notebooks and original electronic files from the research conducted at WIV. Since EHA failed to provide these records and WIV was unable to fulfill its duties for the subaward, NIH notified EHA on August 19, 2022, that it would be terminating the WIV subaward for failure to meet award terms and conditions.
- In order to maintain a higher level of oversight, NIH imposed additional SACs for all EHA awards for a minimum of three years. These SACs included doubling the frequency of the required scientific progress and financial reports EHA is required to submit to NIH. In addition, EHA is required to conduct onsite inspections of all its subawardees every six months to confirm that all terms of subaward agreements are being fully and appropriately executed.

NIH acknowledges prior cooperation and substantial improvement in EHA processes and recognizes EHA is still working on implementing corrective actions. However, given the seriousness of these challenges, NIH will provide additional oversight of EHA's management of its grant awards while EHA addresses the material deficiencies related to financial reporting and subrecipient monitoring. Accordingly, NIH is immediately imposing four additional SACs on NIH awards to EHA. These include requiring EHA to develop or improve written policies to comply with the NIH Grants Policy Statement (GPS) and requiring EHA to receive prior approval of subaward written agreements from NIH to ensure EHA complies with all requirements in the NIH GPS.

In addition, NIH is removing EHA's eligibility for unrestricted advance drawdowns of funds—which means NIH is converting EHA from an advance payment method to a reimbursement method. This will require EHA to submit monthly reimbursement requests with a detailed list of actual expenses incurred and the supporting documentation. The reimbursement method will provide NIH with stronger oversight of EHA's accounting practices. Lastly, NIH is requiring EHA to obtain an independent third-party accounting system audit to conduct a comprehensive review of EHA's accounting practices and financial responsibilities under the terms and conditions of the NIH awards.

NIH believes these additional monitoring mechanisms will allow NIH stronger oversight of EHA to ensure that the grantee meets the responsibilities required to receive federal funding. In a continued effort towards full transparency, NIH has attached the letter to EHA laying out the additional SACs. I hope this information is helpful.

Sincerely,

Michael S. Lauer, M.D.

Enclosures:
Letter from NIH to EHA on April 26, 2023

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

23 October 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

I am following up on Mr. Krinsky's August 13, 2020, letter on behalf of EcoHealth Alliance, Inc. ("EcoHealth") responding to NIH's suspension of grant R01AI110964, which funds the project *Understanding the Risk of Bat Coronavirus Emergence* (the "Project"). Per my letter of July 8, 2020, NIH reinstated the grant but suspended all award activities because we have concerns that the Wuhan Institute of Virology (WIV), which previously served as a subrecipient of the Project, had not satisfied safety requirements that applied to its subawards with EcoHealth, and that EcoHealth had not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance. EcoHealth objected to the suspension on the grounds that WIV has no *current* connection to the Project of EcoHealth's research, and EcoHealth had not issued any subawards in connection with the Grant *at the time of the suspension.*

The fact that EcoHealth does not currently have a subrecipient relationship with WIV and had not issued subawards to WIV at the time of suspension does not absolve EcoHealth of any past non-compliance with the terms and conditions of award for grant R01AI110964. While EcoHealth did not issue a subaward to WIV for year 6 of the grant, WIV served as a subrecipient for years 1 through 5. NIH awarded EcoHealth grant R01AI110964 in 2014, with a project period of June 1, 2014, through June 30, 2024, as renewed. In EcoHealth's grant application, EcoHealth listed Drs. Zheng Li Shi and Xing Yi Ge of WIV as co-investigators and senior/key personnel. It stated that "Drs. Shi, Zhang, and Daszak have collaborated together since 2002 and have been involved in running joint conferences, and shipping samples into and out of China." EcoHealth listed WIV as a Project/Performance Site Location. In describing WIV's facilities, EcoHealth described WIV as China's premier institute for virological research" and touted WIV's "fully equipped biosafety level 3 laboratory" and "a newly opened BLS-4 laboratory." In support of the application, Dr. Zheng Li Shi's personal statement indicated that "My lab will be responsible for diagnosis, genomics and isolation of coronavirus from wild and domestic animals in Southern China and for analyzing their receptor binding domains." The application stated that "Wuhan Institute of Virology and the Wuhan University Center for Animal Experiment BSL-3

lab have an Internal Biosafety Committee and are accredited BSL-2 and BSL 3 laboratories. All experimental work using infectious material will be conducted under appropriate biosafety standards. Disposal of hazardous materials will be conducted according to the institutional biosafety regulations."

EcoHealth requested funding specifically for activities to be carried out by WIV. NIH awarded EcoHealth a total of $749,976 for WIV's work in the following annual amounts for years 1 through 5:

	-Yr 1	-Yr 2	-Yr 3	-Yr 4	-Yr 5
Total Direct Costs	$123,699	$128,718	$147,335	$147,335	$147,335
F&A Costs @ 8%	$9,896	$10,297	$11,787	$11,787	$11,787
TOTAL COSTS	$133,595	$139,015	$159,122	$159,122	$159,122

As stated in the Notices of Award for each budget period of the grant, the awards were subject to terms and conditions, which include the NIH Grants Policy Statement (GPS) and applicable HHS grant regulations. As I indicated in my letter of July 8, 2020, as a term and condition of award EcoHealth was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). See also, 45 C.F.R. § 75.342(a) ("The non-Federal entity is responsible for oversight of the operations of the Federal award supported activities."). Moreover, EcoHealth was required to "Establish and maintain effective internal control over the Federal award that provides reasonable assurance that the non-Federal entity is managing the Federal award in compliance with Federal statutes, regulations, and the terms and conditions of the Federal award[.]" 45 C.F.R. § 75.303(a). The Notice of Award stated that as a term and condition of award, "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]." Moreover, the NIH GPS provides that NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients, so these terms applied to WIV. 45 C.F.R. § 75.101.

As I stated, NIH has concerns of non-compliance with terms and conditions of award—namely, that WIV had not satisfied safety requirements under the award and that EcoHealth Alliance had not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance. Accordingly, NIH suspended all activities related to R01AI110964, pursuant to 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare.

In my letter of July 8, 2020, I provided EcoHealth with the opportunity to object and to provide information and documentation challenging the suspension. Specifically, I sought information and materials that speak to WIV's lab safety and EcoHealth's oversight of its subrecipient, and an inspection of WIV's laboratory records and facilities. I indicated that as a specific condition of award, during the period of suspension, EcoHealth Alliance may not allow research under this

project to be conducted and that no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients.

EcoHealth objected to the requests on the grounds that "NIAID is not authorized under 45 CFR§§ 75.371, 75.205, and 75.207, entitled *Specific Award Conditions*, to impose, *inter alia*, conditions that consist of demands for information regarding entities that are neither subrecipients of grant funds nor project affiliates."

These provisions are irrelevant to NIH's requests. NIH is required to permit the opportunity for recipients to object and provide information and documentation challenging a suspension, 45 C.F.R. § 75.374, so we specifically gave EcoHealth the opportunity to provide information that speaks to NIH's concerns. Moreover, as a granting agency, NIH is required to "manage and administer the Federal award in a manner so as to ensure that Federal funding is expended and associated programs are implemented in full accordance with U.S. statutory and public policy requirements: Including, but not limited to, those protecting public welfare [and] the environment[.]" 45 C.F.R. § 75.300(a). In addition to seeking information that speaks to compliance with terms and conditions of award, NIH is entitled to "make site visits as warranted by program needs." 45 C.F.R. § 75.342. As a term and condition of award, NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. § 75.364); and must have "timely and reasonable access to the non-Federal entity's personnel for the purpose of interview and discussion related to such documents" (id.). These requirements flow down to subawards to subrecipients. 45 C.F.R. § 75.101. "Non-Federal entities must comply with requirements in [45 C.F.R. Part 75] regardless of whether the non-Federal entity is a recipient or subrecipient of a Federal award." 45 C.F.R. 75.101. As the grantee, EcoHealth was required to have in place, "A requirement that the subrecipient permit the pass-through entity and auditors to have access to the subrecipient's records and financial statements as necessary for the pass-through entity to meet the requirements of this part." 45 C.F.R. § 75.352(a)(5). For each of these reasons, NIH is justified in seeking the materials, information, and a site visit specified in my letter of July 8, 2020.

In addition to objecting to NIH's authority to seek the materials, information, and a site visit, EcoHealth has responded that it lacks knowledge or information regarding the requests; that it is not in possession, custody, or control of the specified items; and that it has no authority to grant NIAID and the U.S. National Academy of Sciences access to WIV's facility to conduct an inspection. EcoHealth's responses have not satisfied NIH's concerns that EcoHealth had failed to adequately monitor the compliance of its subrecipient, and that the subrecipient, WIV, had failed to comply with safety requirements.

Notwithstanding this, NIH is providing an additional opportunity for EcoHealth to provide information and documentation challenging these concerns of non-compliance. Accordingly, in addition to reiterating our prior requests (1) through (6) per our letter of July 8, 2020, NIH requests the following information and materials, which must be complete and accurate:

1. Provide copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety.
2. Describe EcoHealth's efforts to evaluate WIV's risk of noncompliance with Federal statutes, regulations, and the terms and conditions of the subaward.
3. Provide copies of all WIV biosafety reports from June 1, 2014 through May 31, 2019.

During the ongoing period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further assess whether EcoHealth Alliance and WIV complied with the terms and conditions of award, including compliance with other terms and conditions of award that may be implicated. We remind you that during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the continued suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 C.F.R. Part 75, including, but not limited to, terminating the grant award or disallowing costs. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

cc: Dr. Erik Stemmy (NIAID)
Ms. Emily Linde (NIAID)

EcoHealth Alliance

Dr. Michael Lauer
Deputy Director for Extramural Research,
NIH, Bethesda, MD.

Response to the Reinstatement and immediate suspension of 2R01AI110964 "Understanding the Risk of Bat Coronavirus Emergence"

April 11th 2021

Dear Dr. Lauer,

I am responding your letters of 7/8/2020 and 10/3/2020 regarding the reinstatement and immediate suspension of NIH grant 2R01AI110964 "*Understanding the Risk of Bat Coronavirus Emergence*", that was terminated "for convenience" on 4/24/2020. In particular, this letter addresses the conditions you state would need to be fulfilled in order for us to have access to the funds to continue this work.

As you know, we had not set up any subcontracts to the Wuhan Institute of Virology under this renewal R01. Immediately following NIH's letter on 4/19/2020 that the WIV was being 'investigated', we suspended all plans for contractual work with WIV. This termination of a funded relationship with the institute makes it extraordinarily difficult and more likely impossible to provide the information requested about an autonomous foreign organization – as would also be the case for a domestic one - that our organization neither works with currently, nor has control over.

Additionally, our collaborative work with the Wuhan Institute of Virology prior to your grant termination letter of 4/24/2020 and that planned in the suspended grant, is wholly unrelated to many of the conditions listed below. These conditions also pertain to certain events and situations that in no way involve EcoHealth Alliance or are not under our control. Thus, most of the conditions below are either unrelated to EcoHealth Alliance's planned research in our highly rated, approved and funded grant application, and/or to the biosafety of our continued research funded by the suspended grant when it is reinstated in full.

Furthermore, in our recent correspondence with NIH regarding the latest in a series of FoIA requests, we were informed (1/26/2021 – see email correspondence at the end of this letter) by an NIH staff member Garcia-Malene Gorka that "any indication from my program that there is an ongoing investigation into WIV can now be disregarded, as we recently confirmed there are no pending investigations into that organization." Because this was the explanation in your initial letter of 4/19/2020 for the decisions from your office regarding restrictions on, termination of, then reinstatement and suspension of our grant, we believe that these decisions should now be reassessed.

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

Despite our concerns about the relevance, fairness, or ability to fulfil the conditions as set forth in detail below, I have made extensive efforts to satisfy NIH's broad concerns, and have provided details of how these are relevant to each condition below. This includes serving as an expert on the WHO-China joint Mission on the Animal Origins of COVID-19, which involved 1 month on the ground in China (including 2 weeks locked in quarantine), at great personal burden and risk to me, to our organization, and to my family. I undertook this mission at a time when I have had increasing levels of personal attack and harassment, including a white-powder letter to my home address a few weeks after the details of our grant termination went public, and death threats that begun at the same time and continue to this day. It is clear in the wording of these attacks that many are a direct result of dangerous conspiracy theories inadvertently amplified by NIH's grant termination, and repeated in the conditions listed below. This type of harassment has accelerated to the point that personal security guards are now stationed at my home address, where I have also had to install invasive equipment and set up procedures to protect my family against expected violent attacks. Additionally, I now meet regularly with FBI agents and others at my home to monitor these threats. As I am sure you appreciate, this has a significant toll on my work, my personal life and my family.

Below, I detail our response to each of the conditions placed on our suspended grant, in an effort to provide as much information as possible and to explain the limitations on what we can do to respond. I look forward to your reply and hope that these will allow NIH to lift the suspension on funding so that we can continue our work to help protect our nation, indeed the global population, against future coronavirus pandemics. Should you wish, I feel certain we may discuss these points without legal counsel in a scientist-to-scientist conversation, as you have suggested verbally to others at NIH, and they have conveyed to me.

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
We believe this condition is effectively impossible for us to fulfil, for the following reasons. Firstly, there is no scientific nor administrative rationale for us to attempt to obtain a SARS-CoV-2 aliquot given that it is not part of our funded collaboration with WIV. Secondly, EcoHealth Alliance scientists do not have any capacity to work on such an aliquot (EHA does not conduct virological laboratory work on SARS-CoV-2) in the USA. This further reduces the validity of a scientific basis for this request to WIV. Thirdly, EcoHealth Alliance scientists were not part of the work that WIV conducted to determine the viral sequence of SARS-CoV-2, and this was not part of our (then active) R01 funded collaboration. This is publicly stated by the lack of EHA authors listed on the paper and the lack of acknowledgement of our grant as a funding source for this work. This publicly discounts any claim of sample ownership or control. Fourthly, the collaborative research laid out in our now-suspended grant does not include the shipping of human viral isolates out of China. Finally, during the last 16 months, there has been a series of vitriolic attacks from the US Government accusing China of bioengineering and releasing SARS-CoV-2 or of otherwise allowing COVID to become pandemic. Given these attacks, and WIV's status as a government entity, it seems to us incredulous that any request, particularly without scientific rationale, from a US non-profit to a Chinese Government laboratory for an active sample of a pathogenic human virus would likely be successful. We note that 1) to our knowledge China has not supplied such an aliquot to any formal request from a government; and 2) that if circumstances were reversed and a Chinese non-

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

governmental institution requested a similar pathogenic viral aliquot from a US government BSL-4 laboratory, this would also be unlikely to be fulfilled.

While we understand that it may be of scientific interest to some US-based researchers to analyze this viral sequence, this scientific interest could easily be satisfied without the need for an aliquot. The full genome of this viral sequence was uploaded to a freely accessible database on January 10 2020 and has been used widely by scientists in the USA (included those funded by NIH) and around the world in their work. Furthermore, isolates of the virus from patients in Thailand and Australia during early 2020 are essentially the same, and have been shared extensively.

2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
International experts on the WHO COVID-19 origins mission, including myself, asked direct questions on this issue to staff at WIV, including the Director of the institute, the P4 Lab Director, Dr. Shi and others. The response from all was consistent, as stated in the WHO mission report published 3/30/2020: "This person according the WIV staff was an alumnus who graduated in 2015 and was now working in a different province and did not accept to talk with media. The person had been contacted and tested and ascertained to be healthy."

Given that the WHO team was not given access to this individual and that China's personal privacy laws are preclude our ability to insist on a meeting, it is difficult to see how a request from a US non-profit would have been approved. It seems at the least to be significantly outside the remit of a US-based non-profit organization to inquire further about the whereabouts of a citizen of a foreign country who has never to our knowledge been involved in our work, and over whom we have no control, influence, nor legal responsibility.

Finally, while many conspiracy theorists have suggested that the lack of a web presence of this person suggests some nefarious activity, there are dozens of unremarkable and routine reasons why a person may be removed from a web listing of employees or students. Not least of these is when a staff member leaves an institution, or a student graduates.

3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
We believe that WIV senior staff comments reported in the WHO COVID origins mission report directly address this request in that they publicly state that no significant safety issues were found in their laboratory prior to, or following, the emergence of COVID. Any questions regarding the safety of the WIV also need to be put into the context of the widely published history of this lab as being built to international safety engineering standards, adhering to international safety practice standards indicated in the BMBL, and with lead WIV staff trained in safety in the United States by a known authority running the BSL-4 lab at the University of Texas Medical Branch in Galveston (as reported in the U.S. Dept of State cables). Furthermore, no verifiable evidence of safety issues have been reported prior to, or following the U.S. Dept of State cables.

EcoHealth Alliance
460 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.7460
EcoHealthAlliance.org

Regarding the U.S. Dept. of State cables, these do not in fact provide evidence of safety concerns at the laboratory. Neither do they convincingly imply safety issues. In fact, they may be simply interpreted as a request for funding from a diplomatic mission set up to further joint US-China research. It is important to note that initially only very limited phrases from these cables were selectively leaked by a Washington Post reporter in an opinion piece that did not verify nor quote direct sources. This opinion piece is demonstrably incomplete in its reporting, however it has been widely cited as providing evidence of safety issues at WIV (https://www.washingtonpost.com/opinions/2020/04/14/state-department-cables-warned-safety-issues-wuhan-lab-studying-bat-coronaviruses/). I have some detailed knowledge of the background to these cables because the diplomatic visit to WIV that they report was a direct result of our NIH-funded work. As part of EcoHealth Alliance's work in China over the past 15 years, including that funded by NIAID, I visited the US Embassy in Beijing regularly and was involved in discussions with US Embassy staff to set up a field visit to the WIV in order to generate goodwill between the US and China at a time when President Trump was planning a state visit. I did this out of a sense of duty to our government, and to the NIH so that our project could help foster goodwill between our countries, as well as provide an indication of the importance of NIH's work. Following the US Embassy staff mission, I was told by people privy to the cable's contents that the articles were positive and supportive of the work we were doing under NIAID funding, and that the trip was a success.

Now that the full text of these cables (embedded at the end of this letter) has been released with minor redactions (https://news.slashdot.org/story/20/07/20/0611205/full-text-of-us-state-department-cables-finally-released-showing-safety-in-chinese-lab), it seems that this more positive interpretation is justified. As you can see in the excerpts below, the request for more laboratory technician support could be reasonably interpreted as simply a request for the funding for more laboratory technician support, rather than a statement that the lab was unsafe, particularly given that the visit was set up as part of an effort to further develop US-China collaborative research opportunities. Furthermore, the cables are extremely positive about the importance of the collaborative work we were conducting with WIV under NIAID funding:

"**REDACTED** noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this they would welcome more help from U.S. and international organizations as they establish "gold standard" operating procedures and training courses for the first time in China."

"The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study **REDACTED** (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS

EcoHealth Alliance
460 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like corona viruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention."

4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.

The WIV staff categorically stated to the WHO mission that their lab is audited annually and no unusual events have been identified. The reports of diminished cell-phone traffic and roadblocks have not been verified or published by reliable sources. Furthermore, should hard evidence of diminished cell-phone traffic and roadblocks exist, it is not necessarily indicative of any issues related to concerns about the laboratory studies underway or safety or security incidents within the laboratory. These issues could be explained by any one of a series of issues that occur regularly in the US without nefarious connotations. For example, they could be due to roadwork or other infrastructure repair or maintenance, technical problems with cell-phone transmission, or rerouting of traffic as regularly occurs in Washington DC and other cities due to transport of visiting dignitaries or other events. Finally, there is no credible reason to think that any request a US non-profit might make to the Chinese government for an explanation of traffic or cell-phone issues would result in any response.

5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.

Since your letter of 7/8/2020, it has been widely reported that WIV scientists have published an addendum to their original paper in *Nature* that described SARS-CoV-2 and compared it phylogenetically to RaTG13. In this follow-up publication, they explain the rationale for conducting work in this mine, and any potential connection to the miner's illnesses and deaths. Importantly, they state that serological results in their lab at the time of the incident did not show that these miners were positive for SARSr-CoVs as some media articles have suggested. They then re-tested the miner samples in 2020 using a range of assays, and found no evidence of SARS-related CoV, nor of SARS-CoV-2 specific antibodies or nucleic acid. During the meeting of the WHO mission team with WIV staff, they were asked a series of questions about the miner's illnesses. The responses were that, while symptoms identified were similar to COVID in that they had pneumonia (a common occupational hazard for miners), their symptoms were also similar to other bacterial or fungal pneumonias. This, and the lack of evidence for SARSr-CoV infection, led them to conclude that SARS or COVID infection was not the cause of these miner's illnesses.

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV fieldwork (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.

The WHO mission was negotiated at the very highest levels as the legitimate way to proceed in an investigation of COVID-19 origins, particularly with such critical geopolitical ramifications from this pandemic. Given the intensity of political attacks and conspiracy theories around this lab, it is unreasonable to expect that the Chinese government or WIV would respond to a request from a US non-profit for an outside inspection team. The 11 international expert members of the WHO team included authorities on epidemiology, animal-origin viral infections and One Health. Members of this team have extensive experience conducting lab audits (e.g. Dr. Peter Ben Embarek), running laboratories dealing with human clinical samples (e.g. Drs. Dominic Dwyer, Thea Fischer), and commissioning, managing and accrediting laboratories in foreign countries (myself, Dr. Fabian Leendertz). The WHO-China Joint Study report details the field site visits to multiple labs in Wuhan, including the WIV and summarizes our findings. This includes information on the management of the WIV, safety at the labs, audits and training and testing of staff. I acted in good faith to try to conform to the WHO terms of reference while ensuring that as much information on the laboratory was provided in the report. This information specifically addresses one of your questions above, with categorical statements from WIV senior staff that they did not have SARS-CoV-2 in their possession prior to December 2019.

After returning to the USA, and in the weeks prior to the publication of the report, I worked hard to make sure this critical information was shared as rapidly as possible with the US Government and agencies, including by:

- Briefing Drs. Anthony Fauci and Clifford Lane of NIAID on the findings of the mission;
- Presenting a full talk about the work to the NIAID COVID PI group that meets weekly
- Briefing FBI and other US Government intelligence agency staff
- Briefing members of the US NASEM Forum on Microbial Threats
- Briefing staff on the White House National Security Council
- Briefing staff on the House Committee for Science, Space, and Technology

7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System.

This has been done and all subawards fully reported as soon as we could once you notified us of this requirement in your letter of 7/8/2020.

8. Provide copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety.

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

As we related in response to your letter of 4/19/2020 that asked us to suspend work with WIV, we had not yet set up a subcontract with WIV for the period of this award, therefore no such subrecipient agreements exist. Our plan was to monitor WIV's compliance as we had in the 5 years prior, by means of semi-annual meetings with the lead investigator and assessments of compliance against all conditions of the award. Additionally, following the NIH's termination, then reinstatement and suspension of our funding, we have contracted with a leading lab biosafety contractor based in Southeast Asia (Dr. Paul Selleck) who has extensive experience commissioning, accrediting and auditing BSL-2, -3, and -4 labs, and has worked for over a decade at the BSL-4 Australian Animal Health Lab. We will be using their services where appropriate for foreign lab subcontractees to assess lab biosafety procedures and conduct audits, including following the full reinstatement of 2R01AI110964. Finally, we have appointed a Senior Field Veterinarian who will oversee all EcoHealth Alliance fieldwork in the region and ensure continued compliance with biosafety when conducting animal capture, sampling and sample handling. We have done this at EcoHealth Alliance's own expense, despite our unblemished record on biosafety, to pre-empt calls for further sanctions against our work given the continued attacks against EcoHealth Alliance in the press after the termination of our NIH grant.

9. Describe EcoHealth's efforts to evaluate WIV's risk of noncompliance with Federal statutes, regulations, and the terms and conditions of the subaward.
Over a 15-year period of collaboration with WIV, we have found no evidence to suggest that there was any element of noncompliance with any of the conditions of the grants or contracts covering our collaboration. Our interactions with all staff at the institute have been professional, respectful, open, and with a focus on the science at a very high level. This has contributed to a relationship built on trust and one that is entirely comparable to our scientific collaborations with laboratories in the US, Europe, Australia, Thailand and over 20 other countries. We continue to believe that this laboratory is highly competent and is an extremely low risk for undisclosed accidental release of virus, and there is no verifiable indication as to why we should not continue to believe so. We would of course consider a change in this assessment if significant and verifiable evidence of lab biosafety issues or breach of other Federal statutes are brought forth, but to date we are aware of none.

10. Provide copies of all WIV biosafety reports from June 1, 2014 through May 31, 2019.
Given the intense geopolitical pressure around the accusations that WIV intentionally or accidentally released SARS-CoV-2 (something which the WHO mission deemed 'extremely unlikely'), obtaining such information is not a plausible option at present.

11. Additional information, re. Lack of ongoing investigation into Wuhan Institute of Virology by NIH:

From: Garcia-Malene, Gerka (NIH/OD) [E] [redacted]
Sent: Tuesday, January 26, 2021 12:20:51 PM
To: [REDACTED]
Cc: [REDACTED]; Bartok, Lauren (NIH/NIAID) [E]; NIH FOIA
Subject: [EXT] FW: FOIA Case No. 55702 re: EcoHealth Alliance & Grant No. R01AI110964-6

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

Good afternoon, **[REDACTED]** –

I'd like to insert myself into the unfolding FOIA conversation in hopes of providing some helpful context. Our records show that this competing renewal has in fact been funded. In addition, any indication from my program that there is an ongoing investigation into WIV can now be disregarded, as we recently confirmed there are no pending investigations into that organization. If we can agree on the above, all that would remain is to receive your proposed redactions to the records sought under the FOIA request.

Please let me know if there are any questions. I look forward to facilitating the Pre-Disclosure Notification process as efficiently as possible.

Best regards.

Gorka Garcia-Malene | FOIA Officer for the National Institutes of Health

From: [REDACTED]
Sent: Monday, January 25, 2021 5:21 PM
To: Bartok, Lauren (NIH/NIAID) [E] [redacted]
Cc: [REDACTED]
Subject: FOIA Case No. 55702 re: EcoHealth Alliance & Grant No. R01AI110964-6

Dear Ms. Bartok:

As you may recall, this firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance"), with respect to certain FOIA requests, including the instant request, FOIA Case No. 55702. The instant request seeks the same documents sought last year in FOIA Case No. 53996, regarding the research project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant 2R01AI110964. A copy of our prior letter regarding FOIA 53996 is available via the link provided below using the password **[REDACTED]**. On the grounds set forth in the letter, FOIA 53996 was denied in its entirety.

Likewise, FOIA 55702 should be denied and the grant documents should be withheld. First, grant 2R01AI110964-06 remains an unfunded competing renewal grant that is the subject of a pending first-level appeal and, thus, the materials are not subject to disclosure under NIH Grants Policy Statement §2.3.11.2.2. Moreover, in the context of the appeal, NIH has made multiple requests for further information regarding The Wuhan Institute of Virology ("WIV"), which requests indicate that a law enforcement investigation concerning WIV remains ongoing. Second, as demonstrated by the recent attack on the US Capital fueled by disinformation and conspiracy theories, the need to protect the privacy of EcoHealth Alliance's employees and affiliates is more important than ever. Last, while EcoHealth Alliance did not initially identify that the grant proposal contained confidential-commercial and propriety information, this is not dispositive. Moreover, since the

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4490
EcoHealthAlliance.org

filing of the renewal application, there has been a global COVID-19 pandemic, which has sparked international and highly competitive research in the area of bat coronaviruses.

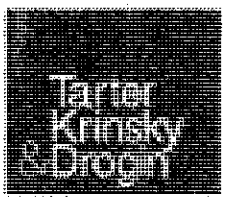
At the very least, the responsive documents will require significant redactions. While the grant documents were previously reviewed and redacted in connection with FOIA 53996, we require a further opportunity to review the documents to confirm, *inter alia*, that all personnel information has been removed given the heightened risk of harm in this unprecedented political environment. Accordingly, EcoHealth Alliance respectfully requests a forty-five (45) day extension of time to respond to FOIA 55702, to allow sufficient time for EcoHealth Alliance to conduct a further review of the responsive documents and provide an updated letter response that incorporates recent developments and specific justifications for additional redactions.

Please confirm that NIH will deny FOIA 55702 in its entirety or that NIH is agreeable to EcoHealth Alliance's request for an extension of time to provide a particularized response to FOIA 55702. Please also confirm NIH's receipt of this email.

Thank you.

Best,
[REDACTED]

FOIA Case No. 53996 - EcoHealth Alliance's Letter Response to FOIA Request, dated June 5, 2020 (With Exhibits)
[REDACTED]



[REDACTED]

Tarter Krinsky & Drogin LLP
1350 Broadway | New York | NY | 10018
www.tarterkrinsky.com | LinkedIn
COVID-19 RESOURCE CENTER

12. Publicly released details of U.S. Department of State Cables regarding visit to Wuhan Institute of Virology, as cited in condition #3 above. These are available from a number of sources, including the Washington Post and (https://news.slashdot.org/story/20/07/20/0611205/full-text-of-us-state-department-cables-finally-released-showing-safety-in-chinese-lab).

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

UNCLASSIFIED
SBU

MRN:	18 BEIJING 138
Date/DTG:	Jan 19, 2018 / 190739Z JAN 18
From:	AMEMBASSY BEIJING
Action:	WASHDC, SECSTATE *ROUTINE*
E.O.:	13526
TAGS:	SHLH, ETRD, ECON, PGOV, CN
Captions:	SENSITIVE
Reference:	17 WUHAN 48
Subject:	China Opens First Bio Safety Level 4 Laboratory

1. (SBU) **Summary and Comment:** The Chinese Academy of Sciences (CAS) has recently established what is reportedly China's first Biosafety Level 4 (BSL-4) laboratory in Wuhan. This state-of-the-art facility is designed for prevention and control research on diseases that require the highest level of biosafety and biosecurity containment. Ultimately, scientists hope the lab will contribute to the development of new antiviral drugs and vaccines, but its current productivity is limited by a shortage of the highly trained technicians and investigators required to safely operate a BSL-4 laboratory and a lack of clarity in related Chinese government policies and guidelines. (b)(5)

(b)(5)

(b)(5) **End Summary and Comment.**

China Investing in Infectious Disease Control

2. (U) Between November 2002 and July 2003, China faced an outbreak of Severe Acute Respiratory Syndrome (SARS), which, according to the World Health Organization, resulting in 8,098 cases and leading to 774 deaths reported in 37 countries. A majority of cases occurred in China, where the fatality rate was 9.6%. This incident convinced China to prioritize international cooperation for infectious disease control. An aspect of this prioritization was China's work with the Jean Merieux BSL-4 Laboratory in Lyon, France, to build China's first high containment laboratory at Wuhan's Institute of Virology (WIV), an institute under the auspices of the Chinese Academy of Sciences (CAS). Construction took 11 years and $44 million USD, and construction on the facility was completed on January 31, 2015. Following

two years of effort, which is not unusual for such facilities, the WIV lab was accredited in February 2017 by the China National Accreditation Service for Conformity Assessment. It occupies four floors and consists of over 32,000 square feet. WIV leadership now considers the lab operational and ready for research on class-four pathogens (P4), among which are the most virulent viruses that pose a high risk of aerosolized person-to-person transmission.

Unclear Guidelines on Virus Access and a Lack of Trained Talent Impede Research

3. (SBU) In addition to accreditation, the lab must also receive permission from the National Health and Family Planning Commission (NHFPC) to initiate research on specific highly contagious pathogens. According to some WIV scientists, it is unclear how NHFPC determines what viruses can or cannot be studied in the new laboratory. To date, WIV has obtained permission for research on three viruses: Ebola virus, Nipah virus, and Xinjiang hemorrhagic fever virus (a strain of Crimean Congo hemorrhagic fever found in China's Xinjiang Province). Despite this permission, however, the Chinese government has not allowed the WIV to import Ebola viruses for study in the BSL-4 lab. Therefore, WIV scientists are frustrated and have pointed out that they won't be able to conduct research project with Ebola viruses at the new BSL-4 lab despite of the permission.

(b)(6)

(b)(6) Thus, while the BSL-4 lab is ostensibly fully accredited, its utilization is limited by lack of access to specific organisms and by opaque government review and approval processes. As long as this situation continues, Beijing's commitment to prioritizing infectious disease control - on the regional and international level, especially in relation to highly pathogenic viruses, remains in doubt.

(b)(6) noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this, (b)(6) they would welcome more help from U.S. and international organizations as they establish "gold standard" operating procedures and training courses for the first time in China. As China is building more BSL-4 labs, including one in Harbin Veterinary Research Institute subordinated to the Chinese Academy of Agricultural Sciences (CAAS) for veterinary research use (b)(6) the training for technicians and investigators working on dangerous pathogens will certainly be in demand.

Despite Limitations, WIV Researchers Produce SARS Discoveries

6. (SBU) The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study, (b)(6) (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS-coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like coronaviruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention. (b)(5) (b)(5) WIV scientists are allowed to study the SARS-like coronaviruses isolated from bats while they are precluded from studying human disease causing SARS coronavirus in their new BSL-4 lab until permission for such work is granted by the NHFCP.

1. Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al. (2017) Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 13(11): e1006698. https://doi.org/10.1371/journal.ppat.1006698

Signature: BRANSTAD

Drafted By: (b)(6)
Cleared By:
Approved By:
Released By:
Info: CHINA POSTS COLLECTIVE *ROUTINE*

Dissemination Rule: Archive Copy

UNCLASSIFIED
SBU

We await your response at the earliest opportunity.

Yours sincerely,

[redacted]

Dr. Peter Daszak
President

(t) [redacted]; (e) [redacted]
cc. Dr. Aleksei A. Chmura (Chief-of-Staff)

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

13 April 2021

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964 and your letter of April 11, 2021

Dear Drs. Chmura and Daszak:

Thank you for your letter of April 11, 2021. We are reviewing your responses in detail.

In the meantime, though, and in interest of expediting our review, we would note that our previous letters were concerned with NIH Grant R01AI110964 (which started/started on June 1, 2014 as documented in RePORTER) and not solely with 2R01AI110964-06. Therefore, as we asked on October 23, 2020, please send us copies of *all* EcoHealth Alliance – WIV subrecipient agreements as well as any and all other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety. While we understand that you may not have activated a subaward for year 6 we would expect there to be substantial documentation of your oversight of WIV subaward activities during years 1 through 5.

Also, as we asked, please send us copies of *all* biosafety reports; we would expect that as part of your oversight you would have copies of all such reports through at least year 5.

As a reminder, as a term and condition of award, NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. § 75.364); and must have "timely and reasonable access to the non-Federal entity's personnel for the purpose of interview and discussion related to such documents" (id.). These requirements flow down to subawards to subrecipients. 45 C.F.R. § 75.101. "Non-Federal entities must comply with requirements in [45 C.F.R. Part 75] regardless of whether the non-Federal entity is a recipient or subrecipient of a Federal award." 45 C.F.R. 75.101. As the grantee, EcoHealth was required to have in place, "A requirement that the subrecipient permit the pass-through entity and auditors to have access to the subrecipient's records and financial statements as necessary for the pass-through entity to meet the requirements of this part." 45 C.F.R. § 75.352(a)(5). For each of these reasons NIH is justified in seeking the materials, information, and a site visit as requested.

Sincerely,

[redacted]

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: [redacted]

EcoHealth Alliance

Dr. Michael Lauer
Deputy Director for Extramural Research,
NIH, Bethesda, MD.

Re: R01AI110964 and 2R01AI110964
"Understanding the Risk of Bat Coronavirus Emergence"

April 23rd 2021

Dear Dr. Lauer,

I am responding your letter of 4/13/21 regarding our response to conditions placed on the suspended NIH grant 2R01AI110964 "*Understanding the Risk of Bat Coronavirus Emergence*". In particular, this letter addresses your request for documentation on our assessment of WIV's compliance with terms of our subcontracts from the initial (now expired) 5-year award:

"*...copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any and all other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award .... NIH must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. § 75.364); and must have "timely and reasonable access to the non-Federal entity's personnel for the purpose of interview and discussion related to such documents" (Id.). These requirements flow down to subawards to subrecipients. 45 C.F.R. § 75.101. "Non-Federal entities must comply with requirements in [45 C.F.R. Part 75] regardless of whether the non-Federal entity is a recipient or subrecipient of a Federal award." 45 C.F.R. 75.101. As the grantee, EcoHealth was required to have in place, "A requirement that the subrecipient permit the pass-through entity and auditors to have access to the subrecipient's records and financial statements as necessary for the pass-through entity to meet the requirements of this part." 45 C.F.R. § 75.352(a)(5)...*"

As requested, we have supplied all EcoHealth Alliance-WIV subrecipient agreements, as well as documents pertaining to EHA's monitoring of WIV's compliance with the terms and conditions of award. The attached documents demonstrate that we have fulfilled all requirements in the CFR codes listed in your letter excerpted above. These documents include:

1. EcoHealth Alliance 2016-2019 Subrecipient Monitoring Forms for WIV. EcoHealth Alliance began this formal subrecipient monitoring policy in 2016 as per OMB Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards (2 CFR 200) ("Uniform Guidance"), specifically §200.331.
2. 2006-2018 WIV Annual Reports. In addition, NIH has full reports on the programmatic results that we filed annually.
3. Wuhan Institute of Virology contracts and invoices for all 5 Years of Grant R01AI110964: 2014-2019
4. Federal Funding Accountability & Transparency Act Reports for WIV. From 2015 – 2019
5. Annual Independent Audit Reports from 2014-2019
6. Inter-Institutional Agreements from DHHS for WIV 2014 & 2019

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

We hope these documents satisfy your request by demonstrating that EcoHealth Alliance maintained detailed records of our appropriate monitoring of WIV's performance against the conditions of our initial (now expired) R01 grant and our contracts with them.

We also would like draw your attention to our letter dated 4.11.2021 regarding plans for biosafety monitoring for the renewal R01, under which we had not yet set up a subcontract with WIV, specifically:

"8. Provide copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety.
As we related in response to your letter of 4/19/2020 that asked us to suspend work with WIV, we had not yet set up a subcontract with WIV for the period of this award, therefore no such subrecipient agreements exist. Our plan was to monitor WIV's compliance as we had in the 5 years prior, by means of semi-annual meetings with the lead investigator and assessments of compliance against all conditions of the award. Additionally, following the NIH's termination, then reinstatement and suspension of our funding, we have contracted with a leading lab biosafety contractor based in Southeast Asia (Dr. Paul Selleck) who has extensive experience commissioning, accrediting and auditing BSL-2, -3, and -4 labs, and has worked for over a decade at the BSL-4 Australian Animal Health Lab. We will be using their services where appropriate for foreign lab subcontractees to assess lab biosafety procedures and conduct audits, including following the full reinstatement of 2R01AI110964. Finally, we have appointed a Senior Field Veterinarian who will oversee all EcoHealth Alliance fieldwork in the region and ensure continued compliance with biosafety when conducting animal capture, sampling and sample handling. We have done this at EcoHealth Alliance's own expense, despite our unblemished record on biosafety, to pre-empt calls for further sanctions against our work given the continued attacks against EcoHealth Alliance in the press after the termination of our NIH grant."

We believe the attached documents lay out details of how we had previously monitored compliance according to the federal codes you cite, and the above response lays out an appropriate plan for biosafety monitoring. Together, we believe they appropriately and fully addresses your condition #8 for full reinstatement with access to funding for the renewal phase of the R01.

Yours sincerely,

[redacted]

Dr. Peter Daszak, President
(t) [redacted] (e) [redacted]

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
+1 212.380.4660
EcoHealthAlliance.org