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Report to
Congressional Requesters

April 2024

VIRUS FIELD RESEARCH

Policy Options to Help Reduce Risks and Enhance Benefits

GAO-24-106759

GAO Highlights

Highlights of GAO-24-106759, a report to congressional requesters

April 2024

VIRUS FIELD RESEARCH

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Why GAO Did This Study

Researchers estimate that 75 percent of emerging infectious diseases come from nonhuman animals. Virus field research—the collection of virus samples from wildlife and the environment and subsequent virus characterization—allows scientists to monitor viral populations, understand their biology, and obtain information that may help predict, prevent, and respond to future viral outbreaks.

Congressional requesters asked GAO to identify the benefits and risks of virus field research and whether alternative technologies may reduce the need for, or replace, field work. This report describes (1) whether field-based collection of virus samples from wildlife and the environment improves our ability to predict, prevent, or respond to pandemics; (2) risks associated with field-based virus collection, transport, and laboratory characterization to identify viruses with pandemic potential; and (3) technologies, other than field-based researchers' collection of virus samples, that may help predict future outbreaks and pandemics.

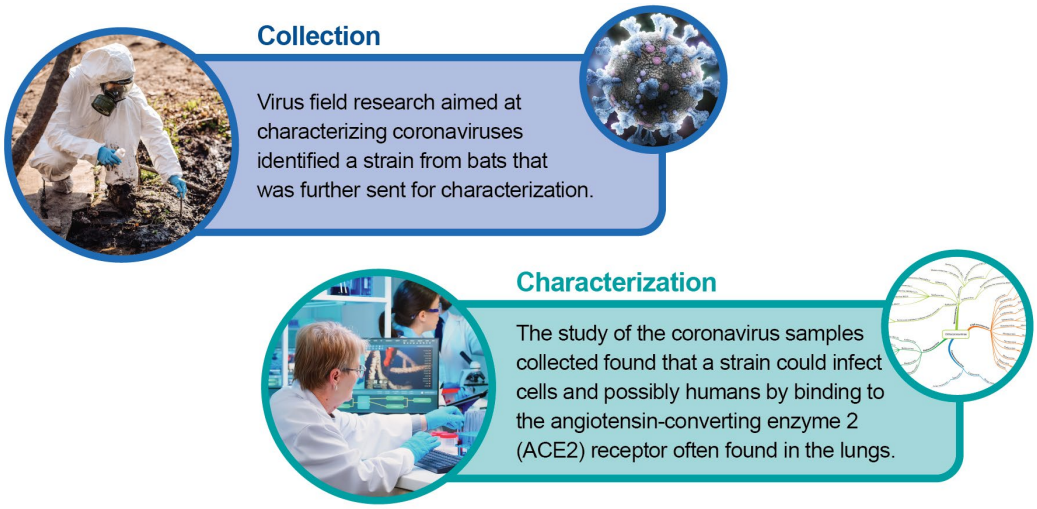
GAO conducted a literature review, convened a multiday 12-person subject matter expert meeting, analyzed documents from six agencies engaged in virus field research, and interviewed agency officials and others knowledgeable in the field. GAO identified three policy options that may help enhance the benefits and decrease the risks of virus field research.

USAID provided a written response in which they neither agreed nor disagreed with our findings.

View GAO-24-106759. For more information, contact Karen L. Howard at (202) 512-6888 or HowardK@gao.gov.

What GAO Found

Virus field research shows benefits in responding to outbreaks and some predictive ability. However, identifying specific preventative benefits of such research is challenging in part because determining the impact of the research on prevention outcomes is difficult to establish with certainty. Experts told us that there are multiple examples of prevention measures that have been taken in an effort to stop an outbreak from occurring, in part because of knowledge gained from virus field research.



Source: GAO analysis of published literature (data); Chatchawal/dottedyeti/DC Studio/kseniyaomega/stock.adobe.com (images). | GAO-24-106759

Virus field researchers face a variety of environmental, occupational, and infectious risks while conducting virus field research. In addition, virus field sample collection is subject to varying levels of regulation. As a result, virus federal field research practices vary, with agencies using their own guidelines for exposure and infection reporting.

Alternative approaches can help reduce the risks of virus field research activities, but virus field sample collections are a necessary source of data for technologies such as disease modeling which can help predict potential transmission and outbreaks. There are also technologies and methods that can be used to reduce exposure risks present during these sample collections and contribute to the understanding of diseases and outbreaks. These technologies include satellite sensing and mapping, field drone technology, field inactivation of samples, and field sequencing.

GAO identified three policy options that may help address these challenges. These policy options are not mutually exclusive and represent possible actions that policymakers—who may include Congress, federal agencies, state and local governments, academic and research institutions, industry, and international organizations—could consider taking.

Policy Option	Opportunities	Considerations
Policymakers could require researchers to include in federal research proposals a risk assessment that identifies the potential risks and benefits of the research as well as the personnel training to mitigate such risks. This policy option could help address the challenge of how to determine the effectiveness of virus field research in preventing pandemics.	Risk assessments could help focus research on high-risk human-animal interfaces where spillover into the population is most likely to occur, to maximize the potential benefit of virus field research. Could help identify opportunities to use other risk reduction approaches, including new technologies.	Standardized approaches for evaluating risks may need to be developed so that assessments are sufficiently consistent between federal agencies, international organizations, and researchers to allow for reliable and usable assessments. Potential benefits may not be directly connected to research (e.g., scientific capacity building) or may not become apparent for a long time.
Policymakers could establish a federal working group to develop standardized tracking and reporting guidelines for potential exposures and infections that occur during virus field work. This policy option could help address the challenge of varying levels of regulation and reporting requirements between agencies and intramural and extramural research.	Consistent reporting guidelines could help agencies more effectively track potential exposures or infections from virus field research, which may help agencies evaluate risks to researchers and the public. Could allow for better accountability of federal funding and could support further evidence-based policymaking.	Such efforts may involve extensive collaboration, such as between federal agencies or with international stakeholders such as the World Health Organization, to ensure that uniform guidelines are adopted for international field work. It may be difficult to clearly identify the types of exposures and infections that should be reported. Funding recipients and agencies may be hesitant to voluntarily report potential exposures and infections if they thought reports could affect future funding. Agencies and experts may believe that current biosafety and reporting practices are sufficient, so may consider new voluntary guidelines as an additional burden with limited value. It can be difficult to establish a clear linkage between specific field work and an exposure or infection, so it may be difficult to create guidelines that ensure accurate reporting.
Policymakers could fund research and development of technologies that may reduce risks of virus field research. This policy option could help address the challenge that current technologies cannot replace virus field research sample collection by humans.	Technologies that decrease sample handling and transportation by researchers could reduce the risk of zoonotic spillover.	If the replacement technologies require researchers to spend more time in the field, they may increase the risk of exposure to other diseases or hazards. It may be challenging to determine how much a given technology, among other investments, reduces risk, which may make it difficult to justify sustained investment. Technologies may force tradeoffs between reduced risks of exposure or infection and less data overall, or lower fidelity data.

Source: GAO. | GAO-24-106759

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Abbreviations

APHIS	Animal and Plant Health Inspection Service
BMBL	Biosafety in Microbiological and Biomedical Laboratories
CDC	Centers for Disease Control and Prevention
HHS	Department of Health and Human Services
NIH	National Institutes of Health
OSHA	Occupational Safety and Health Administration
SARS	Severe Acute Respiratory Syndrome
USAID	U.S. Agency for International Development
USDA	U.S. Department of Agriculture

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April 22, 2024

The Honorable Cathy McMorris Rodgers
Chair
Committee on Energy and Commerce
House of Representatives

The Honorable Brett Guthrie
Chair
Subcommittee on Health
Committee on Energy and Commerce
House of Representatives

The Honorable H. Morgan Griffith
Chair
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives

Researchers estimate that 75 percent of emerging infectious diseases originate from nonhuman animals. Transmission of diseases from animals to people, called spillover, can occur when people interact with infected animals. For example, the 2002 Severe Acute Respiratory Syndrome Coronavirus1 (SARS-CoV-1) and 2012 Middle East Respiratory Syndrome (MERS) outbreaks resulted from the interaction of animals with people.

Virus field research—the collection of virus samples from wildlife and the environment and subsequent virus characterization—is intended to help scientists to monitor viral populations; understand their biology; and obtain information that may help predict, prevent, and respond to future viral outbreaks. Researchers can travel around the world to collect samples from wildlife, such as animal blood and feces, and from the environment, such as water and soil. The samples are then transported to laboratories where researchers use scientific techniques such as genomic sequencing to characterize any viruses in the samples.

Because pandemics incur large social and economic costs, the ability to predict which viruses might lead to a pandemic would be useful for preparation. Researchers use a variety of approaches, including virus field research, in their efforts to predict, effectively prepare for and respond to infectious diseases outbreaks.

You asked us to identify the benefits and risks of virus field research and whether technologies may reduce the need for, or replace, such field work. This report describes (1) whether field-based collection of virus samples from wildlife and the environment improves our ability to predict, prevent, or respond to pandemics; (2) risks associated with field-based virus collection, transport, and laboratory characterization to identify viruses with pandemic potential; and (3) technologies, other than field-based researchers' collection of virus samples, that may help predict future outbreaks and pandemics with less risk.

The scope of our review included the Department of Health and Human Services (HHS), Department of Defense, Department of State, Department of the Interior, U.S. Agency for International Development (USAID), and U.S. Department of Agriculture (USDA). To answer all three objectives, we reviewed documents and published literature, interviewed agency officials and experts, and convened a meeting of experts knowledgeable in virus field research and with a range of viewpoints on such work. Further information about our methodology can be found in appendix I, and appendix II presents a list of participants in our expert meeting.

We conducted this performance audit from April 2023 to April 2024 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

Virus field research can involve direct sampling from animals or environmental sample collection to assess the viruses contained within. Subsequently, these samples may be transported to laboratories for virus identification and characterization. Sample characterization can include procedures such as genetic sequencing to determine whether the sample contains any viruses, and if so, attempts to identify the virus and test if the viruses can infect cells, which may provide information about the organ targets and disease transmission mechanisms.

Scientific literature suggests that one goal of virus field research is to gain information that may help predict, prevent, or respond to outbreaks and pandemics. As we reported previously, collection of virus field samples

can aid in tracking outbreaks through a population.[1] Access to samples can aid in the development of diagnostics, treatments, or vaccines to respond to outbreaks and pandemics. However, virus field research is not without risks and can expose the researcher to known or novel viruses.

Multiple federal agencies conduct or support virus field research domestically and internationally. Domestically, these include USDA's Animal and Plant Health Inspection Service (APHIS), Interior's U.S. Fish and Wildlife Service and U.S. Geological Survey, HHS's Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH), and Smithsonian Institution.[2] Internationally, these include USAID, CDC, NIH, APHIS, and Smithsonian Institution. Virus field research is supported through multiple approaches, including intramural research (i.e., agency staff conducting research) as well as extramural research conducted through contracts, cooperative agreements, and grants to non-federal entities.[3]

Over the past decade, zoonotic viruses—viruses that are spread between animals and humans—have caused multiple epidemics and one

[1]GAO, *Pandemic Origins: Technologies and Challenges for Biological Investigations,* GAO-23-105406 (Washington, D.C.: Jan. 27, 2023). This report examined the use of serology and epidemiological surveillance for pandemic origin investigations, which include studies examining pathogen spread and disease in animal populations.

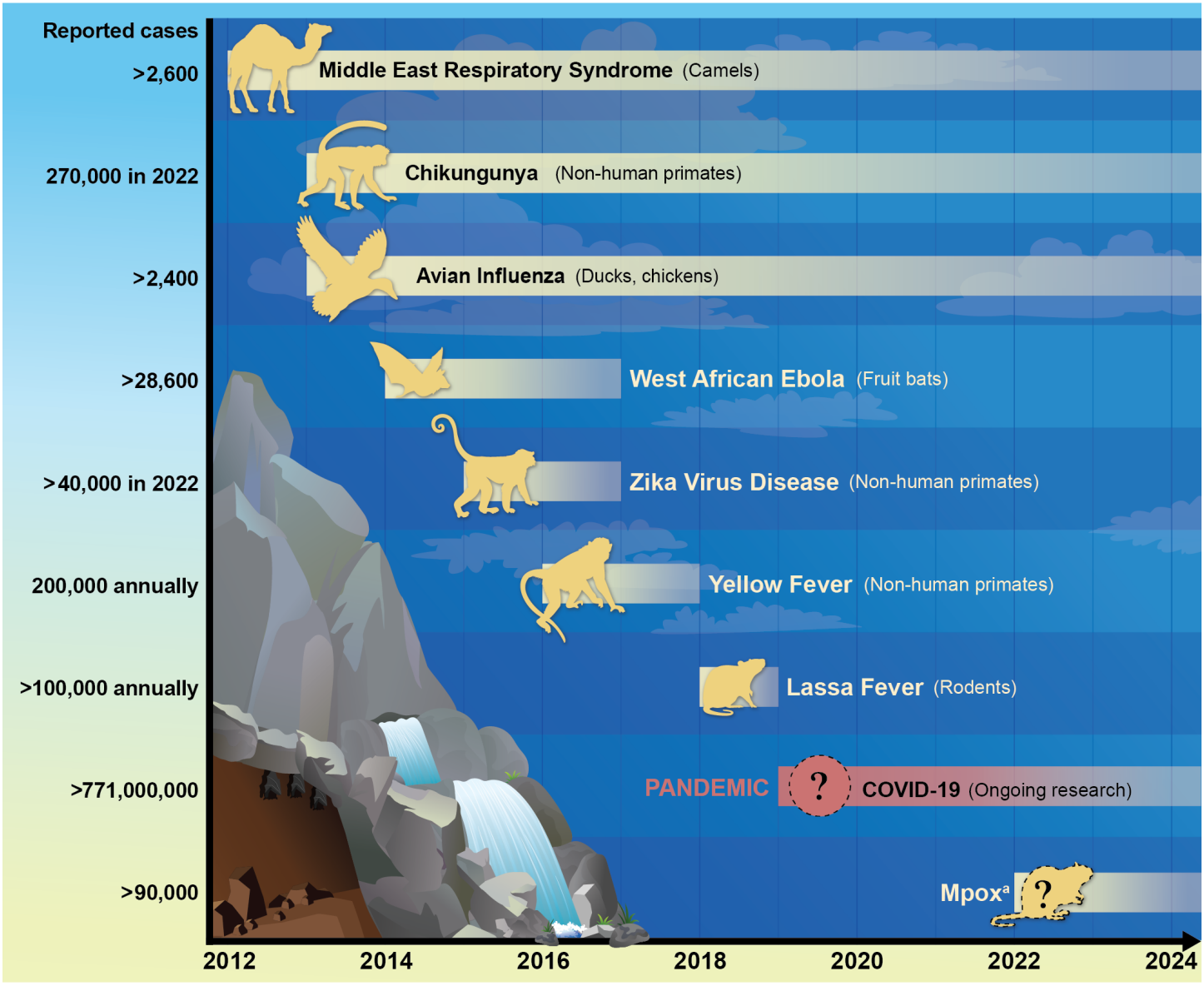
[2]Congress uses and defines various terms for the purpose of prescribing the applicability of a given law or set of laws to certain types of federally created entities. For example, as noted by the U.S. Court of Appeals for the District of Columbia Circuit, the Smithsonian Institution, created by law as "an establishment," meets the definition of "federal agency" for one statute, "instrumentality wholly owned by the United States" under another statute, but does not meet the definition of "agency" under a third statute. *Dong v. Smithsonian Inst.*, 125 F.3d 877 (D.C. Cir. 1997), *cert. denied*, 524 U.S. 922 (1998). However, for the purposes of this report, we refer to the Smithsonian Institution as an agency for the reader's ease, not because we have determined that it is an agency under all laws. Other federal agencies also conduct surveillance of U.S. wildlife. For example, the Department of the Interior's National Park Service is responsible for conducting surveillance of U.S. wildlife within its boundaries. In addition, the Department of Commerce's National Oceanic and Atmospheric Administration is the lead federal agency for surveillance of wild marine mammals, which are outside the scope of our review.

[3]Federal agencies fund two types of researchers—intramural and extramural. Intramural researchers include agency scientists who conduct research, such as in agency laboratories and clinics. Extramural researchers include scientists and research personnel working at universities, academic medical centers, and other research institutions who receive grants and other types of federal funding to conduct research.

pandemic (fig. 1).[4] Zoonotic epidemics happen regularly and originate from a wide variety of animal hosts across many different geographic locations.

[4]CDC defines an epidemic as an increase in the number of cases of a disease above what is normally expected in an area; an outbreak is defined as an epidemic, but in a more limited geographic area; and a pandemic is defined as an epidemic that has spread over several countries or continents. However, these terms are not always used consistently. For example, while some researchers describe MERS as a pandemic, others describe it as an epidemic or outbreak.

Figure 1: Selected Zoonotic Virus Epidemics and One Pandemic and Likely Original Hosts, 2013-2023



Source: GAO analysis of Centers for Disease Control scientific literature (data); Arafat/astira/bullet_chained/jan stopka/julia/kate_kmit/neilras/stock.adobe.com (images). | GAO−24−106759

Virus Field Research Informs Scientific Understanding but Determining Effectiveness for Preventing Pandemics is Challenging

Virus field research—which includes both known and new viruses—has a range of goals, including increasing knowledge about virus transmission and helping predict, prevent, and respond to outbreaks and pandemics. Virus field research has demonstrated benefits in responding to outbreaks and some predictive ability. Identifying specific preventative benefits of such research, however, is challenging because determining the impact of the research on prevention outcomes is difficult to establish with certainty.

Improved Scientific Understanding Can Help Efforts to Predict and Respond to Future Outbreaks and Pandemics

Virus field research has varying goals, depending on the specific aims defined at the beginning of a research study. For example, one goal could be increasing knowledge to help determine a virus's source before an outbreak occurs. In other instances, the goal could be to increase response capabilities.

Prediction. Federal agencies support virus field research through intramural and extramural research. Extramural research resulted in identification and prediction of viruses likely to result in disease outbreaks. For example, prior to the COVID-19 pandemic, research funded by NIH and published in peer-reviewed journals identified disease outbreak risks from bats that harbored coronaviruses. One paper published in 2016, whose authors included federally funded virus field researchers from multiple academic institutes, reported that SARS-like viruses had the potential to cause another coronavirus outbreak.[5] The authors based this determination on laboratory characterizations of virus field samples. This same paper also identified bats as the primary animal reservoir of coronaviruses. Furthermore, an expert we interviewed told us that virus field researchers had identified the viral families that can lead to the most widespread outbreaks, indicating that virus field research has the potential to predict a virus type and animal reservoir most likely to cause outbreaks.

Agencies fund programs that involve virus field collection, with some specifically intending to prevent pandemics. For example, USAID's

[5]The authors showed that coronaviruses had the ability to bind to the angiotensin-converting enzyme 2 (ACE2) receptor and lead to possible reemergence of a coronavirus outbreak. The ACE2 receptor found in human lungs and other organs. Source: V. D. Menachery et al., "SARS-like WIV1-CoV poised for human emergence," *Proceedings of the National Academy of Sciences*, vol. 113, no. 11 (2016).

PREDICT program aimed to proactively strengthen the capacity of countries around the world by identifying viruses that can move between animals and people before large-scale epidemics occur in people. The program, which operated between 2009 and 2020, made multiple discoveries, such as identifying 1,173 viruses. Most of the viruses identified—specifically, 958—were novel.[6] The first phase of PREDICT focused on many viral families, while the second phase concentrated on four viral families with known epidemic and pandemic potential: influenza viruses, filoviruses, paramyxoviruses, and coronaviruses. Such discoveries allow for more rapid detection of diseases, intervention, development of countermeasures, and drug testing. For example, PREDICT identified a new MERS coronavirus variant in a bat species in Uganda, and, in a separate study using machine learning, also determined that coronaviruses can infect a greater number of species more easily than other viruses can. The program's research also found that bats, rodents, and shrews have a higher risk of shedding coronaviruses compared to other mammals, meaning that these species are more likely to transmit coronaviruses to humans.[7] Based on those findings, PREDICT officials worked with local officials in relevant countries to get people to alter their behaviors when interacting with bats to limit the likelihood of exposure, with the goal of preventing pandemics.[8]

Scientists cannot predict exactly where and when such outbreaks may occur due to the numerous variables involved, such as how and when people may interact with infected animals. However, participants in our expert meeting told us that the ability to predict the locations of outbreaks is becoming more accurate, in particular for specific viruses and countries or regions. Additionally, one expert noted that while research predicting outbreaks can be published, there also needs to be a willingness to act

[6]USAID PREDICT Consortium, *Advancing Global Health Security at the Frontiers of Disease Emergence* (Davis, California: Dec. 2020).

[7]Shedding is the expulsion of disease-causing microorganisms into the environment from an infected animal or human.

[8]In 2021, USAID launched another program known as Discovery & Exploration of Emerging Pathogens—Viral Zoonoses. The goal was to collect and characterize over 800,000 virus field samples to determine whether any novel viruses identified had the potential to infect humans. According to agency officials, in June 2023, USAID made a policy decision that funding work with a focus on characterization of novel viruses prior to spillover in humans did not align with current global health priorities. Given this decision, USAID and Washington State University negotiated a revised program description to officially close out the award with an end date of April 2024.

on that information. Furthermore, some researchers have indicated that human infection surveillance should be prioritized over virus field research. One expert told us that in their opinion virus field research had not led to any predictions of which viruses will spill over into humans. In contrast, human infection surveillance tells us which viruses have already spilled over into humans, providing another way to assess the risk of a virus to people. USAID also told us that a combination of human studies in conjunction with wildlife surveillance could be used to locate and identify high-risk human-animal interfaces and that their investments in human disease surveillance are historically significantly greater than investments in virus field research. However, for viruses in humans for which sources are not known, virus field research would still be needed to understand the source of the virus because this knowledge can enhance our understanding of risks and strategies for prevention and preparedness.[9]

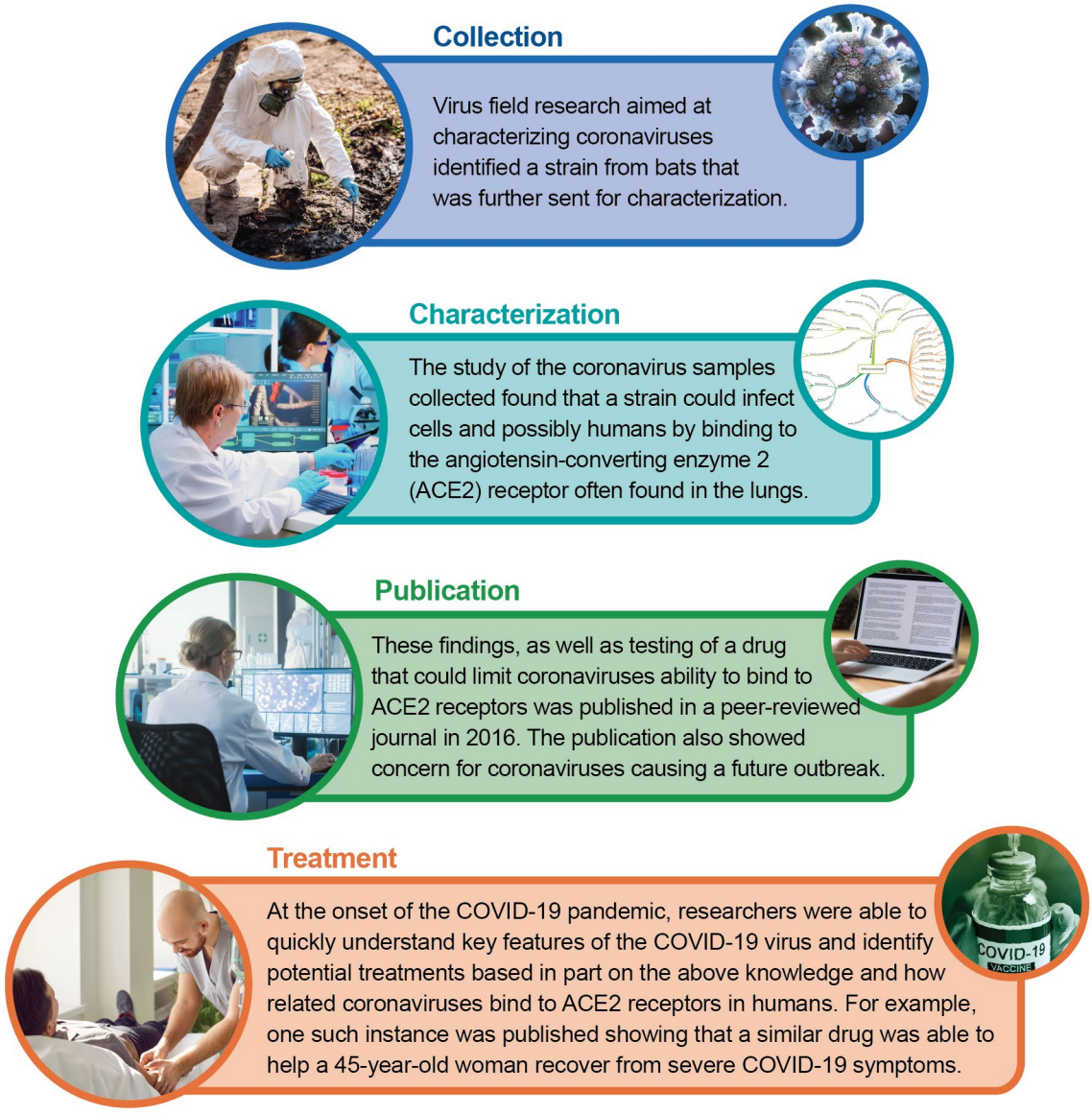
Response. Another goal of virus field research is to increase response capabilities during outbreaks and pandemics. Virus field research can help inform the development of tests to identify and therapeutics to treat viral infections. One expert told us that viruses isolated from field research may inform the development of therapeutics. For example, prior to the COVID-19 pandemic, virus field research aimed at characterizing coronaviruses identified specific characteristics of the viruses; these results facilitated the development of therapeutics in response to the COVID-19 pandemic. As mentioned above, research published in 2016 found that a SARS-like coronavirus used a protein called the ACE2 (angiotensin-converting enzyme 2) receptor as a mechanism of infection. Physicians used this knowledge and the existence of a drug that prevents

[9]USAID told us that most of their investments in global health security contribute to three goals, none of which include virus field research. These goals are 1) global health security capacity strengthening: assisting countries and regions to build the global health security capacities needed to more effectively prevent, detect, and rapidly respond to outbreaks, epidemics, and pandemics; 2) outbreak response: improving outbreak response by supporting countries through effective coordination, consistent messaging, informed decision making, and strategic alignment of USAID's priorities; and 3) multilateral partnerships: working with multilateral partners such as the Pandemic Fund and Coalition for Epidemic Preparedness Innovations to catalyze assistance and strengthen global health security capacities in additional countries.

viruses from binding to the ACE2 receptor and stops viruses from infecting cells to treat a patient.[10] Figure 2 illustrates this example.

[10]This knowledge resulted in some health care providers prescribing existing drugs to treat COVID-19 based on the drug's success in treating other diseases involving the ACE2 receptor. For example, a medical article published in 2020 described a case in a 45-year-old woman whose severe COVID-19 symptoms were controlled with such a drug. Source: Alexander Zoufaly et al., "Human recombinant soluble ACE2 in severe COVID-19." *Lancet Respiratory Medicine,* vol. 9, no. 11 (2020): 1154-1158.

Figure 2: Example of How Virus Field Research Helped in the COVID-19 Pandemic



Source: GAO analysis of published literature (data); Chatchawal/DC Studio/Dottedyeti/Fizkes/Gorodenkoff/Kseniyaomega/Nito/Studio romantic/stock.adobe.com (images). | GAO-24-106759

Notes: For the referenced published studies, see Vineet. D. Menachery et al., "SARS-like WIV1-CoV poised for human emergence," Proceedings of the National Academy of Sciences vol. 113, no. 11 (2016) and Alexander Zoufaly et al., "Human recombinant soluble ACE2 in severe COVID-19." Lancet Respiratory Medicine, vol. 8, no. 11 (2020): 1154-1158. USAID told us that virus field research also helped determine the extent to which mammals were infected with SARS-CoV-1 or SARS- like viruses. This information informs how and where these spillover events may transpire.

According to experts in our meeting, virus field research conducted during the 2002–2003 SARS-CoV-1 outbreak increased scientific understanding of spike proteins in coronaviruses; this knowledge contributed to the rapid development of COVID-19 vaccines.[11] Similarly, a CDC official told us that virus field work is important for developing appropriate tests. Agency officials stated that virus field research gives scientists the opportunity to develop and test materials and methods before an outbreak occurs. For example, in the wake of the 2002–2003 SARS-CoV-1 outbreak, virus field researchers developed novel therapeutics that contributed to the response to the COVID-19 outbreak in 2020.

Quantifying the Effects of Virus Field Research to Prevention Is Challenging

Participants in our expert meeting told us that virus field research has not been shown and cannot be shown to prevent any pandemics. Additionally, experts also indicated that proving whether a specific action prevented a major public health event is challenging, in part because there are no means of determining what would have happened if an intervention was not implemented. For example, it would be unethical to advise one group of people to avoid an animal known to carry a virus, while not informing another group of the same information, in order to compare the results of the two approaches. In addition, it is difficult to isolate the effect of one intervention on the prevention of a pandemic, when there are many other interventions and factors that determine the spread of a disease across the world.

However, experts told us that there are multiple examples of prevention measures that have been taken to stop an outbreak from occurring, in part because of knowledge gained from virus field research. For example, one expert in our meeting told us about initiating a measure to limit the human-animal interaction during tree palm sap collection. Palm sap, a key food source for people in Bangladesh, is collected by scarring a tree and allowing the sap to drain into a gourd. The Nipah virus can be spread to humans when infected bats eat the sap from the gourd. Thus, to limit the possible spread of Nipah virus to humans, virus field researchers designed bamboo screens to be built around the collection gourd. This safely prevented the bats from eating from the sap and reduced the risk that Nipah virus would infect the sap farmers.

[11]Experts in our meeting noted that typically vaccine development does not begin for a new virus until more is known about its potential to make many people sick, in part because vaccine development is so expensive.

Virus Field Research Activities Have Risks and Varying Levels of Regulation

Virus field research activities have risks that include the potential for researchers to be infected with known or novel pathogens and exposed to hazardous environments. In addition, virus field sample collection is subject to varying levels of regulation. As a result, virus field research practices vary, with federal agencies using their own guidelines for exposure and infection reporting.

Virus Field Researchers Face a Range of Risks during Sample Collection

Agency officials and experts at our meeting told us that field researchers face a variety of environmental, occupational, and infectious risks while conducting virus field research. Some risks may be easier to link to specific research activities due to their relative proximity. For example, NIH officials told us that environmental hazards include exposure to inclement weather, falls, or other kinds of injuries. Occupational hazards include cuts or needle sticks from handling equipment used during sample collection. Infectious risks include both endemic and emerging viruses.[12] NIH and CDC officials told us that field researchers are at increased risk of insect or animal bites or stings, which can increase researchers' risks of being infected with locally circulating mosquito-borne viruses, such as dengue virus or West Nile virus, as well as novel zoonotic pathogens. Additionally, researchers can be exposed to zoonotic diseases through other types of direct or indirect contact with an infected animal.[13]

Agency officials and experts told us that using personal protective equipment can help mitigate risks (table 1).[14] Two experts noted that risks cannot be avoided entirely, but one of these experts told us that over the past 10 years, methods for collecting, transporting, and storing samples

[12]According to the CDC, an endemic disease is the constant presence or the usual prevalence of a disease or infectious agent in a population within a geographic area. An emerging disease is an infection that has newly appeared in a population or has existed but is rapidly increasing in incidence or geographic range. Infectious risks also include bacteria, fungi, and parasites.

[13]Exposures via direct contact may occur when a person touches, or gets bitten or scratched by, an infected animal. Exposures via indirect contact may occur when a person comes into contact with an area or object contaminated by an infected animal. Interior officials also noted that researchers present a risk to animals, as diseases may also transmit from humans to animals.

[14]Personal protective equipment is specialized clothing or equipment worn to provide protection against a hazard (e.g., infectious agents and toxins). Personal protective equipment can be as basic as eye protection (i.e., safety glasses or goggles), gloves, or a lab coat or as complex as a "positive pressure suit" that completely isolates a person from the environment.

have improved significantly, which has helped reduce virus field research risks.

Table 1: Virus Field Research Risks and Mitigation Strategies Identified by Agencies

Agency	Risks identified by agency	Mitigation strategies
Centers for Disease Control and Prevention (CDC)	• Animal/insect bites or stings • Zoonotic exposure	• Personal protective equipment[a] • Personnel training • Vaccinations • Sample inactivation[b] • Insect repellents
Department of the Interior, Fish and Wildlife Service and U.S. Geological Survey	• Environmental hazards (e.g., trips and falls) • Zoonotic exposure	• Personal protective equipment • Personnel training
National Institutes of Health (NIH)	• Environmental hazards (e.g., trips and falls) • Animal/insect bites or stings • Sharps injuries (e.g., needle sticks, cuts) • Zoonotic exposure	• Personal protective equipment • Personnel training • Vaccinations • Sample inactivation • Insect repellents
Smithsonian Institution	• Zoonotic exposure	• Personal protective equipment • Sample inactivation
U.S. Agency for International Development (USAID)	• Zoonotic exposure	• Personal protective equipment • Sample inactivation
U.S. Department of Agriculture (USDA), Wildlife Services	• Zoonotic exposure	• Personal protective equipment • Vaccinations

Source: GAO review of agency documentation and interviews with agency officials. | GAO-24-106759

[a]Agency officials gave examples of personal protective equipment, including gloves, respiratory protection (e.g., N95 masks, positive air pressure respirators), eye protection, and Tyvek suits.

[b]Inactivation is a process used to destroy the hazardous effects of pathogens while retaining characteristics for future use. Pathogens can be inactivated using methods such as heat, filtration, ionizing radiation, or chemicals.

Agency officials told us that they were not aware of any reported infections or exposures from researchers conducting virus field research in the past 10 years.[15] CDC officials told us that they were aware of an anecdotal report of researchers getting sick after handling animals, but there was no conclusive evidence linking illnesses with research activities.

[15]USAID informed us of one exposure that occurred recently but did not result in an infection with a known virus as the animal tested negative for the known viral pathogen.

Virus Field Research is Subject to Varying Regulations so Reporting Practices for Exposures and Infections Vary Across Agencies

Potential 2012 Infection with Sosuga Virus

A 2012 example illustrates how difficult it can be to determine whether an illness occurred due to field research. In 2012, a wildlife biologist became infected with a novel virus, later named Sosuga virus, after handling bats and rodents in South Sudan and Uganda.[a] The researcher reportedly used personal protective equipment inconsistently while conducting work earlier in South Sudan, where the Sosuga virus was subsequently detected in multiple Egyptian fruit bat tissue samples. Although scientists were not able to definitively establish that field work led to this researcher's infection, they concluded that these bats were likely the cause.

Source: GAO analysis of published literature (data). | GAO-24-106759

[a]Although these events occurred outside the time frame of our review (which included only events that occurred between 2013 and 2023), we identified this example from an expert interview. Brian R. Amman et al., "A Recently Discovered Pathogenic Paramyxovirus, Sosuga Virus, is Present in *Rousettus aegyptiacus* Fruit Bats at Multiple Locations in Uganda," *Journal of Wildlife Diseases*, vol. 51, no. 3 (2015): 774-779, https://doi.org/10.7589/2015-02-044.

Agency officials we spoke with and our own search results identified laws and regulations that apply to some aspects of virus field research, such as sample transport and laboratory characterization. However, through our literature search we did not identify any federal laws or internationally agreed-upon practices that broadly apply to sample collection. Additionally, agency officials told us that reporting practices varied depending on whether work was conducted as intramural or extramural research, and in the U.S. or internationally.

Both the U.S. and international scientific community have developed safety manuals for laboratory research. In the U.S., the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) manual is a widely accepted source of guidance for all research involving pathogens.[16] The manual outlines principles and practices of biological safety and security and is published in partnership by CDC and NIH. Internationally, the World Health Organization *Laboratory Biosafety Manual* serves as a de facto global standard that presents best practices and sets trends in biosafety.[17] Additionally, multiple federal laws and regulations apply to

[16]U.S. Department of Health and Human Services, Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition, (Bethesda, MD, and Atlanta, GA: revised June 2020).

[17]World Health Organization, *Laboratory biosafety manual, 4th edition* (Dec. 21, 2020).

laboratory research settings in the U.S. and help ensure that safety and health standards are met.[18]

Agency officials told us they were not aware of any substantively equivalent government-issued guidance or regulations that exist for virus field sample collection in the U.S., internationally, or from host countries.[19] Some professional societies and organizations issue voluntary guidelines, such as those issued by the American Society of Mammologists.[20] These guidelines provide best practices for using mammals in research and teaching, including experiments involving wild mammals. The section focusing on human safety notes that risks exist in wild animal research and researchers can protect themselves with appropriate preparation and training, but it provides significant discretion to individual researchers as to how such risks should be identified and evaluated for each research

[18]For example, the Occupational Safety and Health Act of 1970 (OSH Act), as amended, Pub. L. No. 91-596, 84 Stat. 1590 (1970), requires covered employers to comply with occupational safety and health standards promulgated under the OSH Act, and also requires covered employers to provide employees employment and a place of employment which are free from recognized hazards that are causing or likely to cause death or serious physical harm (referred to as the General Duty Clause) (see 29 U.S.C. § 654). Regulations include the Occupational Safety and Health Administration's (OSHA's) Bloodborne Pathogens Standard which prescribes safeguards to protect workers with occupational exposure to blood or other potentially infectious materials against health hazards related to bloodborne pathogens (29 C.F.R. § 1910.1030 (2023)), OSHA's personal protective equipment standards in 29 C.F.R. Part 1910, Subpart I, particularly 29 C.F.R. § 1910.132, and HHS's Public Health Service's regulations on Quarantine, Inspection, and Licensing of Select Agents and Toxins (42 C.F.R. pt. 73 (2023)), promulgated under the authority of 42 U.S.C. § 262a, and USDA's APHIS's regulations on Possession, Use, and Transfer of Select Agents and Toxins (9 C.F.R. pt. 121 (2023) and 7 C.F.R. pt. 331 (2023)) both promulgated under the authority of 7 U.S.C. § 8401.

[19]Department of Labor officials told us that California's Aerosol Transmissible Diseases – Zoonotic regulation may apply to some types of virus field research conducted within the state of California. Cal. Code Regs., tit. 8, § 5199.1 (2023). NIH officials told us that the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* and the *Guide for the Care and Use of Laboratory Animals* are relevant guidance involving the use of vertebrate animals when performing virus field research. This requires the development of an Institutional Animal Care and Use Committee which must ensure that proposed studies do not compromise the health and safety of either animals or persons in the field. However, in our review of these documents we did not identify any substantially equivalent laboratory guidelines to mitigate risks to research personnel conducting virus field research. National Institutes of Health Office of Laboratory Animal Welfare, *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (Bethesda, MD, 2015). Institute for Laboratory Animal Research, *Guide for the Care and Use of Laboratory Animals* (Washington, D. C.: The National Academies Press, 2011).

[20]Robert S. Sikes and the Animal Care and Use Committee of the American Society of Mammalogists, "*2016 Guidelines of the American Society of Mammalogists for the Use of Wild Mammals in Research and Education*," Journal of Mammalogy, vol. 97, no. 3 (2016): 663-688, https://doi.org/10.1093/jmammal/gyw078.

project.[21] Additionally, the National Academies of Sciences, Engineering, and Medicine's Institute for Laboratory Animal Research recently convened a workshop to discuss and understand the challenges associated with using wildlife animals in research.[22] However, this workshop did not seek to establish consensus or make any recommendations on existing guidelines or regulations.

NIH, USAID, and Interior officials told us that for virus field research, they primarily followed occupational safety and health standards issued by the U.S. Department of Labor's Occupational Safety and Health Administration (OSHA). However, agency officials told us that OSHA standards have limited reach, since the agency's standards do not apply outside the U.S. and its territories. In addition, OSHA requirements do not apply to some aspects of virus field sample collection. For example, OSHA's bloodborne pathogen standard only applies to human-to-human exposures, unless the animal is known to be infected with HIV or hepatitis B virus.[23] Virus field research involves handling wild animals, so researchers generally do not know what pathogens are present in a given animal.[24]

Transport of virus field research samples is partially regulated by U.S. import regulations. CDC officials and experts told us that many virus field research samples are collected and characterized outside the U.S. CDC officials said that if these samples are only possessed outside of the U.S. and never imported to the U.S., the select agent and toxin regulations and import permit regulations do not apply, as these regulations only apply

[21]The guidelines state that, "Investigators and institutional animal care and use committee members should remain cognizant that risks from zoonoses vary depending on study species, local environmental conditions, personnel attributes, and the potential pathogens. Accordingly, the safety precautions employed should match potential risks." *"2016 Guidelines of the American Society of Mammalogists for the Use of Wild Mammals in Research and Education,"* page 684.

[22]National Academies of Sciences, Engineering, and Medicine, *Animal Welfare Challenges in Research and Education on Wildlife, Non-Model Animal Species and Biodiversity: Proceedings of a Workshop,* Washington, D.C.: The National Academies Press, 2022. https://doi.org/10.17226/26614.

[23]29 C.F.R. § 1910.1030(b) (2023) (definition of "other potentially infectious materials").

[24]The Department of Labor made us aware of regulation 29 C.F.R. § 1960.18 (2023) which generally states that for the working conditions of agency employees, in the absence of OSHA standards, agencies should develop their own permanent supplementary standards and inform the Department of Labor of these. Agency officials indicated to us they were aware of 29 C.F.R. § 1960.18 and that based on their understanding it did not always apply to virus field research.

within the U.S. CDC officials also told us that select agents or toxins are also subject to additional transport, storage, handling, and reporting requirements under the CDC and USDA Federal Select Agent Program.[25] Anyone wishing to import infectious biological agents, infectious substances, or vectors must first obtain an import permit from CDC.[26] However, CDC officials specified that these regulations only apply once a sample is known to contain an infectious agent, select agent, or toxin and noted that virus field research samples are uncharacterized. As a result, according to CDC officials such samples are not subject to select agent or toxin regulations. Additionally, according to HHS officials field researchers working under a CDC-approved protocol must also adhere to specimen collection, handling, storage and testing procedures outlined in the protocol, in addition to adhering to applicable local regulations for specimen collection, handling, storage, and testing.

We examined agencies' standard operating procedures for reporting potential exposures or infections. We found that there are no comprehensive reporting requirements for potential exposures or infections that occur during virus field research. Additionally, NIH and USAID practices differed for extramural research.

Reporting practices for intramural research

Four agencies—CDC, Interior's Fish and Wildlife Service, NIH, and USDA's APHIS—issue guidelines for reporting potential exposures or infections that occur during intramural research, but these guidelines are not standardized. In contrast, Smithsonian Institution treats exposures or infections as an operational concern (table 2). USDA officials noted that their standard operating procedures were developed based on

[25]The Federal Select Agent Program regulates the possession, use, and transfer of biological select agents and toxins that have the potential to pose a severe threat to public, animal or plant health, or to animal or plant products.-Select infectious biological agents can include, but are not limited to, specific pathogens such as bacteria, viruses, fungi, or protozoa and toxins that have the potential to pose a severe threat to human, animal, or plant health and safety, or to animal or plant products. As of April 2023, the HHS/USDA Select Agents and Toxins list includes 68 select agents or toxins. Centers for Disease Control and Prevention and Animal and Plant Health Inspection Service, "Select Agents and Toxins List," *Federal Select Agent Program* (2023), accessed October 26, 2023, https://www.selectagents.gov/sat/list.htm.

[26]The CDC Import Permit Program regulates the importation of infectious biological materials that could cause disease in humans in order to prevent their introduction and spread into the U.S. 42 C.F.R. § 71.54 (2023). The program ensures that the importation of these agents is monitored and that facilities receiving permits have appropriate biosafety measures in place to work with the imported agents. Centers for Disease Control and Prevention, "About Us," *Import Permit Program* (2023), accessed December 20, 2023, https://www.cdc.gov/orr/ipp/about.htm.

standardized national guidance from the BMBL manual and regulations, such as those that apply to the National Federal Select Agent Program.[27]

Interior's Fish and Wildlife Service officials told us that intramural researchers are directed to monitor their health carefully, and immediately report health incidents (e.g., an occupational injury or illness) to their supervisor and the Fish and Wildlife Service Safety and Health Office. Supervisors are also instructed to assess each potentially hazardous job to determine whether there is a need for the use of a respirator, such as during tasks that could expose an individual to viral infections or during avian influenza surveillance activities.

NIH officials told us that in the event of a potential exposure or development of the signs or symptoms of an infection, an intramural researcher must report the incident to Occupational Medical Service, an office within NIH. Agency protocols contain a framework for "Estimating the risk of exposure and disease in incidents or illness involving a bioagent," which outlines specific steps that should be taken in response to a reported incident or illness.[28] Additionally, HHS officials told us that guidelines for reporting potential exposures or infections may not be standardized due to the different degrees of risk posed by different field sites and varying internal reporting policies followed by each agency.

[27]BMBL includes language on the reporting of biosafety incidents. It states, "Communication is an important aspect of a laboratory biosecurity program. A 'chain-of-notification' should be established in advance of an actual event. This communication chain should include laboratory and program officials, institution management, and any relevant regulatory or public authorities. The roles and responsibilities of all involved officials and programs should be clearly defined." U.S. Department of Health and Human Services, *Biosafety in Microbiological and Biomedical Laboratories*, 127.

[28]National Institutes of Health Occupational Medical Service, *354. Occupational Injury and Illness,* SOP 300.354 (Nov. 2022).

Table 2: Selected Agency Policies for Reporting Potential Exposures and Infections Sustained by Intramural Researchers Conducting Virus Field Research

Agency	Policy
Centers for Disease Control and Prevention (CDC)	Workers who develop symptoms of a mosquito-borne disease should report it to their supervisor and get medical attention. While trapping or sampling small mammals, if a needle stick, bite, or other injury which breaks the skin occurs, the worker should report the injury immediately to medical personnel. If fever and muscle aches or other influenza like symptoms appear within 45 days of the injury, they should seek medical attention and alert the attending physician to the possibility of hantavirus infection. (CDC, National Institute for Occupational Safety and Health, Mosquito-Borne Diseases, https://www.cdc.gov/niosh/topics/outdoor/mosquito-borne/default.html, accessed Oc.t 20, 2023; CDC, Methods for Trapping and Sampling Small Mammals for Virologic Testing, U.S. Department of Health & Human Services Public Health Service, Atlanta, GA, Sept. 1995, page 11.)
Department of the Interior, Fish & Wildlife Service	Project leaders are responsible for reporting when an employee is bitten and exhibits signs or symptoms of tick-borne disease to the Department's Safety Management Information System. The agency does not categorize insect bites as an accident or injury unless there is a reaction to the bite, or the worker seeks medical treatment. The supervisor should only enter insect bites in the Safety Management Information system if a worker experiences an illness or diagnosis of illness associated with insect bites (e.g., Lyme Disease/Rocky Mountain Spotted Fever,). (U.S. Fish & Wildlife Service, Tick-Borne Disease Prevention, 242 FW 5, https://www.fws.gov/policy-library/242fw5, accessed Oct. 11, 2023; U.S. Fish & Wildlife Service, Accident Investigation and Reporting, 240 FW 7, https://www.fws.gov/policy-library/240fw7, accessed Oct.11, 2023.)
National Institutes of Health (NIH)	All work-related injuries and illnesses that occur at NIH facilities must be reported to Occupational Medical Service. In the event that a worker becomes ill or injured while on official travel or a travel-related medical problem develops while on travel or after they return home, they should report the occurrence to Occupational Medical Service. (NIH, Occupational Medical Service, 354. Occupational Injury and Illness (SOP 300.354), Nov. 2022; NIH, Occupational Medical Service, 327. International Travel (SOP 300.327), Nov. 2022.)
Smithsonian Institution	There is no standard operating procedure related to health or disease if a worker were to report an infection from conducting virus field research. Rather, according to an agency official, it is treated like any other operational concern and reported along the supervisory chain as soon as possible following the report. (Interviews with Smithsonian Institution officials.)
U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS)	Workers are responsible for immediately reporting all occupational injuries, illnesses, and exposures, including potential exposures, as well as near misses involving hazardous biological materials of concern, as well as an incident involving infected animals or animal part of a research study, to their supervisor or management chain, and Health Services. In turn, supervisors are to submit a preliminary report using the APHIS First Report of Incident, Accident, Injury, or Illness in a timely manner. (USDA APHIS, Biorisk Management Manual, Feb. 2023.) Animal bites or scratches, splashes in the eyes or mouth, or needle sticks or sharps cut which involved a known or potentially infected animal or contaminated material, must be reported immediately to a worker's supervisor and the National Wildlife Research Center Safety/Biosafety Officer. The employee's supervisor must report the incident to the APHIS Online First Report system as soon as possible. (USDA National Wildlife Research Center, Rabies Vaccinations and Titer Checks HS039.01, 3.9 Accidental exposures, June 2023.)

Source: GAO review of agency documentation and interviews with agency officials. | GAO-24-106759

Reporting practices for extramural research

NIH and USAID officials told us that organizations conducting extramural research were responsible for setting and enforcing their own guidelines and reporting practices. However, NIH provides funding recipients with information on best practices to prevent potential exposures or infections.

For example, NIH funds extramural research programs at universities and other research institutions. All NIH grantees are required to abide by the terms and conditions of the NIH Grants Policy Statement.[29] Grantees are recommended, but not required, to use both the BMBL guidelines and *Prudent Practices for Safety in Laboratories* from the National Research Council to develop operating procedures and practices.[30] Grantees do not need to submit these operating procedures and practices to NIH, but the documentation demonstrating compliance with regulations and guidelines should be available upon request.[31]

In contrast, USAID officials told us that each funding recipient, or implementing partner, was responsible for their own organizational procedures for preventing exposures and reporting incidents.[32] However,

[29]While working overseas, grantees are also expected to comply with all laws and regulations of the host country. National Institutes of Health, *NIH Grants Policy Statement* (Dec. 2022), accessed October 17, 2023, https://grants.nih.gov/grants/policy/nihgps/nihgps.pdf, IIA-25–IIA-26.

[30]National Research Council, *Prudent Practices in the Laboratory* (Washington, D.C.: The National Academies Press, 2011), https://doi.org/10.17226/12654.

[31]NIH officials told us that the agency generally does not do proactive reviews of laboratory safety but conducts reviews of potential non-compliance with laboratory safety regulations and guidance when identified as part of pre-award review or post-award monitoring. One exception is the National Institute of Allergy and Infectious Diseases, which has special procedures for non-U.S. institutions that will conduct NIH-supported foreign select agent research. This process includes a CDC laboratory assessment to establish that the non-U.S. institution's biocontainment facility is equivalent to U.S. standards described in 42 C.F.R. pt. 73 (2023). If any significant departures from U.S. select agent regulations are noted, the National Institute of Allergy and Infectious Diseases will request that the non-U.S. institution submit materials demonstrating its plan to align with U.S. regulations, which the CDC will assess and incorporate into a revised, final CDC assessment report. One instance of potential non-compliance with laboratory safety requirements was identified in which a lack of clear procedures or facilities for safe handling of biohazardous materials was identified during peer review. In September 2023, the funding was restricted until the award recipient submitted an acceptable biohazard management plan. As of December 2023, NIH had received satisfactory evidence of appropriate biohazard management for laboratory safety and lifted the funding restriction.

[32]USAID partners with a variety of institutions, including faith-based and community organizations, private companies, colleges and universities, and non-governmental organizations to conduct programs. The majority of USAID extramural research is competitively awarded through contracts, grants, or cooperative agreements.

agency officials told us that for their most recent set of virus field research funding, which included Discovery & Exploration of Emerging Pathogens—Viral Zoonoses, the agency reviewed and approved funding recipients' biosafety and biosecurity plans. Generally, officials said that implementing partners are responsible for setting their own safety standards and ensuring employees' compliance and the compliance of funding sub-awardees with those standards. Table 3 provides additional information on reporting practices for extramural researchers funded by NIH and USAID.

Table 3: Selected Agency Policies for Reporting Potential Exposures and Infections Sustained by Extramural Researchers Conducting Virus Field Research

Agency	Policy
National Institutes of Health (NIH)	Recipients are responsible for meeting applicable federal, state, and local health and safety standards and for establishing and implementing necessary measures to minimize their employees' risk of injury or illness in activities related to NIH grants. Grant recipient organizations are not required to submit documentation demonstrating their compliance with or implementation of NIH safety regulations and guidelines. However, if requested, recipients should be able to provide evidence that applicable federal, state, and local health and safety standards have been considered and have been put into practice. (NIH, NIH Grants Policy Statement, Dec. 2022, accessed Oct. 17, 2023, https://grants.nih.gov/grants/policy/nihgps/nihgps.pdf, IIA-25–IIA-26.)
U.S. Agency for International Development (USAID)	Each organization conducting research has its own approved institutional procedures, established consistent with any applicable occupational health and safety requirements and host-government requirements, for protecting staff from exposure and reporting any field- or lab-related incidents associated with collection, transport, and testing of samples from animals, humans, or the environment. (Interviews with USAID officials.)

Source: GAO review of agency documentation and interviews with agency officials. | GAO-24-106759

Existing Technologies Cannot Replace Sample Collection by People, but Can Decrease Risk

Virus field research is an important source of data for technologies such as disease modeling which can help predict potential transmission and outbreaks. Researchers can use technologies and methods such as satellite sensing and mapping, field drone technology, field inactivation of samples, and field sequencing to reduce exposure risks during these sample collections and contribute to the understanding of diseases and outbreaks.

Infectious Disease Modeling Can Help Predict Outbreaks but Relies on Data from Virus Field Research

Disease modeling can help predict the behavior of viruses and host interactions, thereby assisting in public health efforts to respond to outbreaks. Models use data and hypotheses describing the demographics, environmental characteristics, transmission opportunities, and health consequences of diseases.

However, these models require data that come from field-acquired samples. NIH officials told us that current technologies cannot replace human collection of samples. An expert told us that while modeling may be useful, it still relies on real data collected from the field to demonstrate trends and detect new viral mutations. CDC officials told us that field research is needed to create the necessary inputs and variables for analysis to inform the newer technologies.

Models vary in their degree of accuracy due to the relevance of new data and assessment of the underlying hypothesis. For example, an expert told us that some models based on flu transmission dynamics proved to be incorrect when used for COVID-19, due to a difference in transmission characteristics of the respective viruses. Another area where modeling can fall short is projecting transmissibility of outbreaks without relying on human infection surveillance. The accuracy of a model requires feedback with new data. A mismatch between the data and the model's projections may challenge the model's assumptions and provide an opportunity to improve it.

Technologies Could Reduce Exposure Risks and May Reduce the Need to Transport Samples

Satellite sensing and mapping. Satellite sensing and mapping can help identify hotspots and inform future sample collection efforts, as they can identify several factors which can create conditions for diseases to propagate and spread. An expert told us that a way of reducing risk may be to target sampling in hotspots and conduct sampling in more effective and efficient ways. Department of State officials told us that using technologies such as satellite remote sensing and geographic information system mapping may help pinpoint areas of higher geographic risks. An expert told us that field studies directed at such viral reservoirs can then provide data on the potential for human outbreaks. For example, Fish and Wildlife Service and U.S. Geological Survey officials told us that virus collection can answer specific epidemiological issues (e.g., is a virus causing morbidity or mortality in wildlife, is it impacting population fitness). Additionally, an animal's environment can be important because animals can carry viruses without getting sick. If something happens in the environment that stresses the population (e.g., habitat change) those viruses can start causing health impacts on animals and people.

Field drone technology. A participant in our expert meeting told us that drones can be used to support virus field research. For example, experts told us about using drones to collect air samples. However, an expert told us that drones are not capable of replacing humans sampling in the field but rather can support virus field research. One expert during our meeting

told us that handling animals requires “tiny and delicate” procedures that current technologies are not capable of performing.

Field inactivation of samples. An expert told us that by inactivating samples in the field, there is a reduced risk to those transporting the samples from the field to the laboratory. Viral inactivation methods prevent a virus from replicating and make it non-infectious and thus facilitate the processing of samples in lower-level biosafety conditions following appropriate safety practices, thus expanding the analysis that can be performed on such samples. Inactivating samples in the field prevents subsequent virus culture and characterization in the lab, but does not affect molecular diagnosis and genome sequencing.

Field sequencing. Genomic sequencing identifies the order—or sequence—of a pathogen’s genetic material. Technologies that can sequence samples in the field could also reduce the risk of possible exposure by reducing or eliminating the need for transportation to a laboratory. Officials with the Smithsonian Institution told us that researchers can collect samples and perform sequencing at the point of detection. The resulting sequencing data gets stored in databases, which can be accessed by the Smithsonian and other institutions. Sequencing devices used in the field provide a fast and real-time option for surveillance and outbreak tracing; however, laboratory-based sequencing is still the gold standard, with several obstacles still facing field-based sequencing. Agency officials also told us that capacity building could reduce the need for transportation of samples from the field. For example, improving in-country laboratory capacity and performing surveillance in wild species could prevent emerging infectious diseases at their source.

Policy Options

As discussed above, we identified three challenges related to virus field research. First, it can be difficult to conclusively demonstrate the potential benefits or risks of virus field research. Second, virus field research activities are subject to varying levels of regulation and reporting requirements vary between agencies and for intramural and extramural research. Finally, current technologies may reduce risks, but cannot entirely replace humans for virus field research sample collection.

GAO identified three policy options that may help address these challenges. These policy options are not mutually exclusive and represent possible actions that policymakers—who may include Congress, federal agencies, state and local governments, academic and research institutions, industry, and international organizations—could consider taking.

Table 4: Policy Options for Virus Field Research

Policy Option	Opportunities	Considerations
Policymakers could require researchers to include in federal research proposals a risk assessment that identifies the potential risks and benefits of the research as well as the personnel training to mitigate such risks. This policy option could help address the challenge of how to determine the effectiveness of virus field research in preventing pandemics.	• Risk assessments could help focus research on high-risk human-animal interfaces where spillover into the population is most likely to occur, to maximize the potential benefit of virus field research. • Could identify opportunities to use other risk reduction approaches, including new technologies.	• Standardized approaches for evaluating risks may need to be developed so that assessments are sufficiently consistent between federal agencies, international organizations, and researchers to allow for reliable and usable assessments. • Potential benefits may not be directly connected to research (e.g., scientific capacity building) or may not become apparent for a long time.
Policymakers could establish a federal working group to develop standardized tracking and reporting guidelines for potential exposures and infections that occur during virus field work. This policy option could help address the challenge of varying levels of regulation and reporting requirements between agencies and intramural and extramural research.	• Consistent reporting guidelines could help agencies more effectively track potential exposures or infections from virus field research, which may help agencies evaluate risks to researchers and the public. • Could allow for better accountability of federal funding and support further evidence-based policymaking.	• Such efforts may involve extensive collaboration, such as between federal agencies or with international stakeholders such as the World Health Organization, to ensure that uniform guidelines are adopted for international field work. • It may be difficult to clearly identify the types of exposures and infections that should be reported. • Funding recipients and agencies may be hesitant to voluntarily report potential exposures and infections if they thought reports could affect future funding. • Agencies and experts may believe that current biosafety and reporting practices are sufficient, so may consider new voluntary guidelines as an additional burden with limited value. • It can be difficult to establish a clear linkage between specific field work and an exposure or infection, so it may be difficult to create guidelines that ensure accurate reporting (i.e., does not lead to false positives or negatives).
Policymakers could fund research and development of technologies that may reduce risks of virus field research. This policy option could help address the challenge that current technologies cannot replace virus field research sample collection by humans.	• Technologies that decrease sample handling and transportation by researchers could reduce the risk of zoonotic spillover.	• If the replacement technologies require researchers to spend more time in the field, they may increase the risk of exposure to other diseases or hazards. • It may be challenging to determine how much a given technology among other investments, reduces risk, which may make it difficult to justify sustained investment. • Technologies may force tradeoffs between reduced risks of exposure or infection and less data overall, or lower fidelity data.

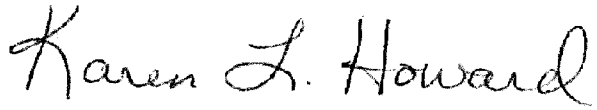
Source: GAO. | GAO-24-106759

Agency Comments:

We provided a draft of this report to the Department of Health and Human Services, Department of Defense, Department of State, Department of the Interior, U.S. Agency for International Development, U.S. Department of Agriculture, and the Smithsonian Institution for review and comment. U.S. Agency for International Development provided written comments, reproduced in appendix III, and technical comments, which we incorporated as appropriate. They also stated that we named projects mainly from their agency despite the scope of this report including other agencies. In our report we have selected one program, PREDICT, to describe in more detail as an example, because it highlighted a program specifically intended to prevent pandemics. Department of Health and Human Services, U.S. Agency for International Development, U.S. Department of Agriculture, and the Smithsonian Institution also provided technical comments, which we incorporated as appropriate. Department of Defense and Department of the Interior did not have any comments.

If you or your staff have any questions about this report, please contact me at (202) 512-6888 or howardk@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made key contributions to this report are listed in appendix IV.

As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to we will send copies to the appropriate congressional committees and the Secretaries of Health and Human Services, Defense, State, Interior, Agriculture, and Smithsonian Institution; the Administrator of the U.S. Agency for International Development; and other interested parties. In addition, the report will be available at no charge on the GAO website at https://www.gao.gov.



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Appendix I: Objectives, Scope, and Methodology

Objectives

This report examines:

1. whether field-based collection of virus samples from wildlife and the environment improves our ability to predict, prevent, or respond to pandemics;
2. risks associated with field-based virus collection, transport, and laboratory characterization to identify viruses with pandemic potential; and
3. technologies, other than field-based researchers' collection of virus samples, that may help predict future outbreaks and pandemics with less risk.

Scope and Methodology

The scope of our review included the following agencies that engaged in virus field research:

- Department of Defense,
- Department of the Interior,
- Department of State,
- U.S. Agency for International Development,
- Department of Health and Human Services, and
- U.S. Department of Agriculture.

Based on interviews and documents we reviewed, we focused our scope on the past 10 years of federal programs for field-based collection of samples of viruses that agencies and subject matter experts identified as having the potential to lead to pandemics. We excluded agencies that mainly focused on foodborne pathogens.

Agency Documentation and Literature Search

To examine all three objectives, we reviewed documents provided by agencies in response to our written questions. These documents included current and past research studies, protocols, and publications that resulted from virus field research programs.

We also conducted a systematic literature search for peer-reviewed publications related to the three objectives in databases including PubMed, scientific journals (e.g., Science, Proceedings of the National Academy of Sciences, Journal of Virology), and trade articles published in the past 10 years. We used a variety of search terms including "zoonotic disease," "virus collection," "pandemic origin," "pathogen biosurveillance," "laboratory characterization," and "field research," among other keywords

relevant to virus field research. We also conducted a broad search of materials published within the last 10 years from federal agencies; trade groups; and the National Academies of Sciences, Engineering, and Medicine. We used the results of our literature search to inform our findings as well as identify experts to interview or invite to participate in our expert meeting. The results of this search were also used to inform our findings on select laws and regulations. We also conducted searches of agency websites and documents we collected during our review to identify relevant laws and regulations regarding virus field research.

Interviews

We interviewed officials with a role in managing or conducting virus field research at each of the agencies and obtained their written responses to follow-up questions as needed. In our interviews, we asked officials about their agencies' roles in virus field research over the past 10 years, and key research outcomes.

We also interviewed a non-generalizable selection of academic and global health experts about their views on virus field research, the efforts of federal and other agencies in this area of research, and the benefits, risks, and technological advances in virus field research. We developed a list of potential experts to interview through a review of selected publications and literature about virus field research. We conducted semi-structured interviews with each expert using the same set of questions for each interview, while allowing for additional follow-up questions specific to an interviewee's responses or context. We also spoke with Department of Labor officials regarding applicable occupational safety and health laws and standards, although it was not an agency included within the scope of the audit since it does not engage in virus field research.

Expert Meeting

To address all of our objectives, we held a 1.5-day virtual expert meeting on August 2 and 3, 2023. This meeting was divided into three sessions: (1) benefits, challenges, and risks of field-based virus collection and characterization; (2) emerging technologies to help predict future outbreaks and pandemics; and (3) possible ways to address gaps and risks in the current approach to conducting field-based virus collection and characterization.

We identified experts based on prior participation in National Academies of Sciences, Engineering, and Medicine expert meetings; GAO expert meetings; the National Science Advisory Board for Biosecurity; Centers of Excellence for Influenza Research and Response; or authorship of technical publications. We selected meeting participants based on their expertise in at least one area related to our objectives and with a view

toward obtaining a range of viewpoints (i.e., experts in favor of and opposed to virus field research). In addition to selecting experts on the basis of their expertise, we determined whether there were any potential conflicts of interest. The experts were determined to be free of reported conflicts of interest and the group as a whole was determined to not have any inappropriate biases.

We conducted this performance audit from April 2023 to April 2024 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for any findings and conclusions based on our audit objectives.

Appendix II: Expert Participation

We convened a 1.5-day meeting of 12 experts to inform our work on virus field research; this meeting was held virtually on August 2 and 3, 2023. The experts who participated in this meeting are listed below. Some of these experts gave us additional assistance throughout our work, including providing assistance during our study by sending material for review or participating in interviews. In addition, we provided the experts with the opportunity to review our draft report for accuracy and two provided technical comments, which we incorporated as appropriate.

Shannon T. Benjamin Ginkgo Bioworks

Dennis Carroll URC

Jocelyn P. Colella University of Kansas

Phil Ferro Paratus Sciences

Ghazi Kayali Human Link

Seema S. Lakdawala Emory University School of Medicine

Juliet S. Lamb The Nature Conservancy

Michael Letko Washington State University

Stephen S. Morse Columbia University Mailman School of Public Health

Steven Salzberg Johns Hopkins University

Stacey L. Schultz-Cherry St. Jude Children's Research Hospital

S. Mark Tompkins University of Georgia

Appendix III: Comments from US Agency for International Development

April 05, 2024

Jason Bair
Managing Director
Internal Affairs and Trade
U.S. Government Accountability Office
441 G Street, N.W.
Washington, D.C. 20226

Re: Virus Field Research Policy Options to Help Reduce Risks and Enhance Benefits (GAO-24-106759)

Dear Mr. Bair:

I am pleased to provide the formal response of the U.S. Agency for International Development (USAID) to the draft report produced by the U.S. Government Accountability Office (GAO) titled, Virus Field Research Policy Options to Help Reduce Risks and Enhance Benefits (GAO-24-106759). The report does not contain any recommendations for action on behalf of the Agency.

Since 2014, USAID has invested almost $2.5 billion in global health security to ensure the necessary systems are in place to prevent, detect and respond to emerging infectious disease threats wherever they exist. A very small portion of that amount has been expended on "identifying viruses that can move between animals and people before large-scale epidemics occur in people." Over the last ten years, less than five percent of the Global Health Security (GHS) budget was expended on this type of work under a previously funded USAID project, PREDICT. The other two USAID projects referenced in this report either don't conduct the type of predictive virus field research the report focuses on (STOP Spillover) or never began implementing field research activities before coming to a mutual termination (DEEP VZN). The vast majority of USAID's investments in global health security contribute to the following three goals, none of which include virus field research:

- Global Health Security Capacity Strengthening: Assisting countries and regions to build the global health security capacities needed to more effectively prevent, detect, and rapidly respond to outbreaks, epidemics, and pandemics;
- Outbreak Response: Improving outbreak response by supporting countries through effective coordination, consistent messaging, informed decision making, and strategic alignment of USAID's priorities; and
- Multilateral Partnerships: Working with multilateral partners such as the Pandemic Fund and Coalition for Epidemic Preparedness Innovations to catalyze

assistance and strengthen global health security capacities in additional countries.

We note that USAID provided a number of comments after the GAO circulated the draft audit report, and we appreciate the GAO considering incorporating those comments prior to issuing the final report. We are submitting this response having not seen any revisions made by the GAO in response to our comments. In our comments, we pointed out that although the scope of the report includes five other Departments and Agencies, only USAID projects were specifically identified and discussed in the draft report. This fact, coupled with the lack of context regarding USAID's GHS program as a whole, created the impression that USAID's work in this space predominates – within the USAID GHS program and the USG more broadly.

USAID also shared more technical comments on the report with the GAO. We would specifically like to highlight the following two:

- The draft report referred to research and sample collection being conducted in "harsh" and "remote" environments. USAID notes that this type of work often takes place in large urban and peri-urban environments with substantial infrastructure.
- The draft report cited an expert opinion that "some researchers have indicated that human infection surveillance should be prioritized over virus field research." USAID did not have the opportunity through this audit to provide information relevant to this expert opinion, specifically evidence of USAID's extensive investments in human disease surveillance, which historically far exceed investments in virus field research.

I am transmitting this letter from USAID for inclusion in the GAO's final report. Thank you for the opportunity to respond to the draft report, and for the courtesies extended by your staff while conducting this engagement. We appreciate the opportunity to participate in the complete and thorough evaluation of our virus field research. We remain committed to strengthening the Global Health Security Program to prevent, detect, and respond to emerging infectious disease threats, wherever they occur in the world.

Sincerely,

Colleen Allen

Colleen R. Allen
Assistant Administrator
Bureau for Management

Appendix IV: GAO Contact and Staff Acknowledgments

GAO Contact

Karen L. Howard, PhD, Director, Science, Technology Assessment, and Analytics (STAA), at (202) 512-6888 or HowardK@gao.gov.

Staff Acknowledgments

In addition to the contact named above, the following STAA staff made key contributions to this report: Hayden Huang, PhD, Assistant Director, Eliot Fletcher, PhD, Analyst-in-Charge and Senior Biological Scientist, Miguel Cortez Jr, General Engineer, Michael Dickens, PhD, Senior Biological Scientist, Eric Lee, PhD, Senior Biological Scientist.

These staff also contributed to this work: Jehan Chase, JD, Senior Attorney, Louise Fickel, Communications Analyst, Joe Rando, Visual Communications Analyst, Amber Sinclair, PhD, Senior Research Methodologist.

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