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Congress of the United States

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November 18, 2020

Mr. Robert R. Redfield, M.D.
Director
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329

Dear Director Redfield:

We write to request information from the Centers for Disease Control and Prevention (CDC) to help determine BioSafety Level (BSL)-3 and Animal BSL (ABSL)-3 laboratory capacity in the U.S. that could be used for COVID-19 preclinical animal model research to help develop vaccines, therapeutics, and diagnostics or for other ongoing research.

The CDC and the National Institutes of Health (NIH) have established four main levels of biosafety (BSL-1 to BSL-4) to guide laboratory researchers in the safe handling of biological agents.¹ Each biosafety level is associated with specific physical and procedural protections. In general, the more dangerous the pathogen is to public health, the higher its recommended biosafety level. Procedures deemed unlikely to produce disease in healthy humans should be conducted at BSL-1; those that may cause disease in healthy humans, but for which immunization or antibiotic treatment is available, should be conducted at BSL-2; procedures that may cause serious or potentially lethal diseases as a result of pathogen exposure should be conducted at BSL-3; and procedures that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease should be conducted at BSL-4.

The virus that causes COVID-19, SARS-CoV-2, is not on the select agent and toxin list, and therefore does not currently require registration with the Federal Select Agent Program

¹ Generally, along with BSL-4 laboratories, BSL-3 laboratories are referred to as “high containment laboratories;” U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, *Biosafety in Biomedical and Microbiological Laboratories (BMBL)*, 5th edition, 2009, *available at* <http://www.cdc.gov/biosafety/publications/bmb15/> (last visited Oct. 30, 2020); U.S. Dept. of Health and Human Services, Public Health Emergency, Science Safety Security, *Biosafety Levels*, *available at* <https://www.phe.gov/s3/BioriskManagement/biosafety/Pages/Biosafety-Levels.aspx> (last visited Oct. 30, 2020).

(FSAP).² However, shortly after COVID-19 was first identified in December 2019 as the cause of an alarming cluster of severe pneumonia cases in central China, the CDC advised that the virus should be isolated and studied in laboratories with advanced containment capabilities, meaning those laboratories with a BSL-3 or higher.³

In addition, the U.S. Food and Drug Administration (FDA) requires animal testing on vaccine and therapeutic candidates before a company can start human clinical trials. At each containment level, there is an equivalent set of biosafety guidelines for work with animals designated as ABSL-2 through maximum containment at ABSL-4. To perform work with animals, ABSL-3 laboratories must meet all the specifications of a BSL-3 facility as well as additional requirements for properly housing and handling animals.⁴ A top priority for COVID-19 preclinical research is to test experimental vaccines by immunizing animals and then “challenging” them with the virus, which are experiments that must be done in BSL-3 laboratories.⁵

In addition, critical equipment and training is needed for personnel for ABSL-3 laboratories. Because COVID-19 is so easily transmitted, there is a high likelihood of cross-contamination between groups of animals. For this reason, ABSL-3 laboratories need to be equipped to allow for single housing, with high efficiency particulate air filters, to prevent transmission of the virus between animals. Thus, strict infection control measures must be instituted by the animal technicians. Not every ABSL-3 laboratory is equipped to deal with pathogens as contagious as COVID-19. Given the CDC restrictions, FDA requirements, and necessary infection control measures there is a strong demand for ABSL-3 laboratories to conduct research with the live SARS-CoV-2.⁶

Based on Minority Committee staff research and discussions with government and non-government experts, available information indicates that the U.S. government lacks complete information on BSL-3 and ABSL-3 laboratory capacity in the U.S. For example, CDC acknowledged there is no national database of all BSL-3 laboratories that work on vaccine efficacy studies for highly transmissible diseases.⁷ Further, for those BSL-3 laboratories being used for preclinical animal studies, the NIH is not tracking COVID-19 vaccine or therapeutic preclinical animal model studies supported by National Institute of Allergy and Infectious

² *Id.*; The Centers for Disease Control and Prevention’s Division of Select Agents and Toxins houses the FSAP.

³ Glenn Rockman, *To accelerate innovation, the CDC should ease limits on which labs can handle the coronavirus*, STAT (Apr. 14, 2020), available at <https://www.statnews.com/2020/04/14/allow-bsl-2-labs-handle-novel-coronavirus/>.

⁴ Email from Centers for Disease Control and Prevention Staff, to Minority Committee Staff (July 22, 2020) (On file with Committee staff).

⁵ Jon Cohen, *Mice, hamsters, ferrets, monkeys. Which lab animals can help defeat the new coronavirus?*, SCIENCE (Apr. 13, 2020), available at <https://www.sciencemag.org/news/2020/04/mice-hamsters-ferrets-monkeys-which-lab-animals-can-help-defeat-new-coronavirus>.

⁶ NIH reported that NIAID has received a number of inquiries regarding services for preclinical animal studies for COVID-19. If appropriate based on the inquiry, NIAID refers requestors to relevant NIAID-supported services. To date, NIAID has referred more than 500 entities to a available NIAID-supported preclinical services. Email from National Institutes of Health to Minority Committee Staff (Oct. 15, 2020) (On file with Committee staff).

⁷ Email from Centers for Disease Control and Prevention Staff, to Minority Committee Staff (July 22, 2020) (On file with Committee staff).

Diseases (NIAID) grants or contracts.⁸ Specifically, NIH project tracking systems do not code for preclinical animal model studies.⁹ In addition, while NIH tracks all COVID-19 supplemental funding in its accounting system, the system does not include details specific to ABSL-3 laboratory projects.¹⁰ The lack of information on BSL-3 laboratory capacity is of concern because it may be contributing to delays and bottlenecks in preclinical COVID-19 research.

Although the BSL-3 laboratory capacity is not fully known, the extraordinary demand for COVID-19 preclinical research may have overwhelmed the known, available capacity. In spring 2020, concerns over the limitations in BSL-3 laboratories and ensuing research delay were raised to Minority Committee staff. For example, a managing partner of an investment firm observed in April 2020 that three of his portfolio companies working around the clock on Covid-19 interventions were stymied by access to BSL-3 labs in recent weeks.¹¹

Further, surveys by the U.S. government and the World Health Organization (WHO) examining BSL-3/ABSL-3 laboratory space suggest concern about laboratory capacity for COVID-19 preclinical research. For example, in its early days, Operation Warp Speed conducted an internal review targeting BSL-3 laboratory capacity and animal models.¹² The review appeared to focus on federal government laboratories, with an interest in facilities and the availability of animals for several vaccine candidates who would potentially need preclinical testing capacity simultaneously. Specifically, the data compilation was driven by the need to understand animal populations, locations, and support capabilities for animal trials to support Operation Warp Speed efforts.¹³

In addition, a WHO working group on COVID-19 models surveyed networks of laboratories to map out global animal laboratory capacity potentially to help with accelerating vaccine and therapeutic evaluation.¹⁴ The list contained information from all laboratories that responded to date, although “a number of BSL-3 laboratories had not yet participated.”¹⁵

Some medical product developers had pre-existing relationships (e.g., contracts or previous collaborations) with entities that had appropriate BSL-3 facilities. Other developers received assistance from NIH or the Biomedical Research and Development Authority

⁸ Email attachment from National Institutes of Health Staff, to Minority Committee Staff (Oct. 15, 2020) (On file with Committee staff).

⁹ *Id.*

¹⁰ *Id.*

¹¹ Glenn Rockman, *To accelerate innovation, the CDC should ease limits on which labs can handle the coronavirus*, STAT (Apr. 14, 2020), available at <https://www.statnews.com/2020/04/14/allow-bsl-2-labs-handle-novel-coronavirus/>.

¹² Email from U.S. Dept. of Health and Human Services Staff, to Minority Committee Staff (Aug. 20, 2020) (On file with Committee staff).

¹³ Email from U.S. Dept. of Health and Human Services Staff, to Minority Committee Staff (Aug. 21, 2020) (On file with Committee staff).

¹⁴ World Health Organization, *Global animal laboratories capacities to support vaccine and therapeutic evaluation* (Aug. 13, 2020), available at <https://www.who.int/publications/m/item/global-animal-laboratories-capacities-to-support-vaccine-and-therapeutic-evaluation>.

¹⁵ Email from the Co-chair of World Health Organization Working Group, to Minority Committee Staff (Aug. 10, 2020) (On file with Committee staff).

(BARDA) in gaining access to government BSL-3 laboratories or were provided guidance on how to find non-government BSL-3 laboratory facilities. Notwithstanding these efforts, there are developers who have experienced delays and bottlenecks in carrying out preclinical work, which means the U.S. COVID-19 research enterprise is not reaching all potential “multiple shots on goal.”¹⁶

Even a large multinational pharmaceutical company initially had difficulties conducting preclinical work on the selected compounds.¹⁷ For example, Pfizer had trouble finding a laboratory that could perform the proper assays.¹⁸ The company scaled down its antiviral research a decade ago and no longer owned a suitable biosafety laboratory to work with the live virus.¹⁹ At one point, Pfizer’s CEO, Albert Bourla, feared that lack of a laboratory would delay the clinical-trial process.²⁰ However, a government medical agency helped the company find a laboratory in a European country.²¹

In addition, some smaller companies also had difficulties accessing BSL-3 laboratory space. A former government biodefense expert informed Minority Committee staff that there is capacity at universities in the NIAID’s Regional Biosafety Laboratories, but it is not easy for small companies to establish agreements, and universities may not have the capacity to lend space for something other than their own research priorities. One company executive told staff that both NIH and BARDA reserved BSL-3 laboratory capacity for their own intramural products or those extramural studies that they are currently funding. The NIH and BARDA have existing contracts that allow multiple vendors in a pre-vetted pool to bid on individual projects. When the COVID-19 outbreak started, NIH and BARDA reserved huge swaths of BSL-3 space in their vendors. For small companies not working with NIH or BARDA support, it has been difficult for them to find laboratory capacity for their studies. In some cases, companies have had to modify their study design to fit around BARDA studies.

In recent months, the difficulties in finding available ABSL-3 laboratories have become apparent. The chief of infectious diseases at the Washington National Primate Research Center, Deborah Fuller, recently said, “[t]he real bottleneck is the access to the ABSL 3... (Scientists) are ready and their products are ready, but now they’re twirling their thumbs.”²² Further, press reports about monkey shortages for COVID-19 preclinical research have also shown limited ABSL-3 laboratory availability.²³ As *The Atlantic* reported, “monkeys infected with COVID-19

¹⁶ Cambridge Network, *'Multiple-shots-on-goal' approach needed to tackle Covid-19, say academics* (Sept. 6, 2020), available at <https://www.cambridgenetwork.co.uk/news/multiple-shots-goal-approach-needed-tackle-covid-19-say-academics>.

¹⁷ Nathan Vardi, *Why Pfizer May Be the Best Bet To Deliver A Vaccine By Fall*, FORBES (May 20, 2020), available at <https://www.forbes.com/sites/nathanvardi/2020/05/20/the-man-betting-1-billion-that-pfizer-can-deliver-a-vaccine-by-this-fall/#46fdd7ab382e>.

¹⁸ *Id.*

¹⁹ *Id.*

²⁰ *Id.*

²¹ *Id.*

²² Adrianna Rodriguez, *America is facing a monkey shortage as demand skyrockets for COVID-19 research, experts say*, USA TODAY (Sept. 10, 2020), available at <https://www.usatoday.com/story/news/health/2020/09/10/covid-vaccine-treatment-trials-create-monkey-shortage-science/5714115002/>.

²³ Sarah Zhang, *America Is Running Low on a Crucial Resource for COVID-19 Vaccines*, THE ATLANTIC (Aug. 31, 2020), available at <https://www.theatlantic.com/science/archive/2020/08/america-facing-monkey->

have to be kept in Animal Biosafety Level 3 laboratories, which have specific design and ventilation requirements to prevent the spread of pathogens. The U.S. has a limited number of ABSL-3 labs.”²⁴

In addition, there are a limited number of BSL-4 laboratories as compared to BSL-3 laboratories, therefore their preclinical research capacity is more ascertainable. NIAID notes that while some of these studies are being performed in BSL-4 facilities, a BSL-4 level of biosafety is not required for SARS-CoV-2 research because such studies can be safely conducted in BSL-3 facilities.²⁵

Biocontainment laboratory capacity is a long-standing concern of policymakers. After the September 11, 2001, terrorist attacks and the subsequent anthrax attacks, the federal government responded with increased focus on and funding for biodefense. A key consideration in this response was addressing shortages in diagnostic, clinical, and research laboratory capacity.²⁶ The surge of interest in high-containment laboratories led NIAID to conduct a survey on laboratory capacity. In a final report presented in June 2005, NIAID identified 277 facilities (with a total of 598 laboratories) in the U.S. with BSL-3 capable laboratories.²⁷ However, the survey had only a 48 percent response rate, did not include federal government laboratories, and did not assess BSL-4 capable laboratories.²⁸ Further, the survey did not assess animal study capacity, or the aerosol capability of these facilities.²⁹

In 2004, Congress enacted the Project BioShield Act that required a report on high-containment laboratory capacity.³⁰ Pursuant to the Project BioShield Act of 2004, the U.S. Department of Homeland Security (DHS) and the U.S. Department of Health and Human Services (HHS) issued the report in January 2007, and estimated that there were 633 BSL-3 and BSL-4 laboratories located within 204 entities or institutions.³¹ Of the 633 biocontainment

shortage/615799/?utm_source=msn; Mallory Pickett, *The Search for a COVID-19 Animal Model*, WIRED (May 11, 2020) (“Only primate research facilities with appropriate biosafety facilities can conduct coronavirus experiments, and these special facilities have very limited capacity.”), available at <https://www.wired.com/story/the-search-for-a-covid-19-research-animal-model/>.

²⁴ Sarah Zhang, *America Is Running Low on a Crucial Resource for COVID-19 Vaccines*, THE ATLANTIC (Aug. 31, 2020), available at https://www.theatlantic.com/science/archive/2020/08/america-facing-monkey-shortage/615799/?utm_source=msn.

²⁵ Email from National Institutes of Health Staff, to Minority Committee staff (September 9, 2020). NIAID reported having three BSL-4 labs in their network, with one BSL-4 lab involved in conducting preclinical studies for COVID-19.

²⁶ Frank Gottron and Dana A. Shea, *Oversight of High-Containment Biological Laboratories: Issues for Congress*, Congressional Research Service (May 4, 2009), available at <https://fas.org/sgp/crs/terror/R40418.pdf>.

²⁷ Constella Health Sciences, *Survey for Determining the Location, Capacity, and Status of Existing and Operating BSL-3 Laboratory Facilities within the United States* (June 2, 2005), available at <https://fas.org/biosecurity/resource/documents/BSL3-Survey.pdf>.

²⁸ *Id.* at 3.

²⁹ *Id.*

³⁰ Sec. 5(d)(1) of the Act requires that “[n]ot later than 120 days after enactment of this act, the DHS and HHS Secretaries will jointly report to the designated congressional committees whether there is a lack of adequate large-scale biocontainment facilities necessary for the testing of security countermeasures in accordance with Food and Drug Administration requirements.”

³¹ U.S. Dept. of Health and Human Services and U.S. Dept. of Homeland Security, *Report Regarding Biocontainment Facilities* (Jan. 2007).

facilities, 39 had the capacity to conduct the animal studies necessary for medical countermeasure testing.³² However, of the 39 facilities, only three facilities met the requirements to conduct aerosol challenge studies in animals (especially non-human primates) and stringent good laboratory practices.³³ The DHS and HHS estimate drew heavily on the number of facilities registered to work with select agents. However, a BSL-3 laboratory does not necessarily work with select agents, and therefore may not be required to hold a registration certificate. In addition, entities registered to work with select agents may or may not use high-containment laboratories.

The Project BioShield Act of 2004 only required the aforementioned report on domestic capacity. Subsequently, the Pandemic and All-Hazards Preparedness Act and its reauthorizations folded many of the annual BioShield reporting requirements into the biennial Public Health and Emergency Medical Countermeasure Enterprise Strategy and Implementation Plan (PHEMCE SIP).³⁴ However, the PHEMCE SIP is not required to have a high containment laboratory capacity assessment as described in the BioShield Act.³⁵ The U.S. Government Accountability Office (GAO) was unable to determine definitively the number of BSL-3 laboratories, but did document an increase in laboratories.³⁶ In 2009, Congressional Research Service noted that “[a] lack of information on existing federal and non-federal high-containment laboratory capacity is hindering more coordinated planning.”³⁷ Further, GAO reported in 2009 that information about non-select agent laboratories is unknown.³⁸ In 2013, GAO was not able to find any detailed projections based on a government-wide strategic evaluation of research requirements based on public health or national security needs. As GAO noted in 2014 testimony, “[w]ithout this information, there is little assurance of having facilities with the right capacity to meet our national needs.”³⁹

Minority Committee staff sought to update the 2007 statistics with the assistance of the CDC. As of August 10, 2020, CDC reported that there are 72 entities registered with the FSAP that maintain ABSL-3 laboratories.⁴⁰ Of those entities:

- 8 entities are registered to perform studies involving large animals;
- 9 entities are registered to perform studies involving non-human primates; and

³² *Id.*

³³ *Id.*

³⁴ 42 U.S.C. 300-10(d).

³⁵ Email from Congressional Research Service Staff, to Minority Committee Staff (Aug. 17, 2020) (On file with Committee staff).

³⁶ U.S. Government Accountability Office, *High-containment Biosafety Laboratories Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*, GAO-08-108T (Oct. 4, 2007), available at <https://www.gao.gov/assets/120/117997.pdf>.

³⁷ Frank Gottron and Dana A. Shea, *Oversight of High-Containment Biological Laboratories: Issues for Congress*, Congressional Research Service (CRS) 15 (May 4, 2009), available at <https://fas.org/sgp/crs/terror/R40418.pdf>.

³⁸ Testimony of Nancy Kingsbury, U.S. Government Accountability Office, *Review of CDC Anthrax Lab Incident: Hearing Before H. Comm. On Energy and Commerce's Subcommittee on Oversight and Investigations*, 113th Cong. (July 16, 2014), available at <https://docs.house.gov/meetings/IF/IF02/20140716/102479/HHRG-113-IF02-Wstate-KingsburyN-20140716.pdf>.

³⁹ *Id.* at 3.

⁴⁰ Email from Centers for Disease Control and Prevention Staff, to Minority Committee Staff (Aug. 14, 2020) (On file with Committee staff).

- 66 entities are registered to perform studies involving small animals (e.g., ferrets, mice).

In contrast to the 39 registered entities for animal research on medical countermeasure testing in 2007, CDC later reported that there are 27 registered entities that intend to perform vaccine studies with avian influenza virus and reconstructed 1918 influenza virus in animals. However, CDC was not able to provide current statistics on the number of BSL-3 entities and the corresponding number of laboratories.

According to the 2019 Annual Report of the FSAP, there were 199 entities registered as BSL-3/ABSL-3 laboratories and 8 entities registered as BSL-4/ABSL-4 laboratories.⁴¹ While this number represents BSL-3 laboratories that are registered to work with federal select agents, since COVID-19 is not registered as a federal select agent, this number does not necessarily include all of the laboratories that are working with COVID-19.

The BSL-3 laboratories in the U.S. conduct critical research on SARS-CoV-2, the virus that causes COVID-19.⁴² These laboratories are not only conducting needed basic research on the pathogen, but they are also playing a key role in generating the critical data necessary to develop new diagnostics, therapeutics, and vaccines effective against COVID-19.⁴³

The NIH Accelerating COVID-19 Therapeutic Interventions and Vaccines program acknowledged the importance of BSL-3 laboratories in Fast Track Area #1 noting that “to develop a collaborative streamlined forum to identify preclinical treatment” the NIH planned to extend access to high-throughput facilities, especially in BSL-3 laboratories, and increase access to validated animal models.

It is critical for the nation’s response to the pandemic to have the best understanding of the totality of such research assets in the U.S. in order to improve access for researchers, maximize research opportunities for identifying medical advances for COVID-19, bring in any underutilized laboratories to help relieve burdens on overworked research entities, and understand through traditional gap analysis whether there is appropriate high-containment laboratory capacity for biodefense strategic planning.⁴⁴

Because the CDC has been a primary source of data for U.S. government assessments for laboratory capacity, we would appreciate the CDC’s assistance to explore ways for obtaining comprehensive data on BSL-3 laboratories and ABSL-3 laboratories in the U.S. To assist our request, please provide the following by December 18, 2020:

⁴¹ U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, U.S. Dept. of Agriculture, 2019 Annual Report of the Federal Select Agent Program, *available at*

https://www.selectagents.gov/resources/publications/docs/FSAP_Annual_Report_2019_508.pdf.

⁴² Email from National Institutes of Health Staff, to Minority Committee Staff (June 25, 2020) (On file with Committee staff).

⁴³ *Id.*

⁴⁴ Frank Gottron and Dana A. Shea, *Oversight of High-Containment Biological Laboratories: Issues for Congress*, Congressional Research Service (May 4, 2009), *available at* <https://fas.org/sgp/crs/terror/R40418.pdf>.

1. What is the best way to get comprehensive information on BSL-3 and ABSL-3 laboratory capacity?
2. Please confirm whether all entities listed in the NIAID national and regional laboratory network have ABSL-3 laboratories, how many of the entities are registered with FSAP, how many ABSL-3 laboratory spaces at each of these entities, and how many ABSL-3 laboratory spaces.
3. CDC requires permits to import SARS-CoV-2, the virus that causes COVID-19, or subsequent transfer of the imported virus into the U.S.⁴⁵ As of August 10, the Division of Select Agents and Toxins(DSAT) has issued 436 permits for import or for subsequent transfer of the imported SARS-CoV-2 into the U.S.⁴⁶
 - a. How many entities have requested import permits to date? How many of these entities are registered with the FSAP?
 - b. How many of those registered with FSAP have ABSL-3 laboratories?
4. How many entities with ABSL-3 laboratories have withdrawn their registrations with the FSAP within the last 10 years? Please provide the number of withdrawals per year. Have any of these entities requested import permits for SARS-CoV-2?
5. How many entities with ABSL-3 laboratories have changed work studies and are no longer registered with FSAP?
6. How many entities have animal permits for non-human primate research?
7. How many entities have animal permits for small animal research that would include Syrian hamsters (a popular animal model in COVID-19 preclinical research)?
8. Could the CDC conduct a questionnaire of all research entities with laboratories to identify ABSL-3 laboratories at entities not registered with FSAP? If so, would CDC be willing to gather this data? If not, which agency or department is the most appropriate for gathering this information? How is the CDC coordinating with other federal agencies to get this information? What barriers does CDC face in order to gather this information?
9. How can FSAP data on ABSL-3 laboratories include information on whether the laboratory has the capability of conducting COVID-19 preclinical animal research?
10. What ideas does the CDC have for obtaining the most comprehensive data on BSL-3 and ABSL-3 laboratory capacity?

⁴⁵ Centers for Disease Control and Prevention, Import Permit Program (IPP), *available at* <https://www.cdc.gov/cpr/ipp/index.htm> (last visited Oct. 30, 2020).

⁴⁶ Email from Centers for Disease Control and Prevention Staff, to Minority Committee Staff (Aug. 14, 2020) (On file with Committee staff).

11. Is there data on ABSL-3 laboratories from animal welfare committees or other organizations, and could CDC obtain this data?

We appreciate your attention to this matter. If you have any questions, please contact Alan Slobodin of the Minority Committee staff at (202) 225-3641.

Sincerely,



Greg Walden
Republican Leader
Committee on Energy and Commerce



Michael Burgess
Republican Leader
Subcommittee on Health



Brett Guthrie
Ranking Member
Subcommittee on Oversight and
Investigations