U.S. Department of Health and Human Services

National Institutes of Health

Sixteenth Meeting of the Clinical Center Research Hospital Board

October 16, 2020

Contents

Clinical Center Research Hospital Board iii

Executive Summary iv

Welcome and Board Chair's Overview 1

NIH Director's Remarks 1

- Therapeutic Agents 1
- Vaccines 2
- Diagnostics 2
- Conclusion 2
- Discussion 2

NIH Clinical Center Chief Executive Officer Update 3

- Annual Awards 3
- Leadership Changes 3
- 2020 Culture of Patient Safety Survey 4
- Hospital Census 4
- 2020 Priorities Closeout 4
- Hand Hygiene Compliance 5
- Influenza Vaccinations 5
- Ongoing SARS-CoV-2 Safeguards 5
- A Peek at 2021 6
- Discussion 6

Patient Safety and Clinical Quality Update 6

- Performance Metrics 6
- Patient Safety Event Reporting 7
- COVID-19–Related Events 7
- Culture of Patient Safety Survey 7
- Expression of Gratitude 8

Discussion 8
Clinical Facilities Update 3
Completed Projects 8
Projects Under Construction 9
Projects Awaiting Funding 10
Discussion 10
Follow-Up Item 11
Rehabilitation Medicine Department Research Highlights 8
Epidemiology and Biostatistics 11
Research Section: Office of Strategic Research 12
Exercise Science Group 12
COVID-19 Care 13
Highlights of the Past 6 Years 13
RMD's Work in Cerebral Palsy 13
Key Principles in Neurorehabilitation 14
Early Intervention in Cerebral Palsy 15
Discussion 15
NIH Responses to COVID-19 11
NIH Role in Diagnostic Research 16
NIH Role in Therapeutic Research 17
Research to Prevent COVID-19 18
Discussion 18
Adjournment 18
Abbreviations and Acronyms 20

Clinical Center Research Hospital Board

Laura Forese, M.D., M.P.H., Executive Vice President and Chief Operating Officer, NewYork–Presbyterian Hospital; and Chair, National Institutes of Health (NIH) Clinical Center Research Hospital Board (CCRHB)

Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, NIH; and Executive Director, CCRHB

Francis S. Collins, M.D., Ph.D., Director, NIH; and *Ex Officio* Member, CCRHB

*Ellen Berty, Special Education Teacher, Book Author, and Former NIH Research Participant

Brig Gen James Burks, M.B.A., M.M.A.O.S., U.S. Air Force (Ret.)

Jeanette Ives Erickson, D.N.P., RN, FAAN, Chief Nurse Emerita, Massachusetts General Hospital; and Executive Committee Chair, Commission on Magnet Recognition, American Nurses Credentialing Center

Julie Freischlag, M.D., Wake Forest University School of Medicine

Steven I. Goldstein, M.H.A., President and Chief Executive Officer, University of Rochester Medical Center

William Hait, M.D., Ph.D., Global Head of External Innovation, Johnson & Johnson

Stephanie Reel, M.B.A., Chief Information Officer Emerita, Johns Hopkins University and Health System

Richard P. Shannon, M.D., Chief Quality Officer, Duke Health

Ruth Williams-Brinkley, M.S.N., President and Chief Executive Officer, Kaiser Foundation Health Plan of the Mid-Atlantic States, Inc.

*Absent

Executive Summary

The Clinical Center Research Hospital Board (CCRHB) of the National Institutes of Health (NIH) convened its 16th meeting via videoconference on October 16, 2020. The meeting was open to the public and was webcast live. A video recording of the meeting is available online.

Laura Forese, M.D., Executive Vice President and Chief Operating Officer, NewYork–Presbyterian Hospital; and Chair, CCRHB, called the meeting to order at 9:01 a.m. ET. She welcomed the newest Board member Julie Freischlag, M.D., of the Wake Forest University School of Medicine.

Francis Collins, M.D., Ph.D., NIH Director, greeted the CCRHB members and highlighted NIH activities focused on developing diagnostics, therapeutics, and preventive vaccines for the coronavirus disease 2019 (COVID-19) pandemic. For the fifth time, *60 Minutes* aired a segment on gene therapies developed under the Cure Sickle Cell Initiative.

James Gilman, M.D., Chief Executive Officer (CEO), NIH Clinical Center, announced the recipients of several Clinical Center awards that recognize exemplary performance. He also noted several changes in Clinical Center leadership and observed that the hospital census has been gradually increasing since being severely curtailed because of the pandemic. The pandemic also led to the deferral of a 2021 priority focused on improving neurologic assessment of patients; the other priorities have progressed despite the pandemic. Dr. Gilman updated the Board on screening and testing of staff and patients for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). He commented on the impending retirement of Laura Lee, RN, Chief, Office of Patient Safety and Clinical Quality, after 32 years of service to NIH.

Ms. Lee briefed the CCRHB on patient and employee safety data, noting several recent encouraging trends. She presented the results of the 2020 Culture of Patient Safety Survey, which showed significant progress in all 12 domains compared with the 2017 survey. Ms. Lee concluded her remarks by thanking Dr. Gilman, the CCRHB, and her team for their support during her tenure at NIH.

Several construction projects have been completed in the Clinical Center, and others are underway. Daniel Wheeland, P.E., Director, Office of Research Facilities, described and provided timelines for eight projects intended to increase patient safety and expand research facilities.

Leighton Chan, M.D., M.P.H., Chief, Clinical Center Rehabilitation Medicine Department (RMD) briefed the CCRHB on the department, noting that it touches nearly every research participant who comes to the Clinical Center. RMD has covered 65% of its $6 million research budget through agreements with other agencies, mainly the Social Security Administration. RMD efforts have contributed to advances in disability assessment, traumatic brain injury biomarkers, and treatment of pulmonary hypertension, systemic lupus erythematosus, cerebral palsy, and Havana syndrome.

Diane Damiano, Ph.D., PT, FAPTA, Senior Investigator and Chief, Functional & Applied Biomechanics (FAB) Section, Clinical Center RMD, is the Chief of RMD's FAB section and runs the FAB laboratory. Dr. Damiano said that the FAB LAB designs and evaluates novel treatments in combination with real-time functional imaging to improve gait and other motor

skills of people who have cerebral palsy. Her research team supports 14 protocols for investigators: 8 in the National Institute of Neurologic Disorders and Stroke and 2 each in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Human Genome Research Institute, and the Clinical Center.

H. Clifford Lane, M.D., outlined the timeline of the SARS-CoV-2 pandemic. The first reports came out of China in early December 2019. The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public–private partnership aims to speed the development of the most promising treatments and vaccines for COVID-19. In addition to private firms and NIH, the Department of Veterans Affairs, the Department of Defense, the Biomedical Advanced Research and Development Authority, the Centers for Disease Control and Prevention, and other federal entities are collaborating within the framework of Operation Warp Speed.

Meeting Summary
Friday, October 16, 2020

Welcome and Board Chair's Overview

Laura Forese, M.D., Executive Vice President and Chief Operating Officer, NewYork–Presbyterian Hospital, and Chair, Clinical Center Research Hospital Board (CCRHB)

The 16th meeting of the National Institutes of Health (NIH) CCRHB took place on October 16, 2020. The meeting participants convened via videoconferencing. The meeting was open to the public and webcast live. A video recording of the meeting is available online.

Dr. Forese called the meeting to order at 9:01 a.m. ET and welcomed everyone. She introduced new CCRHB member Julie Freischlag, M.D., of the Wake Forest University School of Medicine, and noted that Ellen Berty was unable to attend.

NIH Director's Remarks

Francis S. Collins, M.D., Ph.D., Director, NIH; and Ex Officio *Member, CCRHB*

Dr. Collins thanked Dr. Forese for her continued service as chair of the Board.

Dr. Collins reported that the NIH Clinical Center is restarting many activities with appropriate precautions in place to protect staff and patients. Bench scientists and staff involved in patient care have returned to work gradually, and many other employees are still working remotely. Those who have returned to the Clinical Center are working in shifts to minimize the number of people in laboratories and elsewhere in the Clinical Center. Dr. Collins said that employees are continuing to support NIH's mission despite the stress imposed by 7 months of a global pandemic, and he recognized the stress and special challenges faced by those who are working remotely while having children or other family members at home.

Dr. Collins reported that NIH has been highly focused on making progress on diagnostic tests, therapeutics, and vaccine development for coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Therapeutic Agents

NIH is involved in several clinical trials of potential therapeutic agents, including ACTIV-1 IM, the master protocol launched by the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership. ACTIV-1 IM is a randomized, placebo-controlled, adaptive trial comparing the efficacy of three immunomodulatory drugs in hospitalized patients who have COVID-19 complicated by a cytokine storm, a potentially fatal multisystem inflammatory response. Other ACTIV trials include tests of monoclonal antibodies and other therapeutics in outpatients (ACTIV-2) and in a hospitalized population (ACTIV-3). ACTIV-4 is investigating antithrombotic agents, and the adaptive design of ACTIV-5 allows rapid testing of approved or agents in late-stage development. Compounds that show efficacy at the interim analysis will move forward to Phase III trials.

Vaccines
Four vaccine trials are ongoing in the United States; two based on adenovirus-vectored vaccines are on hold while the Food and Drug Administration (FDA) reviews adverse events. Two trials of vaccines based on purified recombinant protein subunits are going to get underway soon. NIH has a significant role with the trial, which is testing Moderna's mRNA vaccine.

Diagnostics
Dr. Collins reported that NIH is supporting the development of 22 creative technology platforms through the Rapid Acceleration of Diagnostics (RADx) initiative for COVID-19 testing. A "shark tank" approach allowed applicants to demonstrate their capabilities and collect advice from experts. The resulting diagnostic platforms should be able to add capacity for 2.2 million tests per day, probably in the next few months. Wider availability of testing for asymptomatic COVID-19 cases is a critical part of public health strategies for isolation and contact tracing to bring the pandemic under control.

Conclusion
Despite the pandemic, NIH's commitment to its mission to support progress on a spectrum from basic science to clinical trials for many diseases continues unabated. For the fifth time, *60 Minutes* aired a segment on the Cure Sickle Cell Initiative led by John Tisdale, M.D. The segments on gene therapy approaches for the disease always result in an outpouring of emails from people seeking cures for their children and themselves.

Dr. Collins noted that he has now served 11 years as Director of NIH. He said that it is a privilege to work with talented and dedicated people who work hard at NIH and at institutions across the country to improve the nation's health.

Discussion
Steven I. Goldstein, M.H.A., inquired about the status of Russia's vaccine development efforts. Dr. Collins said that some limited data on safety and immunogenicity from the Phase I and II trials of the vaccine called Sputnik V. Russia started distributing the vaccine without a Phase III trial, which would be insisted upon in the United States. The lack of safety data on the Russian vaccine may put people at risk.

Dr. Forese read the following resolution into the record: "We thank the NIH for its collective services to our nation during this unprecedented COVID-19 pandemic. On behalf of all of us on the Clinical Center Research Hospital Board, thank you, Dr. Collins, your colleagues, and the many others for the work they are doing every day. It is the privilege of the Board to be part of this important effort in a minor way, and we are proud of the work the NIH is doing."

Dr. Collins expressed appreciation on the behalf of himself and Anthony Fauci, M.D., who has been the voice of reason, evidence, and truth during the global pandemic.

NIH Clinical Center Chief Executive Officer Update

James Gilman, M.D., Chief Executive Officer (CEO), NIH Clinical Center

Dr. Gilman spoke about NIH intramural researcher Harvey J. Alter, M.D., being awarded the 2020 Nobel Prize in Physiology or Medicine along with two other scientists for their contributions to the discovery of the hepatitis C virus. Their accomplishments made the blood supply much safer. A banner honoring Dr. Alter will be hung in the Clinical Center when the hospital is operating more normally.

John Gallin, M.D., Chief Scientific Officer and Scientific Director of the Clinical Center, added to the accolades for Dr. Alter, with whom he had worked for 50 years in the Clinical Center. Dr. Gallin recalled that when Dr. Alter was a fellow, he wanted to learn how to use Ouchterlony plates for detecting antibodies. Dr. Alter won the Lasker Award and then, 20 years later, the Nobel Prize. His success is largely due to having access to many pre- and posttransfusion samples from patients undergoing cardiac surgery. Also, NIH afforded him the ability to undertake chimpanzee studies that enabled his discovery. Dr. Gallin said that the Nobel Prize is a cause for celebration for many at NIH.

Annual Awards

Dr. Gilman announced the following awards honoring Clinical Center personnel:

- Staff Clinician of the Year: Stephanie Goff, M.D., Surgery Branch, National Cancer Institute
- Physician Assistant of the Year: Theresa Jerussi, PA, administrative head of the Blood and Immune Deficiency–Cellular Therapy Program
- Clinical Center Administrators of the Year: Bernard Harper, Chief, Materials Management and Environmental Services; and Patricia Coffey, RHIA, Chief, Health Information Management Other Awards and Honors
- Allies of the Disability Community Award: Diane Damiano, Ph.D., M.S., PT, Chief, Functional and Applied Biomechanics Section, Rehabilitation Medicine Department (RMD)
- SuperSTARS Awards: Ashley Devries, Clinical Research Nurse; Curtin Young, Patient Care Technician; Mary Bowes, Nurse; and Raj Kanagarathinam, Phlebotomist, Department of Laboratory Medicine (DLM)

Leadership Changes

Dr. Gilman reported that Janice Lee, D.D.S., M.D., M.S., was appointed NIH Deputy Director for Intramural Clinical Research. Dr. Lee is a craniofacial surgeon.

The position of Chief Medical Officer (CMO) remains vacant. Colleen Hadigan, M.D., will step in as Acting CMO for the next 6 months. She is a pediatric gastrointestinal medicine specialist. Dr. Gilman acknowledged several other clinicians who have rotated CMO duties since January 2020. A new search for a permanent CMO will start early in 2021.

The position of Chief of the Department of Transfusion Medicine (DTM) has been filled, but the hiring package is not yet finalized. Cathy Cantilena, M.D., has been serving as the Acting Chief since last fall. Dr. Gilman anticipates announcing the new Chief in November 2020.

Dr. Gilman remarked on the departure of Laura Lee, M.S., RN, Director, Clinical Center Office of Patient Safety and Clinical Quality, who is retiring after 32 years of commendable service to the Clinical Center. Ms. Lee plans to join MedStar Health to lead the development of a strategy for high reliability and to prioritize and activate patient safety initiatives across the system's hospitals and ambulatory care sites. Mary Sparks, RN, will step in as Acting Director. Dr. Gilman spoke about the importance of working to ensure that the important changes made by Ms. Lee persist, ensuring that improvements in patient care and clinical quality persist. Dr. Gilman announced that Ms. Lee received the 2019 Secretary's Award for Meritorious Service—the highest award issued by the Department of Health and Human Services.

2020 Culture of Patient Safety Survey

More than 1,000 responses were received. The Clinical Center improved in each of the 12 domains compared with the 2017 scores.

Hospital Census

Dr. Gilman reported that the average daily census is down about 30% compared with the 3-year average, but the census is slowly rising to provide more opportunities for people to participate in clinical trials. Investigators are eager to start seeing more research participants; efforts are underway to open a few more beds. Everyone is aware of the need to guard against COVID-19 and influenza in the fall and winter.

2020 Priorities Closeout

Dr. Gilman reminded the Board members that the 2020 priorities were established before the pandemic; implementation of at least one priority has been delayed.

- *Magnet Recognition Program®:* The official Magnet kickoff event and keynote address occurred on October 1. On October 19, the Clinical Center Patient Advisory Group will receive a briefing. Online resources about the Magnet Journey® will launch in October. The effort to achieve Magnet® status was explained during the July 2020 CCRHB meeting.
- *Talent management:* Dr. Gilman spoke about behind-the scenes efforts to take care of Clinical Center staff. In a large organization with a centralized human resources office, such as NIH, programs that appeal to staff differ. Therefore, it will be important to learn more about employees' goals for their professional lives and tailor programs to meet their needs. He envisions a major initiative to recruit and retain the best of the best supported by a custom onboarding program and individual development plans.
- *Staff safety:* Dr. Gilman recalled briefing the Board on the Anti-Harassment Response Team (AHaRT) and the Behavioral Emergency Response Team (BERT) during the July 2020 meeting. AHaRT is a multidisciplinary group composed of NIH and Clinical Center staff that is addressing inappropriate behavior and harassment by patients and visitors

towards staff. BERT is a multifaceted program that supports nurses and health care staff in managing behavioral emergencies. Both programs are now in place.

- *Simulations and telemedicine:* The Board was briefed on these well-integrated CC programs during the July 2020 meeting.
- *Improved neurologic assessments by physicians and nursing staff:* Dr. Gilman said that progress on this front has stalled because of the pandemic. Therefore, this priority will be reinvigorated in 2021.

Hand Hygiene Compliance

Dr. Gilman said that the Clinical Center implemented the Power of Clean Hands Campaign and a mentoring program on April 1, 2018. Since then, hand hygiene compliance rates have risen from 70% to 90%.

Influenza Vaccinations

About 40% of Clinical Center staff have already received vaccinations for the coming influenza season. The vaccination campaign will continue until November 4, 2020. People who are teleworking may come to campus for COVID-19 surveillance testing or to receive an influenza vaccination.

Ongoing SARS-CoV-2 Safeguards

To protect the health and safety of patients, visitors, and staff, infection control measures remain unchanged. Every person who enters the Clinical Center is screened and given a mask, which is to be worn whenever the person is near another person. Everyone is expected to maintain social distancing except during hands-on patient care. Visitors are not permitted, with a few exceptions for pediatric patients and for patients at the end of life. Visitors permitted under these limited exceptions must remain in the patient room for the duration of the visit. There has been little, if any, evidence of SARS-CoV-2 spread within the Clinical Center.

More than a half million screenings have occurred as people have entered the hospital. Adding another screening spot will make a total of four. Nursing staff oversee screenings, because sometimes clinical decisions are necessary. The FDA has approved use of saliva samples for SARS-CoV-2 testing. Between 15% and 20% of staff request saliva testing. Saliva testing could reduce the need for personal protective equipment and lower staffing requirements, because sample collection is simpler. This is important because of the increasing number of tests.

Some other NIH sites (e.g., Rocky Mountain Laboratories in Montana) collect samples and send them to the Clinical Center's DLM for testing. Turnaround time is typically 24 hours. The rate of positivity continues to hover around 2 or 3 positive results per 1,000 tests.

Morale-boosting activities, including musical performances, are gradually being re-introduced in the Clinical Center. Patients, visitors and staff appreciate the connections to more normal, happier times. Food trucks, outdoor barbecue, and mobile food ordering are expanding dining options for employees. The hope is that the annual gingerbread house exhibit will take place with social distancing measures in place for assembly and viewing.

A Peek at 2021

Dr. Gilman reminded the CCRHB members that the Joint Commission is due for a return visit to the Clinical Center next year. The search for a CMO will continue. Dr. Gilman expects that more Clinical Center staff will return to work on site. Construction and environmental improvements will continue.

Discussion

William Hait, M.D., Ph.D., commented on the remarkably low rate of positive tests for SARS-CoV-2. Nationally, about 10% of tests are positive. Dr. Gilman clarified that 2 or 3 positive tests per 1,000 is the rate for the asymptomatic line. Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, NIH; and Executive Director, CCRHB, confirmed that the positivity rate for in-car tests of symptomatic people is 6%, which mirrors the prevalence in the surrounding county.

Dr. Gilman noted that Clinical Center staff are well informed and conscientious; therefore, they would probably avoid coming to the Clinical Center if they are feeling ill. The staff are accustomed to social distancing and wearing masks. Testing is voluntary.

Dr. Janice Lee thanked Clinical Center leadership for supporting the interface between outstanding research and excellent patient care. She appreciates the opportunity to serve as the Deputy Director for Intramural Clinical Research.

Patient Safety and Clinical Quality Update

Laura Lee, M.S., RN, Director, Clinical Center Office of Patient Safety and Clinical Quality

Ms. Lee thanked Dr. Gilman for his kind remarks.

Performance Metrics

Ms. Lee highlighted several performance metrics from the Executive Dashboard for the Clinical Center:

- *Patient perceptions:* Because the hospital census has been low, few patient perception surveys have been completed. Survey responses continue to show that patients have a positive perception of their care in the Clinical Center and that patients would recommend the Clinical Center to their friends and family. Both measures were well above the benchmarks for both inpatient and outpatient experiences.
- *Infection control metrics:* Handwashing compliance continues to improve. In the second quarter of 2020, compliance reached 95%. Rates of central line–associated blood stream infections (CLABSIs) in the whole house and in the intensive care unit increased during the second quarter of 2020, after being at 0 per 1,000 catheter days during the first quarter. Ms. Lee presented the CLABSI review tool that is used to identify variations in patients and practice that may have increased risk of CLABSI in each case. Catheter-associated urinary infection rates have remained at 0 per 1,000 catheter days for at least 1 year, with the exception of the fourth quarter of 2019 and the first quarter of 2020, when a few cases occurred in the Surgical Oncology Program.

- *Inpatient falls:* Ms. Lee reported slight upward trends in falls and falls with injuries, but rates remain below national benchmarks. Falls are often associated with activities such as toileting and ambulating. Nursing staff are taking action to reduce these rates.
- *Pressure injuries:* Three injuries were reported during the second quarter of 2020. Contributing factors included clinical status and having nasogastric or endotracheal tubes in place. A group dedicated to preventing pressure injuries is developing interventions to reduce risk throughout the hospital and for individual patients.
- *Medication administration barcode compliance:* Compliance hovers between 98% and 99% in areas of the hospital using barcode technology.
- *Occupational injury and illness:* Cases of injuries and illness among employees have fallen steeply during the pandemic. Injuries are mostly related to the musculoskeletal system. The most important metric is days away, restricted, or transferred (DART); during the second quarter of 2020, DART was down to 6 cases from 35 cases reported in the third quarter of 2019.

Patient Safety Event Reporting

Ms. Lee presented the dashboard for the Safety Tracking and Reporting System (STARS), which is used to identify trends in patient safety events. This electronic reporting system is available to all staff to allow them to share information about errors, near misses, process issues, and instances of high-quality service. Numbers of STARS reports have decreased due to offsite teleworking. Only 4% of reports are anonymous. Among the top reported events are incorrect blood sample volumes and failure to enter orders in the Clinical Research Information System (CRIS). Harm events generally related to clinical care, treatment, or service and lapses in reporting use of high-risk medications (e.g., insulin). The large majority of events resulted in mild or moderate harm. Severe harm and death are very rare.

COVID-19–Related Events

Between March 10 and October 7, 2020, 168 total events related to COVID-19 occurred. Most were infections, lapses in procedures, events related to clinical care, and communication issues. The number of events peaked in September at 49. In October, the number fell to six.

Culture of Patient Safety Survey

Ms. Lee reported that over the past 5 years, the Clinical Center has made a strong effort to improve the quality of care. Tools such as the Agency for Healthcare Research and Quality (AHRQ) nationwide survey are essential to track progress on domains of safety culture. NIH last fielded the AHRQ survey in 2017. This year, 1,172 CRIS users and Clinical Center staff participated; 65% of respondents provide direct patient care.

Compared with 2017, the Clinical Center has improved in all 12 domains, with the largest gains being in overall perceptions of patient safety and in handoffs and transitions. In 2017, the Clinical Center ranked below average for AHRQ hospitals across all 12 domains; in 2020, the Clinical Center ranked as well as or better than other AHRQ hospitals in 7 domains. These results provide solid evidence that the Clinical Center's investment in its safety culture has paid off. Ms. Lee thanked NIH leaders and the CCRHB for providing the resources and guidance to achieve these results.

Expression of Gratitude
Ms. Lee thanked Dr. Gilman for his leadership and all the Clinical Center and Institute and Center (IC) staff who serve NIH patients, each other, and the American public. She acknowledged the stellar efforts of her team. Ms. Lee expressed her gratitude to Clinical Center patients for participating in research as true partners in medical discovery.

Discussion
Dr. Forese acknowledged the accomplishments of the Clinical Center Office of Patient Safety and Clinical Quality under Ms. Lee's leadership. Dr. Forese congratulated Ms. Lee and her team on their progress in developing a culture of safety as evidenced by the AHRQ survey results. She noted that former and current patient members of the Board have greatly appreciated Ms. Lee's dedication to patient safety. Jeanette Ives Erickson, D.N.P., RN, FAAN, noted that Ms. Lee leaves the Clinical Center a much safer place thanks to her leadership on the Clinical Center's quality and safety journey. Dr. Erickson applauded efforts to achieve Magnet Recognition®, which will be a testament to Ms. Lee's work. Richard P. Shannon, M.D., congratulated Ms. Lee, saying that he meets with patient safety officers across the nation and that she is second to none. No doubt her team is well prepared to continue this important work. Stephanie Reel, M.B.A., lauded Ms. Lee's accomplishments and thanked her for her work on establishing a successful safety program. Dr. Tabak thanked Ms. Lee on behalf of Dr. Collins and the entire NIH leadership team.

Clinical Facilities Update

Daniel Wheeland, P.E., Director, Office of Research Facilities, NIH

Completed Projects
Mr. Wheeland highlighted several recently completed projects:

- *Expansion of the Interim-Intravenous Admixture Unit (I-IVAU):* The capacity of the existing IVAU was inadequate and not compliant with new U.S. Pharmacopeia (USP) 800 criteria. Construction ended in June 2020. After the commissioning, qualification, and validation (CQV) process, the I-IVAU was turned over to the Pharmacy Department in September 2020. Mr. Wheeland explained that the CQV process covers the facility itself and all facility equipment therein. The process is consistent with FDA regulations, USP 797 and 800, and Good Manufacturing Practice (GMP) regulations.
- *Center for Cellular Engineering Cell-Processing Facility:* The facility, located on the east terrace of the Clinical Center, completed construction in October 2020. The CQV process is underway with facility turnover scheduled in May 2021. The facility is dedicated to cell processing and does not rely on any shared infrastructure, conferring a high degree of resilience and dependability. NIH created an advanced simulation of the facility and to test the building's systems under a range of scenarios to ensure that the facility systems are resilient and can respond and recover in a way that maintains stability and appropriate air quality. The findings of the simulation indicated refinements to the programming of systems and will be incorporated into training of maintenance mechanics to help them respond if a failure occurs.

- *National Cancer Institute Tumor Infiltrating Lymphocytes Cell Processing Facility:* The project has completed the CQV process, and document reviews are pending before it can be officially turned over to NCI. -This new facility complies with GMP and has an emergency generator, redundant systems, and an independent air supply. NIH created an advanced simulation of the facility and test the building's systems under a range of scenarios to ensure that the facility systems are resilient and can respond and recover in a way that maintains stability and adequate air quality. The findings of the simulation indicated refinements to the programming of systems and will be incorporated into training of maintenance mechanics to help them respond if a failure occurs.

Projects Under Construction

Mr. Wheeland described a number of projects that are underway in the Clinical Center:

- *DLM Sterility Laboratory:* The DLM lacked adequate space for testing the sterility of investigational drugs and for assessing APF environmental samples. Due to the lack of space and capacity, much of this laboratory work has been contracted out, which has been expensive and has caused some impacts on throughput and timelines. The project, which is comprised of two separate Aseptic Process Facility (APF) Laboratory spaces with appropriate entry points and gowning areas, will have construction complete in March 2021. The CQV process has started and facility turnover is scheduled in May 2021.
- *Positron emission tomography (PET) and magnetic resonance (MR) scanner turnkey upgrade:* The upgrade will accommodate a new PET/MR 3 Tesla scanner, which will allow patients who need both scans to have them done in a single operation. The turnkey contract was awarded in May 2020, and the goal is to complete the work in May 2021.
- *Renovation of the pharmacy and Permanent Intravenous Admixture Unit (P-IVAU):* The interim IVAU provides temporary space, but it is inadequate in terms of space and lacks a backup plan in case of a facility emergency. Construction of the P-IVAU is under construction. The project is valued at more than $25 million and will greatly improve the quality and amount of space for the pharmacy function in the Clinical Center. Swing space was constructed to vacate the existing Pharmacy Department while construction is ongoing.
- *Building 10 E-Wing renovation:* The renovated wing will house the DTM, primarily on the 12th floor. The renovation will include GMP space for ISO7 tissue culture suites. The Blood Bank and other DTM functions are on lower floors. In addition, some ICs will have basic research programs housed in the E wing. Unforeseen conditions have affected the schedule and budget for the project, which is scheduled for completion in 2022.
- *Utility vault and patient parking garage:* This project will enhance patient safety. The utility vault is outdated and in a vulnerable location. Current parking is under Building 10, presenting a security threat. The new parking garage and utility vault likely will be completed in March 2022.

Projects Awaiting Funding

The CCRHB asked for more information about how funding works for future construction and renovation projects. Dr. Tabak explained that all NIH resources must be allocated by Congress. Construction projects are paid for with Building and Facilities (B&F) funding. Dr. Gilman explained that about a year ago, the National Academies of Science reviewed NIH infrastructure and determined that the Clinical Center needed some new construction. The building has many shortcomings, some of which are the result of poor design and construction in the 1970s and 1980s. Dr. Tabak added that the infrastructure is aging, difficult to inspect, and challenging to maintain and repair. In addition, NIH research is becoming increasingly complex. These factors mean that NIH needs to refresh its facilities and sometimes build new ones.

Mr. Wheeland described plans for the Surgery, Radiology, and Laboratory Medicine (SRLM) Building. The building will include interventional radiology and the catheterization laboratory. The legacy departments of Perioperative Medicine, Laboratory Medicine, and Radiology and Imaging Sciences and the National Heart, Lung, and Blood Institute's cardiac catheterization laboratory will be in this building. Current facilities are beyond repair, with obsolete mechanical, electrical, and plumbing infrastructure that cannot be economically upgraded. This project is partially funded through fiscal year (FY) 2020 Nonrecurring Expenses Fund carryover and B&F FY 2020 carryover funds. The balance of funding has been requested for the design and construction of the SRLM building. These funds can be carried over for 5 years. If there is a full appropriation, another $225 million would allow NIH to award the contract in 2021. The project involves a total of 630,000 gross square feet for new and renovated spaces. Mr. Wheeland described SRLM project milestones, some of which have already been met.

Another project that is still unfunded is the replacement of the electrical power supply for normal and emergency conditions. This is on the critical path and urgent for electrical reliability of the whole complex.

Discussion

Dr. Forese asked about the regulatory framework for reviewing and signing off on Clinical Center projects. Mr. Wheeland described a series of meetings with the FDA before construction on the IVAU and pharmacy began. Dr. Gilman added that work is coordinated with the FDA and any other relevant regulators throughout the design process and construction. The agencies provide advice and eventually will check compliance with regulations. Dr. Gilman pointed out that the guidance of USP and the FDA do not always align. These organizations also check the technology that goes into these demanding systems to ensure that they function as intended. The final review likely occurs when the facilities are actually in use.

Dr. Hait asked about NIH's approach with regard to sustainability, carbon footprint, and other environmental issues. Mr. Wheeland said that NIH takes a broad approach. The facility will be designed for the Leadership in Energy and Environmental Design (LEED) gold level. The laboratories will use chilled beam cooling technology, which uses 30% less energy than the legacy technology. NIH has deployed state-of-the-art technology, such as thermal energy storage. One goal is to drive down utility costs to the extent possible.

Dr. Forese asked about potential challenges with parking facilities for employees, since many will be anxious about using public transit for some time. Mr. Wheeland said that this issue is an important one. On a typical workday, only one parking space is available for every 2.7 staff. That ratio works because of public transportation options, vanpools, and carpools. Limited parking will be a rate limiter as people return to campus. Dr. Tabak added that parking is the third most important concern of staff, after child and elder care. The solution to this challenge will be the passage of time, as the pandemic is brought under control and ridership of public transport goes back up to pre-pandemic levels.

Dr. Shannon suggested that digital health platforms might assist with the Clinical Center's resumption of activities and return to a more stable census. Digital tools can help clinicians keep in touch with patients and even perform some interventions. Dr. Gilman said that the pandemic motivated a rapid adoption of telemedicine at the Clinical Center. Technology has reduced the need for in-person visits for survey completion, for example. NIH has committed to purchasing a better platform that is more user friendly and will integrate with electronic health records. Another advantage of telemedicine is that it could expand trial recruitment beyond NIH's usual catchment area.

Follow-Up Item

- Mr. Wheeland offered to provide the Board with a detailed list of measures that would make the SLRM project as green as possible.

Rehabilitation Medicine Department Research Highlights

Leighton Chan, M.D., M.P.H., Chief, Clinical Center Rehabilitation Medicine Department (RMD); and Diane Damiano, Ph.D., PT, FAPTA, Senior Investigator and Chief, Functional & Applied Biomechanics (FAB) Section, Clinical Center RMD

Dr. Chan briefed the CCRHB on RMD, which touches nearly every research participant who comes to the Clinical Center. In his presentation, he focused on the Office of Strategic Research, the Epidemiology and Biostatistics section, and the FAB section.

Epidemiology and Biostatistics

Three NIH staff and 23 contractors staff this section. The Social Security Administration (SSA) funds much of the research. The focus is on improving the Social Security disability adjudication process. SSA runs two of the largest disability insurance programs in the world: the Social Security Disability Insurance and Supplemental Security Income programs, which receive 2 million to 3 million new applications every year. Benefits are 75% of a beneficiary's prior income, amounting to $700 to $1,700 per month plus health insurance, on average. The annual cost to the government is $187 billion in disability payments. The adjudication process entails very long wait times and many overturned decisions.

RMD has had an interagency agreement with SSA for more than 10 years. The agreement has brought more than $31 million to RMD to fund studies and pay for infrastructure and contract staff. NIH's goal is to improve SSA decision making in terms of accuracy, consistency, and timeliness.

SSA's number one problem is data reduction. Only a certain number of adjudicators are available to review applications, meaning that they can only dedicate 8 minutes per case review. Often, each case comes with huge volumes of data. RMD scientists are studying the use of machine learning and natural language processing to rapidly identify the most relevant documents for adjudicators' decision making.

Off-the-shelf software was inadequate. Most software focuses on diagnoses rather than functional information. Also, available software did not have the necessary terminology or structure to achieve NIH's goal. The work to create a system requires many clinicians to read and annotate documents and give meaning to phrases. It is possible to build software to "read" documents and create rules about which documents to present to adjudicators. The software package is now in the SSA pipeline for evaluation.

Another problem SSA has is spending too much time confirming diagnoses. Diagnosis alone is a poor predictor of work disability, which is the gap between an individual's functional abilities and their job demands. For example, a partial hand disability would have a greater impact on a concert pianist than on an elementary school teacher. RMD developed the Work Disability Functional Assessment Battery (WD-FAB), which people can complete on a computer in about 20 minutes. Applicants' scores on physical and mental health function are the two major bases for disability applications. The WD-FAB score gives adjudicators a snapshot of how a person is doing compared to norms.

RMD's Epidemiology and Biostatistics group has provided SSA with tools that could lead to meaningful improvements in efficiency and cost reductions. The assessment tool is being translated for use by social insurance programs in the European Union.

Research Section: Office of Strategic Research

This section comprises four NIH staff and six contractors. The work on traumatic brain injury (TBI) is supported by the Department of Defense. Other work is focusing on exercise science and on Havana syndrome, a condition experienced by certain Department of State personnel stationed in Cuba.

Exercise Science Group

This group is examining the effect of aggressive aerobic training on disease progression, functional capacity, and quality of life. The scientists are focusing on conditions with few treatment options and poor quality of life: pulmonary hypertension, systemic lupus erythematosus (SLE), idiopathic pulmonary fibrosis, and TBI. Some early success has been achieved with pulmonary hypertension. Until 2000, the recommendation was to limit physical activity, but this recommendation was challenged. A randomized clinical trial conducted by the Exercise Science Group demonstrated that vigorous exercise, characterized by perspiration and high heart rate, improved participants' quality of life and 6-minute walking time with only minimal adverse events. The results led to a change in the clinical guidelines.

More recently, this group collaborated with the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) on a pilot study in SLE. Fatigue is a major problem among those who have the condition. A pilot study showed that exercise reduced fatigue and

improved quality of life. Dr. Chan hopes that the pilot results will lead NIAMS to fund a larger, well-powered study.

COVID-19 Care

Dr. Chan said that many people will have a long path to recovery after having COVID-19. The plan is to learn whether aerobic exercise training is beneficial for improving functional outcome and recovery among survivors of COVID-19. The block-randomized trial will enroll 90 adults who have residual physical limitations or fatigue after recovering from COVID-19. Outcomes include 6-minute walking time, quality of life, physical activity, vascular function, and blood biomarkers.

Highlights of the Past 6 Years

Dr. Chan reported that between 2014 and 2020, RMD published approximately 250 peer-reviewed papers, brought more than 1,200 outpatients into the Clinical Center, and covered 65% of the department's $6 million research budget through agreements with other agencies. RMD efforts have contributed to advances in disability assessment, TBI biomarkers, and treatment of pulmonary hypertension, SLE, cerebral palsy, and Havana syndrome.

RMD's Work in Cerebral Palsy

Dr. Damiano has been with RMD for 12 years. She is the Chief of the FAB section and runs the laboratory. Dr. Damiano is reportedly the first physical therapist to receive tenure in the NIH/CC intramural research program Her laboratory currently has 5 IRB protocols, which are actively recruiting, 4 of which she is the PI on (the exoskeleton project which she initiated more than 10 years ago is led by her staff scientist, Dr. Tom Bulea as PI).

The major focus of research in her section is on cerebral palsy, a group of brain disorders or injuries of multifactorial etiologies, which is the most prevalent motor disability originating in childhood. WHO recently stated that CP has the highest global burden in across all chronic rehabilitation conditions, due to its prevalence and severity and the fact that it persists across the lifespan. There is no cure for cerebral palsy, but some recent neuroprotective advances, such as magnesium sulfate to reduce prematurity and head cooling, have reduced its prevalence and severity. Recent advances in neuroscience (mainly in animal models) suggest that intensive motor training, particularly if initiated very early in life, may significantly alter the motor prognosis in CP, although data to support this in humans are minimal at best.

When Dr. Damiano came to NIH, the biomechanics laboratory was transformed into one that integrates biomechanics with neuroscience and neuroengineering to investigate motor impairments in cerebral palsy. The two primary goals are to uncover the brain mechanisms underlying the various brain abnormalities exhibited in those with CP and then to utilize this knowledge to design and evaluate novel treatments to improve gait and other motor skills of people who have cerebral palsy. Towards these goals, Dr. Damiano noted that her laboratory was among the first to study brain activity during motor tasks. They use mobile brain imaging (MoBI) with functional near-infrared spectroscopy (fNIRS) and/or electroencephalography (EEG) in combination with precise quantification of joint movements and muscle activity to study brain activation during motor tasks in those with and without CP. Because of the uncontrolled movements resulting from the disorder approximately half of children who have CP

cannot undergo magnetic resonance imaging but virtually all can be studied with these other technologies. Other advantages of mobile brain imaging techniques are that the fact that they can be done very cost-effectively in the laboratory and during any motor task, including walking. FNIRS works by projecting near-infrared light at two different wavelengths through the scalp into the outer layer of the cortes and then recording the reflected light from each wavelength gives a measure of light absorbance by oxygenated and deoxygenated hemoglobin, reflecting hemodynamic responses associated with neuronal activity. This BOLD (blood oxygenation level dependent) signal is the same as that recorded in functional MRI. EEG records the electrical activity of large groups of neurons activated during any desired motor or cognitive task using electrodes places over the entire scalp region. The major advantage of EEG is that it can demonstrate brain activity in real time. We are about to embark on a study using EEG as neurofeedback to train new motor capabilities in CP, which has not yet been attempted in this population.

Some of our major findings in CP using these technologies were: 1) the demonstration of the loss of muscle selectivity and somatotopic organization as shown by larger areas of brain activation and higher magnitudes in the sensorimotor brain regions of those with CP than seen in children with typical development; 2) extensive brain reorganization in those with unilateral brain injuries whereby one side of the brain may control movements on both sides; 3) tremendous variability in patterns of brain activation across individuals with CP even in those with similar motor deficits; and 4) decreased rate of cortical maturation as shown by slower frequencies of brain waves in children with CP compared to age-matched peers. We have clearly demonstrated that tasks that were simple for controls were harder for those with CP especially as the degree of neurological impairment increases, and that excessive muscle effort is strongly related to excessive brain activity. We are also gaining insights into normal motor control in adults and children. For example, we reinforced other preliminary findings of substantial cortical activity during constant speed walking on a smooth surface, which contradicts a prevailing belief that this is mainly controlled by locomotor circuits in the spinal cord (from spinalized cat studies). Dr. Damiano stated they are now applying these technologies to infants with and without CP within the first years of life. This work was featured in *Washingtonian Magazine* last winter. .

Key Principles in Neurorehabilitation

Effort, engagement, and error are the main principles behind neurorehabilitation. Effort means that the patient, rather than the device or the therapy, puts in most of the work. Engagement means that the person should be cognitively involved and motivated to do the task. Error is important because people need to learn what they are doing wrong so they can actively correct their movement errors. Most robotics use assist-as-needed or impedance control, but they are not effective, because instead of "fighting" devices, users just let the device do the work, reducing benefit. The solution is to have the device do slightly less than what is required for the task.

Dr. Damiano said that the pediatric exoskeleton for treating crouch gait was first developed at NIH. The person controls their own knee motion, but the motor injects torque at two points in the gait. A video showed how a child's gait improved with the device.

Early Intervention in Cerebral Palsy

Dr. Damiano explained that neuroplasticity is greater in early development; capabilities may be lost permanently unless intervention occurs early. Nearly half of neurons die in infancy. Children who have cerebral palsy may not be getting the right inputs for normal development. Animal evidence suggests that the window for neural recovery is between 3 and 6 months of age.

Two trials showed that robotics can help young children learn how to move more normally. A more portable version is being developed for clinics for treating children as young as 4 months old.

In addition to their own research, Dr. Damiano's research team also supports 14 protocols for investigators: 8 in the National Institute of Neurologic Disorders and Stroke and 2 each in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Human Genome Research Institute, and the Clinical Center

Discussion

Ms. Reel asked about measuring SSA's adoption of the assessment tool developed by RMD. Dr. Chan said that this is a key question. The science behind RMD's work with SSA is interesting, but the biggest challenge is getting interventions adopted. RMD did a great deal of validation to ensure that SSA was satisfied with the disability assessment tool, which is being used in some cases during the review process for reevaluating beneficiaries. Dr. Chan anticipates that the tool is likely to be widely adopted in Europe first.

Ms. Reel asked whether the disability assessment tool would have a role in eliminating or reducing fraud and abuse. Dr. Chan said that this is a major concern of RMD and SSA. A great deal of effort has gone into addressing fraud and abuse. Neuropsychologists are looking into tools to ferret out fraud. The instrument was designed to make it difficult for people to game.

Dr. Forese asked about getting technologies out of the laboratory to help children with movement disorders. Dr. Damiano said that children should not required to be in therapy their whole lives; they need to be able to control their own health. Wearable robotics could be worn at home and in the community; eventually, we anticipate that we can wean them from the device and they move more normally after training even without the device.

Dr. Hait asked about the impact of music on brain function and whether music might help with training. Dr. Damiano noted that there are scientists exploring the effects of music therapy in those with CP because it increases engagement may very likely have a powerful effect on rehabilitation.

Dr. Gallin congratulated Dr. Chan and his team for bringing in funding to support RMD research and Clinical Center services, particularly imaging.

NIH Responses to COVID-19

H. Clifford Lane, M.D., Clinical Director, National Institute of Allergy and Infectious Diseases (NIAID)

Dr. Lane reviewed the timeline of the COVID-19 pandemic. In early January 2020, the story about a novel human coronavirus causing an outbreak of pneumonia broke. The disease seemed to be linked to a seafood market in China.

Two key events occurred on January 20: The first U.S. case was identified in a recent traveler to Wuhan, China, and the *Diamond Princess* departed Yokohama for a 14-day cruise. On January 25, a passenger aboard the ship was diagnosed with the disease. Among the 3,711 passengers and crew, 712 (19%) became infected, of whom 14 (2%) died.

The outbreak on the *Diamond Princess* accelerated NIAID initiation of an international randomized, controlled trial of remdesivir, the most promising antiviral drug at the time, in a study known as the Active COVID-19 Treatment Trial (ACTT-1). In addition, using the published sequences and samples from the first U.S. survivors, work at the NIAID Vaccine Research Center (VRC) focused on developing countermeasures, including an RNA vaccine (collaboration with Moderna) and a monoclonal antibody (collaboration with Lilly).

In China, the first cases were diagnosed in early December 2019. Some but not all cases were linked to the seafood market. The coronavirus was directly sequenced and cultured from a bronchoalveolar lavage on December 30, 2019. As of February 20, 2020, more than 75,000 cases were confirmed in the country. Dr. Lane served as a member of the World Health Organization–China Joint Mission on COVID-19. In China, people were highly compliant with wearing masks and maintaining social distance. There was a well-organized, whole-of-society effort. Daily counts were posted publicly. Messaging was consistent and pervasive. People were subject to periodic traffic stops for temperature checks. Strict quarantine measures were put in place and enforced in ways that might not be acceptable to American society.

NIH plays a key or leadership role in the federal government's response to the pandemic, including the White House Task Force, Operation Warp Speed, and the ACTIV public–private partnership. Dr. Fauci has been a forceful presence on the White House Task Force chaired by Vice President Pence. Operation Warp Speed is a national program to accelerate the development, manufacture, and distribution of COVID-19 vaccines, therapeutics, and diagnostics. NIH launched the ACTIV public–private partnership to standardize and share preclinical evaluation methods, minimize overlap, advance vaccine development, and prioritize and accelerate therapeutic candidates.

NIH Role in Diagnostic Research

The Director of the National Institute of Biomedical Imaging and Bioengineering is taking the lead on the diagnostic aspect of Operation Warp Speed. The RADx initiative is seeking a way to fund innovative ideas for COVID-19 testing and finding novel ways to obtain rapid, inexpensive, and accurate test results. The program consists of four subprograms:

- RADx Tech: Develop new strategies in a "shark tank" format.
- RADx Underserved Populations: Develop testing strategies in real-world settings.
- RADx Radical: Investigate nontraditional approaches (e.g., artificial intelligence, biosensors).

- RADx Advanced Technology Platforms: Increase capacity of advanced technology platforms.

NIH Role in Therapeutic Research

Dr. Lane reported that NIH's extramural programs are supporting a variety of studies of investigational treatments for COVID-19. Some studies are supported through Operation Warp Speed and the ACTIV partnership.

The randomized controlled trial ACTT, which uses an adaptive design, is enrolling adults hospitalized with COVID-19 and evidence of pulmonary disease. The study opened in February to study remdesivir and has since completed two versions. It is now enrolling the third version comparing remdesivir and remdesivir plus interferon beta. The final report on the trial that tested remdesivir as a treatment for COVID-19 was published in *The New England Journal of Medicine* on October 8, 2020. The study demonstrated a significant decrease in time to recovery for those randomized to remdesivir. A trend toward decreased mortality with remdesivir was observed, but the confidence interval overlapped with 1.

NIH used its funding mechanisms and those available through the NCI and their Federally Funded Research and Development Center at Ft. Detrick to rapidly activate study sites. Dr. Lane highlighted the five ACTIV trials.

Dr. Lane described the structure of SARS-CoV-2. Several companies have monoclonal antibodies that are currently being tested singly or in combinations. Convalescent plasma and immune immunoglobulin are also being tested.

Dr. Lane highlighted some intramural clinical protocols, including studies of small molecules, plasma collection, pathogenesis, genomics, and markers of thrombosis. In total, 28 intramural therapeutic protocols are being conducted across 12 ICs.

In addition, a panel of U.S. experts convened at the request of the White House Task Fore and HHS Secretary developed the *Coronavirus 2019 (COVID-19) Treatment Guidelines* as a living document that will be updated often as new clinical data are produced. The guidelines had 1 million views the first week; since then, the document has had 4.8 million views. The guidelines have undergone five updates so far. Key recommendations include the following:

- The COVID-19 Treatment Guidelines Panel recommends against the use of chloroquine or hydroxychloroquine for the treatment of COVID-19 in hospitalized patients.
- The Panel recommends remdesivir for 5 days or until hospital discharge for patients who require supplemental oxygen but not those who require high-flow oxygen or mechanical ventilation.
- The Panel recommends 6 mg dexamethasone per day for up to 10 days or until hospital discharge for the treatment of COVID-19 in hospitalized patients who are mechanically ventilated.
- There are insufficient data to recommend either for or against the use of convalescent plasma for the treatment of COVID-19.

Research to Prevent COVID-19

Dr. Lane described studies investigating monoclonal antibodies for prophylaxis in nursing homes and family settings. In addition, multiple vaccine candidates are being evaluated in separate but harmonized protocols. Investigational new drug applications are held by the companies. Four vaccines have entered Phase III trials. One Phase III data and safety monitoring board is currently overseeing all U.S. Phase III trials except the Pfizer mRNA vaccine trial.

Dr. Lane reviewed FDA guidance for Emergency Use Authorization (EUA) for a COVID-19 vaccine. He explained the evidence that companies will have to assemble for an EUA:

> "Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2 (Section 564 of the FD&C Act [21 U.S.C. 360bbb-3]). Phase III findings to support an EUA would need to include:
>
> - A point estimate of efficacy of at least 50%
> - A lower bound confidence interval of at least 30%
> - A median follow-up duration of at least 2 months
> - A total of five more cases of severe disease in the placebo group
> - Safety data in patients with prior SARS-CoV-2 infection."

Dr. Lane concluded by saying that NIH is playing a major role in the research effort to study the pathogenesis, diagnosis, treatment, and prevention of SARS-CoV-2 infection and COVID-19. Early successes include demonstration of the clinical efficacy of remdesivir, launch of coordinated therapeutic and diagnostic research portfolios, and involvement in the launch of three of the four ongoing Phase III vaccine trials. By working to keep these efforts coordinated and setting clear priorities, it is hoped that the most effective countermeasures will get to the greatest number of people in the shortest period of time.

Discussion

Dr. Forese thanked Dr. Lane for his service along with other NIH leaders, including Dr. Fauci. Dr. Gilman added that Dr. Fauci is surrounded by many great Americans who are doing this work. Dr. Fauci is an excellent risk communicator to the American people and the scientific community. He can do that because scientists such as Dr. Lane and others to help lead the effort to apply rigorous science and collect evidence to support the safety and efficacy of therapeutics and vaccines.

Adjournment

Dr. Forese thanked the Board members and NIH leaders. On the behalf of Dr. Collins and himself, Dr. Tabak thanked Ms. Lee, the CCRHB members, and Gretchen Wood and others who organized the meeting.

Dr. Forese adjourned the meeting at 1:01 p.m.

_____

Laura Forese, M.D., M.P.H.
Chair, NIH Clinical Center Research Hospital Board
Executive Vice President and Chief Operating Officer, NewYork–Presbyterian Hospital

_____

Lawrence A. Tabak, D.D.S., Ph.D.
Executive Director, NIH Clinical Center Research Hospital Board
Principal Deputy Director, NIH

_____

Francis S. Collins, M.D., Ph.D.
Ex Officio Member, NIH Clinical Center Research Hospital Board
Director, NIH

Abbreviations and Acronyms

ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines
ACTT	Active COVID-19 Treatment Trial
AHaRT	Anti-Harassment Response Team
B&F	Buildings and Facilities
BERT	Behavioral Emergency Response Team
CCRHB	Clinical Center Research Hospital Board
CEO	Chief Executive Officer
CLABSI	central line–associated bloodstream infection
CMO	Chief Medical Officer
COVID-19	coronavirus disease 2019
CQV	commissioning, qualification, and validation
CRIS	Clinical Research Information System
DART	days away, restricted, or transferred
DLM	Department of Laboratory Medicine
DTM	Department of Transfusion Medicine

EEG	electroencephalography
EUA	Emergency Use Authorization
FAB	Functional & Applied Biomechanics
FAB LAB	FAB laboratory
FDA	Food and Drug Administration
fNIRS	functional near-infrared spectroscopy
FY	fiscal year
GMP	Good Manufacturing Practice
ICs	Institutes and Centers
IVAU	Intravenous Admixture Unit
LEED	Leadership in Energy and Environmental Design
MoBI	mobile brain imaging
MR	magnetic resonance
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH	National Institutes of Health

PET	positron emission tomography
P-IVAU	Permanent IVAU
RADx	Rapid Acceleration of Diagnostics
RMD	Rehabilitation Medicine Department
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SLE	systemic lupus erythematosus
SRLM	Surgery, Radiology, and Laboratory Medicine
SSA	Social Security Administration
STARS	Safety Tracking and Reporting System
TBI	traumatic brain injury
WD-FAB	Work Disability Functional Assessment Battery