



MEMORANDUM

December 6, 2021

To: Subcommittee on Health Members and Staff

Fr: Committee on Energy and Commerce Staff

Re: Hearing on “The Future of Biomedicine: Translating Biomedical Research into Personalized Health Care”

On Wednesday, December 8, 2021, at 10:30 a.m. (EST), in the John D. Dingell Room, 2123 of the Rayburn House Office Building, and via Cisco WebEx online video conferencing, the Subcommittee on Health will hold a hearing entitled, “The Future of Biomedicine: Translating Biomedical Research into Personalized Health Care.”

I. BACKGROUND

This year marks the 20th anniversary of the publication of the Human Genome Project, which provided the first look at the human genome’s nearly complete sequence.¹ Since this landmark effort, scientists have built upon this knowledge to deepen our molecular understanding of the biological processes that govern human health and disease.² Fundamental discoveries in deciphering the significance of the genetic code, coupled with advances in bioengineering and computational sciences, have paved the way for personalized health care, driving new developments in diagnostics and treatments.³ For example, there are now 22 cell and gene therapies approved by the Food and Drug Administration (FDA),⁴ large-scale clinical

¹ National Human Genome Research Institute, *20th Anniversary of Landmark Human Genome Project Publications* (www.genome.gov/human-genome-project/20th-anniversary-of-landmark-human-genome-project-publications).

² *Id.*

³ *Id.*

⁴ Food and Drug Administration, *Approved Cellular and Gene Therapy Products* (www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products) (Oct. 26, 2021).

trials are underway for blood tests that can detect multiple types of cancer in asymptomatic people,⁵ and individualized cancer vaccines are currently being developed.⁶

A. Basic Scientific Research

Basic biomedical research answers fundamental questions about the principles, mechanisms, and processes that underlie living organisms.⁷ The knowledge gained from this type of research forms the basis of biomedical innovation and serves as the foundation for advances in human health, but often this research does not have immediate direct applications to medicine when the research studies are undertaken.⁸

The goal of basic biomedical research is to understand how disease functions, not necessarily to predict, prevent, diagnose, and treat disease, and the timelines from foundational discovery to clinical application are often long.⁹ Basic research into biological processes can lead to the identification of potential drug targets or treatments and it can also lead to the development of platform technologies. For example, the emerging field of cancer immunotherapy was borne out of decades of research into how immune cells function on a molecular level and clustered regularly interspaced short palindromic repeats (CRISPR) gene editing technology was first discovered through curiosity-driven studies of how bacteria protect themselves from invading viruses.^{10, 11} The return on investment in basic research over time, however, is significant.¹² For example, the first scientific articles on mRNA were published in

⁵ Scientific American, *The Quest for Cancer-Detecting Blood Tests Speeds Up* (www.scientificamerican.com/article/the-quest-for-cancer-detecting-blood-tests-speeds-up/) (July 1, 2021).

⁶ National Geographic, *New Cancer Treatments may be on the Horizon—Thanks to mRNA Vaccines* (www.nationalgeographic.com/science/article/new-cancer-treatments-may-be-on-the-horizonthanks-to-mrna-vaccines) (July 8, 2021).

⁷ National Institutes of Health, *Basic Research – Digital Media Kit* (www.nih.gov/news-events/basic-research-digital-media-kit) (Mar. 12, 2021).

⁸ *Id.*

⁹ *Id.*

¹⁰ Paula Dobosz and Tomasz Dzieciatkowski, *The Intriguing History of Cancer Immunotherapy*, *Frontiers in Immunology* (Dec. 17, 2019).

¹¹ National Institutes of Health, *Gene Editing – Digital Media Kit* (www.nih.gov/news-events/gene-editing-digital-media-kit) (Nov. 5, 2021).

¹² *See* note 7.

1961, and the first mRNA vaccine was approved by the FDA for the coronavirus disease of 2019 (COVID-19) in 2021, sixty years later.^{13, 14, 15}

Funding for basic scientific research accounts for approximately 51 percent of the National Institutes of Health (NIH) budget and the economic and scientific return on this investment is significant.¹⁶ NIH contributed to published research for every one of the 210 new drugs approved by FDA from 2010 to 2016, and 90 percent of this research was basic.¹⁷ According to NIH, an increase of one dollar in public basic research stimulates \$8.38 in industry research and development investment after eight years.¹⁸

B. Translational Scientific Research

Translational research builds upon and informs basic science research.¹⁹ Translational research is the process of transforming scientific discoveries into new treatments and advances in medical practice that improve the health of both individuals and the population.²⁰ Following basic scientific discoveries, the translational science spectrum includes preclinical research, clinical research, clinical implementation, and public health.²¹

Preclinical research is the stage at which scientists develop model interventions to further understand the basis of a disease or disorder and find ways to treat it.²² This testing is carried out in cell and animal models and is the phase of translation where interventions may have potential,

¹³ Sydney Brenner et al., *An Unstable Intermediate Carrying Information from Genes to Ribosomes for Protein Synthesis*, *Nature* (May 13, 1961).

¹⁴ Francois Gros et al., *Unstable Ribonucleic Acid Revealed by Pulse Labelling of Escherichia Coli*, *Nature* (May 13, 1961).

¹⁵ Food and Drug Administration, *FDA Approves First COVID-19 Vaccine* (www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine) (Aug. 23, 2021).

¹⁶ See note 7.

¹⁷ *Id.*

¹⁸ National Institutes of Health, *Turning Discovery Into Health* (www.nih.gov/sites/default/files/about-nih/impact/impact-our-nation.pdf) (Sept. 2015).

¹⁹ Christopher P. Austin, *Translating Translation*, *Nature Reviews Drug Discovery* (Apr. 20, 2018).

²⁰ National Center for Advancing Translational Sciences, *Translational Science Spectrum* (ncats.nih.gov/translation/spectrum) (Nov. 10, 2021).

²¹ *Id.*

²² *Id.*

but their feasibility, safety, and efficacy is not yet established.²³ This early stage of applied research and development represents a high risk of failure, leading to a public and private financing gap and the deferment of potentially fruitful avenues of research.²⁴ This phase of translating basic research into early stage human clinical trials has been referred to as the “valley of death” due to the attrition caused by poor basic science reproducibility, clinical relevance, time-consuming collaboration between researchers and clinicians, and predictably expensive late-stage clinical trials.²⁵

Clinical research includes studies that aim to better understand a disease in humans, such as clinical trials to test interventions for safety and effectiveness, behavioral and observational studies, and outcomes and health services research.²⁶ In an analysis of clinical trials completed between 2000 and 2019, 3.8 percent were funded by the NIH or other United States government agencies, with the majority sponsored by industry and other sources.²⁷ The stage of clinical implementation is the adoption of interventions into routine clinical care and includes implementation research to assess the real-world effect of interventions for patients.²⁸ At the stage of public health, researchers study health outcomes at the population level to determine the effects of diseases and efforts to prevent, diagnose, and treat them.²⁹

C. Precision Medicine

Precision medicine is an emerging practice of medicine that utilizes knowledge of an individual’s genetic profile and other molecular markers, as well as lifestyle and environmental factors, to make decisions regarding the prevention, diagnosis, and treatment of disease.³⁰ Treatments that are effective for some patients may be ineffective for others. For example, for 75 percent of cancer patients, 43 percent of diabetes patients, and 38 percent of patients on antidepressants, a particular drug within the class of drugs used to treat the condition will be ineffective.³¹ In contrast to a one-size-fits-all approach, precision medicine allows health care

²³ Attila Seyhan, *Lost in Translation: The Valley of Death Across Preclinical and Clinical Divide – Identification of Problems and Overcoming Obstacles*, Translational Medicine Communications (Nov. 18, 2019).

²⁴ *Id.*

²⁵ *Id.*

²⁶ *See* note 20.

²⁷ Gillian Gresham et al., *Assessment of Trends in the Design, Accrual, and Completion of Trials Registered in ClinicalTrials.gov by Sponsor Type, 2000-2019*, JAMA Network Open (Aug. 26, 2020).

²⁸ *See* note 20.

²⁹ *Id.*

³⁰ National Human Genome Research Institute, *Personalized Medicine* (www.genome.gov/genetics-glossary/Personalized-Medicine).

³¹ B B Spear et al., *Clinical Application of Pharmacogenetics*, Trends in Molecular Medicine (May 2001).

providers to combine molecular data from diagnostic tests with an individual's medical history to develop targeted prevention and treatment plans.³² Precision medicine has advanced the standard of care in fields such as pharmacogenomics, rare diseases, cancer immunotherapy, and precision oncology.³³ For example, in 2020, the FDA approved the first liquid biopsy next generation sequencing (NGS) diagnostic tests as companion diagnostics for selecting advanced cancer treatments.³⁴

Precision health expands upon precision medicine by integrating this approach with an emphasis on disease prevention and health promotion activities.³⁵ Central to this is the concept of a knowledge network that connects the wealth of information that already exists from basic molecular research, clinical insights, environmental data, and others.³⁶ Example sources of this data include laboratory experiments and genetic sequencing data, clinical trial data, electronic health records, demographic data sets, and digital health technologies.³⁷ Integration of diverse data types provides the opportunity to uncover new patterns and testable hypotheses with applications such as new insight into biological processes, the discovery of effective drugs and diagnostics, and the evaluation of the effectiveness of health interventions.³⁸

D. Diversity and Inclusion in Biomedical Research

Racial and ethnic minorities are underrepresented in both clinical trials and biomedical research. For the 53 new drugs and biologics that were approved by the FDA in 2020, clinical trial participants were 75 percent White, eight percent Black, six percent Asian, and 11 percent Hispanic.³⁹ As of 2018, individuals included in genomic studies were 78 percent White, two percent Black, ten percent Asian, and one percent Hispanic.⁴⁰ By contrast, the United States

³² Personalized Medicine Coalition, *The Personalized Medicine Report: Opportunity, Challenges, and the Future* (Nov. 2020).

³³ National Institutes of Health, *The Promise of Precision Medicine* (www.nih.gov/about-nih/what-we-do/nih-turning-discovery-into-health/promise-precision-medicine) (Feb. 12, 2021).

³⁴ National Cancer Institute, *FDA Approves Blood Tests That Can Help Guide Cancer Treatment* (www.cancer.gov/news-events/cancer-currents-blog/2020/fda-guardant-360-foundation-one-cancer-liquid-biopsy) (Oct. 15, 2021).

³⁵ Centers for Disease Control and Prevention, *Precision Health: Improving Health for Each of Us and All of Us* (www.cdc.gov/genomics/about/precision_med.htm) (Aug. 14, 2020).

³⁶ Precision Medicine at UCSF, *Building the Knowledge Network* (precisionmedicine.ucsf.edu/building-knowledge-network).

³⁷ *Id.*

³⁸ Precision Medicine at UCSF, *Computational Health* (precisionmedicine.ucsf.edu/computational-health-sciences).

³⁹ Food and Drug Administration, *2020 Drug Trial Snapshot Summary Report* (www.fda.gov/media/145718/download) (accessed August 25, 2021).

⁴⁰ Giorgio Sirugo et al., *The Missing Diversity in Human Genetic Studies*, *Cell* (Mar. 21, 2019).

population is 60 percent White, 13.4 percent Black, 5.9 percent Asian, and 18.5 percent Hispanic.⁴¹ The effects of these disparities are exacerbated by the disproportionate impact that some diseases and conditions, such as Alzheimer’s disease and some cancers, have on certain racial and ethnic subgroups.^{42, 43} Diverse biomedical datasets provide insights into the underlying differences in disease presentation and can inform drug and diagnostic development.⁴⁴ Genetic variation among populations can also affect drug effectiveness or the likelihood of an adverse event in a specific subgroup, exacerbating health disparities.⁴⁵ In 230 trials leading to FDA oncology drug approvals from 2008 to 2018, race was only reported in 63 percent of clinical trials and race subgroup analyses were reported in just 25 percent of trials.⁴⁶ An FDA review of drug approvals between 2008 and 2013 found that approximately one-fifth of new drugs demonstrated some differences in exposure and/or response across racial and ethnic groups.⁴⁷

There are many barriers to inclusive participation in biomedical research and clinical trials, including a perception that it is more difficult and expensive to recruit diverse patients, a lack of diverse investigators, restrictive inclusion and exclusion criteria, language or health literacy differences, burdensome trial logistics, historical mistrust of clinical trial ethics, study site location, and others.⁴⁸

II. CONGRESSIONAL ACTION

A. Precision Medicine

The Committee on Energy and Commerce has played a leading role in helping to advance precision medicine and greater equity in its implementation. The 21st Century Cures Act authorized \$4.8 billion dollars to NIH for four innovation projects: the Precision Medicine

⁴¹ United States Census Bureau, *Quick Facts United States* (www.census.gov/quickfacts/fact/table/US/PST045219).

⁴² Centers for Disease Control and Prevention, *New Estimates of Americans with Alzheimer’s Disease and Related Dementias Show Racial and Ethnic Disparities* (www.cdc.gov/aging/data/infographic/racial-ethnic-disparities-ad.html) (Sept. 20, 2018).

⁴³ Jonathan Loree et al., *Disparity of Race Reporting and Representation in Clinical Trials Leading to Cancer Drug Approvals From 2008 to 2018*, *JAMA Oncology* (Aug. 15, 2019).

⁴⁴ See note 41.

⁴⁵ Food and Drug Administration, *Collection of Race and Ethnicity Data in Clinical Trials Guidance for Industry and Food and Drug Administration Staff* (Oct. 26, 2016).

⁴⁶ See note 44.

⁴⁷ A Ramamoorthy et al., *Racial/Ethnic Differences in Drug Disposition and Response: Review of Recently Approved Drugs*, *Clinical Pharmacology & Therapeutics* (Dec. 13, 2014).

⁴⁸ Food and Drug Administration, *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies Guidance for Industry and Food and Drug Administration Staff* (Sept. 12, 2017).

Initiative, the BRAIN Initiative, the Cancer Moonshot, and the Regenerative Medicine Innovation Project.^{49, 50} NIH estimates that over 80 percent of participants in certain Precision Medicine Initiative projects are underrepresented in biomedical research.⁵¹ With \$1.4 billion in funding over ten years, the Precision Medicine Initiative established the All of Us Research Program, which aims to build a diverse biomedical research database of genomic data, electronic health records, and other health information for over one million participants.⁵² As of November 2021, more than 350,000 participants have enrolled in the All of Us Research Program.⁵³ The 21st Century Cures Act also authorized \$500 million to FDA to accelerate drug development, innovation, and professional recruitment.⁵⁴

B. Diversity and Inclusion in Biomedical Research

Improving diversity in biomedical research has been a focus for Congress in recent years. The NIH Revitalization Act of 1993 directed the NIH to establish guidelines for inclusion of women and minorities in clinical research.⁵⁵ Section 907 of Food and Drug Administration Safety and Innovation Act (FDASIA) directed the FDA to develop a report addressing the extent to which clinical trial participation and the inclusion of safety and effectiveness data by demographic subgroups is included in applications to the FDA.⁵⁶ FDASIA also directed FDA to develop an action plan that recommended medical product applications submitted for marketing

⁴⁹ National Institutes of Health, *The 21st Century Cures Act* (www.nih.gov/research-training/medical-research-initiatives/cures).

⁵⁰ 21st Century Cures Act, Pub. L. No. 114-255.

⁵¹ National Institutes of Health, *Media Advisory: NIH's All of Us Research Program Records Significant Progress in Participant Diversity and Research Underway* (June 11, 2021) (allofus.nih.gov/news-events-and-media/announcements/media-advisory-nihs-all-us-research-program-records-significant-progress-participant-diversity-and-research-underway).

⁵² National Institutes of Health, *All of Us Research Program Overview* (allofus.nih.gov/about/all-us-research-program-overview).

⁵³ National Institutes of Health, *National Institutes of Health's All of Us Research Program Gathers Data on Social Environment for Precision Medicine Database* (<https://allofus.nih.gov/news-events-and-media/announcements/national-institutes-healths-all-us-research-program-gathers-data-social-environment-precision-medicine-database>) (Nov. 4, 2021).

⁵⁴ Food and Drug Administration, *Selected Amendments To the FD&C Act, 21st Century Cures Act* (www.fda.gov/regulatory-information/selected-amendments-fdc-act/21st-century-cures-act) (Jan. 31, 2020).

⁵⁵ National Institutes of Health, *NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research* (grants.nih.gov/policy/inclusion/women-and-minorities/guidelines.htm) (Dec. 6, 2017).

⁵⁶ FDA Innovation Act of 2012, Pub. L. No. 112-144.

approval to improve their demographic subgroup data’s completeness, quality, and availability.⁵⁷ The FDA Reauthorization Act of 2017 directed the FDA to release guidance on enhancing the diversity of clinical trial populations, including eligibility criteria, enrollment practices and trial design.^{58, 59} The guidance, released in November 2020, advised sponsors to work to ensure clinical trial eligibility criteria have a representative sample of the population for whom the drug has been developed, and recommended that sponsors consider adaptive clinical trial design, which can allow for broader enrollment.⁶⁰ On January 5, 2021, Congress passed the Henrietta Lacks Enhancing Cancer Research Act, which directed the Government Accountability Office to complete a study and provide recommendations on how federal agencies can address barriers to participation of underrepresented populations in federally-funded cancer clinical trials.⁶¹

III. WITNESSES

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⁵⁷ Food and Drug Administration, *FDASIA Section 907: Inclusion of Demographic Subgroups in Clinical Trials* (www.fda.gov/regulatory-information/food-and-drug-administration-safety-and-innovation-act-fdasia/fdasia-section-907-inclusion-demographic-subgroups-clinical-trials) (Mar. 28, 2018).

⁵⁸ FDA Reauthorization Act of 2017, Pub. L. No. 115-52.

⁵⁹ Food and Drug Administration, *Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry* (Nov. 2020).

⁶⁰ *Id.*

⁶¹ Henrietta Lacks Enhancing Cancer Research Act of 2019, Pub. L. No. 116-291.