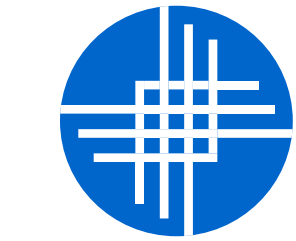

COVID-19 Silver Linings for Biomedical Innovation: *Implementation Roadmap*

About the Milken Institute

The Milken Institute is a nonprofit, nonpartisan think tank. We catalyze practical, scalable solutions to global challenges by connecting human, financial, and educational resources to those who need them. We leverage the expertise and insight gained through research and the convening of top experts, innovators, and influencers from different backgrounds and competing viewpoints to construct programs and policy initiatives. Our goal is to help people build meaningful lives in which they can experience health and well-being, pursue effective education and gainful employment, and access the resources required to create ever-expanding opportunities for themselves and their broader communities.

About FasterCures

FasterCures, a center of the Milken Institute, is working to build a system that is effective, efficient, and driven by a clear vision: patient needs above all else. We believe that transformative and life-saving science should be fully realized and deliver better treatments to the people who need them.

Background

While the response to the COVID-19 pandemic has exposed many of the fault lines in the biomedical innovation ecosystem that have slowed progress for decades, we have also shown ourselves capable of innovating in ways we perhaps did not think possible. FasterCures wants to ensure that the lessons of this crisis are not lost when the current urgency subsides—not only for combatting future infectious disease outbreaks but also for conducting every other aspect of biomedical R&D.

In the second half of 2020, informed by over three dozen interviews with key actors involved in the pandemic response from various sectors, we set out to capture the silver linings during the COVID-19 public health emergency, many of which will not remain in place unless collective action is taken. The resulting white paper, **"Lessons Learned from COVID-19: Are There Silver Linings for Biomedical Innovation?"** identified broad opportunities for focus in the areas of research collaboration, accelerating product development, clinical trial innovation, the collection and use of real-world data and evidence, and addressing racial and ethnic disparities in health care and research.[1]

With input from a working group of external advisors, we built upon the themes that emerged from our white paper to identify specific near-term goals and actions that stakeholders can take to begin to leverage our collective learnings from COVID-19 for the benefit of the whole biomedical research ecosystem—and ultimately for patients suffering from a broad range of deadly and debilitating conditions.

Goals include:

1. Preserve and repurpose infrastructure created during the pandemic and target it at other urgent public health needs.
2. Prioritize investment in platform technologies and research infrastructure that can benefit many researchers and developers.
3. Promote greater adoption of efficient clinical trial practices utilized during the pandemic, such as master protocols, seamless trials, pragmatic trials, and decentralized trials.
4. Initiate a public dialogue about how regulation can become more agile based on need in light of the COVID experience.

Opportunities to achieve these goals in the near term may include proposed 21st Century Cures 2.0 legislation, the Prescription Drug User Fee Act (PDUFA) VII authorizing process, and several executive branch "COVID-19 lessons learned" processes that have and will be set in motion.

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1. FasterCures has launched a separate initiative around improving diversity and inclusion in clinical research, so we are not pursuing those issues with the action plans recommended here.

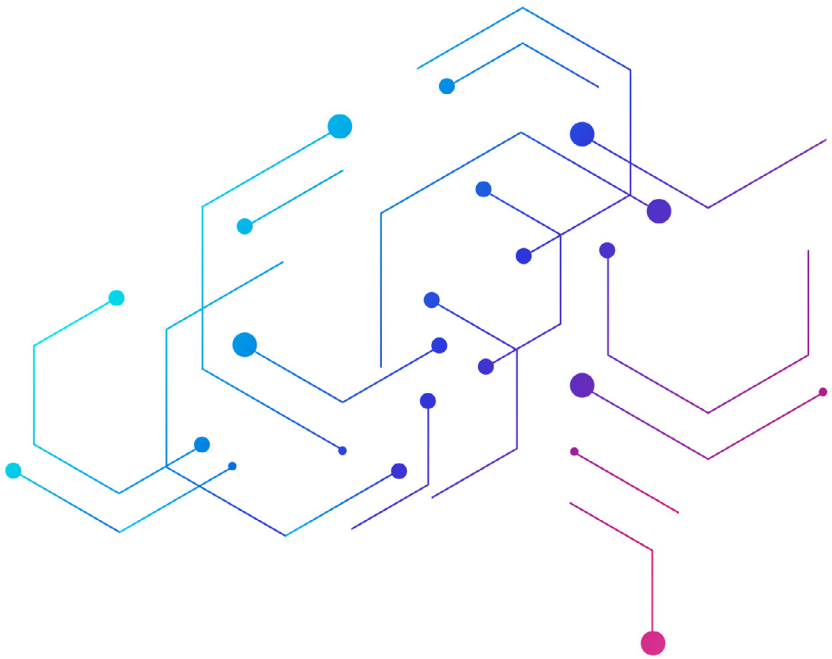
GOAL #1: Preserve and repurpose infrastructure created during the pandemic and target it at other urgent public health needs.

Collaborative infrastructure born out of the public health crisis facilitated more public-private partnerships, enabled the accelerated timeline of COVID-19 vaccines and therapeutics development, and encouraged increased sharing of real-world data and evidence. These initiatives and platforms could help accelerate progress against other prioritized health challenges.

ACTOR	ACTION
National Institutes of Health (NIH) Office of the Director	• Direct that an externally-led evaluation be conducted of **government-funded networks** and partnerships built and utilized for COVID-19 (such as Accelerating COVID-19 Therapeutic Interventions and Vaccines, Rapid Acceleration of Diagnostics, and the National COVID Cohort Collaborative) to assess their strengths, weaknesses, gaps, and fitness for application beyond the public health emergency (PHE).
NIH National Center for Advancing Translational Science (NCATS)	• Create and execute an action plan for maintaining the **National COVID Cohort Collaborative** (N3C), a Clinical and Translational Science Awards (CTSA) data sharing/analytics platform, for future research. NIH should consider requiring participation in N3C as a condition of receiving CTSA awards in the future. • Maintain, expand (e.g., to include other government-funded health systems like Veterans Affairs, Department of Defense, Federally Qualified Health Centers) and utilize **NIH's Clinical Trial Capacity Inventory** created during COVID-19 for other priority research.
Secretary of the US Department of Health and Human Services (HHS)	• Develop and execute a plan for setting and funding research challenges to train and keep this research base active. • Convene a **Grand Challenges Working Group** consisting of representatives of NIH, US Food and Drug Administration (FDA), Centers for Medicare & Medicaid Services, Centers for Disease Control and Prevention, and other agencies that support biomedical research (Defense Advanced Research Projects Agency, National Science Foundation), along with an advisory group of external representatives of patients, industry, academic research institutions, public health experts, and other stakeholders to prioritize research challenges to support via this infrastructure. The working group could consider high public health needs, high health-care costs, and low innovation activity as criteria for prioritizing disease categories.
Advanced Research Projects Agency for Health (ARPA-H) (if created as proposed)	• Be a vehicle for advancing prioritized research into platform technologies that can benefit many conditions and stakeholders.

(Continued)

Congress	• Provide **funding** (through ARPA-H and/or other existing agencies and programs) for research challenges prioritized by the newly established HHS Grand Challenges Working Group.
Public/private/ nonprofit stakeholders involved in COVID-19 collaborations (e.g., Reagan-Udall Evidence Accelerator, industry COVID R&D Alliance, etc.)	• Evaluate initiatives and partnerships—including the agreements that underpinned them—built and utilized for COVID-19 to assess their strengths, weaknesses, gaps, and fitness for application beyond the PHE. » This should include COVID-19 **real-world data/real-word evidence platforms and initiative**s. Organizations engaged in these initiatives should share learning broadly related to standards, methods, and quality of data and evidence. Identify incentives for private-sector participation.
White House Office of Science and Technology Policy	• Hold a high-level summit/convening to highlight learnings from efforts, particularly those initiated outside the US government, and determine what application they could have post-pandemic.



GOAL #2: Prioritize investment in platform technologies and research infrastructure that can benefit many researchers and developers.

While much of the compressed COVID-19 R&D timelines is due to an extraordinary investment of financial and human capital, some is also due to long-term investments made by the government, philanthropy, and industry in critical platform technologies and infrastructure that benefit many researchers and developers. To prevent another global health crisis and speed the pace of medical innovation, these actors must identify other critical health platform technologies and guide investment in these new areas.

ACTOR	ACTION
NIH Office of the Director	• Perform a landscape assessment of **platform technologies and research** infrastructure (e.g., mRNA, prototype pathogens, trial networks, etc.) that impacted the biomedical ecosystem during the PHE and report to Congress on the im-pact of these long-term investments.
Congress	• Fund the President's Budget proposal for an **ARPA-H** program to define and invest in critical platform technologies and research infrastructure. Congress should also provide stable and predictable funding to the Biomedical Advanced Research and Development Authority (BARDA) to "de-risk" novel scientific platforms and promote innovation. » Consider extending **BARDA Ventures** as a model to leverage additional private-sector investment in critical health technologies beyond infectious disease.
Leaders in health/ medical philanthropy	• Convene a roundtable with **philanthropic funders** on opportunities to support collaborative infrastructure and initiatives brought to the fore during the pandemic.
Congress and the Administration	• Identify **clinical trials networks** as "national critical research infrastructure" and ensure funding for the maintenance and expansion of standing research capacity and its readiness. • Consider whether clinical research is adequately represented within the government's "Critical Infrastructure Sectors" health care and public health sector definitions and action plans, as well as other federal efforts aimed at sustaining critical national infrastructure.
NIH Office of the Director, in collaboration	• Identify and address gaps in existing government-funded and commercial trial networks and barriers to participation to build, engage, and support more **community-based institutions and networks** to improve representativeness and the ability to deploy pragmatic trials. » This effort should examine existing models such as the National Cancer Institute (NCI) Community Oncology Research Program.
Secretary of HHS	• Direct the Health Resources and Services Administration (HRSA) to evaluate the capacity of the **Federally Qualified Health Centers** to conduct clinical research and determine what resources are needed to enable them to participate more readily. • As above (see p. 2), convene a cross-agency **Grand Challenges Working Group** to develop and execute a plan for setting research challenges to train and keep this research base active. Congress should ensure funding for such research priorities.

GOAL #3: Promote greater adoption of efficient clinical trial practices utilized during the pandemic, such as master protocols, seamless trials, pragmatic trials, and decentralized trials.

Innovative trial designs and approaches have been increasing during COVID-19. These approaches are not new, but they had not been widely adopted because of unfamiliarity or concerns about their risk from a regulatory standpoint. The pandemic's urgency pushed researchers to use these approaches more broadly, increasing familiarity and the potential for more routine use across therapeutic areas. Institutional review boards also proved themselves more nimble and flexible during the pandemic.

ACTOR	ACTION
Food and Drug Administration (FDA)	• Review and report on the experience of sponsors and the agency with **master protocols and other adaptive designs**, and update guidances to reflect learnings and promote greater adoption of these approaches. • Consider whether there are additional ways the agency can incentivize adoption, including **enhanced engagement by sponsors** with the agency. • Review pandemic guidance on non-COVID trial conduct, track sponsors' experience using remote tools during COVID, and determine need for post-pandemic guidance/ flexibilities to enable more decentralized/hybrid trials.
Industry organizations	• Review and report on sponsors' experiences with adaptive designs and pragmatic trials during the pandemic and make recommendations as to what actions would increase adoption.
HHS Office for Human Research Protections	• In conjunction with the Secretary's Advisory Committee on Human Research Protections, should conduct an analysis of how processes were accelerated during the pandemic, particularly by **Institutional Review Boards**, evaluate what worked and what didn't, and identify approaches that can improve efficiency for all research going forward.

GOAL #4: Initiate a public dialogue about how regulation can become more agile based on need, in light of the COVID experience.

The COVID-19 experience has highlighted key areas in which FDA can accelerate its work while protecting public safety and highlighted how regulatory approaches might be tailored based on need, rather than following "cookie-cutter" approaches traditionally used by regulatory bodies. The pandemic has opened up a dialogue about the right balance between speed and safety under specific circumstances.

ACTOR	ACTION
Congress	• Call for a report on how FDA was able to accelerate processes during the pandemic and their appropriateness and applicability in non-emergency conditions. » This analysis should specifically focus on the **types of meetings** available to sponsors, how they were used in the context of COVID-19, and the potential for more rapid and regular interaction with the agency going forward, including ongoing submission and review of applicable data. » This analysis should also identify ways in which the agency was able to create more **cross-disciplinary collaboration** within the agency. » Consider linking this analysis to the PDUFA authorization process. • Direct the FDA to undertake an internal review to reevaluate in light of the COVID-19 experience its plans and frameworks around how **real-world evidence and data** is collected, analyzed, and used in decision-making, as well as its technology modernization plan.
External organizations	• Create **briefing materials and events for lawmakers** around lessons learned from the COVID-19 pandemic regarding accelerated regulatory processes, benefit/risk evaluation, innovative clinical trial models, and other novel practices that were employed out of necessity due to the PHE, including case studies of where and how it led to benefits for innovation and patients.
FDA	• Review its approach to **guidance** in light of the COVID experience to determine how it might make the process more rapid and iterative, looking at the Oncology Center of Excellence's efforts to streamline many guidances as a model.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