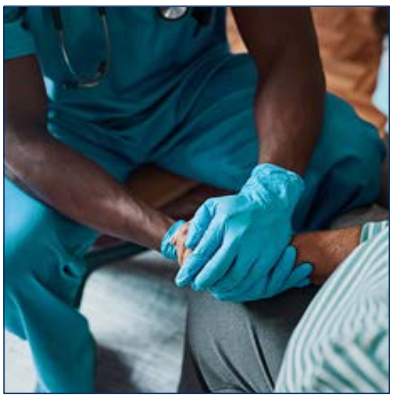
U.S. Department of Health & Human Services
Office of the Assistant Secretary for Preparedness & Response

Recommendations from the National Biodefense Science Board (NBSB): |

Enhancing Benefits from Federal Investments in the Development and Production of the Next Generation of COVID-19 Vaccines and Therapeutics

November 30, 2023

ASPR



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Introduction

Vaccines and antiviral therapeutics for Coronavirus Disease 2019 (COVID-19) that are available in 2023 are effective at preventing serious illnesses and death. In May 2023, the U.S. Government (USG) announced *Project NextGen*, a joint program between the Biomedical Advanced Research and Development Authority (BARDA) and the National Institutes of Health (NIH) National Institute of Allergy and Infectious Diseases (NIAID), to accelerate and streamline the development of the "next generation" COVID-19 vaccines and therapeutics. The goal of that investment portfolio is to achieve improved and sustained protection against COVID-19.

In addition to equity considerations, regarding which the NBSB issued recommendations in the report Prioritization of Product Attribute Categories to Maximize Access for Next Generation COVID-19 Vaccines and Therapeutics earlier this year, BARDA is exploring factors that ensure an equitable relationship with private companies in the development of the next generation of COVID-19 vaccines and therapeutics. BARDA aims to invest in later-phase development of products that promote increased uptake by all populations while ensuring that national leaders and the American people recognize a favorable return on investment of taxpayer funds. To that end, BARDA sought advice from the NBSB to help ensure that the federal government achieves optimal benefits from investments in private companies. More details on this request are provided in Appendix 2 of this report. As a result of deliberations between September 6 and November 9, 2023, this report contains the NBSB's findings and advice on this topic.

Issue Overview

The U.S. government (USG) seeks equitable investment considerations with industry partners, whose efforts are necessary to develop and produce emergency medical countermeasures (MCM). The NBSB firmly believes that the SARS-CoV-2 virus is likely to continue to spread and mutate, which means that new and improved countermeasures are critical to avoiding another surge in cases and deaths. As of the publication of this report, a considerable amount of additional funding has already been awarded for next generation vaccines and therapeutics; BARDA will continue to invest in later-phase research and development (R&D) while communicating the overall value of those decisions to the public.

Appropriators in the U.S. Congress and other external stakeholders have expressed concerns that USG funding be more heavily balanced in the interest of the U.S. taxpayer. The concern, as publicly stated, is that private drug companies that receive public funds during an emergency gain excessive profit at the cost of public benefit. Financing, economics, and politics in the pharmaceutical industry is complicated and beyond the scope of the NBSB, but there are several key observations that are relevant to the board members' advice and recommendations in this report.

Federal funding for R&D such as BARDA's is unique in that it addresses the "market failure" for medical products that are deemed essential for national health security.[1] Health security products often have very limited uses and are often simply added to the Strategic National Stockpile rather than sold commercially in significant quantities. Such products are not viable to produce and sell for profit because they are only needed for highly specific threats when they occur. The federal government invests in development of health security products because private investors will not or cannot do so quickly enough to meet emergency requirements. BARDA and other federal funders absorb some of that financial risk, including the opportunity costs that comes with halting other R&D projects that could be more financially lucrative. Private companies may be required to prioritize federal requirements and deadlines and may have to halt work on multiple projects, which companies need to hedge against "normal" product development failures. Lastly, the faster that products must be developed, the more risk of failure the federal government must absorb.

Private investors are incentivized by the promise of financial return and therefore private companies (regardless of the industry) must return a profit that is paid to shareholders in exchange for investments. Under normal circumstances, biomedical R&D is inherently complicated, financially risky, and competitive, but a combination of private and public investment leads to innovation. Pharmaceutical companies must eventually sell FDA-approved products at a price that covers many years (sometimes decades) of investment. The fact is that about 90% of all investigational compounds fail to result in a new drug, and companies may plan for seven or more years of revenue from a single drug's sale to cover such costs. Federal funding for emergency MCM development must be substantial, and with reasonable conditions, so that private companies will accept contracts and the risks associated with potentially failing to generate revenue.

Findings and Recommendations

Developing and negotiating contracts for emergency MCM product development is complex, influenced in part by the unique structure of the U.S. health care system. There are many private companies and organizations involved in developing, manufacturing, procuring, distributing, and administering vaccines and therapeutics, all of which have some impact on costs and prices. Comprehensive analysis of the pros and cons of every possible private industry consideration and federal incentive structure are beyond the scope of the NBSB's charter and this report. The board members and other subject matter experts noted, however, that it would be very difficult to conduct such an analysis without much more information about the private costs of R&D, which are publicly unavailable. The following findings, advice, and recommendations are aimed

[1] National health security is a state in which the Nation and its people are prepared for, protected from, and resilient in the face of disasters or emergencies with health consequences. See National Health Security Strategy for more details on the current U.S. government approach.

at helping BARDA and others to ensure that the Nation continues to benefit from development of COVID-19 products in a cost-responsible way.

First and foremost, BARDA's model of investment works in the interest of the American taxpayer. BARDA's webpages are replete with examples of biomedical innovations that strengthen national preparedness for health emergencies and the health consequences of disasters. Many of those products would likely not exist or not be available at a reasonable cost without federal investment in their development and production. BARDA is not alone in that effort; the NIH and Department of Defense, among others, provide large amounts of funding for biomedical discovery and innovation that leads to health security products.

Considerations, in the context of this report, are forms of return or benefit that the federal government receives from a private pharmaceutical company receiving public funding for R&D of emergency medical products. The federal government does not receive an equity-stake in private companies as do stockholders but may claim a portion of profits or set other requirements that ensure that the Nation receives an appropriate benefit. The success of this financing model has been recognized by other countries, with work ongoing to emulate this form of public-private partnership. The NBSB fully endorses the ongoing work of BARDA and the USG emergency MCM enterprise more broadly and offers the following advice and recommendations.

1. **Communicate publicly, more clearly (in relatable terms), and more frequently about the benefits and risks related to developing emergency MCMs, as well as the role of the federal government.** At the beginning of the pandemic, the United States needed effective solutions very quickly at a massive scale, which was only possible through large amounts of funding to many companies simultaneously. While the pharmaceutical industry and BARDA have a kind of "playbook" for this situation, the outcomes will always be uncertain. Only some of the companies that receive funding at the earliest phase of a response will generate revenue or profit; all others will fail in their efforts, and some may go bankrupt. Today, the situation with COVID-19 remains unpredictable. Will the virus continue to evolve and cause illnesses and deaths, including among those who have been infected with prior variants or previously vaccinated? Will there be another massive wave of the pandemic? On the other hand, will COVID-19 become less significant, with declining motivation for new vaccines and little need for treatments, resulting in products with low commercial value? Currently, only 7% of U.S. adults have opted for the latest COVID-19 vaccine, evidencing vaccine fatigue and concerns about costs following the expiration of federal subsidies. Public funding reduces risks to pharmaceutical companies by investing in public health security but does not completely eliminate those risks. Those decisions by BARDA and other components of HHS that lead to equitable, effective, and safe emergency MCM should be constructed and

communicated as a "win-win" for the taxpayer, private industry, and the innovation economy.

2. **Ensure that all production contracts include controls for fair pricing of commercial products**. While approval for commercial sale is beyond the authority of BARDA, funding agreements for R&D that could lead to future commercial products should include considerations for fair pricing. Fair pricing means a reasonable profit that is in line with public expectations and norms. The details related to the price of potential products (in relationship to the products' value) could be disclosed earlier in the development process, transparently accounting for cost-sharing, manufacturing, and the unique structure of the U.S. healthcare system, as well as "last mile" costs associated with distribution and administration. Conditions or "prizes" the allow higher pricing could be based on the degree of innovation involved, delivering the final product ahead of schedule, rapid development for pediatric use or the needs of other at-risk populations, and qualities of the product related to efficacy, stability, equity, and ease of administration. Costs for new commercial vaccines for COVID-19 should be consistent with prices for similar products, such as the vaccines against influenza or the respiratory syncytial virus, as well as the prices charged in other high-income countries.
3. **Claim additional royalties for new products, which are used for future R&D.** Because compensation and performance awards for federal employees is strictly limited, federal law allows for federal scientists to receive a portion of royalties from their inventions while working for the federal government. Research and development funded by BARDA does not directly result in inventions (e.g., the patents are already privately or publicly owned), but BARDA could negotiate additional royalty payments from the sale of commercial products, which could then be put back into federal R&D. Unlike royalties claimed in private arrangements, public royalties would be relatively small, but could serve as an incentive for controlling the cost of R&D while ensuring that the taxpayer is "compensated" when there is a successful commercial product, with those funds being put to good use to develop future health security products.
4. **Establish advanced purchase agreements for commercial products**. When negotiating considerations related to royalties or fair pricing, agreements with private companies should include an agreement to purchase a minimum quantity at market price, to include an amount that will be provided free-of-charge in public health programs in the United States. This also necessarily means that companies must first provide the USG with the quantity promised before selling to other buyers. While purchase guarantees may incentivize companies, those prices should also be at negotiated at reasonable rates as the USG is not in the work of guaranteeing profits for private companies. While patient assistance programs have been criticized for providing nominal benefit to patients,

companies could be required to establish some form of program that ensures that therapeutics (in particular) continue to be available at low or no cost after FDA approval for the un- or under-insured.

In addition to the types of considerations from private companies that could be beneficial to the American taxpayer, the board members talked about a variety of incentives that might be useful to use in conjunction with such considerations. For the NBSB, considerations (benefits to the public) and incentives (benefits for private companies) go hand in hand. These additional recommendations are offered to assist with current and future investment decisions.

1. **Establish a system of milestone payments or prizes for cutting edge and emergency R&D.** BARDA could further reduce risks related to cutting edge or emergency R&D and entice more companies to partner with the federal government by using a system of milestone payments that reward progress, even though a product may ultimately fail. This could be combined with a system of prizes (potentially recognizing first place and second place "winners") that escalate payments for exceptional performance or value. Payments (whether as a milestone or a prize) could be tied to the speed of development, reduction in research costs, reductions in expected or actual production costs, collection of data specific to equity or at-risk individuals (especially children), enhanced safety and efficacy, the need for few doses, specific markers of biological effectiveness, innovative storage or administration systems, or shelf-stability. Prizes could include a variety of other incentives in partnership with other agencies, such as priority review vouchers, funding for other types of research, or access to an existing clinical trial network, or the option to charge a higher price at some point.
2. **Explore options to develop facilities in the United States that support good manufacturing practices and are available for future emergency production.** The NBSB does not believe that the federal government should own or operate biomedical manufacturing facilities, but there should be investment in manufacturing infrastructure that increases the availability of domestic manufacturing for emergency products when needed. Because manufacturing large quantities of pandemic emergency vaccines and therapeutics can be expected to be relatively time-limited—though in the case of COVID-19, it appears that the United States will need SARS-CoV-2 vaccines and treatments for some time—facilities that uphold good manufacturing practices need to be able to produce other commercial products between emergency uses. Arrangements should be in place for specific facilities to shift as quickly as possible, potentially with additional federal funding, to production of emergency MCMs, then shift back to normal production when no longer needed for emergency response. To this end, as an example, the federal government could enable MCM production companies to use the government's existing networks of contract drug manufacturing organizations (CDMOs)

and contract research organizations (CROs) to mitigate capacity constraints when emergency manufacturing is needed. The network of CDMOs and CROs could use government resources and preliminary technical transfer activities to support emergency manufacturing of promising vaccines and therapeutics. The NBSB recognizes that there are very high standards for biomedical manufacturing that typically inhibit rapid changes to product lines as described, but this is an opportunity for experimentation and innovation, such as just-in-time manufacturing.

3. **Coordinate with NIH and other agencies to reduce costs of R&D and the time required for clinical trials.** The federal government could take additional steps to lower the overall costs and complexity of R&D for novel vaccines and pharmaceuticals (and potentially other MCM) by streamlining access to the federally sponsored "R&D ecosystem." Examples of such in-kind incentives include access to pre-existing clinical trial networks for adults, children, and other at-risk individuals, vouchers for rapid FDA review of any new drug, purchase agreements for other (non-emergency, but widely beneficial) medical products, or government-backed loans for capital investment or R&D. These could be a standard feature of contracts, part of a milestone award, or a prize for first and/or best candidates.

Appendix 1: Roster of the National Biodefense Science Board (November 2023)

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Appendix 2. Details of Request from the Biomedical Advanced Research and Development Authority (BARDA) to the National Biodefense Science Board (NBSB)

Examples of key equitable investment considerations BARDA has contemplated include:

1. High-Income Country Equivalence Consideration: The USG would require that it not pay more for a product developed with USG funding than would be paid by any other high-income country.
2. Royalty Consideration or USG Credit/Foundation Consideration: The USG would receive percentage of every product sold on a commercial market. That royalty payment could be used by BARDA as a USG credit for further research and development (R&D) efforts by the company or to a foundation for further investments.
3. Performance Incentives Consideration: Create incentives for speed, overall R&D costs, and/or total end cost such as 2% increase in overall contract value to spend on more R&D or an increase/renegotiation of a higher fee.
4. Loan Consideration: Provide financing in the form of loans that would need to be repaid. This would only be considered if BARDA receives loan authority which it currently does not possess.
5. "As Is" Consideration: Accounting for all the current factors in USG investment (including delivering lifesaving medical countermeasures, cost-sharing, generating jobs, supporting the development of infrastructure, lost opportunity cost, etc.), there is already a significant amount of consideration the USG receives.
6. US Patient Assistance Programs: Require awardees that bring a product to the commercial market to create a robust patient assistance program in the US to help ensure equitable access for all US populations.
7. Push/Pull Consideration: BARDA provides *push* funding with contract and Other Transaction Authority (OTA) mechanisms; but could increase the use of *pull* funding mechanisms (e.g., prizes, milestone-based payments). For example: If a company reaches a certain development threshold, they will receive a "prize" (to be defined). This would enable risk-sharing with the partners and only reward success.
8. Government Facility Consideration: If USG provides infrastructure to assist product development or production, then the company has to provide a consideration to the USG. This could include access or ability for a company to develop a product it could not have otherwise.

BARDA intends to apply considerations on a case-by-case basis—selecting and scaling the consideration(s) based on the unique circumstances and characteristics of each Project NextGen-funded company and project. Potential company and project circumstances and characteristics include: size and revenue of the developer, technology readiness level of the candidate, amount of USG funding provided to the developer, and commercial potential of the product.

BARDA seeks input from the National Biodefense Science Board (NBSB) regarding considerations needed to establish equity between the USG and industry while ensuring that the interests of both parties are adequately met; and how they should be prioritized for next generationCOVID-19 vaccines and therapeutics. BARDA would like to request the NBSB to consider the following questions:

1. Are there additional considerations beyond the eight that BARDA identified?

2. What are the unique company and product characteristics and circumstances that BARDA should evaluate to select equitable investment considerations when required?

3. How should BARDA determine (i.e., scale) the investment relative to consideration – amount ($1M vs. $50M vs. $500M NextGen investment) or percentage (funding 1%, 10%, or 100%) of the work (thus risk)—to ensure the product might be licensed?

4. In a situation when BARDA identifies a promising candidate for which the company has decided to proceed with development only if it receives a nominal or 'in kind' consideration, how should BARDA factor public benefit (i.e., potential for the product to achieve a public health objective/outcome) into its investment decisions given limited taxpayer dollars? How should BARDA think this through?