

Lessons for SPIs from Novel Developments in Emerging Biotechnologies

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Abstract

Rapid advances in emerging biotechnologies have created controversies and generated important lessons for science policy interfaces (SPIs). Based on empirical research, we identify three key lessons. First, public sector investment in the life sciences was essential during the COVID-19 pandemic and should remain a well-funded part of governments' R&D portfolios. Second, when gathering clinical evidence, governments should use gold-standard randomized control trials (RCTs) to avoid collecting faulty evidence and fuelling misinformation. Third, global science diplomacy efforts should focus on improving access to and building resilient supply chains for novel biotechnology reagents and products. Together, these lessons would help SPIs better adapt and harness the benefits of novel emerging biotechnologies.

In recent years, the world has seen substantial innovation in critical and emerging biotechnologies, including mRNA vaccines and chimeric antigen receptor (CAR) T-cell therapies. In the long term, these technologies will likely be joined by other innovations, including gene therapies, precision medicine, and more. The rapid development of these technologies, however, has been accompanied by controversies related to access to these novel technologies and misinformation around them, generating important lessons for science-policy-society interfaces (SPIs) to consider in their decision-making processes.

Key lessons in emerging biotechnology development

We reviewed qualitatively reviewed past literature on novel emerging biotechnologies and identified three key lessons for global policymakers to consider.

Supporting public sector investment in life science research

Public sector investment in life science research refers to grants, pre-market commitments, and other financing tools often offered to research institutions and firms to support the development of critical and emerging biotechnology products. In recent years, public-sector investment has been an increasingly crucial part of the drug development pipeline.

Prior to the COVID-19 pandemic, public-sector investment already played a critical role in developing transformative drugs like sofosbuvir for the treatment of hepatitis C (Barenie et al., 2021). Indeed, drugs developed with public funds accounted for 19% of the 248 drugs approved by the U.S. Food and Drug Administration between 2008 and 2017 and were more likely, on average, to be innovative, first-in-class products (Nayak et al., 2019). However, during the

COVID-19 pandemic, the importance of public sector investment grew even further. More than ten countries made crucial public-sector investments in developing over 190 vaccine candidates against COVID-19 (GAVI, 2023). For the most innovative biotechnologies, like mRNA vaccines, researchers estimate that the U.S., Canada, Germany, and other countries collectively invested more than \$30 billion to develop these products for global use (Lalani et al., 2023).

Beyond magnitude, this public-sector investment is also critical, as it is targeted in emerging biotechnology sectors where the private sector often underinvests. For example, in critical sectors like antibiotics, poor commercial sales and high failure rates during development have caused private-sector funding of antibiotic development to wane (Wasan et al., 2023). This underinvestment is particularly concerning given antimicrobial resistance (AMR) poses substantial risks and could kill nearly 10 million annually through 2050 and cause billions in economic damage (Capozzi et al., 2019). Facing this tide, public-sector actors, including domestic and international government bodies, non-government organizations, and public-private partnerships, have become the primary funders supporting the development of critical antibiotics against resistant bacteria (Wasan et al., 2023).

However, political and resource constraints for SPIs mean that public funding is often constrained and limited. Given that biotechnology research and development is incredibly expensive, many SPIs lacking resources often forgo investing in life science research, causing a net loss for global innovation. Similarly, even in countries with extensive financial resources, public-sector investment often pales in comparison to the private sector (Schulthess et al., 2023). Absent reforms, this status quo risks leaving late-stage biotechnology development and commercialization largely to the private sector, which may be problematic for SPIs given that many firms' underinvest in key biotechnologies and

because of the aforementioned positive association between public-sector funding and more innovative therapies.

Maintaining high-quality evidence collection standards

The COVID-19 pandemic produced significant challenges in the collection of high-quality evidentiary data. Prior to the pandemic, randomized control trials (RCTs) remained the primary gold-standard tool to gather evidence used to gather data on the efficacy and safety of novel biotechnology products (Munnangi & Boktor, 2022). Most regulatory agencies worldwide often require or primarily review RCT data to determine if a product should receive regulatory approval in a given country.

During the COVID-19 pandemic, however, difficulties in conducting RCTs led regulatory bodies to grant emergency use authorizations or approvals based on limited or non-rigorous scientific evidence, such as observational studies. Some have argued that greater acceptance of such studies by regulatory bodies should be encouraged, given that such studies often require fewer resources and are more feasible in resource-poor settings. However, while potentially justified when traditional evidence-gathering is impossible, this shift to non-rigorous studies presents several dangers of which SPIs should be aware.

Such dangers are most notably seen in the case of hydroxychloroquine (HCQ), a drug used primarily as an antimalarial (Manivannan et al., 2021). Researchers originally suspected that HCQ had potential antiviral uses, and during the early pandemic, researchers ran several studies analyzing its efficacy versus COVID-19. Several observational studies — nonrigorous studies in which patients did not randomly receive HCQ or a placebo — indicated that HCQ was an effective therapy against COVID-19 (Manivannan et al., 2021). Given these studies' deviation from traditional RCT methodologies, these studies faced major scientific criticism, and later gold-standard RCTs found HCQ to be ineffective or potentially harmful, leading many governments to limit its use (Manivannan et al., 2021). However, this flip-flop resulted in widespread misinformation online and significantly hampered public trust in SPIs worldwide.

The tale of HCQ and other similar products highlights that SPI reliance on observational studies and non-rigorous forms of evidence presents credible dangers to the global public's trust in SPIs. Decisions to withdraw

products after approval risk causing allegations that governments chose to withdraw products from their markets due to political, ideological, or even conspiratorial reasons, especially among polarized segments of society. At a minimum, it degrades the perceived competency and credibility of SPIs, reducing public trust in future SPI decision-making. Such a result can even prevent SPIs from wielding effective policymaking tools in future crises.

Improving global science diplomacy

Global science diplomacy efforts, especially at the multilateral level, remains a critical part of international dialogue. However, in recent years, SPI diplomacy has faced significant difficulties in achieving multilateral objectives related to the Sustainable Development Goals (SDGs), especially in ensuring global access to critical biotechnology products.

From an ethical and institutional responsibility perspective, SPIs must first tackle sizeable global health disparities in product access, as seen with the persistent imbalances in the global distribution of COVID-19 vaccinations, therapeutics, and personal protective equipment (PPE). Such disparities not only risk enabling the rise of dangerous new variants of diseases but represent an ethical failing by international institutions on behalf of the individuals they serve. In many cases, despite the best efforts of the UN Medicines Patent Pool (MPP) and other actors who negotiated voluntary licensing (VL) agreements to scale up global medicines production, such agreements often had a limited impact (Pepperell et al., 2022). First, demand continued to outstrip supply despite the VL agreement, and second, many countries struggled to both diagnose which individuals needed these therapies and then deliver these products to the populations who needed them (Pepperell et al., 2022).

Second, moreover, such agreements fail to address the key supply chain issues displayed at the onset of the COVID-19 pandemic. Immediate pandemic-related disruptions to global supply chains for personal protective equipment (PPE) resulted in shortages at key medical institutions, especially in developing countries (Francis, 2020). A lack of institutional communication channels between medical institutions and PPE suppliers forced many medical care providers to hunt for contracts at a time when suppliers were inundated with requests (Francis, 2020). Later, as COVID-19 vaccines emerged, there was a rapid global scale-up of reagent suppliers and vaccine producers (Bown &

Bollikky, 2022). However, in many cases, this scale-up of global supply was hindered by shortages of upstream inputs and raw materials needed to make new vaccines (Bown & Bollikky, 2022). This shortage of upstream and raw materials appears largely driven by suppliers lacking both the needed production capacity and being dispersed across numerous locations worldwide, thus leaving them vulnerable to cross-national trade and regulatory barriers (Bown & Bollikky, 2022).

Policy recommendations

On each of the three key issues raised, SPIs should take evidence-based steps to more effectively harness the opportunities presented and counter the challenges posed by novel emerging biotechnologies.

On the issue of public sector investment, governments, international organizations, and other actors should increase their R&D investment in basic life science research, especially in critical sectors like antibiotics and new frontier technologies where the private sector often underinvests. Given funding constraints faced by individual governments, regional states should consider pooling resources and developing multilateral investment funds to foster greater biotechnology innovation. Similarly, individual governments could also sponsor public-private partnerships to expand the pool of funds available for investment. However, such partnerships should include guidelines to target a significant portion of partnership investments to critical sectors like antibiotics.

Second, on the issue of collecting rigorous evidence, global policymakers should avoid relying on non-rigorous studies and instead adopt more innovative methods for conducting traditional randomized control trials (RCTs), as was done in the UK's RECOVERY trial that helped reveal the utility of dexamethasone for the treatment of severe COVID-19 (RECOVERY et al., 2021). Such innovative RCT approaches ensure that collected evidence is reliable for use in regulatory decision-making and is less likely to lead to misinformation and distrust of SPIs. To ensure RCTs can be conducted across many countries, multilateral efforts should also be made to invest in supplying diagnostics and data-gathering tools to countries worldwide to increase the diversity of settings in which RCTs may be performed.

Lastly, to improve global access to emerging biotechnologies, international policymakers should invest in building diagnostic and delivery capacity worldwide to ensure products scaled up via VL agreements can reach populations in need. Meanwhile,

on supply chain resilience, national policymakers should convene forums and build online interfaces to connect medical institutions with key suppliers, ensuring hospitals, clinics, and other care providers can rapidly secure contracts in a time of crisis. Governments should also convene new working groups and forums to coordinate new investments in the global production of upstream inputs and raw materials for biotechnology products. Multilateral coordination for such investments will be essential to overcome national regulatory barriers and support suppliers located in geographically disparate locations worldwide.

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