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## DA – Innovation

#### Pharmaceutical innovation is accelerating now – new medicines are substantially better than existing treatments.

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Despite recent concerns over an innovation crisis, this analysis shows pharmaceutical innovation has actually increased over the last several decades based on the structural novelty of approved NMEs. The higher proportion of Pioneers over the most recent decade is a sign that innovation within the industry is accelerating rather than slowing. It is also an encouraging sign for the state of innovation in drug discovery that these Pioneers are significantly more likely to be the source of promising new therapies that are expected to provide substantial clinical advantages over existing treatments. Drug hunters are discovering Pioneers in newer and less explored regions of chemical space as they are increasingly found on scaffolds first reported in the CAS REGISTRY five or less years prior to their IND year or on scaffolds populated with 50 or less other compounds at the time of IND.

As scale becomes less of a strategic advantage, Big Pharma’s share of Pioneers has decreased even though the number of Big Pharma originated Pioneers has increased. This has created a structural innovation gap between Big Pharma and the Rest of Ecosystem which has widened over the last two decades as the Rest of Ecosystem is now responsible for originating almost 3 out of every 4 Pioneers. Pioneers originated by the Rest of Ecosystem are increasingly on new scaffolds, while a majority of Big Pharma originated Pioneers have historically been on new scaffolds.

The work presented here was intended as a study of drug innovation at a macro level. As a result, it included substances of various sizes with different degrees of complexity belonging to a range of functional and drug classes. Even though it was outside the scope of the present work to study specific subsets, such focused studies could yield additional insights into how innovation at a more micro level has changed over time. Other interesting subsets of our data set are the shapes and scaffolds of the Settlers and Colonists. Many of these shapes and scaffolds are privileged in the sense that they are seemingly capable of serving as ligands for a diverse array of target proteins. A separate study of the Settlers and Colonists as well as their side chains could provide insights into possible target-specific innovation trends.

As it often takes more than 10 years after initial discovery for an experimental drug to gain FDA approval, any measure of drug innovation that relies on the time of approval incorporates a significant time lag between initial discovery and ultimate approval. However, characterizing drug innovation based on structural novelty provides a means to assess the forward-looking innovation potential of an experimental drug at the time of initial discovery by comparing its framework information (at the scaffold and shape level) with prior FDA-approved drugs. Therefore, a separate study of drug candidates with publically disclosed structures currently in clinical development could provide additional insights into innovation trends at an FDA regulatory review level and serve as a leading indicator of innovation trends at an FDA approval level.

Given the tremendous opportunity represented by the vast amount of chemical space yet to be explored, drug-hunters of all types will continue pushing the boundaries to find promising new therapies in previously unexplored areas of chemical space. The race to discover these new drugs will be fueled by further advancements in screening approaches and in-silico methods (including innovations related to machine learning algorithms and molecular representations). However, comprehensive data on known shapes and scaffolds can fast track the identification of meaningful open areas of chemical space (shapes or scaffolds that are potentially important but have never been used as the basis for a molecule) to further explore.

#### The biopharmaceutical industry is uniquely reliant on IP protections – undermining them would kill innovation by making an already expensive process completely unfeasible.

Kristina M. Lybecker, PhD, 17 [PhD Economics, Associate Professor of Economics @ Colorado College], “Intellectual Property Rights Protection and the Biopharmaceutical Industry: How Canada Measures Up,” Fraser Institute, January 2017, <https://www.fraserinstitute.org/sites/default/files/intellectual-property-rights-protection-and-the%20biopharmaceutical-industry.pdf> C.VC

The unique structure of the innovative biopharmaceutical industry necessitates a variety of intellectual property protection mechanisms. In particular, the industry is characterized by a research and development (R&D) process that is lengthy, expensive, uncertain, and risky. According to DiMasi and colleagues, the estimated cost of developing a new medicine is US$2.6 billion (DiMasi, Grabowski, and Hansen, 2016).2 In addition, the time required to develop a new drug is also significant, averaging 10 to 15 years without any guarantee of success (PhRMA, n.d.). While these figures are highly controversial, biopharmaceutical innovation is unquestionably an expensive and lengthy undertaking.3 For the biopharmaceutical industry, innovation and its protection are essential and the source of both profits and growth. As such, patent protection is disproportionally more important for ensuring that the innovator appropriates the returns to R&D for the biopharmaceutical industry than virtually any other. Extending the findings of the 1987 “Yale Survey” (Levin, Klevorick, Nelson, and Winter, 1987), the “Carnegie Mellon Survey” established that while patents are again considered “unambiguously the least effective appropriability mechanisms,” the drug industry and other scholars regard them as strictly more effective than alternative mechanisms (Cohen, Nelson, and Walsh, 1996). The industry’s disproportionate reliance on patents and other forms of intellectual property protection is confirmed in numerous other studies.4

In essence, IPR protections provide innovative biopharmaceutical firms with an assurance of some return on their investment, thus creating incentives for the development of new technologies that could otherwise be easily replicated and sold by competitors. Due to the tremendous fixed costs required to develop new treatments and cures, a significant potential exists for free riding by follower firms, a market failure that would prevent investment in innovation were it not for the patents and other forms of intellectual property protections that provide a limited period of market exclusivity or other such incentives. Fundamentally, patents amount to an efficiency tradeoff. Society provides innovators with a limited period of market exclusivity to encourage innovation in exchange for public access to this knowledge. In exchange for the temporary static loss from market exclusivity, society gains complete knowledge of the innovation through disclosure, a permanent dynamic gain. Through this tradeoff, the existing patent system corrects the market failure that would stymie innovation. In its Apotex Inc. v. Wellcome Foundation Ltd. finding, Justice Binnie wrote for the Supreme Court of Canada, “A patent, as has been said many times, is not intended as an accolade or civic award for ingenuity. It is a method by which inventive solutions to practical problems are coaxed into the public domain by the promise of a limited monopoly for a limited time. Disclosure is the quid pro quo for valuable proprietary rights to exclusivity which are entirely the statutory creature of the Patent Act” (para. 37).

The biopharmaceutical industry is characterized by a number of legal and economic issues that distinguish it from other research-intensive industries. Danzon (1999) describes three features that are particularly noteworthy. First, given that the biopharmaceutical industry is characterized by an unusually high rate of R&D, intellectual property protection provides for the potential for significant market power and monopoly pricing that raises numerous public health policy questions surrounding prices and profits. Second, virtually every aspect of the industry is heavily regulated, from safety and efficacy to promotion and advertising, to pricing and reimbursement. Danzon describes the impact of these regulations as “profound and multidimensional even within a single country, affecting consumption patterns, productivity, R&D and hence the supply of future technologies” (Danzon, 1999: 1056). Lastly, while research and development costs are borne solely by the innovator, the resulting product is a global public good. “Each country faces an incentive to adopt the regulatory policies that best control its pharmaceutical budget in the short run, free-riding on others to pay for the joint costs of R&D and ignoring cross-national spillovers of national regulatory policies through parallel trade and international price comparisons” (Danzon, 1999: 1056). The combination of these characteristics defines a set of unique economic and legal challenges for the innovation of new drugs and the public health policies that surround their production, marketing, and distribution.

Innovative companies make far greater investments in time, resources, and financial support than do generic firms. Notably, innovation-based companies spend more than 200 times that which generic companies spend on the development of a particular drug (CIPC, 2011: 10). In addition, the investment of time, from laboratory to market, is also close to double for innovative companies relative to generic producers. Table 1 highlights the differences in the drug development processes of innovative and generic companies. For innovative biopharmaceutical companies, the development process is expensive, risky, and time consuming, all of which points to the need for strong IP protection to encourage investment and ensure companies are able to recover their investments.

The risk involved in biopharmaceutical development is starkly illustrated in a recent report by Biotechnology Innovation Organization (BIO), which reports that less than one of every 10 drugs that enter clinical trials is ultimately approved by the Food and Drug Administration in the United States. The report finds a success rate of merely 9.6%, a calculation that is significantly smaller than the widely-cited 11.8% figure from a 2014 study by the Tufts University’s Center for the Study of Drug Development.5 The International Federation of Pharmaceutical Manufacturers and Associations (2012) estimates that more than 3,200 compounds were at different stages of development globally in 2011, but only 35 new medicines were launched (Dawson, 2015).

Fundamentally, research-based biopharmaceutical companies incur greater expenses and risk in the development of their products than do generic manufactures. These investments of time and financial resources should be recognized and the effective patent life should be sufficient to recoup these investments. Continued investment and innovation are contingent upon strong, effective intellectual property protection and the ability of innovative firms to recoup their investments. Patents and other forms of intellectual property protection are disproportionally important to the research-based biopharmaceutical industry. Consequently, the legal architecture necessary to foster a robust innovation-based industry is multifaceted and is a powerful force shaping the biopharmaceutical industry, its profitability, productivity, and innovative future.

**Pharmaceutical innovation is key to protecting against future pandemics, bioterrorism, and antibiotic resistance.**

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As key actors in the healthcare innovation landscape, pharmaceutical and life sci-ences companies have been called on to develop medicines, vaccines and diagnostics for pressing public health challenges. The COVID-19 crisis is one such challenge, but there are many others. For example, MERS, SARS, Ebola, Zika and avian and swine flu are also infectious diseases that represent public health threats. Infectious agents such as anthrax, smallpox and tularemia could present threats in a **bioterrorism con-text**.1 The general threat to public health that is posed by **antimicrobial resistance** is also **well-recognised** as an area **in need of pharmaceutical innovation**. Innovating in response to these challenges does not always align well with pharmaceutical industry commercial models, shareholder expectations and compe-tition within the industry. However, the expertise, networks and infrastructure that industry has within its reach, as well as public expectations and the moral imperative, make pharmaceutical companies and the wider life sciences sector an **indispensable** partner in the search for solutions that save lives. This perspective argues for the need to establish more sustainable and scalable ways of incentivising pharmaceu-tical innovation in response to infectious disease threats to public health. It considers both past and current examples of efforts to mobilise pharmaceutical innovation in high commercial risk areas, including in the context of current efforts to respond to the COVID-19 pandemic. In global pandemic crises like COVID-19, the urgency and scale of the crisis – as well as the spotlight placed on pharmaceutical companies – mean that contributing to the search for effective medicines, vaccines or diagnostics is **essential** for socially responsible companies in the sec-tor.2 It is therefore unsurprising that we are seeing indus-try-wide efforts unfold at unprecedented scale and pace. Whereas there is always scope for more activity, industry is currently contributing in a variety of ways. Examples include pharmaceutical companies donating existing com-pounds to assess their utility in the fight against COVID-19; screening existing compound libraries in-house or with partners to see if they can be repurposed; accelerating tri-als for potentially effective medicine or vaccine candidates; and in some cases rapidly accelerating in-house research and development to discover new treatments or vaccine agents and develop diagnostics tests.3,4 Pharmaceutical companies are collaborating with each other in some of these efforts and participating in global R&D partnerships (such as the Innovative Medicines Initiative effort to accel-erate the development of potential therapies for COVID-19) and supporting national efforts to expand diagnosis and testing capacity and ensure affordable and ready access to potential solutions.3,5,6 The primary purpose of such innovation is to **benefit patients** and wider **population health**. Although there are also reputational benefits from involvement that can be realised across the industry, there are likely to be rela-tively few companies that are ‘commercial’ winners. Those who might gain substantial revenues will be under pres-sure not to be seen as profiting from the pandemic. In the United Kingdom for example, GSK has stated that it does not expect to profit from its COVID-19 related activities and that any gains will be invested in supporting research and long-term pandemic preparedness, as well as in developing products that would be affordable in the world’s poorest countries.7 Similarly, in the United States AbbVie has waived intellectual property rights for an existing com-bination product that is being tested for therapeutic poten-tial against COVID-19, which would support affordability and allow for a supply of generics.8,9 Johnson & Johnson has stated that its potential vaccine – which is expected to begin trials – will be available on a not-for-profit basis during the pandemic.10 Pharma is mobilising substantial efforts to rise to the COVID-19 challenge at hand. However, we need to consider how pharmaceutical innovation for responding to emerging infectious diseases can best be enabled beyond the current crisis. Many public health threats (including those associated with other **infectious diseases**, **bioterror-ism** agents **and antimicrobial resistance**) are **urgently in need of pharmaceutical innovation**, **even if their impacts are not as visible** to society **as COVID**-19 is in the imme-diate term. The pharmaceutical industry has responded to previous public health emergencies associated with infec-tious disease in recent times – for example those associated with Ebola and Zika outbreaks.11 However, it has done so to a lesser scale than for COVID-19 and with contribu-tions from fewer companies. Similarly, levels of activity in response to the threat of antimicrobial resistance are still **low**.12 There are important policy questions as to whether – and how – industry could engage with such public health threats to an even greater extent under improved innova-tion conditions.

#### Bioterrorism and future pandemics cause extinction.

Hamish De Bretton-Gordon, 20 [Director @ DBG Defense, Consultant on CBRN and Biosecurity], “Biosecurity in the Wake of COVID-19: The Urgent Action Needed,” Combatting Terrorism Center Sentinel, November/December 2020, Volume 13, Issue 11, <https://ctc.usma.edu/biosecurity-in-the-wake-of-covid-19-the-urgent-action-needed/> C.VC

Policymakers around the world did not grasp just how large the impact of a bio threat could be. Beyond the enormous human and economic impact, the current pandemic has exposed the weakness, lack of preparedness, and poor responsiveness of healthcare systems of even highly developed countries like the United States and the United Kingdom. And the virus has inflicted carnage, even though SARS-CoV-2 (the virus that causes COVID-19) is not especially virulent. The world may be confronted with other viruses in the future whose combination of virulence (the harm a pathogen does to its host), transmissibility, and other characteristics pose much greater danger.

While overwhelming evidence points to SARS-CoV-2 spontaneously spreading to humans, the advances in synthetic biology and the growth in the number of Level 3 and 4 biocontainment facilities around the world storing deadly viruses1 mean there is also the very real possibility that in the future, bad actors will try to engineer or steal/obtain a highly transmissible and highly virulent virus and unleash it onto the world. Another risk is accidental releases from such biocontainment facilities.

COVID-19, a highly transmissible but not very virulent pathogen, has had a devastating global impact, a fact that will not have gone unnoticed by rogue states and terror organizations. Advances in synthetic biology have created tools that could be put to malevolent use. In the last two decades, scientists synthesized the poliovirus from its genetic sequence,2 recreated the 1918 Spanish flu virus,3 and succeeded in modifying the H5N1 avian flu virus so that it resulted (in a research laboratory) in airborne transmission among mammals.4 In the future, we should think of weaponized biology as no less of an existential threat to the planet than weaponized atomic science. It should also be noted that the fear and panic that even a medium-scale bioterror attack could create could have dangerous implications that may rival or even surpass the immediate loss of life.

The Need to Rethink Likelihood

Given the fact that in late 2019 when, as far as is known, COVID-19 cases first started emerging in China, it had been more than a century since the previous catastrophic outbreak (the 1918-1919 “Spanish flu” pandemic),d it was unsurprising that many thought of such pandemics as a one-in-a-100-year event. Such assumptions should no longer hold. The encroachment of human settlements into areas that had previously been sanctuaries for wildlife5 and the popularity in some parts of the world of markets where people and wild animals are brought into proximity have made it more likely viruses will make the species leap to human beings.e And when they do, as the COVID-19 pandemic illustrated, the interconnectedness of a world in which millions of people fly each day6 means they can spread very rapidly.

There is also growing concern about engineered viruses. Not only have advances in synthetic biology (SynBio) created growing capacity for extremely dangerous viruses to be engineered in a laboratory, but the number of people with access to potentially dangerous ‘dual use’ technology has greatly expanded and continues to expand, making malevolent use of such technology ever more likely.

In the August 2020 issue of this publication, scientists at the U.S. Military Academy at West Point warned that:

The wide availability of the protocols, procedures, and techniques necessary to produce and modify living organisms combined with an exponential increase in the availability of genetic data is leading to a revolution in science affecting the threat landscape that can be rivaled only by the development of the atomic bomb. As the technology improves, the level of education and skills necessary to engineer biological agents decreases. Whereas only state actors historically had the resources to develop and employ biological weapons, SynBio is changing the threat paradigm.

The cost threshold of engineering viruses is also lowering, with the West Point scientists warning that synthetic biology has “placed the ability to recreate some of the deadliest infectious diseases known well within the grasp of the state-sponsored terrorist and the talented non-state actor.”7

As already noted, another source of vulnerability is that deadly viruses could be stolen from or escape from a research laboratory. There are now around 50 Biosafety Level 4f facilities around the world, where the deadliest pathogens are stored and worked on, and this figure is set to increase in the next few years.g This is a large increase over the last 30 years, creating bigger risk of a breach. Of equal, if not greater concern are the thousands of Biosafety Level 3 labs globally,8 which handle deadly pathogens like COVID-19.9

Given what has been outlined above, the risk of a future destructive biological attack or another devastating global pandemic should no longer be seen as low. From this point forward, there should no higher priority for the international community than biosecurity.

## Case

Extinction outweighs

**Industrial manufacturers are cooperating now with developing countries – that solves better because states can’t produce vaccines on their own, even without IP restrictions. BUT, reducing their profit motive removes the incentive to cooperate, which makes vaccine access worse**

**Silverman 20** [Rachel Silverman is a policy fellow at the Center for Global Development, where she leads policy-oriented research on global health financing and incentive structures. "Would Exempting COVID-19 Vaccines from Intellectual Property Rights Improve Global Access and Equity?" <https://www.cgdev.org/debate/would-exempting-covid-19-vaccines-intellectual-property-rights-improve-global-access> No Date Listed -- Earliest possible publication is 2020]

Innovator companies are under **enormous** commercial and geopolitical **pressure** to scale **as quickly as possible** to meet enormous, immediate demand. Their profit-driven interest, in this case, is aligned with the **global imperative** to increase production. To do so, they are already **cooperating** widely with competitors and generic manufacturers, including via **voluntary licenses**, **contracted production**, and proactive **technology transfer**. Diluting that commercial incentive may **reduce their interest** in pursuing the voluntary horizontal collaborations that are already driving scale.

It is also not clear that any additional generic manufacturers are “**standing by**” ready to produce. Under existing TRIPS flexibilities, countries can already issue compulsory licenses to produce vaccines without permission from the patent-holder. None have done so. Voluntary licensing and technology transfer from originator companies can help increase long-term manufacturing capacity, especially if paired with public investment; originators also have an interest in enforcing safety and quality control standards while doing so, which is especially important in the context of widespread **vaccine hesitancy**. Their cooperation is important for both speed and quality, and so far they seem **willing to play ball**.

**It doesn’t solve – there are tons of barriers to access to vaccines, especially in developing countries. Even if it’s legal to make generics, lack of raw materials, expertise, and production facilities mean the plan is a drop in the bucket for responding to global covid**

**Herper** et al **21** [Matthew Herper Senior Writer, Medicine, Editorial Director of Events at STAT. "Waiver of patent rights on Covid-19 vaccines, in near term, may be more symbolic than substantive." https://www.statnews.com/2021/05/06/waiver-of-patent-rights-on-covid-19-vaccines-in-near-term-may-be-more-symbolic-than-substantive/]

Prashant **Yadav**, a supply chain **expert** and senior fellow at the Center for Global Development, said the **biggest barrier** to increasing the global **vaccine supply** is a lack of raw **materials** and **facilities** that manufacture the billions of doses the world needs. Temporarily suspending some **intellectual property**, as the U.S. proposes to do, would have **little effect on those problems**, he said.

“My take is: **By itself**, it will not get us much benefit in increased manufacturing capacity,” Yadav said. “But as part of a larger package, it can.”

That larger package would include wealthy nations like the U.S. mounting an Operation Warp Speed-style effort to invest in manufacturing in low-income countries, he said, using their vast financial resources to actually produce vaccine doses rather than solely targeting patents.

Lawrence Gostin, director of the O’Neill Institute for National and Global Health Law at Georgetown Law, said the waiver is necessary but hardly sufficient. It will likely take months of international infighting before the proposal would take effect, he said, months during which would-be manufacturers would not have the right to start producing vaccines.

“We’re not talking about any **immediate help** for India or Latin America or other countries going through an enormous spread of the virus,” Gostin said. “While they’re going to be negotiating the text, the **virus** will be **mutating**.”

**COVID vaccines aren’t like aspirin – they require extraordinarily complicated chemistry, advanced production facilities, and tons of experts – even if making generics became legal, it would be nearly impossible to produce them in developing countries**

**Herper** et al **21** [Matthew Herper Senior Writer, Medicine, Editorial Director of Events at STAT. "Waiver of patent rights on Covid-19 vaccines, in near term, may be more symbolic than substantive." https://www.statnews.com/2021/05/06/waiver-of-patent-rights-on-covid-19-vaccines-in-near-term-may-be-more-symbolic-than-substantive/]

That underscores the drug **industry’s case** that patents are just **one facet** of the **complex process** of producing vaccines.

“There are currently **no generic vaccines** primarily because there are **hundreds of process steps** involved in the manufacturing of vaccines, and thousands of **check points for testing** to assure the quality and consistency of manufacturing. One may transfer the **IP**, but the transfer of **skills** is not that simple,” said Norman Baylor, who formerly headed the Food and Drug Administration’s Office of Vaccines Research and Review, and who is now president of Biologics Consulting.

While there are factories around the world that can reliably produce generic Lipitor, vaccines like the ones from **Pfizer and Moderna** — using messenger RNA technology — require skilled **expertise** that even existing manufacturers are having **trouble sourcing**.

“In such a setting, imagining that someone will have staff who can create a new site or refurbish or reconfigure **an existing site** to make mRNA [vaccine] is highly, **highly unlikely**,” Yadav said.

There are already huge **constraints** on some of the raw **materials** and **equipment** used to make vaccines. Pfizer, for instance, had to appeal to the Biden administration to use the Defense Production Act to help it cut the line for in-demand materials necessary for manufacturing.