incubate Policy Lab

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The Impact of Price Controls on Investment into Small Biotech Innovation

About incubate Policy Lab

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Incubate is a 501(c)(4) organization of venture capital organizations representing the patient, corporate, and investment communities whose aim is to educate policymakers on the role of venture in bringing promising ideas to patients in need. The advocacy organization recently launched its research arm, Incubate Policy Lab, which explores various policy initiatives and potential effects on the biopharmaceutical industry. Thank you to our members for their insights and contributions to this report.

Executive Summary

In the US, policymakers have expressed interest in different forms of federal price controls for innovative medicines, which could reduce the amount of biopharmaceutical revenue in the US market significantly. To better understand the potential implications of US government price controls and their effect on investment into early-stage innovation in the US, CRA organized discussions with experts working in the pharmaceutical industry (n=4) and venture capital (VC) firms who invest in small biotech companies (n=6). We find a series of position are shared by both companies and VC companies, leading to a set of policy implications (Table 1).

Table 1: Summary of expert positions and policy implications

Expert positions	*Implications*
1. All forms of price control would be detrimental to innovation, but international reference pricing (IRP) was noted to have the largest impact	IRP would create global implications for access to medicines outside of the U.S., with companies likely choosing to delay or not launch in countries the U.S. included within their reference basket.
2. Price control would first stifle early-stage innovation	Small, entrepreneurial biotech companies that are major contributors to innovation within the industry would be highly sensitive to price control.
3. Innovator behavior would change in response to price controls	Price control policies will shift innovation away from areas of high unmet need towards incremental improvements in therapy areas with lower costs of development and risk of return.
4. Transformational innovation in therapy areas with high unmet need would suffer	Price control policies would have lasting negative effects on transformative innovation and patient access to medicines.
5. The current price control debate is causing market uncertainty and already impacting investment decisions	Early-stage investment decisions are sensitive to pricing policies. Moving the policy focus towards broader health system reforms could also lead to greater investment into innovation.

Background and Objectives

In the U.S., policymakers have expressed interest in different forms of federal price controls for innovative medicines with the objective to control spending. Depending on the scope of the policy, these price controls could reduce the amount of biopharmaceutical revenue in the U.S. market significantly. Incubate asked Charles River Associates (CRA) to investigate the likely implications of price control policies, and the associated reduction in biopharmaceutical revenues, on investment by smaller biotech firms which are a growing source of new innovative medicines.

CRA's approach

To better understand the potential implications of U.S. government price controls and their effect on investment into medicine innovation in the U.S. by smaller biotech firms, CRA organized discussions with experts working in the pharmaceutical industry (n=4) and venture capital (VC) firms who invest in small biotech companies (n=6). Experts were selected to represent VC firms focusing specifically on life sciences investment and both small biotech and large pharma companies with portfolio products across a range or therapy areas. Together, participating experts provided a broad representation across leadership roles within the industry, particularly relating to early-stage innovation.

Discussions were undertaken on a confidential basis and held between June and August 2021 with each interview lasting 45-60 minutes. The interviews covered the impact of price controls in general terms, defined as a system where the federal government takes price setting out of the hands of private industry which currently negotiates with private insurers, and instead establishes the price for branded medicines (or at least a substantial portion of them) centrally. Three mechanisms of price controls were discussed:

1. ***International reference pricing (IRP):*** *sets an upper price limit equal to the minimum, or average price within a basket of reference countries, usually selected for having similar characteristics to the referencing country*
2. ***Value assessment:*** *sets a price limit that references prices based on value assessment frameworks (e.g., ICER is the most prominent framework in the U.S.*[1]*), which include factors such as cost-effectiveness, comparative clinical effectiveness, or budget impact*
3. ***Domestic reference pricing:*** *sets a price limit based on a reference price benchmark or in comparison to other currently available treatments*

We summarize the key findings from the interviews below.

[1] Institute for Clinical and Economic Review (ICER), https://icer.org/our-approach/methods-process/value-assessment-framework/.

Expert Consensus

We find a series of position are shared by both pharmaceutical companies and VC firms:

- **Position 1:** All forms of price control would be detrimental to innovation, but IRP was noted as expected to have the largest impact
- **Position 2:** Price control would first stifle early-stage innovation
- **Position 3:** Innovator behavior would change in response to price controls
- **Position 4:** Transformational innovation in therapy areas with high unmet need would suffer
- **Position 5:** The current price control debate is causing market uncertainty and already impacting investment decisions

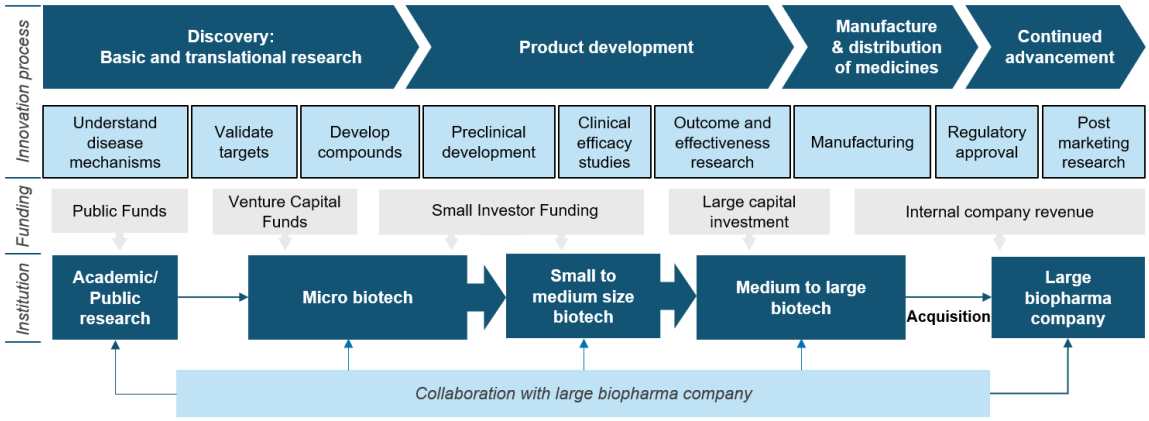
Position 1: All forms of price control would be detrimental to innovation, but IRP was noted as expected to have the largest impact

There was consensus across the experts we interviewed that, while all three forms of price controls would reduce innovation, IRP would be the most detrimental due to lack of nuance in considering the therapy area and clinical traits of certain drugs. Furthermore, IRP would have implications for access to medicines outside of the U.S., with many companies likely choosing to delay or not launch in countries that the U.S. would include within the reference basket. Following IRP, domestic reference pricing was considered the second most harmful form of price control. VC representatives noted that since domestic reference pricing can involve price comparison to currently available treatments, it is especially detrimental to venture investment, which is typically focused on transformative innovations and for which there are no relevant comparisons and comparisons might be made to generics in current medical practice. Traditional value assessment approaches also tend to undervalue the benefit of medicines; however, respondents considered this form of price control the least detrimental due to the ability to inform the assessment with data and evidence to better capture the holistic benefit of new medicines.

Position 2: Price control would first stifle early-stage innovation

Experts interviewed highlighted that the effects of price controls would be first felt by smaller biotech firms. This means that innovation at the early stage of the development pathway (**Error! Not a valid bookmark self-reference.**) would be disproportionately impacted by price controls.

Figure 1: The healthcare value chain for biotech innovation



Source: CRA analysis

Interviewees highlighted that small biotechs need to be able to articulate the potential for meaningful returns in order to be attractive to VC. The return to VC is often predicated on a transaction with larger pharma companies with the transaction price determined by the future value of the asset, which is directly linked to the potential for commercial market sales. Price controls would be likely to have the biggest impact on high-risk innovative medicines that have few current alternatives, therefore decreasing the transaction price for innovation between large pharma and small biotech. This could significantly reduce investment by VC in smaller biotech companies. There was broad agreement among experts that early-stage innovation is particularly sensitive to price controls. A VC representative noted that, while there is a perception of high prices within the pharmaceutical industry, pharmaceutical portfolios are considered to be higher risk than other industry portfolios. This may explain why although VC deals in the healthcare sector have been steadily increasing over the past 20 years, growth has been relatively slower compared to VC deals in other sectors.[2]

In addition, a pharma representative noted there is considerable uncertainty. Only after approximately 10 years from when the policy is implemented would there begin to be sufficient data to measure the effects of price control legislation and the impact on innovation.

Position 3: Innovator behavior would change in response to price controls

VC experts interviewed noted that the impact of price controls would vary depending on the focus of a VC firm. Generalist VC firms, which invest in several sectors, would eventually shift to tech and other industries outside biopharma offering higher rewards or focus investment on products unlikely to be as affected by a price control policy. VC firms that specialize exclusively in the life sciences and cannot as easily switch industries would instead choose to invest less in transformative, high risk therapies.

Experts noted that larger pharma companies would respond to a price-controlled market

[2] Chandra, A., Foroughi, C. & Mostrom, L. "Venture Capital Led Entrepreneurship in Health Care," NBER Chapters, January 29, 2021, https://www.nber.org/system/files/chapters/c14383/c14383.pdf.

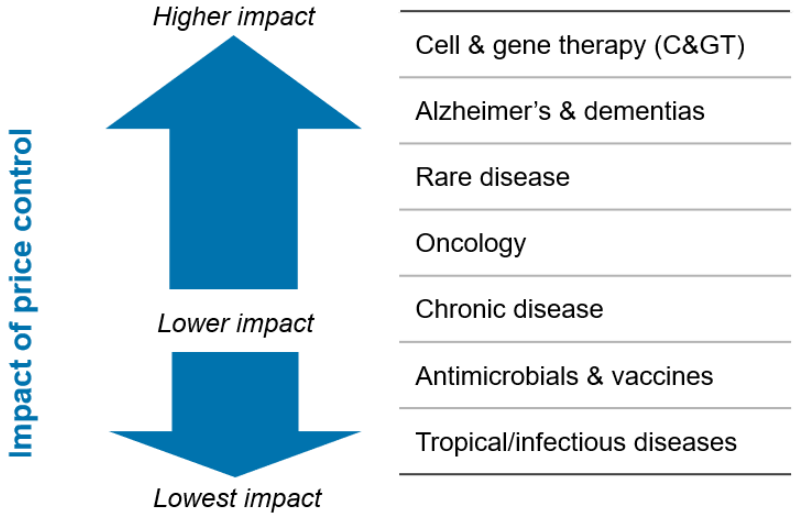
by cutting R&D budgets or shifting away from transformative to less expensive, lower risk R&D. As discussed above, a decline in large pharma R&D budgets would lead to less willingness to invest in smaller biotechs. This would result in reduced investment by VCs. As a result, the size of the biotech sector of the industry would decrease, perhaps substantially, under a regime of price controls.

Proponents of price control suggest that savings to federal medicine spending could be redirected into public investment in R&D, making up for any private investment lost from price controls.[3] However, experts highlighted that the public sector would lack the capacity and ability to make up for the shrinking biotech sector. The industry experts we interviewed warned that despite the important role of public agencies such as the National Institute of Health (NIH) within the Department of Health and Human Services (HHS), the Department of Defense (DOD) and private academic institutions in the innovation pathway, knowledge translation from basic science to product regulatory approval and distribution requires a tolerance for risk that is incompatible with public institutions and academic centers. This risk is considerable given that 80–90% of interventions that are tested in humans for the first time are never approved.[4] The result is that with price control legislation, the number of new medicine approvals would decline.

Position 4: Transformational innovation in therapy areas with high unmet need would suffer

The experts we interviewed stated there would be a differential impact from price controls on certain therapy areas. As summarized in Figure 2, experts noted that the required investment within a given therapy area and related impact of price control is affected by the difficultly in translating basic science into early-stage discovery, the cost of late-stage development (as a result of the likelihood of clinical trial success), and the market potential post-approval, considering patent life and population size.

Figure 2: Impact of price controls on innovation by drug class, along the innovation lifecycle



[3] Robinson, J.C. "Funding of pharmaceutical innovation during and after the COVID-19 pandemic," January 14, 2021, *JAMA*, 325(9):825–826, https://jamanetwork.com/journals/jama/fullarticle/2775400.

[4] Dowden, H., & Munro, J. "Trends in clinical success rates and therapeutic focus," *Nature reviews. Drug discovery,* May 8, 2019, 18(7), 495–496. https://doi.org/10.1038/d41573-019-00074-z.

Source: CRA interviews with large pharma, biotech and VC representatives

Experts highlighted that **cell & gene therapies (C&GTs)** often developed to treat oncology and rare disease, tend to be transformative therapies with higher prices. There are significant challenges in late-stage development from manufacturing and distribution, with C&GTs facing a much smaller profit margin than some small molecule therapies, such as chronic disease. C&GTs require sufficient returns to reward high scientific risks and high cost of development that recognize the value of a curative promise within typically small patient populations. For these reasons, experts stated C&GTs would be most impacted by price control policy and face reduced investment, especially in disease areas for which there are non-gene therapy treatment alternatives.

With **Alzheimer's** and other dementias, knowledge gaps exist within basic and translational research.[5] Due to the high failure rates inherent in the discovery and development of new medicines in this therapy area, price control policy that limits the size of reward, would result in fewer new treatments or cures for Alzheimer's and other dementias. However, due to potentially large population sizes, as well as significant unmet need, investment into therapies for Alzheimer's and other dementias areas may remain attractive. Furthermore, even in a potentially large therapeutic area like Alzheimer's there may be medicines with potential for a subset of the population that would be less commercially viable in a price-controlled environment.

Experts perceive a medium impact of price control **on oncology and rare disease** (outside of G&CTs) innovation because of relatively lower development costs, such as smaller clinical trial sizes. Oncology often has a large volume of patients in need of treatment and for rare diseases, supportive policies such as the Orphan Drug Act have created commercial opportunities for innovation. For these reasons, commercialization, though still challenging, would to be expected to have a relatively lower impact from price controls compared with C&GTs and Alzheimer's Disease.

Price control is expected to have a lower impact on **mass market chronic disease** categories relative to other therapy areas discussed. Experts interviewed highlighted that the science around the ability to treat is well developed for symptomatic treatments within this category. Therefore, price controls may cause a shift to incremental over transformational innovation, such as changes to route of administration or dosing intervals. This type of innovation has a higher likelihood of success as it involves making changes to therapeutics for which the science or mechanism of action has already been proven to be effective.[6] However, even in this case, the search for a transformative cure, a more challenging form of innovation, continues and becomes even higher-risk relative to incremental innovation. The drive for such transformative innovation would be reduced.

Finally, experts noted that there remains significant unmet need in **antimicrobials and vaccines and infectious and tropical diseases.** The lack of innovation in these therapy areas is linked to the limited commercial viability: novel antimicrobials are saved

[5] Mauricio, R., Benn, et al., Therapeutics for Dementia Consortium, "Tackling gaps in developing life-changing treatments for dementia," *Alzheimer's & dementia* (New York, N. Y.), June 25, 2019, 5, 241–253, https://doi.org/10.1016/j.trci.2019.05.001.

[6] Pammolli, F., Magazzini, L. & Riccaboni, M. "The productivity crisis in pharmaceutical R&D," *Nature reviews. Drug discovery*, June 1, 2011, 10, 428–438, https://doi.org/10.1038/nrd3405.

as a last resort and are therefore used in few patients. Infectious and tropical disease medicines are typically used in low- and middle-income countries that cannot afford or lack cohesive healthcare systems to pay value-based prices. Experts highlight that even though the impact may be less, these therapy areas would be further harmed by the implementation of price controls.

Position 5: The current price control debate is causing market uncertainty and already impacting investment decisions

Uncertainty and market size impact investment decisions.[7] In our discussions, there were different opinions as to whether the risk of price controls is already being incorporated into business decisions. One pharma representative noted that they had already observed volatility in the market for biotech acquisitions and partnerships over the first half of 2021 due to the policy debate on price control. VC representatives noted that VCs watch public markets, but most have not historically considered the impact of legislative changes in their investment decisions until after a bill is passed. However, the current debate is unprecedented and VC decisions are not immune to influence from the current policy debate: one VC representative shared a recent decision they had made to not invest in a potential cure for an ultra-rare disease due to the risk of price control legislation being implemented and reducing the potential return on funding of the product.

[7] Acemoglu, D. & Linn, J. "Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry," *The Quarterly Journal of Economics*, August 1, 2004, 1049–1090, https://doi.org/10.1162/0033553041502144.

Conclusions from Expert Interviews

Policy discussions about price controls often consider the impact on large pharmaceutical companies - the most visible stakeholder in the medicine development industry. The policy debate generally neglects assessing the potential impact of price control on the smaller development-stage biotech companies who are a significant contributor to the innovation of new medicines. CRA conducted interviews with representatives from large pharma, VCs and biotechs familiar with investment decisions to understand the potential impact of price control in the U.S. on the innovation ecosystem. Interviews revealed the consequences of price controls:

- **International Reference Pricing would be the most detrimental form of price control discussed.** All forms of price control would harm innovation, however IRP would create global implications for access to medicines outside of the U.S., with many companies likely choosing to delay or not launch in countries that the U.S. included within their reference basket.
- **Small, entrepreneurial biotech companies that are major contributors to innovation within the industry would be highly sensitive to price control.** These companies would face reduced investment from VC and large pharma. Over time, this would reduce the number of biotechs.
- **Price control policies would shift innovation away from areas of high unmet need towards incremental improvements in therapy areas with lower costs of development and lower risk of return.** There would be a reduction in investment from large pharma and VC in small biotechs and valuations for high-risk innovative treatments and there would be an investor preference for less risky development. The development of transformative and potentially curative treatments would decline. This effect would be counter to supportive policies which aim to encourage transformative innovation.
- **Price control policies would have lasting negative effects on transformative innovation and patient access to medicines.** The industry operates in ten-year cycles; therefore, the full effects of price control legislation would persist in the long-term. Ultimately, this would lead to large reductions in new product launches in the market. Policymakers should consider the long-lasting implications of price control on future health and therapeutic advances.
- **Early-stage investment decisions are sensitive to consideration of pricing policies.** Experts noted that investment decisions are already being affected by price control proposals. This suggests that capital for VC investment for new innovations are at risk. Policymakers should consider policy options which

do not compromise a stable market for innovation while providing broad access to medicine.

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