

The Bioethical Problems in Applying the Defense Production Act to Pharmaceuticals: A Case Study of Horizon's Tepezza

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INTRODUCTION

Since the start of the COVID-19 pandemic, there have been calls for the President to invoke a Korean-war-era law, the Defense Production Act ("DPA"), to effectively nationalize the supply of critical medical supplies (e.g., N-95-grade masks, ventilators) and speed up vaccine production. The reasoning for employing the DPA is simple: it can immediately ramp up the industrial production of critical supplies and material resources and direct their distribution to areas of greatest need.¹ The Trump administration used the DPA 18 times to aid vaccine development.² The Biden administration has followed suit, invoking the DPA in February.³ While the Defense Production Act has enabled a massive mobilization of crucial resources for vaccine development, it has also had negative, downstream effects, which raise ethical concerns surrounding resource allocation. Evaluating the effect of the DPA on Tepezza (teprotumumab-trbw; Horizon Therapeutics), a non-COVID-19 medication, demonstrates how the DPA is not adequately designed to address pharmaceutical manufacturing, and point to a potential need for further legislation.

ANALYSIS

By its nature, the DPA is a very blunt and fast-moving instrument that should be used sparingly. Originally signed into law by President Truman at the outset of the Korean War in 1950, the DPA gives the President the authority to order private sectors to produce essential goods in times of emergency.⁴ In particular, it allows the President to compel corporations to immediately prioritize orders from the federal government irrespective of previously agreed-upon contracts. The typical rules of supply and demand economics are overridden, and legally binding agreements are nullified. Thus, the power of the DPA facilitates its ability to redirect resources in a swift, absolute manner.

Over the years, the general scope of the DPA has steadily extended beyond military preparedness to include natural disasters and homeland security. In January 2001, both President Clinton and President G. W. Bush invoked DPA powers to ensure that emergency supplies of electrical power and natural gas continued

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flowing to California utilities during the 2000 - 2001 energy crisis.⁵ In 2017, the Federal Emergency Management Agency (FEMA) used the DPA to prioritize contracts for food, bottled water, and the restoration of electrical systems after Hurricane Maria struck Puerto Rico.⁶

December 2020 had a record number (65,000) of US COVID-19 deaths and over 118,000 COVID-19 patients in U.S. hospitals.⁷ Vaccines were still predominantly being allocated to healthcare workers and residents of long-term care and assisted living facilities. While the federal government created demand for COVID-19 vaccines by contracting with pharmaceutical and manufacturing companies, vaccine supply remained low. Private companies needed more time to alter their production schedules and get out of existing contracts before they could fulfill the government contracts. The government invoked the DPA to expedite vaccine production, enabling companies to break existing contracts and start production.

On December 17, 2020, Horizon Therapeutics, a biopharmaceutical company, announced that its drug Tepezza would experience a serious supply shortage⁸ due to the abrupt cancellation of manufacturing slots at Horizon's sub-contractor Catalent Pharma Solutions. Catalent, a drug manufacturer, packager, and distributor, was also a producer of Moderna's new COVID-19 vaccine, manufacturing both Tepezza and the Moderna vaccine on the same production line. Operation Warp Speed, used the DPA to direct the immediate reallocation of Catalent's manufacturing slots to Moderna.⁹

The abrupt disruption of Tepezza production had a "dramatic effect" on patients.¹⁰ Tepezza is the only FDA-approved medication to treat adults with Thyroid Eye Disease (TED), also known as Graves' Ophthalmopathy, a rare autoimmune condition wherein the muscles and fatty tissues behind the eye become inflamed, causing the eyes to push forward and bulge outward. Symptoms include eye pain, light sensitivity, difficulty closing the eye, and, in severe cases, blindness.¹¹ While TED impacts a small number of individuals, the disease can be incapacitating, preventing individuals from performing important daily activities, like driving or working. On the prescribed course of treatment for TED, patients take a total of eight intravenous injections of Tepezza, one every three weeks.¹² When supplies were disrupted, some patients stopped receiving Tepezza in the middle of treatment. While the effects of stopping midway are unknown, symptoms may worsen during the hiatus or premature stoppage. People who had not yet begun treatment had to delay starting, sometimes remaining in pain and risking vision loss from optic nerve compression. To alleviate symptoms, some patients may have opted for eye surgeries instead of waiting for Tepezza.¹³

When the federal government invoked the DPA, it inadvertently put two interests at odds with each other – providing medication for a rare but serious disease and speeding up vaccination rates against the coronavirus. Prior applications of the DPA affected the supply and demand of machinery and raw materials – not pharmaceuticals, which have a direct and immediate impact on human health. In 1967, for instance, President Johnson invoked the DPA requiring Chrysler to prioritize production of the M1 Abrams Tank, the Army's new main battle tank, over cars. Around the same time, President Johnson also used the DPA to expand chemical plants' production of herbicides, such as 2,4,5-T and 2,4-D, to make Agent Orange.¹⁴ Most recently, the Trump administration used the DPA to require GE and 3M to prioritize the production of critical medical equipment (e.g., ventilators, personal protective equipment).¹⁵ None of these examples impacted access to pharmaceuticals.

There are, however, significant ethical issues at stake in the use of the DPA to abruptly alter pharmaceutical manufacturing, even temporarily. Catalent was just one of many Moderna COVID-19 vaccine manufacturers. The number of doses of Tepezza needed to supply patients was small given the low prevalence of TED. An investor reported that if Horizon had access to the facility for even a few hours, it

could have met the demand.¹⁶ If Operation Warp Speed had worked more closely with Horizon Therapeutics and asked Catalent to briefly make additional doses given its short manufacturing time, the negative effects on patients with TED could have been avoided.

But the DPA, by design, approaches an emergency from a utilitarian perspective, rapidly redirecting resources to achieve the greatest good for the greatest number of people. A significant portion of the American population, including Tepezza's patient population, was at risk of contracting the coronavirus and experiencing severe symptoms, and the DPA order had the potential to save many lives. But pharmaceutical supply chains are complex, fragile, and highly time sensitive. A sudden disruption can have a significant, long-lasting effect on patients' health. We need to be cognizant of these ethical issues and weigh competing claims before proceeding. The decision to employ the DPA to take over the assembly line of Tepezza resulted in *de facto* rationing of supplies without proper ethical analysis. During the COVID-19 pandemic, we have been fortunate that the DPA did not do more damage to the supply chains of life-saving drugs.

CONCLUSION

We should reconsider whether the DPA, in its current form, should apply to the pharmaceutical industry. The government should carefully analyze the ethics before redirecting pharmaceutical production. Instead, the federal government should create a different process in the DPA, which I call the "Pharmaceutical DPA", for assessing when to divert pharmaceutical production, perhaps with a goal of preserving the ability to produce drugs for serious illnesses, even if the illnesses are rare. While a pharmaceutical DPA could still compel pharmaceutical and manufacturing companies to prioritize government contracts and break pre-existing contracts, the companies should have more latitude to decide *when and how* to start complying with the DPA's directives. With a new two-tiered law, the federal government would have the ability to redirect non-pharmaceutical resources as it does currently and pharmaceutical ones in a way that gives a limited amount of discretion to pharmaceutical companies. Given that so many excess doses of the vaccine remain unused,¹⁷ arguably the diversion of resources away from Tepezza did not effectively further the government's target vaccination goals due to a decision by many people not to receive the vaccine.

Production of Tepezza resumed in April 2021, not because the DPA was lifted, but because Horizon submitted a prior approval supplement (PAS) to the Food and Drug Administration (FDA) to support the increased scale production of Tepezza by other manufacturers.¹⁸ Although the short-term supply shortage has been corrected, the case of Tepezza shows that the DPA needs to be carefully reconsidered in the context of the pharmaceutical industry because of the potential consequences to patients. If the DPA were flexible enough to allow Catalent to manufacture Tepezza for a few more hours in total, the company could have avoided the shortage. The creation of a pharmaceutical DPA would prevent this from happening in the future, enabling the original Act's provisions to be used more like a scalpel than a blunt instrument.

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⁹ Kansteiner, F. “Horizon’s Tepezza supply dwindles as manufacturer Catalent pivots to Warp Speed vaccines” Fierce Pharma (2020), accessed July 23, 2021, <https://www.fiercepharma.com/manufacturing/horizon-faces-tepezza-disruptions-as-manufacturer-catalent-tapped-for-warp-speed>

¹⁰ Kuchler, H. “Push to make Covid vaccines causes US drug shortages,” Financial Times (2021), accessed July 22, 2021, <https://www.ft.com/content/b3ac261e-2675-4679-9356-53aa6d812ad7>

¹¹ “FDA approves first treatment for thyroid eye disease,” FDA (2020), accessed July 22, 2021, <https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease>

¹² “Tepezza Dosing and Administration” Tepezza, accessed July 23, 2021, <https://www.tepezza.com/hcp/tepezza-dosing-and-infusion-information>

¹³ It should be noted that there are currently no academic sources on the effects of the Tepezza shortage to the TED patient population.

¹⁴ Bell, D. “‘A Little-known Bill of Great National Significance’: The Uses and Evolution of the Defense Production Act, 1950 – 2020,” US Army Heritage and Education Center (2020), accessed September 23, 2021, https://ahec.armywarcollege.edu/documents/Defense_Production_Act_1950-2020.pdf

¹⁵ “Applying the Defense Production Act,” FEMA (2021), accessed September 23, 2021, <https://www.fema.gov/press-release/20210420/applying-defense-production-act>

¹⁶ Author personally attended a small group conversation with the investor and attests to the accuracy of the statement.

¹⁷ Eaton J., Murphy, J. “15 million Covid vaccine doses thrown away in the U.S. since March, new data shows,” NBC News (2021), accessed October 1, 2021, <https://www.nbcnews.com/news/us-news/america-has-wasted-least-15-million-covid-vaccine-doses-march-n1278211>

¹⁸ “Statement on TEPEZZA® (teprotumumab-trbw) Availability,” Horizon (2021), accessed July 22, 2021, <https://www.horizontherapeutics.com/media-center/horizon-resources/statement-on-short-term-tepezza-supply-disruption>