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Recapturing the Orphan Drug Act: An Analysis of Proposals

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RECAPTURING THE ORPHAN DRUG ACT: AN ANALYSIS OF PROPOSALS

I. INTRODUCTION AND BACKGROUND

On January 4, 1983, President Ronald Reagan signed into law the Orphan Drug Act ("ODA").[1] The ODA would later become a model for similar acts around the world, as various countries tackled the problem of orphan diseases.[2] "Orphan" diseases are rare diseases whose low prevalence has caused drug companies to "orphan" them because the effort and financial resources required to research, develop, and treat them are simply not profitable.[3] The Orphan Drug Act sought to remedy this problem by providing financial incentives to pharmaceutical companies that developed treatments for orphan diseases, thereby developing the eponymous "orphan drugs." The ODA provided two major incentives: seven-year market exclusivity that was stronger than standard intellectual property protections such as patents and a tax credit for 50% of the clinical trial costs.[4] Thus, pharmaceutical companies would have a monopoly over any treatments they developed for orphan diseases, as well as lower market entry costs. Because of the first-mover advantage for diseases that would not likely yield profit without the tax credit, this monopoly had a high chance of persisting beyond the statutory window. The initial and potential persistent monopolies did come with the standard monopoly concerns of price gouging, lack of competitive innovation to provide better solutions, etc. However, the monopoly also made for a very potent incentive. Furthermore, the tax *credit*, rather than a tax *deduction*, was calculated based off an extremely expensive step in bringing a drug to market, thus providing significant reductions in tax burden for these pharmaceutical companies. This paper will not focus on the history of the ODA but will provide a brief overview so as to give context to the incentive analysis that follows.

1. Barbara Andraka-Christou, *Policy Process Lessons from the Orphan Drug Act: Applications for Health Policy Advocates*, 4 J. ENTREPRENEURSHIP & PUB. POL'Y 278, 278–97 (2015).

2. *Id*.

3. *Id*.

4. *Id*.

Before the Bill

The ODA did not easily reach the President's desk to be signed into law. Patient-activist organizations such as the National Organization for Rare Disorders ("NORD") came to realize that while academics were doing research into cures for rare diseases, those diseases were not of any interest to the pharmaceutical companies. Working together, they decided to focus on the goal of pressuring Congress to make pharmaceutical companies bring drugs for rare diseases to market. They began, without the support of the pharmaceutical companies, lobbying Congress and engaging in public relations campaigns. Pharmaceutical companies pushed back, and initially proposed legislation stalled. Then, by moving to an incentive-driven approach, the activist organizations were able to bring pharmaceutical companies on board. By bringing national attention to the issue via television and newspaper, the organizations helped create the necessary political climate for Representative Henry Waxman of California to propose the legislation that would become the Orphan Drug Act. Republicans in the Senate pared down the benefits, but the bill was passed.[5]

Legal scholars have examined the Orphan Drug Act from the perspective of various policymaking frameworks. Klingon's Multiple Streams theory is the oldest such lens through which we can analyze the ODA.[6] According to the theory, there are three "streams" that flow through a policy system: problems, policies, and politics. A "policy entrepreneur" can, during a "policy window," bring these three streams together to implement a policy. When looking at the ODA in this way, legal scholars have shown that identifying the problem as a market failure for orphan drugs rather than that pharmaceutical companies were "heartless" was much more likely to succeed. The policy most likely to be successful was thus a market-based and incentive-generating proposal built by specialists at advocacy groups like NORD and pharmaceutical company lobbyists. Lastly, the politics around the situation were influenced by the media attention and politicians' desire to help their constituents and be reelected. This meant that the three streams could come together with NORD as the policy entrepreneur taking advantage of media attention in television dramas, etc. to ensure the policy was implemented.[7]

5. *Id*.
6. *Id*.
7. *Id*.

The Advocacy Coalition Framework is another framework through which legal scholars can seek to understand how policies come to pass. This framework suggests that policymaking occurs when specialists in different subsystems come together to make coalitions that tackle complex problems.[8] These specialists are necessary because of the intricacies of modern policymaking, and they will negotiate and struggle with one another due to deep core beliefs that vary across subsystems. In the case of the ODA, the relationship between the government, advocacy groups like NORD, and the pharmaceutical companies formed the coalition. By negotiating and focusing on the shared core beliefs, the three parties were able to generate a policy.

Social Constructionism Theory suggests that policymakers distribute benefits and burdens in accordance with how they've sorted people and entities into various groups.[9] The theory posits that the main groups are: (1) "advantaged" groups with significant power who are deserving of benefits because of what they provide to society; (2) "contender" groups with significant power and influence who are undeserving of benefits due to not needing them or not providing significant social value as a result of those benefits; (3) "dependent" groups who have little power or influence and yet are deserving due to misfortune, sympathy, etc.; and (4) "deviant" groups who are low-powered and undeserving such as criminals or other groups considered a permanent underclass by society. In the case of the ODA, the people with rare diseases are "dependent," but it took shifting the pharmaceutical companies from "contender" to "advantaged" to make the policy successful.

After the Signing

At its signing, the Orphan Drug Act included guidelines to the FDA for what qualified as an "orphan" disease. Originally, there was only one criterion for designation as orphan: "disease or condition which occurs so infrequently in the United States that there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug."[10] In 1984, very soon after the passing of the ODA, Congress passed an amendment, adding a second criterion: diseases

8. *Id*.

9. *Id*.

10. Matthew Herder, *What is the Purpose of the Orphan Drug Act?*, 14 PLOS MED. (Jan. 3, 2017), https://doi.org/10.1371/journal.pmed.1002191.

with a prevalence of under 200,000 individuals within the United States.[11] Since this amendment, virtually all drugs developed for orphan diseases qualified under this criterion.[12]

Due to concerns that the prevalence-based criterion was being abused in order for "Trojan" orphan drugs (orphan drugs that do not necessarily deserve their status), the FDA moved in 1991 to increase the rigor of qualifications.[13] The 1991 proposed regulations were meant to address "salami slicing," a practice wherein the pharmaceutical company would very strictly define the limits of a disease, or subdivide the disease into multiple different classifications, in order to ensure that the prevalence was under the 200,000 brightline, thus granting the drug in development orphan drug classification.[14] The proposed regulations stated that a subset of a common disease or condition "would qualify for designation only if the subset is medically plausible" and that "'arbitrary' subsets would be unacceptable."[15] In 1992, however, the regulations offered little clarity or definition on "medically plausible" and completely dropped the "arbitrary" restriction.[16] Due to this lack of clarification, this regulation did not appreciably change the situation, which the FDA later acknowledged.[17]

The next attempt to regulate overuse of the ODA was in 2013.[18] This next round of regulation began by acknowledging the failures of the "medically plausible" guidelines and removed the term from the guidelines.[19] Instead, the FDA's Final Rule sought to define the orphan subset in such a way that nonrare diseases or conditions could not be "artificially subdivided" into smaller groups for designation.[20] There was some initial academic concern, though analyses suggested that the new, more rigorous definition provided reason to be optimistic.[21] Unfortunately,

11. *Id*.
12. *Id*.
13. Shannon Gibson & Barbara von Tigerstrom, *Orphan Drug Incentives in the Pharmacogenomic Context: Policy Responses in the US and Canada*, 2 J. LAW BIOSCI. 263, 263–91 (2015).
14. Herder, *supra* note 10.
15. Gibson & von Tigerstrom, *supra* note 13, at 269.
16. *Id*.
17. *Id*.
18. *Id*.
19. *Id*.
20. *Id*.
21. *Id*.

later empirical analysis has suggested that the new regulation was not as helpful as the FDA had hoped, and artificial "salami slicing" persisted.[22]

Congress notably sought to remedy abuse of the Orphan Drug Act at two points after the 2013 updated regulations. The 2017 Tax Cuts and Jobs Act ("TCJA") cut the tax credit from 50% to 25% of clinical trial costs.[23] This measure was opposed, unsurprisingly, by pharmaceutical companies and interest groups lobbying on behalf of individuals with rare diseases.[24] A few years later, the House passed a version of the Build Back Better Bill, which included an amendment to the Orphan Drug Act.[25] It restricted the application of the tax credit only to the first orphan use of the drug.[26] However, the Senate version has not passed, and while orphan drug credit reform was considered for the Inflation Reduction Act, there was nothing passed beyond an exception to drug negotiation provisions for orphan drugs.[27] Consequently, the current status quo is a post-TCJA number with the existing 2013 regulation from the FDA and an increased incentive to classify nonorphan drugs as orphan drugs to avoid the negotiation provisions.

The ODA Today

Drug companies and advocacy groups for rare diseases consider the ODA a success.[28] Since its passing, over 400 orphan drugs have been brought to market.[29] In recent years, the numbers have increased, with the FDA estimating that nearly 200 drugs enter development for orphan drugs each year, and one third of FDA approvals are for orphan diseases.[30] Some academics have also cited the Orphan Drug Act as spurring innovation in treatment and therapies.[31]

22. Herder, *supra* note 10.

23. Christopher Gerry, *Risky Business: The Far-Reaching Consequences of Slashing the Orphan Drug Tax Credit*, SCI. NEWS. (Jan. 8, 2018), https://sitn.hms.harvard.edu/flash/2018/risky-business-far-reaching-consequences-slashing-orphan-drug-tax-credit/.

24. *See id.*

25. Rohan Narayanan, *NORD Response to New Draft of the Build Back Better Act*, NAT'L ORG. FOR RARE DISORDERS (Oct. 29, 2021), https://rarediseases.org/nord-response-to-new-draft-of-the-build-back-better-act/.

26. *Id*.

27. 42 U.S.C. § 1320f-1(e)(1)(A).

28. Gibson & von Tigerstrom, *supra* note 13.

29. *Id*.

30. *Id*.

31. *Id*. at 264.

Some, especially those in academic circles, though, are more skeptical. Critics of the ODA in its current state contend that the ODA does not actually provide the incentives it purports to. Because of this contention, they argue the drugs would have been developed even without what the ODA provides.[32] Many of the drugs developed under the umbrella of this ODA have been incredibly profitable, such as Provigil, Crestor, or Humira. Furthermore, empirical research has shown that the ODA is unable to reach a variety of genuinely rare diseases.[33] Together, this raises concerns of price gouging on the part of the pharmaceutical companies due to having a small captive market while simultaneously benefiting from government funding meant to help those people, not exploit them and their condition. Henry Waxman, the original author of the ODA, has since expressed regret and remorse that the ODA has been used to enrich pharmaceutical companies while many rare diseases languish and remain underserved.[34]

Additional criticism has been raised with respect to how the ODA interacts with the market. The market discourages certain types of research, such as that performed to benefit pregnant women, minority, and underserved groups; diseases that are unlikely to impact an American market; etc. Critics have pointed out that the ODA neglects the potential social welfare gains of funding for these situations.[35] The ODA also does not engage with the severity, morbidity, or transmissibility of diseases when establishing orphan status; these are also points of criticism.[36]

II. ANALYSIS

Equity

The ODA has a number of equity concerns, both in broad concerns about burdens and benefits, as well as traditional forms of equity analysis along vertical and horizontal axes. The fundamental question is whether it is appropriate for the government, and for society as a whole, to pay to save people with rare diseases. This paper argues that yes, the general

32. Herder, *supra* note 10.

33. Aaron S. Kesselheim, *Biomarker-Defined Subsets of Common Diseases: Policy and Economic Implications of Orphan Drug Act Coverage*, 14 PLOS MED. (Jan. 3, 2017), https://doi.org/10.1371/journal.pmed.1002190.

34. Michael J. Berens & Ken Armstrong, *Pharma's Windfall: The Mining of Rare Diseases*, SEATTLE TIMES (Nov. 9, 2013), https://apps.seattletimes.com/reports/pharma-windfall/2013/nov/9/mining-rare-diseases/.

35. Herder, *supra* note 10.

36. *Id*.

social benefits such an investment provides makes the general principle behind the ODA worthwhile. Caring for those with rare diseases is a form of the government's obligation to care for the less fortunate and disadvantaged. Additionally, research into rare diseases can have beneficial externalities. Pharmaceuticals can often be cross applied to different diseases as we learn more and as diseases develop. This means that the initial steps to bring an orphan drug to market can actually help many people beyond just that specific subset. As diseases change and new threats evolve, an arsenal of knowledge and options about a variety of treatments is generally helpful. This base of knowledge can also aid if the orphan disease is substantively related to a prevalent new disease, thus providing a more concrete foundation for treatment. Lastly, our Constitution does include an interest in promoting science; research into otherwise unprofitable drugs certainly advances this goal.[37]

In a burden/benefit analysis, the initial questions are: (1) who bears the burden in this situation, and (2) is that burden equitably distributed? In this case, pharmaceutical companies make substantial or even, to some, excessive amounts of profit; operate thanks to the human capital and infrastructure of this country; and rely on the public goodwill to at least some degree. Thus, they have at least some capacity to bear the burden of the cost of development for these rare drugs for the good of the society supporting them. Currently, the burden is borne by the public in aggregate. The Treasury, in 2021, estimated that the tax expenditure for the tax credit in the year 2022 was $1.72 billion, and $55.26 billion over ten years.[38] Despite being a comparatively small tax expenditure in the grand scheme of the budget, it is still money that is not going to the government that represents the public but rather going to private entities who have substantial wealth.

As for benefits, the ODA as written certainly benefits specifically the people with rare diseases, as they are much more likely to have therapies developed to treat them. As previously discussed, the ODA as written does not provide enough incentive to help *all* people with rare diseases, but it does also have some spillover benefits to society at large. Furthermore, individuals do not exist in a void. They have work connections, family connections, and social connections. Improving their quality of life provides financial, emotional, and spiritual benefits to this greater societal web. It benefits the pharmaceutical companies in that their costs of

37. U.S. CONST., art. 1, § 8, cl. 8.

38. U.S. TREASURY, *Tax Expenditures*, https://home.treasury.gov/policy-issues/tax-policy/tax-expenditures (last visited Nov. 18, 2022).

production are offset, as well as rehabilitating their public image from that of a "contender" to "advantaged" under social constructionism theory.[39] They receive the goodwill from bringing the drug to market. The government and the politicians that make up the government benefit because they fulfill their burden to take care of disadvantaged groups, satisfy interest groups, and promote economic growth by introducing a stimulus. Furthermore, they can "outsource" some of the administrative burden of caring for people with rare diseases to the pharmaceutical companies, since they do not have to institute a state-run development. Thus, the ODA can be considered a win-win-win from a benefit perspective. Taken together, this means there are fairly widespread benefits that can be argued to outweigh the burdens shouldered by the public.

Further equity analysis requires an examination of horizontal and vertical equity. Horizontal equity in this situation can be between various pharmaceutical companies and various members of the public. Between pharmaceutical companies, there can be concerns around horizontal equity *between* companies. This measure certainly rewards drug companies who are well equipped or interested in rare diseases rather than drug companies who are not. Because it is a percentage-based tax credit, the amount of money recompensated to each company will also vary. However, this mitigates concerns about vertical equity between different orphan drugs that are harder or easier to develop; the abilities of bigger companies to handle difficulties cheaply, which smaller companies cannot; etc. It can be argued these equity concerns generally outweigh the horizontal equity concerns; if companies wish to also take advantage of this credit, nothing is stopping them from stepping in to aid patients in need.

The concerns of patients in need are also a matter of horizontal and vertical equity. There is a question about horizontal equity between patients: do patients in the same situation receive the same results? The ODA's tax credit itself does not push an equitable result between two patients with different rare diseases that have relative parity in said disease's nature. However, the ODA as a whole does because if a drug is developed for Patient A with Disease A, there is exclusivity for that treatment and companies are thus more likely to look to Patient B with Disease B. Since Diseases A and B have rough parity, the profit analysis that leads to a drug being developed for A suggests such a drug would also be developed for B. This theoretically achieves horizontal equity.

39. Andraka-Christou, *supra* note 1.

The ODA certainly promotes vertical equity from many perspectives. It promotes vertical equity between rare and nonrare diseases. Because rare diseases are less likely to be profitable and have less influence due to less prevalence, they are comparatively disadvantaged. Thus, aiding them is a positive move for vertical equity. The proportional nature of the tax credit also incentivizes vertical equity in that comparatively expensive to develop drugs are attractive as they will theoretically have the highest reduction on the company's tax burden. It also provides a positive effect on vertical equity in society as a whole; we are caring for the disadvantaged. The ODA also somewhat promotes vertical equity between the needs of patients because of the exclusivity doctrine: if the easiest diseases are covered by exclusivity, the harder diseases will be much more attractive.

The ODA is not perfect when it comes to vertical equity, however. It does not provide any *additional* credit beyond the proportional credit to extremely disadvantaged rare diseases. Thus, those diseases are highly likely to be left behind when they are the ones in most need. By providing a captive market and a lack of competition for the people in need, it leaves them vulnerable to additional burdens like price gouging or a lack of competition and innovation to make competing drugs. Also, it is not necessarily vertically equitable on a societal level: there is no consideration as to the socioeconomic standing of the population that tends to have rare diseases that drug companies focus on. There is no guidance to suggest that diseases frequent among wealthy people, men, white people, certain geographic areas, and other similarly privileged groups are not going to be preferred by drug companies. Lastly, as shown by the benefit and burden analysis, there can be vertical equity difficulties because the advantaged, wealthy, profit-motivated pharmaceutical companies are receiving a benefit on the backs of the less-advantaged public.

Overall, the potential and already demonstrated good that comes from the ODA and the commitment to care for those in the most need tip the scale for me in this equity analysis. The government seems to have agreed in implementing the measure, though that does not preclude efforts to increase equity of the ODA.

Efficiency

The primary aim of the ODA is to ensure that effective drugs are developed for orphan diseases. Because pharmaceutical companies are private entities beholden primarily to a profit motive, they are unlikely to

produce drugs that are unprofitable. Orphan drugs cost significantly more (approximately five times) than nonorphan drugs to develop.[40] Prior to the establishment of the ODA, drug companies claimed routine development of "public service" drugs for orphan diseases as an altruistic action.[41] NORD, though, was able to show that this was not the case, and the pharmaceutical industry was an adversary to research into orphan diseases.[42] Economic game theory analyses of the ODA have also demonstrated that absent government intervention, patients will suffer, and drug development will not occur.[43] Hence, for the ODA or any amended measure to succeed in its purpose, it should "tip the needle" to ensure effective drugs to help orphan diseases are brought to market.

The incentive system setup should ideally minimize exploitation while maximizing development for rare diseases. The intent of Congress and the public is to care for individuals with orphan diseases, not simply enrich pharmaceutical companies.[44] This has implications because the ODA only compensates successfully developed drugs. By doing so, the public disincentivizes abuse of the ODA and unnecessary expenditures on unproductive research. On the other hand, there is an efficiency cost in that risky or difficult research may be avoided for fear of failure and a lack of compensation. By compensating clinical trials specifically, the ODA does lower the incentive for a company to be efficient in this particular step of development. However, the incentive is powerful, as demonstrated by its historical success and by its theoretical nature. It is reliable, predictable, and thus attractive. Together, this suggests that the incentive is at least somewhat efficient at achieving the goals of Congress.

Game theory analysis has also been applied to the ODA.[45] This analysis suggests that orphan drugs will not be developed without any government incentive, and that government incentive will be effective at doing so, thus providing results to the public and profits to the companies.[46] That means that the core idea behind the ODA is theoretically sound. The game theory analysis did determine that endogenous pricing of drugs resulted in less yields to the public, but

40. *Id*.

41. *Id*.

42. *Id*.

43. *See* Wendy Olsder, Tugce Martagan & Christopher S. Tang, Improving Access to Rare Disease Treatments: Subsidy, Pricing, and Payment Schemes (June 9, 2022) (unpublished manuscript), https://ssrn.com/abstract=3481150.

44. Andraka-Christou, *supra* note 1.

45. Olsder, Martagan & Tang, *supra* note 43.

46. *Id*.

exogenous pricing required a heavier subsidy from the government despite reaching a more optimal balance between profit and yields to the patients.[47] The exact value of this subsidy and comparative efficiency between additional costs versus better yields to patients is a matter for expert negotiation and political determinations.

This notion of deciding appropriate prices of subsidies is a matter of efficiency from the perspective of the taxpayer. Is the ODA generally an efficient use of money? Traditional tort principles, while harsh to a layperson, do provide methods of estimating the value of a person's life to the public. Typical Value of a Statistical Life ("VSL") numbers estimate approximately $10 million.[48] Given the estimated cost of the ODA per year at $1.72 billion, the ODA would only need to save 172 people per year to break even and be efficient.[49] The National Conference of State Legislatures estimates that there are 25 million people with orphan diseases in the United States.[50] Together, this suggests that the numerical efficiency of the ODA is in reality incredibly high, and thus it is thus an excellent use of taxpayer money. This is important to keep in mind when evaluating problems with the ODA and potential solutions. Clearly the FDA and Congress are interested in amending and fine-tuning the ODA, but it is not overall desperately necessary. There is a large margin of error, and the actual yield of the ODA even without peak efficiency is relatively high.

That said, there are inefficiencies within the ODA. The most glaring is the previously mentioned salami slicing. This is a form of abuse of the statute, where due to the existence of a bright line, companies are able to obtain orphan drug status for drugs that probably were not meant to qualify. As a matter of legislative regulation, this is fixable by Congress and/or the relative agencies. There are also inefficiencies in line with the monetary analysis previously performed and the equity analysis. The drug companies, when selecting which drugs to develop, do not necessarily seek the drugs that would have the largest public good or monetary gain to the government; they instead seek private profit. Aligning the two more closely would theoretically yield better results. There are also potential inefficiencies in terms of confounding factors that lower the representation

47. *Id*.

48. Gina Cioffi et al., Evaluation of the Societal Burden of Rare Diseases in the United States (Oct. 11, 2021) (unpublished manuscript), https://doi.org/10.21203/rs.3.rs-936611/v1

49. U.S. Treasury, *supra* note 38.

50. Nat'l Conf. of State Legis., *Rare and Orphan Diseases*, https://www.ncsl.org/research/health/rare-and-orphan-diseases.aspx (last visited Nov. 18, 2022).

of further market-disadvantaged drugs even if the goal of the ODA is to achieve treatments for them because the ODA does not include additional incentives targeted to those market-disadvantaged drugs. Together, these failures mean that to some degree we are missing out on "real" orphan drugs in favor of orphan drugs that are relatively profitable to drug companies but not to the public and purpose of the ODA. We also do not know if as a result of the ODA's brightline prevalence distinction, we are missing out on drugs that could be close to the brightline but are now overshadowed. A disease with a prevalence of 250,000, for example, could now be in a "no man's land" where it cannot compete with the drugs that fall under ODA designation for attention, but neither can it compete with the significantly more prevalent diseases. This is also a potential inefficiency.

As previously discussed, the sheer yield of the ODA means the inefficiencies are more easily overlooked, as even most possible solutions will still end up incredibly efficient. This does not excuse attempts at or consideration of progress, however. In Section III, a number of proposals will be evaluated.

Administrability

Just as for equity and efficiency, there are multiple positive and negative concerns around administrability. The ODA in its current form is comparatively easy to administer: the prevalence criterion is straightforward and predictable for both the government and for the drug companies. Furthermore, its thirty-plus year tenure means that when it comes to this particular provision, there is established precedent and established expertise on the part of the companies and the government. Changes to this would inherently increase the administrability burden at least temporarily, even if there were a theoretical improvement down the line. However, that does not mean that prevalence is an open-and-shut criterion to administer, simply that it is *comparatively* easier. There are several loopholes, definitional contentions, and attempts by pharmaceutical companies to gain the most for the least. Thus, keeping abreast with developments in the field, methods of ensuring abuses are not occurring, etc. do add an administrative burden that requires expertise to manage. These do weigh down the administrability of the ODA.

Political Considerations

There are also a few attendant political considerations. Firstly, pharmaceutical companies are incredibly potent interest groups, so any efforts to curtail their benefits will be politically difficult, while increasing vulnerabilities in the ODA will be politically incentivized. At the same time, though, there can be public political pressure resulting from the needs of the sick, advocacy groups, and frustration at inefficiency or inequity insofar as the drug companies are characterized as unfairly taking funds they are not entitled to. Because the history of the ODA had pharmaceutical companies working in conjunction with NORD, while opposition met failure, drumming up this public support will not be easy even if theoretically viable.

III. PROPOSALS

Various proposals will be listed below, before concluding with the proposal that is arguably the "best" option for the government to take. The previous analysis factors of equity, efficiency, and administrability will be broadly considered, as well as the political process, policymaking framework considerations, and the economic game theory information where applicable. Because the current ODA is in fact quite equitable and quite efficient, the goal of these proposals is improvement rather than stripping back something successful.

Status Quo/Build Back Better Amendment

The current status option is perhaps the easiest and simplest solution. By "staying the course" and maintaining the status quo, the government and academics can collect additional data and determine with greater certainty what changes need to be made. The ODA's equity, efficiency, and administrability considerations have been previously discussed, and those would remain the same. The FDA could, under this proposal, attempt to tighten its requirements as needed in the vein of the 1998 and 2013 revisions.[51] This would increase the administrability burden but ideally offset that by improving the equity and efficiency of the ODA. Politically, there are a number of advantages to this proposal. It would require the least effort on the part of lawmakers, as well as avoid negative lobbying from pharmaceutical companies and rare disease advocacy groups. However,

51. Gibson & von Tigerstrom, *supra* note 13.

there is a political concern in that as lawmakers look for funding to finance their other agendas, raising revenue by eliminating this tax expenditure becomes politically attractive.

This option would imply not passing the Build Back Better Bill's amendment. This would almost universally be a win across most metrics. The Build Back Better Bill only applies the credit to the first time a drug is given orphan status.[52] Because drugs are widely cross-applicable, this would be deeply inequitable. It would take away necessary lifesaving treatment from people who need it, perhaps because their disease gained attention later, because it was more difficult to treat or research, etc. It would also be inequitable to rising pharmaceutical companies that would be unable to apply the credit to their own research simply because an established company had already used the drug in some other situation. It would be inefficient because a large number of potential drugs that the ODA sought to have developed simply would never reach market as per game theory analysis. While administrability may seem easier due to not needing to oversee as many drugs receiving the credit, the various permutations and combinations of drugs would still pose some administrability burdens. It would also be politically easier because the drug companies and the interest groups would not spend effort opposing the tightening restrictions.

The Build Back Better amendment does have some advantages. The overuse of the ODA via methods such as salami slicing would certainly be curtailed. There would be more room for competition if fewer drugs had exclusivity. The government would have additional revenue, which it could use in other areas. However, as history and the game theory analysis have shown us, the actual development of the needed treatments simply would not occur in those cases where the ODA's incentive was not provided. This severe cutback would undermine the ODA to the point where it would frustrate the fundamental purpose of the provision. This means the status quo option is the better of the two.

Remove the Prevalence Criterion

The next, most intuitive proposal is to remove the second criterion passed in 1984.[53] This would mean that *only* drugs for which there was no reasonable expectation of profitability within the United States could receive the credit. This proposal has academic support and is appealing for

52. Narayanan, *supra* note 25.
53. Herder, *supra* note 10.

many reasons.[54] It would ensure that some equitability concerns are met because the people whose diseases are genuinely disadvantaged by the market would be the primary focus. It could substantially increase efficiency as there would be a lot less room for abuse via salami slicing based on arbitrary prevalence brightlines. With fewer applicants, the administrative burden may also lessen. On the other hand, it may decrease efficiency because fewer drugs are in development or produced. To ensure that the genuinely unprofitable drugs *were* produced, the incentive would likely have to be increased, which could be seen as spending on pharmaceutical companies. Also, there may be continued room for abuse if a subset can be defined in such a way that the subset is unprofitable while other subsets are not, analogous to salami slicing. Abuse can also exist if the drug companies use the even smaller prevalence of these orphan diseases to engage in price gouging. The credit would also not *necessarily* ensure that all drugs disadvantaged in the American market now gain attention, leading to the continued influence of the previously mentioned structural difficulties such as a lack of interest in research for pregnant women. Furthermore, the administrative burden to determine what is in fact "unprofitable" at the outset is far more difficult than a mere prevalence-based approach. Politically, it could also be more difficult as it would likely be opposed by drug companies and interest groups for people with rare diseases who *do* have potentially profitable drugs being developed for their treatment. Also, the likely necessary increased spending as a percentage of the development costs could be politically difficult even if the actual monetary amount flowing out of the government goes down.

Public Production

Public production of drugs theoretically eliminates any equity concerns around not serving the right people and around advantaging otherwise wealthy drug companies at the expense of the public. It is also theoretically far more efficient, as there is no concern about overcoming a profit motive, no concern about overuse of the tax credit, etc. It could be advantageous for politicians who could take direct credit for the lifesaving treatments. On the other hand, direct government control is extremely difficult administratively. The burden would be quite significant, and the government lacks the expertise in the process of developing the drugs as opposed to mere oversight. Furthermore, it would be expensive because

54. *See* Herder, *supra* note 10, at 4.

the government would need to go through start-up costs, would lack some of the necessary expertise, and would be covering the entirety of the cost rather than simply a portion. This exacerbates equity considerations with regards to how much the public can afford to spend on the lives of minorities. It also would not be able to facilitate competition to spur innovation, which is an efficiency downside, as well as typical concerns about the efficiency of government spending. The traditional political climate in America is also not favorable to such state-run solutions, so implementing it would likely be significantly more difficult than a private sector subsidy. This means that while some academics have found that it is ideal, it is unlikely to be a credibly feasible proposal.[55]

Direct Grants

Similar to the public production proposal, the government directly funding specific drug development is a promising option. The government would theoretically be able to target the proper populations to prevent abuse, provide a variable and appropriate amount of funding depending on the circumstances of each specific case, etc. There would of course be concerns about abuse in the application process, but there would not be a brightline loophole as the status quo provides. This is a theoretically vast improvement in efficiency due to the targeted nature of the relief; structural difficulties could be avoided through judicious and ethical grant acceptances.

However, this theoretical improvement comes with significant costs and difficulties. Just as in the case of removing prevalence as a criterion, there is a significant cost associated with moving the truly disadvantaged diseases to a state where the pharmaceutical company will agree to develop. The expertise required to truly determine which diseases are in need of the aid is also quite difficult to obtain and not necessarily something the government immediately has. Without perfect knowledge and perfect systems of approach, there is also likely to be a reduction in efficiency as the government may simply be incorrect about the amount of grant money required or the proper diseases to allocate the grant to. The administrative burden to acquire this would be significant. There is still potential for abuse if regulatory capture or the complexities of politics influence the grant process. Drug companies also would not be able to easily rely on the presence of a guaranteed tax cut and would have to spend effort to produce grant proposals, which would lower efficiency and add

55. *See* Andraka-Christou, *supra* note 1.

potential dead weight loss. Granting money in this way is also less likely to be politically feasible due to being more overt spending and could be a point for further political struggles in the future. Advocacy groups are also unlikely to be happy because they must leave the decision for if their drug gets financed up to the government rather than a transparent metric. Thus, this option is not necessarily optimal.

Orphan Drug Cap-and-Trade

This proposal originated from considering disincentives as opposed to positive incentives that can be abused. The essence of the proposal is imposing a harsh tax on pharmaceutical companies for nonorphan drugs that can be offset by a generous credit for orphan drugs. This is analogous to, though not exactly, a cap-and-trade system, such as those proposed for carbon and fossil fuels.[56] This would theoretically increase efficiency because even if the profit margins for less profitable orphan drugs are slimmer, the comparative profit margin would be substantially increased, increasing the likelihood that the drug companies would seek to develop orphan drugs. There is also an equity advantage in that pharmaceutical companies have the capacity to pay so they would be bearing an increased, volitional burden for not producing the orphan drugs. This system, though, has multiple flaws. Firstly, there would be an even stronger incentive to abuse the orphan drug categorization, and determining which drugs are standard rather than genuinely orphan can be extremely difficult prospectively rather than retroactively. There could also be an equity concern across drug companies as not all companies are capable of or have the expertise to develop orphan drugs. The bookkeeping for tracing profits would also add an administrative burden. Politically it would also likely be an uphill battle as pharmaceutical companies would want to avoid a blanket tax and would lobby against it. Also, as is often the concern with *levying* a tax, the government needs to be concerned about how much of the tax is passed on to consumers. If much of it is passed on to consumers, then people who need treatment for nonorphan diseases may be inequitably burdened, while the efficiency does not substantially change. While price controls can, as the game theory analysis demonstrated, help ease this difficulty, on its own this would be the major variable that decides the utility of this proposal. This variable is difficult to determine, therefore the proposal in part H is preferable as it offers more certainty.

56. *See e.g.*, Lawrence H. Goulder & Andrew R. Schein, *Carbon Taxes Versus Cap and Trade: A Critical Review*, 4 CLIMATE CHANGE ECON. 1350010 (November 18, 2013).

Price Controls if Using ODA

Just as price controls could aid the prior proposal, and in fact many of the other proposals, they are a viable independent solution. The core equity argument behind them is that if you take public money meant to care for people with orphan diseases, you are not entitled to make an excessive profit off the very people the public deemed disadvantaged and in need of aid. It becomes a matter of fundamental fairness, as well as an efficiency matter in truly fulfilling the purpose of the ODA. Thus, price controls would be implemented for any drugs developed when taking advantage of the ODA. The game theory analysis of the ODA also concluded that exogenous pricing rather than pricing determined by the drug companies would be far more likely to produce good results for the patients.[57] And yet, there are still fundamental concerns that make this option difficult on its own. There is a reverse equity argument that it is not the government's place to place a cap on the market's determination of price, especially in cases where the drug companies are allegedly producing drugs that help people in great need. There's an efficiency argument, as demonstrated by the game theory paper, that the attendant subsidies provided to the drug companies would need to be even higher to "tip the needle" and may, in some cases, lead to some drugs not being produced at all. It also would not necessarily eliminate the incentive to abuse the ODA, nor would it change the flawed criteria by which drug companies currently abuse the ODA. Furthermore, the administrative burden of determining an appropriate price point to cap each drug is difficult and costly. Politically, this would not be popular with drug companies, and American politicians generally do not particularly like price control. However, the equity considerations are so significant that price control *should* be seriously considered, especially in conjunction with other proposals to address issues that price controls do not address.

Loss Recompensation

The third original proposal is one that intuitively leads to the final and ideal proposal. In this proposal, rather than an upfront tax credit, orphan drugs that *end up* unprofitable after the seven-year exclusivity period will get compensated by the tax credit. The fundamental goal is to recenter the ODA on the unprofitable drugs it was meant to facilitate and assure drug companies that they can afford to take the risk into that market. Because

57. *See* Olsder, Maragan & Tang, *supra* note 43.

this is retrospective rather than prospective, there would theoretically be much more accurate information, thus ensuring equitability, streamlining efficiency, lowering administrative costs, and being monetarily cheaper.

The main problem with this proposal is that because of the first-mover advantage, it is entirely possible that the drug's price will simply skyrocket *after* the exclusivity period, resulting in deferred prices that may be even higher to compensate for lost profit in the previous years. Drug companies could abuse this along with abusing the designation loopholes. "Kicking the can down the road" is not a viable strategy for long-term health of the plan, though this is a case where longer-term price controls could mitigate the downside. Also, the incentive would be weaker due to the time value of money, and the administrative burden of analyzing the exact profitability of the drug could be quite heavy. Because of the weakness of the incentive and the burden on the government, this policy is inferior to the recapture policy in section H.

Recapture

This policy is an original policy that has the most potential to be successful across all axes. Based on prior analysis, it would be even more successful if combined with price controls. However, price controls may not be strictly necessary in order to make the proposal function. This flexibility itself is an asset as it makes space for legislative and policymaking compromise. The essence of this policy is recapture, much in the vein of other forms of tax recapture such as depreciation recapture. Depreciation reduces tax burden, but when a realization event occurs that reflects a difference between the depreciation and the actual value, the overly depreciated tax burden must be made whole. In much the same way, a "recapture" can be applied to the ODA. The incentive can be broadly granted at the time the drug is brought to market. This incentive could be the current incentive, a much higher percentage than 50% to draw in more drugs. In the event that the drug is excessively successful and thus a genuinely profitable drug that should not have had the advantages of the ODA, the company must repay the tax credit at a variable rate dependent on the scale of the profits made, perhaps over the seven years of exclusivity. The exact rate of repayment, thresholds for profit, etc. would be determined by experts and ideally would be flexible from case to case and year to year as the landscape of drug development and disease understanding evolves. The idea of "repaying" a tax credit is not unheard

of. The advance child tax credit is similar and NOL tax credits are an inverse where a tax credit can be amended due to a separate loss.[58]

This proposal has many significant advantages, though it does not fix some issues itself. It also is highly flexible and can be implemented in conjunction with a subset of the prior proposals to result in a better overall policy. The first advantage, of course, is an equity advantage like that of the price controls. It ensures that the drug companies do not make excessive amounts of profit financed by public funds, though they would still be entitled to a reasonable profit to ensure the drugs were developed. The second advantage is that it lowers (though it does not eliminate) the incentive to abuse the ODA, because the only remaining benefits would be the first-mover advantage that comes with market exclusivity and the time value of money associated with the upfront credit. This time value of money is another advantage in that it maintains an incentive for drug companies to participate in orphan drug development even if the theoretical profit has been decreased. Thus, the drugs do get developed, and people do get treatment. It also has more flexibility in efficiency because the amount recaptured can vary rather than stay fixed. A company who developed a moderately excessively profitable drug would not have to recompensate the government as much as a company who developed an extremely excessively profitable drug. This variability and lack of a bright line also makes it harder for companies to strategize around ways to abuse it. Politically, it is more feasible because it would lower government spending, not be as unpalatable to the pharmaceutical companies, and allow politicians to demonstrate to the people that they are not simply giving money to companies without oversight.

There are, of course, downsides to this approach. There would need to be additional administrative overhead for the government and for companies to track this recapture and deal with greater complexity in the tax code. It also does not completely eliminate the incentive to abuse the ODA. The concerns about later price gouging that existed due to the limited time window in the loss recompensation proposal would exist here as well, though theoretically with less severity.

The proposal, though, appeals to me in part because of its flexibility. It can complement prior proposals to create an optimal framework. For example, if the prevalence criterion was removed to remove the salami

58. *See, e.g.*, I. R. S. 2021 Child Tax Credit and Advance Child Tax Credit Payments — Topic A: General Information, https://www.irs.gov/credits-deductions/2021-child-tax-credit-and-advance-child-tax-credit-payments-topic-a-general-information; I. R. S. Publication 536 (2021), Net Operating Losses (NOLs) for Individuals, Estates, and Trusts, https://www.irs.gov/publications/p536.

slicing style abuse, this proposal would be able to complement it by ensuring that any increased incentive to offset the increased unprofitability is not exploited. The recapture proposal could also synthesize with price controls to avoid gouging after the window, relying instead on the time value of money of the heavy tax credit and first-mover advantage to incentivize production of the drugs. This substantially increases equity because the people who need the drug are not going to be charged too high an amount, while the public via the government can rest easy knowing that they are not being fleeced for too much money.

From a policymaking framework perspective, the abuses of the pharmaceutical industry threaten them with returning to the contender status. By curtailing excessive profits, they return closer to an advantaged status, which makes any other abuses more palatable. As far as the three streams framework can be applied, this proposal is a policy that seeks to find a nexus between the problem of pharmaceutical abuse of the ODA and a political climate that wants a more efficient ODA without expending unnecessary political capital due to extreme opposition from either rare disease advocates or pharmaceutical companies.

Overall, this proposal is arguably optimal despite its imperfections. While it certainly is not a panacea to the struggles around companies seeking to gain the most while doing the least for people in need, it does provide a certain elegant backstop to an excessive amount of abuse. The other proposals run into difficulties in part due to overreaching. This proposal maintains a healthy incentive for companies to produce orphan drugs and puts a limit only if they truly egregiously abuse the drug. The drugs are thus still developed and go toward the ultimate goal of helping people in need.

III. CONCLUSION

The Orphan Drug Act has successfully provided many people with rare diseases in the United States with lifesaving treatment. It brought a solution to a problem posed by the unprofitability of those diseases and helped bring drug companies into a better place ethically and from a policymaking framework perspective. The measure is generally equitable, has high efficiency, and does not suffer from an excessive administrative burden. However, it is not perfect, and issues such as salami slicing create an impetus for the ODA to be better and deliver more to the people who need it. The recapture method was the best suggestion, as determined after an analysis of many proposals. The recapture method will allow the government to ensure that excessive profits are not being made off the

back of public funds while maintaining a potent incentive, thereby increasing the efficiency and equitability of the ODA. The recapture method is also flexible and can be integrated into other approaches, resulting in remedies for flaws that other proposals may face.

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