Interaction between technological and social factors in recent US pharmaceutical developments

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Introduction

Rare diseases, or conditions that affect only a small percentage of the population, are a major challenge in public health. Although each individual rare disease affects few people, collectively 6 to 8 percent of the global population is affected by at least one rare disease (Auvin et al., 2018). These diseases often severely disrupt the patients' normal life, due to the symptom severity, as well as the difficulty of getting treatment. Patients with rare diseases have historically been underserved by commercial drug development (Drummond et al., 2007). These patients face several major challenges, including deficient diagnostics systems, inadequate knowledge, difficulty in clinical trials (Sharma et al., 2010), which all contribute to difficulty of getting treatment. Thus, it is important to understand how this landscape was formed, and the relationship between key relevant events.

In this paper, I will argue that the major events in the US drug development industry from the 1950s to 1980s, including the Thalidomide tragedy, Kefauver-Harris Amendment, Orphan Drug Act, and various major shifts in technological patterns exemplify a cyclic pattern. These show that interactions between technological and social changes in drug development in the US cannot be simply explained by a cause-and-effect relationship proposed by the technological determinism theory. Rather, there is a co-dependent, cyclic relationship between them, where each influences the other. This paper examines the theory of technological determinism in depth, which has a reductionist nature at its core, and thus fails to paint a complete picture. It is unable to capture the complex dynamics between technological developments and social changes, when considering the complicated history of the biomedicine field.

The events examined in this paper are some of the most important events in the context of the orphan drug field, especially the early years of its development. These events

and the connections between them highlight the reciprocal influence between technology and society factors. Through analysis into the history of the drug development industry, this paper demonstrates that there is indeed evidence pointing to technological developments wielding significant influence over social changes in some cases. However, the paper also points out that this is far from the whole truth, as technological developments are also in turn influenced and shaped by social forces. This can be seen in the responses in the drug development industry's response to social changes such as regulatory reforms. With various complex dynamics at play, societal changes have both influenced and been influenced by technological developments, often in cyclic developments.

The significance of this paper is its ability to enhance the understanding of developments in biomedicine, which has profound implications on public health. By analyzing the relationships between several key events and refuting the narrative that technological advancement has the power to drive social change by itself, the paper provides insight into the complex processes behind developments in the drug development industry. Recognizing the nuance and complexity of these events and how they have influenced orphan drug development is essential for understanding the landscape of orphan drug development and its challenges. This facilitates guiding policies and strategies that can effectively address the challenges of the contemporary biomedicine field.

Literature review

There is extensive existing literature about the major developments in the drug development field. Government actions playing an important role in guiding the direction of technological developments has been the central premise in many studies. Specifically, two pieces of landmark legislation, the Kefauver-Harris Amendment, and the Orphan Drug Act, have been examined extensively for their impact.

The Kefauver-Harris Amendment of 1962 introduced efficacy and safety proof requirements. It has been argued that it has played a crucial role in ensuring drug safety (Greene & Podolsky, 2012). On the other hand, some literature has also focused on its negative impacts, notably driving up costs and keeping small companies out of the market (Klinch et al., 2019). Some drug development companies' effort to lessen the amendment's effectiveness has also been studied (Jacobson, 2018).

The Orphan Drug Act of 1983 was passed to incentive the development of orphan drugs. Its various aspects have been examined in depth. Bagley et al. (2019) discusses the act's overall effects on drug development in the thirty-five years following its adoption, as well as its implications for the future. Pulsinelli (1999) examines the key provisions intended to incentivize orphan drug development and their effectiveness. There has also been literature criticizing the Orphan Drug Act's negative implications, such as the looser regulations for orphan drugs leading to pharmaceutical safety incidents in the case of Makena (Kim, 2012). Some literature discusses how the market exclusivity incentive has led to more monopolies and higher prices for consumers (Sarpatwari et al., 2018). An important aspect of policy reforms in drug development is the crucial role played by patient advocacy groups (Aymé et al., 2008). Through lobbying, these organizations (Gammie et al., 2015) have been successful in advocating for funding and policy reform that expand access to treatments for rare diseases. Novas (2009) examines the impact of patient group lobbying on the passage of the Orphan Drug Act in depth.

Additionally, there is literature about the relevant technological developments this paper will examine. The background and implications of the Thalidomide tragedy (Ridings, 2013; Vargesson, 2013), as well as the evolving technical focus of pharmaceutical companies (Wastfelt et al., 2006) have both been studied. Within the public health domain, there is

extensive literature about technological advancements driving social changes. These examples span various sub-domains, both at the macro level such as epidemiology (Yairi & Ambrose, 2013), and at the micro level such as toxicology (Choudhuri et al., 2018) and virology (Zuo et al., 2024). These advancements include direct progress such as vaccines and new drugs, but also developments in the related natural science fields that serve as a foundation of biomedicine, as well as overall better understanding of public health. These technological developments have greatly improved public health outcomes, as exemplified by the drastic increase in life expectancy and ever decreasing mortality rates (Kinsella & Velkoff, 2022). These improvements have brought about a lot of positive social changes. These changes include improved economic productivity and social stability at the population level, and the improvement in quality of life at the individual level, exemplified by longer, healthier, and happier lives (Veenhoven, 2005). Furthermore, there have been changes in the attitudes and value judgements of the general population. Specifically, the improvements in public health outcomes have led to a continuously "growing public acceptance of disease control as both a possibility and a public responsibility" (Division of Health Care Services & Committee for the Study of the Future of Public Health, 1988), as exemplified by the increasing vaccination rates and improvements in personal hygiene habits.

Since the focal point of this paper's analysis is the interaction between technological and social developments, technological determinism provides a useful starting point. As demonstrated by existing literature on the subject, there have been cases where certain technological developments have had profound influence over societal dynamics. Technological Determinism's emphasis on technology's role provides useful insights into an essential part of the interactions between technology and society. Technological determinism itself is a controversial framework within social sciences and has been applied broadly in analysis across a variety of fields, including new media (Hauer, 2017), educational

technology (Oliver, 2011), semiconductor development (Ceruzzi, 2005), journalism (Appelgren, 2023), just to name a few. Within the context of the drug development field, although not explicitly stated in most cases, the central idea of technological determinism is very prevalent in a lot of analysis (Drews & Ryser, 1997; see also Athar et al., 2021; Vangapandu et al., 2007). Technological determinism has been used in analysis as the main framework to make sense of the of technological developments in the context of social changes. It has been applied to theoretical discussions of the relationship between technical and social factors, the responses of policy makers to challenges about new technologies, as well as the public's reaction to new technologies (Wyatt, 2008).

Merritt Roe Smith, an influential critic of technological determinism, identified an important means through which the idea manifested in society, narratives. He argued that psychological appeal was pushed to the public by associating technology with intangible desires, appealing to efficiency, modernity, and status (Smith & Marx, 1994). This factor played a prominent role in the pharmaceutical industry, the public was constantly exposed to medicine advertisements in everyday life. These advertisements had great psychological effects due to its critical role as it relates to health, even life and death. Technological advancements extensively manipulated the public's fears of death, disease, and suffering (Wolinsky, 2005), as well as the hope for a longer healthier life, which has been present throughout history.

Methods

The research question this paper seeks to investigate is: How is technological determinism insufficient in explaining the pattern of interaction between the major technological developments and social changes in the US pharmaceutical field? The process of investigation into this question comprises of employing various forms of analysis,

including historical analysis, case study analysis, and policy analysis.

By utilizing historical analysis, this paper analyzed the major events, both technical developments and social changes in the US. Specifically, the focus of the analysis was the causes and effects of these events, how they connect to each other was assessed in depth especially. Due to the nature of the subject and the focus of this study, historical analysis is the most appropriate for examining several key past events in the US that aid in the understanding of their effects. The paper mainly studies events in the timeframe ranging from the 1950s (starting with the development of Thalidomide) to the 1980s (passage and adoption of the Orphan Drug Act). As these are some of the most important events leading to the current landscape of orphan drug development. The paper argues that these events are all connected in a complex way. As enough time has passed since these events' initial developments, there are more secondary sources available. These sources can provide a comprehensive review and paint a more complete picture. Moreover, historical analysis fits with the overall scheme of this paper's analysis because of the STS framework employed. Traditional technological determinism theory reduces the interaction of technical and socio-economic factors simply to technology driving society in an inevitable manner. But through analysis and assessment of historical events and the connection within, the paper demonstrates the limitations of such thought and theory, as well as the necessity of more nuanced understanding of history and society.

This paper also utilizes the method of case study analysis in its investigation of the development of the biomedicine field. Within the scope of this paper's analysis, both technological developments and social changes in the field are primarily driven by a few influential events. To facilitate analysis and better understanding of the field, the paper simplifies the continuous, ever-evolving dynamic of relevant historical developments by

grouping them into discrete cases. The main cases this paper analyzes include the development of Thalidomide, adoption of the Kefauver-Harris Amendment, subsequent recession in the drug development industry, adoption of the Orphan Drug Act, and the resulting shift in focus in drug development. Classifying many related small events together into one unified case allows for comprehensive analysis into the complex dynamics around key events. Looking at the big picture cases effectively rids the analysis of noise from trivial events. The resulting focus on the influence of major events, as well as interaction between events can provide a clearer and more complete picture and insights into the biomedicine field during this time.

Moreover, considering the nature of the case studies this paper examines, the method of policy analysis was also utilized in the analysis to some extent. Two pieces of influential policy, specifically the Kefauver-Harris Amendment and the Orphan Drug Act, were part of this paper's analysis. Policy analysis into both the societal and the technological background can help put these policies into the proper context, as well as provide insights into their causes and effects. This method is appropriate for this paper's analysis into technological developments and societal changes, since policy is a central part of the social changes this paper discusses. Additionally, a key part of policy analysis is about certain policies addressing specific technological issues. This is also a crucial part of this paper's analysis, and fits into the grand scheme of interactions between technological developments and social changes.

There were various types of secondary sources examined in aid of this paper's analysis, namely academic research papers, policy analysis, and agency reports. In addition to these secondary sources, primary sources also played an important role in this study. The documents surrounding the most influential pieces of legislation relevant to this paper's

analysis were especially important. These documents include not only the legal texts themselves, but also documents produced during the legislative process, such as the transcripts of relevant congressional hearings. The examination of these documents can provide direct insights into the deeper levels of social change, especially the roles and perspectives of various relevant social groups, such as testimony from patient advocacy organizations.

Analysis

The consequences of the development of the drug Thalidomide were the main contributing factor of various subsequent social changes, some of which turned out to be very influential in other ways. As the root cause of one of the biggest medical disasters in recent history, Thalidomide was originally developed as "a sedative and anti-hypnotic" (Vargesson, 2009, p. 1327) in the 1950s. Later it was also widely used across the world to relieve morning sickness for pregnant women. Several years later it was discovered that this drug was the main cause for birth defects in tens of thousands of newly born children, especially to "the limbs, ear and eye, peripheral neuropathies and internal organ defects" (Vargesson, 2009, p. 1327). Thalidomide was taken off the market almost completely at the time due to social pressure. More importantly, this tragedy led to significant and widespread reforms in the biomedicine industry. Pharmaceutical testing and regulation were still very much in its primal stages at the time, so much so that Thalidomide was never approved where it was developed (Hofland, 2013). The tragedy of Thalidomide brought the testing and approval process of pharmaceutical products into public focus and attention, which eventually resulted in the adoption of systematic and extensive testing requirements, as well as a stricter approval process (Ridings, 2013). One of the most significant responses in the United States in the aftermath of the Thalidomide tragedy was the Kefauver-Harris Amendment, passed in 1962,

as an amendment to the Federal Food, Drug and Cosmetic Act.

The Kefauver-Harris Amendment was influential in ensuing technological developments. It ensured that "the efficacy of drugs now reaching the market has been proved to a much greater degree" (Hollister et al., 1968, p. 69) through increasingly strict review criteria. It also elevated the level of clinical studies of drugs through more exacting requirements for data (Hollister et al., 1968) in place of outdated testimonial studies. The Kefauver-Harris Amendment drastically improved the pharmaceutical safety standards and effectively protected the public from potentially dangerous drugs through more regulations. On the other hand, the regulatory burdens imposed by the new provisions dramatically increased drug development costs. As a response, most drug development companies began to shift focus towards developing "treatments for common diseases with large potential markets in order to maximize the possibility of recouping research and development costs and generating significant revenues" (Cheung et al., 2004, p. 184). This was a good example of how social factors were able to exert their influence on the direction of technological development. The barrier of entry resulting from the stricter testing and approval requirements precluded many companies from continuing to participate in the market. This can be attributed to various factors, including insufficient experience, monetary support, or incentive of these companies to conduct the necessary clinical trials (Klinch et al., 2019). As a result, many drugs on the market at the time were discontinued. Data have shown that the drug development industry started to recede following the Kefauver-Harris Amendment, more than half of the medicines available prior to its passage were lost following its adoption (Klinch et al., 2019).

Subsequent technological developments in the drug development industry exemplify well the cyclic nature of the interaction between technological developments and social

changes. The adoption of the Kefauver-Harris Amendment led to the "gap between common versus rare diseases widened to the point where either very few or no treatment options were available for some disease conditions" (Cheung et al., 2004, p. 184). Thus, the availability of drugs for rare diseases became a focal point for patient advocacy organizations, who questioned the role of the regulatory procedures in preventing the development of orphan drugs (Novas, 2009), which refer to drugs for conditions with no reasonable expectation of US sales supporting its development or conditions with a prevalence of 200,000 patients (Kesselheim, 2011). These organizations' activism raised public awareness and brought attention to orphan drugs as a political issue. Eventually the lobbying led to the successful enactment of several measures taken by the federal government, the most important of which was the 1983 Orphan Drug Act (Novas, 2009). As exemplified in this case, the social changes were influenced by various factors, both technical and social, and cannot be simply attributed to being driven by technological developments.

The Orphan Drug Act is a landmark legislation in the context of US drug development and marked a turning point. It is a great example of a case where social factors have been very influential in shaping the technological landscape and led to certain technological developments. Thus, it is crucial to assess, in depth, its historical context and effects on subsequent developments. The Orphan Drug Act, which was signed into law by President Reagan in 1983 and signified a major social change in the drug development industry. Intended to encourage the development of drugs for rare diseases (called orphan drugs), the bill pushed radical regulatory overhauls and government involvement in drug development. Major incentives included "seven-year market exclusivity for firms, …, tax credits equal to half of the development costs, carry-forward … and carry-back provision" (Cheung et al., 2004, p. 185). There have been extensive studies showcasing the effects of the Orphan Drug Act on technological developments in the pharmaceutical industry.

One of the most effective incentives offered by the Orphan Drug Act to drug development companies is marketing exclusivity and the related patent reforms. Regardless of the size of the potential market, the development process of a drug is not only expensive and time consuming, but it also carries a lot of risk. For most drugs, because of the large potential markets, drug development companies seek to recover the cost and make a profit from the sales. In this regard, orphan drug development already becomes extremely difficult just due to the limitations with potential market size. This is further exacerbated by the fact that many orphan drugs were unpatentable according to existing regulations before the Orphan Drug Act (Pulsinelli, 1999). It was extremely difficult for pioneering drug development companies to safeguard their interests against unfair competition (Arno et al., 1995). This meant that drug development companies had no incentive at all to develop orphan drugs. The special case incentive for orphan drugs, introduced by the bill, immediately created interest from pharmaceutical companies. Critics have raised numerous concerns. Some have argued that it has led to unintended consequences in the drug development industry that exacerbates issues in other ways and brought about new concerns. These consequences are mainly about the creation of monopolies (Pulsinelli, 1999) and the impedance of innovation due to the incentives provided (Kesselheim, 2011), which could preclude the development of similar drugs for a larger population, instead of the small subset of conditions. But the Orphan Drug Act has achieved immense success, as demonstrated by the enormous increase in orphan drugs available to patients. Almost 100 new drugs specifically developed for orphan diseases were able to reach the consumer market in the first decade following the passage of this bill (Arno et al., 1995), in stark contrast with the fact that there were fewer than ten such drugs in the decade prior to this bill's adoption (Daly 2002). It highlights the need to recognize that there is nothing deterministic about these developments in the pharmaceutical industry, both technical and social.

Conclusion

This paper analyzes the complex relationships between technological developments and social changes, in the context of the US drug development field. Through in-depth examination of key events that took place from the 1950s to the 1980s, the paper demonstrates that the relationship is not the one-directional, deterministic relationship proposed by technological determinism. Instead, there is a dynamic codependent relationship where technological developments and social changes exert influences over each other in a cyclic fashion. The paper reveals the insufficiency of technological determinism due to its nature. This new understanding has important real-world implications. For example, governmental regulatory agencies could consider more adaptive regulations that are responsive to both technological advancements and social changes. Specifically, more upfront tax credit incentives for development costs could be considered in place of overly broad monopolies granted. There could also be more coordination between these regulatory agencies, pharmaceutical companies, and patient groups, such as more public-private partnership. Such as sharing of research facilities and coordination to assist clinical testing, which could enhance transparency and public health outcomes.

It is important to note, however, that there are limitations to this paper due to its scope. Its analysis is limited to the drug development field in the US during a specific period, thus the ability to generalize the findings to other contexts may be limited, and further research would be useful. Specifically, more research on the key events relevant to orphan drugs in other countries can provide more insights into the relationship between technological and social factors in this context, and how it's affected by the unique cultural and economic circumstances. Moreover, there are other events potentially relevant to the current orphan drug landscape, such as the Hatch-Waxman Act of 1984 that established the generic drug

system, and the Prescription Drug Marketing Act of 1987 that tightened regulations on prescription drugs. Future research could also focus on events in more recent decades, assessing how the relationships between technological and social developments has changed and what factors have contributed to this change,

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