The role of regulators in mitigating uncertainty within the Valley of Death

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Abstract

The essential cause of the 'Valley of Death' (VoD) is the reluctance of the private sector to invest in technologies which are perceived as immature. However, uncertainty about whether a new product or technology complies with regulatory frameworks may also have an important effect on private sector investments. We use the cases of the Critical Path Initiative, in the pharmaceutical industry, and the Advanced General Aviation Transportation Experiments, in the general aviation industry, to analyze the role of regulatory agencies in decreasing three different types of regulatory uncertainty along the VoD. We find that regulatory agencies play an important role as a social glue which helps coordinate industry-wide efforts. Based on the comparison between the two cases, we create theory to explain the effect of regulatory uncertainty on the shape of the VoD. Our theoretical framework may help agencies detect the major sources of regulatory uncertainty, and adapt their policies accordingly to facilitate the traverse of emerging technologies across the VoD.

Keywords: valley of death; regulation; uncertainty; technology adoption; pharmaceuticals; aviation

Highlights

- Regulatory uncertainty is an important driver of investment decisions
- Regulators may act not only as gatekeepers but also as innovation enablers
- We identify three types of regulatory uncertainty
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Classification codes

O250 Industrial Policy

O310 Innovation and Invention: Processes and Incentives

O320 Management of Technological Innovation and R&D

O330 Technological Change: Choices and Consequences; Diffusion Processes

O380 Technological Change: Government Policy

1 Introduction

The Valley of Death (VoD) is usually understood as a phase in the maturity of an emerging technology, after public sector investment in early proof of principle research, and before the private sector is willing to accept the level of uncertainty associated with proprietary application development and scale-up. (Butler, 2008; NRC, 2004; Weyant, 2011). One of the factors which may accentuate this uncertainty is the existence of a stringent and/or evolving regulatory framework, and the uncertainty about how to ensure the new technology can comply with existing and future laws and rules (Gallaher et al., 2007; Marcus, 1981). As regulatory uncertainty increases, venture capitalists may be less willing to invest, and often shift their interest to less uncertain endeavors (Fleming, 2015). Industries where regulatory uncertainty is an important driver of investment decisions include renewable energy (Mowery et al., 2010), telecommunications (Henisz and Zelner, 2001), life sciences (Oye, 2012; Pisano, 1997), and aviation (Nakamura et al., 2013).

Regulatory uncertainty affects firms' investments in different ways. Firms might be aware of a potential change in regulations, but are unable to estimate the impact on their operations (Gerard and Lave, 2005; Milliken, 1987; Mowery et al., 2010). With pharmaceuticals or advanced equipment, rules determine market approval, but products need to undergo extensive real-life testing to assess compliance–some technological uncertainty can only be assessed in the later stages of development (Downer, 2007; Kola and Landis, 2004; Maine and Garnsey, 2006). With novel technologies such as nanotechnology or genome editing, existing rules might not be appropriate. If agencies hesitate to approve new products until new rules are written, this creates an important barrier to market entry (Jones, 2015; Oye, 2012; Rip, 2018).

Despite regulatory uncertainty being a well-known barrier for the commercialization of new products, the literature on the VoD has not incorporated those insights to explain variations in technology investments. Furthermore, the government's role in traversing the VoD has mostly been studied from a funding perspective. We extend the literature on the VoD by incorporating regulatory uncertainty as a factor complementary to funding. Our contribution is two-fold: first, we provide insights about how regulatory uncertainty affects the VoD, and how regulatory

agencies can reduce such uncertainty. Second, acknowledging the diverse nature of regulatory uncertainty, we provide a taxonomy with three types of regulatory uncertainty in the VoD. We explain the different impact of each type on the VoD, and propose specific actions for regulatory agencies to help industry overcome existing uncertainty.

We study two different cases: the Critical Path Initiative (CPI) in the pharmaceutical industry, and Advanced General Aviation Transport Experiments (AGATE) in the general aviation industry. For both, we analyze the industrial context behind the creation of the consortium, its organizational structure, and the regulatory changes implemented to bridge the VoD. We gather data from 22 interviews and approximately 90 sources of archival data.

We find that regulatory agencies play an important role as innovation enablers, not only by creating or revising rules, but also by establishing strong collaborative networks with industry members to facilitate the two-way exchange of technical and regulatory information. Our findings can help agencies identify the major types of uncertainty, the stakeholders who can bring the technical knowledge required to reduce those uncertainties, and show how to align program outcomes with regulatory goals to accelerate the development and diffusion of emerging technologies.

2 Theoretical Background: Regulatory Uncertainty affects the VoD

The term VoD refers to the dearth of investment in promising emerging technologies at an intermediate stage in their development, between proof of concept R&D and prototype demonstration and commercialization (Biemans and Huizingh, 2020). The technology has matured beyond traditional public sector funding for early-stage research, but is not mature enough for firms to invest in the development and scale-up of proprietary applications (Butler, 2008; NRC, 2004; Weyant, 2011). The 'depth' of the VoD, or in other words, the reluctance of the private sector to invest in commercializing a relatively immature technology, is typically a function of industry's perceived risk (Murphy, 2003). This reluctance will be higher as the time to market, and the uncertainty surrounding the performance of the final product, increase (Hollister, 2009).

To help companies overcome the VoD, the U.S. government has conceived innovation awards such as the Advanced Technology Program (and its successor the Technology Innovation Program) and the Small Business Innovation Research Program, which provide funding for early-stage technology development (Wessner, 2005). Complementarily, governments have provided funding and legal frameworks to create collaborative structures for technology acceleration and demonstration, such as SEMATECH for semiconductors (Browning et al., 1995), or more recently, the National Network for Manufacturing Innovation (now known as Manufacturing USA) (Sargent, 2012).

The VoD, traditionally considered a problem due to lack of investment as a function of technological maturity, is usually defined in terms of Technology Readiness Level (TRL) 4 to 7 (McIntyre, 2014). Studies on this topic, however, usually lack insights on how regulatory uncertainty affects private investments. Uncertainty whether a certain product or technology complies with existing or future regulations may discourage firms to invest, as the profitability of the new product cannot be accurately assessed (Marcus, 1981). Furthermore, the industrialization of an emerging (product) technology may also require innovation and development of relevant production technologies and other engineering tools, which may themselves be subject to technological and regulatory uncertainty (Featherston et al., 2016; Tassey, 2004).

2.1 Types of Regulatory Uncertainty

Research analyzing the effect of regulatory uncertainty on firms' investments and innovative performance cover diverse fields such as law, economics, management, and industry-specific studies. Comparisons across the various literature streams reveal several types of regulatory uncertainty, some in an industrial context, while others are typical of emerging technologies, and therefore more relevant to the VoD.

One literature stream analyzes whether firms' beliefs in a potential policy or regulatory change affect their attitude to investing in new technologies (Hoffmann et al., 2009). Such change is expected to happen within the lifecycle of the product and to have a strong impact on its profitability (Patiño-Echeverri et al., 2009), especially if the new rules are applied retroactively

(Coleman, 2016; Mir-Artigues et al., 2018). This uncertainty is a specific case of a broader concept known as 'environmental uncertainty' in the management literature (Duncan, 1972; Krishnan et al., 2016). We call this specific case 'rule content' uncertainty.

Environmental uncertainty is caused by insufficient understanding of how external actors will behave, the potential effect of such behavior, and how a firm can respond (Milliken, 1987). Empirical industry studies suggest that environmental uncertainty often drives firms to postpone or reduce their R&D investments. Manufacturing firms anticipating a change in pollution-abatement regulations may hold their investments in emission-control technologies until that uncertainty is dissipated (Gerard and Lave, 2005; Viscusi, 1983). Extreme cases where uncertainty might negatively impact R&D investments are: industries subject to large capital expenditure and which need a stable institutional environment to be amortized, such as energy (Mowery et al., 2010; Narayanamurti et al., 2011), and telecommunications (Henisz and Zelner, 2001); also where new products are based on long-term basic research, such as biotechnology (Freeman and van Reenen, 2008; Oakey, 1990). For these cases, governments and regulatory agencies need to make a 'credible commitment' so that the new rules are socially accepted and not perceived as transient (Bergek et al., 2008; North and Weingast, 1989). Environmental uncertainty can, however, have a positive effect on certain innovative activities. Large corporations may decide to expand their business portfolios as a diversification strategy under uncertainty (Carrera et al., 2003), avoiding investments seen as 'irreversible' and focusing on flexible technology investments which may offer larger returns in the long term (Rugman and Verbeke, 1998). Hoffmann et al. (2009) suggest that firms invest under environmental uncertainty to secure competitive resources, leverage complementary resources, and alleviate long-term normative pressures (e.g. to reduce carbon emissions). Firms may also decide to invest in technology if they believe that regulatory changes are likely to have a beneficial effect on their operations (McGrath, 1997).

A second literature stream examines uncertainty in situations where the rules are clear and not expected to change, but firms cannot ensure their new products will comply with existing regulation until later stages in their development, even after commercialization. In other words,

uncertainty is intrinsic to the new product and does not depend on external factors. We refer to this as 'final compliance' uncertainty.

Laboratory testing might not suffice to measure a product's performance, and large-scale, real-life testing might be needed to assess compliance (Downer, 2007). This uncertainty is common in complex technological systems such as aircraft manufacturing (Mowery and Rosenberg, 1981), advanced materials (Maine and Garnsey, 2006), and pharmaceuticals (Kola and Landis, 2004), all of which typically have very long development times. Some side effects or undesired behaviors are only detected once the product has reached the market (Lortie, 1986; Williard et al., 2013). In the worst case, products might be recalled from the market (Kleinke and Gottlieb, 1998; Song et al., 2014; Zuckerman et al., 2011), causing significant financial and social losses both to manufacturers and their customers.

Given the unpredictability of compliance and long development time of these products, venture capitalists might be reluctant to invest during the early stages (Fleming, 2015; Hoerr, 2011). To minimize the chances of failure during certification, firms might focus their efforts on incremental improvements to existing products (DiMasi and Faden, 2011), rather than the commercialization of radically different products which can bring unexpected technical problems and costly delays during certification (Nakamura et al., 2013). Smaller, more innovative firms may struggle to bring their products to market, as they do not have the same regulatory experience or access to regulatory officers as larger firms (Heemstra et al., 2008). Consequently, entrants may need to establish alliances with larger firms to further commercialize their innovations (Audretsch and Feldman, 2003; Rothaermel and Deeds, 2004).

A third literature stream examines the inherent uncertainty in introducing new technologies, and how to build regulatory frameworks which limit technological uncertainty, without hampering the technology's long-term innovation potential (Bonnín Roca et al., 2017; Kuhlmann et al., 2019). Examples of these fields include nanotechnology (Rip, 2018), genome editing (Jones, 2015), and blockchain (Yeoh, 2017). Not only is it uncertain how new technology will perform, existing rules can be inadequate to guarantee its safety and need to be rethought. We call this 'qualification method' uncertainty.

Table 1: We identify three types of regulatory uncertainty in the literature which are relevant to the VoD

Type of regulatory uncertainty	Definition	Examples
Rule content uncertainty	Firms and investors are unable to anticipate how rules will evolve. The details and specifications of the final rules, and their impact on business operations, are unknown.	Investments on telecommunications infrastructure depend on the existence of a stable, favorable institutional landscape (Henisz and Zelner, 2001) Manufacturing firms may hold investments in emission-control technologies if they believe environmental regulations may change (Gerard and Lave, 2005)
Final compliance uncertainty	Firms and investors do not know whether a product will comply with existing rules until it has been tested in real-life conditions.	Efficacy and safety of drugs assessed through several stages of clinical trials, with low success rate (Kola and Landis, 2004) The safety of self-driving cars can only be assessed through large-scale testing on the road (Banerjee et al., 2018).
Qualification method uncertainty	Firms are unsure how to comply with regulations because existing product rules were not designed for the new technology. New rules may be required as existing ones might be insufficient or inadequate.	Rules to approve drugs are inadequate to approve biosimilar products (Wang and Chow, 2012). Guidelines to ensure the structural integrity of machined metallic components are insufficient to ensure the integrity of 3D-printed components (Bonnín Roca et al., 2017).

Regulators themselves face important epistemic barriers, as the relevant technical knowledge is concentrated in a handful of firms trying to exploit their competitive advantage (Mandel, 2009). These knowledge asymmetries force regulators to establish strong collaborative ties with the

private sector to proactively seek knowledge, allowing agencies to gather technical know-how, and revise their regulatory system as the technology matures (McCray et al., 2010; Petersen and Bloemen, 2015). However, this greater interaction between private and public sectors may also increase the risk of regulatory capture, and result in degradation of the original social goals (Dal Bó, 2006).

2.2 Role of government agencies in reducing regulatory uncertainty

Traditionally, regulatory agencies' role in the innovation process has been analyzed from the perspective of law and economics, focusing on the design and evaluation of rules and oversight approaches to drive innovation (Ashford et al., 1985; Coglianese and Lazer, 2003; Dudek et al., 1992; La Pierre, 1976; Thomas, 1990a). However, such analyses might not be adequate for emerging technologies if agencies lack the scientific evidence to write new rules (Bonnín Roca et al., 2017; Downer, 2010). To improve this situation, the community of innovation researchers has proposed mechanisms called 'adaptive governance' (Folke et al., 2005), 'anticipatory governance' (Guston, 2014), or 'tentative governance' (Kuhlmann et al., 2019), to balance the need for safety while leaving enough scope for technological experimentation. These new approaches differ from traditional methods in three ways: 1) rather than merely reacting to movements in industry, regulators become knowledge-seeking, proactive actors; 2) regulators become coordinating agents between scientists and firms; and 3) regulators seek flexibility, rather than rigidity in the rules, to allow scope for adaptation to technological change (Bonnín Roca et al., 2017; Folke et al., 2005; Guston, 2014; Kuhlmann et al., 2019; McCray et al., 2010; Oye, 2012).

Government initiatives devote resources to developing publicly available scientific tools and databases, which can later become the industry standard (Demortain, 2017; Hamburg, 2011; NSTC, 2014). Given the public nature of these tools, it is unlikely that only firms invest in their development, creating a case for public intervention (Featherston et al., 2016; Tassey, 2004). At the same time, high-quality input from industry and academia is crucial for developing common tools (Link and Metcalfe, 2008; Schofield et al., 2010). To support the creation of public-private partnerships for technology development and ensure alignment with their regulatory goals, regulators may therefore need to enhance their role as innovation brokers (Fleming and

Waguespack, 2007; Howells, 2006). Fulfilling this intermediation role means walking a very fine line, given that regulators should remain neutral and avoid picking winners (neither technologies nor firms) (Marchant, 2008), even though that neutrality might be suboptimal (Greenberg, 2015).

As it is still a nascent field, much of the literature on regulating new technologies is no more than theoretical constructs with little technical detail (Folke et al., 2005; Guston, 2014; Kuhlmann et al., 2019); for example a survey of institutes and organizational structures regulating emerging technologies (McCray et al., 2010), or an analysis of sector-specific rules affecting the commercialization of certain products (Oye, 2012; Rip, 2018). We contribute to the literature by focusing on the diverse nature of regulatory uncertainty and how it could be reduced by regulatory agencies, at different stages of technological maturity. To do so, we showcase two public initiatives within highly regulated industries: the Critical Path Initiative (CPI), in the pharmaceutical industry; and the Advanced General Aviation Transportation Experiment (AGATE).

3 Methods

We use grounded theory-building methods (Eisenhardt, 1989; Glaser and Strauss, 1967) to gain insight into the role of regulatory agencies in helping technologies bridge the VoD. They underline our aim to provide "tentative answers to novel questions of how and why … suggesting new connections among phenomena" (Edmondson and McManus, 2007, p.1158) and "clear enough categories and hypotheses so that crucial ones can be verified in present and future research" (Glaser and Strauss, 1967, p.3). We focus on two public initiatives through which regulatory agencies have tried to overcome the VoD: the Critical Path Initiative (CPI) in the pharmaceutical industry, and Advanced General Aviation Transport Experiments (AGATE) in the aviation industry (Table 2). Our unit level of analysis is the public-private partnership. We present multiple cases which create "better grounded, more accurate, and more generalizable" theory (Eisenhardt and Graebner, 2007, p.27) than single-case studies.

3.1 Theoretical sampling

We selected industries where: regulation represents an important barrier to entry; regulatory agencies have to interact systematically with firms over long periods of time; and R&D intensity is high, therefore any reduction in uncertainty could greatly impact innovative productivity. We focus on U.S. agencies given their explicit mandate to engage in technology transfer activities through the Stevenson-Wydler Technology Innovation Act of 1980, and the Federal Technology Transfer Act of 1986. Aviation and pharma are both heavily regulated industries. In both cases, due to technical complexity and lengthy certification processes, early-concept to commercialization may take more than ten years (Bonnín Roca et al., 2017; Sternitzke, 2010), thus discouraging firms from introducing radically new products with a greater likelihood of not being approved (Kroo, 2004; Miller, 2010). Consequently, firms and agencies establish strong working relationships and interpersonal ties (Downer, 2010; Pisano, 1997). R&D intensity is typically high (Bustinza et al., 2019; Watanabe et al., 2002). The regulatory agencies in the two selected industries, the Federal Aviation Administration (FAA) and the Food and Drug Administration (FDA), are endowed with substantially larger budgets than other regulatory agencies. In 2018, FAA's budget was $16.1B and FDA's budget $5.1B, considerably higher than the National Highway Traffic Safety Administration ($0.9B) or the Occupational Health and Safety Administration ($0.5B) (OMB, 2017). We focus on AGATE and CPI because industry members highlighted these programs as being particularly relevant for studying how agencies try to enable innovation.

To validate and provide stronger arguments for our findings, we examined industry-level differences between general aviation and pharma. The pharmaceutical industry is dominated by vertically integrated, large corporations ('big pharma'), which have established expertise in engaging with regulators (Rafols et al., 2014). New entrants that use venture capital to fund their early-stage R&D activities, lack resources and tend to have less regulatory expertise (Styhre and Remneland-Wikhamn, 2016). Because its knowledge is science-based and easy to appropriate, pharma has a strong intellectual property (IP) regime (Grabowski, 2002) which can impede inter-firm collaboration. General aviation manufacturers are much smaller (GAMA, 2017), and their R&D capabilities are lower (Masson, 2005). Their supply chain is international

and complex (Soshkin, 2016; Zeng, 2003), pushing industry to seek new forms of inter-firm collaboration (Esposito, 2004). Interactions with regulators happen through designees assigned to original equipment manufacturers (OEM) (Florio, 2016). Technical knowledge is highly tacit and therefore hard to appropriate (Frischtak, 1994), making IP protection less of a concern than in pharma.

Table 2 Overview of the two cases considered in this study, CPI and AGATE

Critical Path Initiative (CPI)	Advanced General Aviation Transport Experiments (AGATE)
Due to the decline in the pharmaceutical industry's R&D productivity, FDA launched the Critical Path Initiative (2004-present) to promote tighter collaboration among government, firms, and external stakeholders like doctors or patient groups, through multiple consortia. FDA co-funded the Critical Path Institute, a neutral third party creating data tools to accelerate drug development. Its efforts often required new rules and certification pathways to validate new products, and incentivize investment in less commercially attractive diseases. We illustrate these efforts with examples in the field of biomarkers and dynamic disease simulation tools.	AGATE (1995-2000), a consortium co-financed by NASA and FAA to modernize the general aviation industry, which was at the time subject to strict liability laws, and inappropriate certification guidelines inherited from commercial aviation. We highlight FAA's efforts to promote collaboration among industry competitors and implement new rules reducing the cost and time of the certification process. Examples of avionics and composite materials show how FAA successfully reduced uncertainty in developing new aircraft.

3.2 Data sources

We combined insights from 22 semi-structured interviews and approximately 90 archival sources, whenever possible publicly available databases (such as drug approval rates, market and safety data), as our primary source of information. As AGATE was conceived in the early 1990s, we believe archival data may be a less-biased source of information about its origins and impact than interviews. NASA's Technical Reports Server was especially useful for accessing numerous reports containing data about the program's goals , experimental programs (RTI, 1997), organizational structure, and evaluation (Gale, 2002; Masson, 2005). In the case of CPI,

we obtained most data by comparing articles across a variety of medical, biotechnology, and health policy journals, as well as relevant material on the FDA and CPI websites. This material includes initial reports justifying the launch of CPI (FDA, 2006, 2004) and descriptions of the collaborative structures established between industry and government to foster pre-competitive sharing (Maxfield et al., 2017; Woosley et al., 2010).

We interviewed consortia members to obtain undocumented information, such as the personal stories and drivers behind the establishment of the program, the challenges and lessons learned from coordinating industry-wide efforts, whether political changes affected the program goals, and perspectives on the consortia's outcomes and impact. Our target was top level officers with more than twenty years' experience in their industries, as we required people with strong technical and regulatory backgrounds. Once we had exhausted the pool of potential interviewees, we approached managers in the private sector and intermediary research institutes. This enabled us to check the consistency of our findings between the public and private sectors. Our interviewees included two program directors, six certification officers, five project managers at collaborating research centers, and three industry representatives.

Interviews lasting on average an hour were conducted between 2015 and the first half of 2019, in three distinct phases. We conducted 11 interviews for AGATE, and 11 for CPI. We started by reaching out to regulators to understand their own opinions about the role of regulatory agencies in the innovation process. It was not unusual to have to wait months to schedule an interview, given the high position of officers in their organizations. Regulators were extremely helpful with providing relevant archival data, and snowball-sampling (Denzin and Lincoln, 2011) our next set of interviewees. The second interview round consisted of people who were active members in both consortia, including collaborating organizations. At this point, we had gathered enough data to compare and highlight the differences between CPI and AGATE. A third round of interviews clarified the nature and potential reasons for these discrepancies. To validate our findings, we e-mailed a draft report to eight interviewed program and project managers who were interested in reading our work. Four of them provided additional clarifications.

3.3 Data collection and analysis

Without any structure, "*grounded theory research would be presented as a jumble of literature consultation, data collection, and analysis [...] neither efficient nor comprehensible*" (Suddaby, 2006, p.637). To illustrate our findings and improve their readability, we use an analytical framework based on existing literature. We have structured sections 4.1 and 4.2 in line with the five levels defined by Hodge and Greve (2017) to assess public-private partnerships' performance: industry context and culture, governance style, policy, organizational form, and project.

To evaluate the effect of regulatory uncertainty in the VoD, we consider the three types of uncertainty summarized in section 2.1. Labelled 'rule content', 'final compliance' and 'qualification method' they revolve around the questions 'what' rules are in place, 'whether' the product will comply with those rules, and 'how' to prove compliance with the rules. Section 4.3 summarizes how agencies tried to address the three types of uncertainty.

Coding was performed iteratively between archival data and interviews throughout data collection. The first step, performed independently for CPI and AGATE, was manually coding, paragraph-by-paragraph, the archival data (about 50 documents) containing relevant information on the consortia and their impact on the VoD. Interview protocols were based on this code, and divided into two sections: the first set of questions to understand the interviewee's role in the program, and the overall expected effect of regulatory uncertainty in the VoD; the second set to understand the differences observed between CPI and AGATE.

Interview coding was done independently by the first author, who conducted all the interviews, and then by the second author, who was thus able to analyze the data from an unbiased perspective. We constructed an initial code for CPI and another for AGATE, both containing *in vivo* codes given the large amount of jargon in the regulatory world. After coding, we added new sources of archival data, often provided by our interviewees. This iteration between archival data and interviews continued until we reached theoretical saturation. At that point, we created a focused code equally applicable to CPI and AGATE. For instance, the initial codes 'surrogate endpoints' and 'equivalence sampling exercise' became 'new validation processes'.

4 Findings

For the sake of clarity, we present the CPI and AGATE cases separately in the following sections. For each consortium, we analyze regulatory agencies' attempts to reduce uncertainty at industry, consortium, project, and rule levels. We compare the cases in section 4.3.

4.1 The Critical Path Initiative

4.1.1 Industrial context: productivity crisis in pharma

Commercializing a new drug takes an average of 12 years, and the approval of new medical devices, an average of 7 years (Van Norman, 2016). After pre-clinical testing, clinical trials for a new drug are conducted in three phases: Phase I assesses the safety of the drug and the optimal dosage; Phase II assesses the efficacy of the drug and potential side effects; and Phase III, the longest one, involves large-scale, randomized testing. In most cases, this long process fails: "W*e are still approving 1/10 models, that's so f***ed up*" (Program director). Half of the drug candidates reaching Phase III fail (Van Norman, 2016). High failure rates led to a productivity crisis. Between 1993 and 2003, approval of new molecular entities fell more than 75%, while global R&D spending doubled (FDA, 2004; Woodcock and Woosley, 2008). New drug development costs have been steadily rising in the past decade, sometimes reaching more than US$2B (Mullard, 2014). Pharma has witnessed a trend of companies avoiding these high costs by focusing on commercializing less innovative treatments such as 'me-too' drugs, which are almost chemically equivalent to already approved drugs, and therefore more likely to obtain regulatory approval (Gagne, 2011).

Any help in reducing these failure rates or better estimating which drugs are likely to fail before Phase III, could have a profound impact on firms' investments: "*The actual benefit would be to improve the predictive power by X%. When 90% fail, that's a great deal of money on the table. Even if you had a marginally better tool*" (Program director). To aid this mission, FDA published a report (2004) to 'identify and prioritize the most pressing development problems and areas that provide the greatest opportunities for rapid improvement and public health benefits'. This report sparked setting up CPI, public-private partnerships to enhance collaboration among regulators, doctors, scientists and patients in creating tools to accelerate drug development (FDA, 2004; Mahajan and Gupta, 2010; Woodcock and Woosley, 2008).

Besides developing new tools, FDA created four types of expedited reviews to cut, in specific cases, the length of the certification process to a couple of years (Sherman et al., 2013). Expedited review methods aimed to bridge the VoD in small markets, probably not the most attractive for firms, usually to treat serious conditions for which there is no available treatment, or significantly improve existing treatments. These expedited reviews seem to have attracted firms' attention. In 2014, approximately 70% of the drugs approved by the FDA used one of these four expedited methods, so that drugs might 'be approved at earlier stages based on less rigorous clinical testing' (Kesselheim et al., 2015, p.4).

4.1.2 Organizational structure

CPI goals are pursued under a myriad of public-private partnerships, each tackling a different disease. Since the launch of the CPI, FDA has participated in more than 25 consortia (Maxfield et al., 2017). In 2004, FDA created the Office of Critical Path Programs to coordinate efforts and offer financial support (FDA, 2009). In 2008, CPI received direct support from U.S. Congress (FDA, 2009), although the funding was probably insufficient to fully develop the cutting-edge tools it required (Fox, 2010).

However, as FDA officials commented: "*FDA isn't a research organization, this is a big ecosystem problem and we were trying to encourage others*" (Program director), and "*this is not a single-person task, this is a philosophy change. It is a responsibility for all stakeholders to be a part of this*" (Scientific advisor). Leadership of the consortia was progressively transferred to the Critical Path Institute (C-Path), created in 2005 with the unique purpose of working with FDA on CPI, and acting as a 'neutral third-party' (Woosley and Cossman, 2007). Participating companies gain many benefits: "*they get to participate in meetings with FDA, access to data, they get to have regulatory input, key opinion leaders who usually cost 10K/day for free, and coauthor papers with famous people*" (Project manager). Sometimes, companies are reluctant to participate, due to IP concerns: "*When I was in industry they told me I could go there but say nothing… They're concerned about losing IP but at the end of the day, young people understand that the competitive advantage is the molecule itself… All the other stuff should be pre-competitive*" (Project manager). Tools developed by C-Path are released to the public before becoming part of a consensus report or submission to the FDA (Woosley et al., 2010).

Within C-Path, each consortium has its distinct membership and cost-sharing structure, which is adapted to slightly different market contexts. Their mission, however, remains the same: "*we provide legal, data sharing and regulatory frameworks for all these stakeholders to work together. Another is … to develop these shared tools. The tools may not be the same, but the overarching goal is to have a forum to share data*" (Project manager).

4.1.3 Regulatory changes to streamline qualification

CPI efforts to modernize industry practices were further legitimized in 2016, when the U.S. House of Representatives passed the 21st Century Cures Act, 'designed to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently' (FDA, 2018). The Cures Act encourages FDA to design non-traditional clinical trials, use new data analysis tools, and accelerate drug approval pathways (Avorn and Kesselheim, 2015). The Act also authorized an 'FDA Innovation Account', for which FDA submitted a plan to spend US$500M from 2017 to 2025, 'to help accelerate medical product innovation while reducing regulatory burden' (FDA, 2017, p.1).

FDA has promoted numerous consortia to achieve the goals established by CPI and the Cures Act. Two of these consortia relating to the commercialization process are: the Biomarker Qualification Program and the Fit-For-Purpose Initiative. They represent two complementary ways FDA can reduce regulatory uncertainty. In the case of biomarkers, FDA legitimizes research into a disease by providing an *informal* endorsement called 'Letter of Support', which informs companies about the most promising opportunities; in the case of the Fit-For-Purpose Initiative, FDA created an entirely new, *formal* regulatory framework, for data tools (rather than drugs) to reduce the cost of clinical trials.

4.1.3.1 Efforts towards the qualification of biomarkers

One of the CPI's early objectives was to create a qualification process of biomarkers for drug development; this would promote standardization, thus facilitating a path for developing predictive biomarkers (FDA, 2004). The World Health Organization defines biomarkers as 'any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease' (WHO, 2001, p.1). Biomarkers accelerate drug development programs because they can assess the safety and effectiveness of a drug on a

certain patient at a lower cost than clinical outcomes studies, and organize patient groups based on objective criteria (Altar, 2008). One of the first consortia (2006) promoted by the Office of Critical Path Programs was the Biomarkers Consortium, managed by the Foundation for the National Institutes of Health (FNIH) (Wagner et al., 2010). The Biomarkers Consortium is helping to improve the validation and standardization of biomarkers, and addressing the lack of reliable data for clinical trials by pooling resources across different sectors (Wholley, 2014). This work has, for instance, helped the FDA create an accelerated approval pathway for drugs to treat breast cancer (Prowell and Pazdur, 2012).

FDA complemented the Biomarkers Consortium's activities with the creation of the Biomarker Qualification Program. Traditionally, companies could, under a confidentiality agreement, use a certain biomarker to tackle a single condition. FDA aims to create a database of qualified biomarkers which can be used in multiple applications, sharing resources across consortia members (Amur et al., 2015). To help create the required data infrastructure, C-Path launched the Biomarker Data Repository (Sauer et al., 2016). Furthermore, for biomarkers not yet qualified, but for which there is substantial scientific evidence of their potential, the FDA created a new type of guidance called 'Letters of Support' (Amur et al., 2015). This informal endorsement represented an important change for researchers developing data tools and for industry: "*The whole idea behind the Letter of Support was pretty much new ground… This is more subtle because it is the type of thing people in the field will follow. We were looking at our data but we didn't have enough to put the stamp of certification… [now] they can publicly state their belief in the value of this program*" (Program director).

4.1.3.2 Pioneering the approval of dynamic simulation tools

Computational tools such as disease or statistical models can accelerate drug development by optimizing the design of clinical trials and simulating the dynamic effect of drugs in patients (Romero et al., 2014). Thus, these new tools can reduce development times and uncertainty in the early stages. FDA wanted to formally endorse these tools. However, these algorithms need periodic updates in their input data, which may translate into changes in their output. This dynamic nature clashed with pre-existing endorsement mechanisms, which typically require final products to remain unchanged. "[FDA] *they didn't feel the qualification process would be*

applicable to trial tools, because of the dynamic process" (Project manager). To solve this problem, FDA developed a special approval process under the 'Fit for Purpose Initiative'. The first approved fit-for-purpose tool was an Alzheimer's Disease clinical trial simulation tool, created by C-Path (Romero et al., 2015). The approval process of this tool was lengthy and built on a close partnership between firms, scientists at C-Path, and FDA, which would have been difficult to achieve outside the consortium (Romero et al., 2014).

The motivation to create the tool was because in the previous decade, several drugs for Alzheimer's Disease had failed during Phase III trials (Extance, 2010). How clinical trials are designed is one of the major reasons that drug trials fail. Although it is desirable to find early-stage patients and avoid being 'too late', it can also be difficult to assess the degree of cognitive impairment if it is 'too early' (Kozauer and Katz, 2013). C-Path's drug-disease-trial simulation model uses data from previous clinical trials; it can determine optimal sample size, trial duration, and treatment effect time as well as perform sensitivity analyses based on predetermined sources of variability (Romero et al., 2014). "*We have heard from companies that they now use this as part of trial preparation. They used it retrospectively, and if they had had this tool, they would have designed the trials different*" (Program director). This tool "*could have predicted the failure of multimillion Phase III drugs trials. Each of those trials… billions of dollars*" (Project manager).

4.2 Advanced General Aviation Transport Experiments (AGATE)

4.2.1 Industrial context: innovation crisis in the aviation sector

In the early 1990s, the general aviation sector was in a deep crisis. Between the late 1970s and 1990s, the annual demand for general aviation aircraft had plummeted by about 95%, and the number of pilot licenses by roughly 35% (GAO, 2001). The reasons were diverse: a large increase in the price of insurance due to manufacturers being subject to strict liability rules; high fatality rates; a dramatic reduction in the number of air traffic controllers; and costly certification processes (Grenville and Kleiner, 2004; Metz and Bowen, 2005; OTA, 1982). All these factors increased the costs of new aircraft, and made manufacturers more risk-averse to introducing innovations (Holmes, 1996). Some models of small aircraft have actually been in production since the 1950s, with only minor modifications (Dowling, 2017).

In 1994, the U.S. Congress passed the General Aviation Revitalization Act, reducing the liability period to eighteen years (McAllister, 1995). NASA, with its technical expertise and industry leadership, and FAA, with its regulatory expertise, were tasked to create a consortium with industry to foster technology development (Metz, 2002). New aircraft would 'mimic as closely as possible the ease of operating an automobile' (Zyskowski, 1995, p. 847). In economic terms, AGATE's objective was 'to develop the technology to create a single-engine, four-passenger aircraft with improved avionics and crashworthiness features that will sell for approximately US$100,000' (Cole, 2001, p.ii).

4.2.2 Organizational structure: NASA and FAA coordinate different work packages

AGATE was created as a NASA Joint Sponsored Research Agreement (JSRA), whereby industry develops specific R&D projects aligned with a program's high-level goals, and IP rights are shared among members (Masson, 2005; NASA, 2014). Just information relating to the standardization of new technologies and system architectures can be released to the public, and only after a certain time (Masson, 2005). AGATE was coordinated by an Executive Council, which had one representative for each work package, one NASA and one FAA representative, and parties invited by the General Aviation Program office. Each work package had a Technical Council, usually with a NASA leader and an FAA member (Grenville and Kleiner, 2004; Metz and Bowen, 2005).

AGATE targeted technology groups such as: flight systems; propulsion; design and manufacturing; platforms for integration and ice protection (Metz, 2002). While NASA had the technical leadership of each work package, FAA supplied in-kind expertise. "*We had an FAA expert [on our project] and we had also someone getting their hands dirty with industry, deciding what to pursue, and a person on the certification side helping develop guidance to certify these new technologies. He would attend the meetings, sit there, ask questions, provide guidance and take it back to the FAA*" (Research manager). Industry, on the other hand, "*came with their own self-regulatory style, created a team to present results to regulators. It was the private sector who had the knowledge about how to standardize production and maintenance*" (Program designer). As a result of such close regulatory collaboration, AGATE offered an

excellent opportunity to revise outdated certification procedures, reliant on expensive testing and qualification methods (Grenville and Kleiner, 2004).

To choose the best SME candidates for fostering industry's innovation capabilities, NASA designed topic-specific grants under the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, which were aligned with AGATE's goals (Masson, 2005). Awardees of these grants were invited to join the consortium (NASA, 2010). The first to respond were "*mid-tier companies… to compete with the largest companies*" (Program director). Some larger companies were reluctant at first: "*I had companies tell me I was crazy…they quit, that it was nonsense, that it was not practical… They came back about a year later*" (Program director).

4.2.3 Regulatory changes to create industry-wide standards

Due to the wide variety of technologies being developed, FAA had to assemble from all over the country, a specific group of staff specialized in each field of technical research. The group, informally called 'AIR AGATE' (AIR being the Aircraft Certification Service), was responsible for meeting firms' representatives to assess what type of regulatory changes were required to create more consistent industry-wide standards (Masson, 2005). FAA members participated in all the Technical Council meetings, constructively steered the discussions and formulation of the proposed standard, and informed and educated people within the FAA about the proposal, thereby helping to effectively guide the document through the FAA approval process.

FAA's activities during AGATE led to the revision, or issuance, of eight different policy documents (Table 3), mostly advisory circulars (Gale, 2002). The effect of such policies on the VoD was two-sided: first, they increased the reliability of aircraft, with the expectation of lowering accident rates, which should reduce insurance costs; second, they reduced the certification time and cost of new technologies.

Table 3 FAA policies issued as a result of AGATE, and their impact on the VoD

Policy documents	Impact on VoD
23.1309.1C Equipment Systems and installation in Part 23 Airplanes	Increases reliability of technologies to address pilot errors and weather-related accidents
23.1311-1A Installation of Electronic Display in Part 23 Airplanes	Creates a new risk assessment model to lower avionics certification costs
20-53B Protection of Aircraft Fuel Systems Against Fuel Vapor Ignition due to Lightning	Improves safety in lightning strikes which could affect new electronic systems
20-105B Reciprocating Engine Power Loss, Accident Prevention and Trend Monitoring	Reduces accidents through engine monitoring programs and increased pilot awareness
20-140 Guidelines for Design Approval of Aircraft Data Policy Memorandum	Supports the adoption of data communication technologies for future navigation systems
Policy Memo ACE-00-23.613-01: Material Qualification and Equivalency for Polymer Matrix Composite Material Systems	Establishes a generic procedure to reduce time and costs of qualifying composite materials
21-16D RTCA Document DO-160D Environmental Conditions of Communications Systems and Test Procedures for Airborne Equipment	Establishes acceptable standards for the environmental testing of installed equipment

We now describe in greater detail the regulatory changes in two special AGATE technology groups: electronics ('avionics') and composite materials. The case of avionics highlights the regulatory changes needed to adopt technology initially developed for a less safety-critical industry, automotive. Conversely, in the case of composite materials, the new regulatory framework enabled a more safety-critical sector, commercial aviation, to take advantage of technology developed under the AGATE program, with little adaptation. They thus represent two complementary faces of technology transfer.

4.2.3.1 Guidelines for the certification of avionics

AGATE's goal was to substitute traditional cockpits with 'glass cockpits' and integrated instruments which would be easier to read. Technology was immature "*this was the 1990s even before LCD panels were available*" (Program director), but the price-performance of new hardware was expected to drop following the general computing trend (Zyskowski, 1995). In terms of technology, there was a substantial overlap between the navigational and safety

systems used in automobiles (such as GPS or collision avoidance sensors) and the AGATE goals (Cole, 2001). Being able to transfer those technologies, together with the data communication protocols, to aircraft would substantially reduce both equipment and certification costs. The main challenge FAA faced was how to create certification guidelines which could take advantage of cheaper technology, but at the same time increase safety.

Rules for the certification of avionics were inherited from those applicable to airliners, which require a much higher reliability (AC 23.1309-1C, 1999). For instance, the old rules required a reliability of one error per million hours, which in airliners is achieved normally through redundancy (Downer, 2011), but in general aviation would lead to excessive weight and cost additions. The AIR-AGATE team's philosophy was to create guidelines for the system as a whole, instead of specifying thresholds for each component (Gale, 2002). A new analytical model was built to take into account interaction effects among the different components in a glass cockpit, which could analyze all the different subsystems and perform sensitivity analyses (Thompson et al., 1999). Outcomes were published as advisory circulars.

The first AGATE Concepts Demonstrator was built in 1997 for the Annual National Air Transportation Association (NATA) Convention (RTI, 1997). By 2003, the first 'glass cockpits' were introduced, and by 2007 they already represented 90% of the cockpits installed in new aircraft (Hennig, 2002). "*Clearly customers like the glass, features and capabilities for the most part. Industry went through a couple of iterations where the first were a bit harder to use. Soon enough graphical terrain and weather and automated frequency management made things better*" (Program director). In addition, some manufacturers started to retrofit old aircraft with new cockpits, using a supplemental type certification (Babbitt, 2010).

4.2.3.2 New qualification method for advanced composite materials

AGATE aimed to lower the cost of certifying advanced composite materials for aircraft. Composite materials offer valuable features for aviation: their usage translates into important fuel savings (Slayton and Spinardi, 2015); little corrosion; and they do not suffer from fatigue, an important problem as aircraft age (Soutis, 2005). In 2008, general aviation aircraft in the U.S. were on average 40 years old (GAMA, 2017). The manufacture of composite materials is both capital and labor intensive, material prices are high, and the low volume of general aviation

makes it difficult to achieve economies of scale. In addition, the certification of advanced materials for aircraft structures is a complex, costly process. For materials which are not standardized, applicants have to certify each material individually, potentially requiring thousands of samples (OTA, 1988; RAND, 2001).

To reduce qualification costs, AGATE pioneered a new low-cost certification method, with the help of the National Institute for Aviation Research (NIAR) at Wichita State University. One major incentive is that it "*is a canned process, meaning that you can take it right off the shelf and apply it to ANY material. That means they [OEMs] don´t have to write up test plans which then get sent to the FAA and then have 30 days to review, and then send back and ask for corrections, and then another 30 days to review, so it is essentially removing the OEM having to actually write all the material database test plans*" (Research manager).

Consortium members select by consensus which materials they want to have qualified, and share the costs of testing activities. Once testing is completed, NIAR publishes a report with the expected material properties and error margins, so "*anybody can use those material properties to begin the design phase of an aircraft*" (Research manager). Manufacturers wanting to use materials in the AGATE database only need to undergo an 'equivalency sampling exercise' by producing a small sample of components to prove they can reproduce the properties stated in the database (Ng, 2010). Using the AGATE database cuts certification costs by an order of magnitude, and certification time by 75% (Tomblin et al., 2002). The process is also more cost-effective for material suppliers, who can tap into a larger market once their product is standardized, and for companies outside the aviation industry that benefit from having reliable material properties (Berenberg, 2003).

This new certification process was so successful, that it soon caught the attention of the large commercial aircraft manufacturers: "*essentially people said 'hey, this is great, we really love having this information, but is there a way we can get these reports certified by the FAA? So we can use this material as a certified material to then start designing our aircraft*'" (Research manager). The AGATE process was adapted for commercial aviation's more stringent needs, and approved by the FAA in 2010 (Ashforth et al., 2014).

4.3 A comparison of regulatory agencies' actions

We summarize in Table 4 how CPI and AGATE attempt to reduce the various levels of regulatory uncertainty. Despite the significantly different nature of the pharmaceutical and aviation industries, both consortia have taken similar actions to increase the number of innovations reaching the market. Rule content uncertainty was reduced by providing quick access to feedback from regulatory agencies, and encouraging innovative firms to participate in consortia. Final compliance uncertainty was reduced by pooling industry's resources and endorsing novel data tools to assess the chances of success in the early stages of product development. Qualification method uncertainty was reduced by creating expedited certification pathways for products considered strategic, and novel regulatory frameworks for products which could not be properly assessed using preexisting rules.

Table 4: Examples of CPI and AGATE actions to reduce the various types of regulatory uncertainty

	Action and motivation	CPI	AGATE
Rule content	Establishing regular communication channels between government and industry (typically initiated by government) helps companies learn agencies' plans before formal rules are approved. Regulators learn about firms' priorities and become more proactive. A neutral third party could reduce the risk of regulatory capture.	The Critical Path Institute (C-Path), co-funded by the FDA and the State of Arizona, serves as a neutral bridge between academia, industry, and agencies. It provides consortia members with a legal framework which enables collaboration and access to FDA officers' regulatory knowledge.	AGATE is co-funded by FAA and NASA acting as the neutral party. AGATE assigns at least one FAA officer per work package. A specific group AIR AGATE was established to work with industry representatives on revising outdated rules.
	Firms may not initially be interested in collaborative arrangements due to fear of losing their competitive advantage, or too much organizational inertia. Agencies may seek younger, more innovative firms, through the strategic selection of funding programs.	CPI projects focus on diseases which are rare or simply not commercially appealing to established companies, or on creating simulation tools for a variety of diseases.	NASA and FAA design several SBIR solicitations to find companies in and outside the aviation industry that contribute the most to implementing novel technologies in small aircraft.
Final compliance	Generating data to assess the compliance of a new technology is a lengthy and expensive process. By pooling consortia members' resources, sponsored research centers can create publicly available databases of products proven compliant.	FDA has created a database of qualified biomarkers which is accessible to industry members. FDA also issues new Letters of Support to signal promising biomarkers for which there is insufficient evidence for approval.	FAA co-funds the creation and maintenance of databases with the mechanical properties of advanced materials. Data is publicly available and ready to use by companies in their early design phases.
	Often, compliance of a new product cannot be assessed until it is tested in the real world. Simulation tools help companies improve their risk assessments in the early stages. Agencies can fund the development and formally endorse the usage of these tools.	C-Path developed the world's first drug-disease-trial simulation model, enabling companies to assess the potential efficacy of new drugs for Alzheimer's in the early stages; and designed clinical trials with a better selected pool of patients.	Rules for avionics were the same as for commercial aircraft, making the adoption of newer, safer technologies too expensive. FAA developed with industry a new risk assessment model better adapted to the reality of smaller aircraft. It can be used in the design stage, long before flying the first prototype.
Qualification method	Agencies may decide to create expedited certification pathways to reduce the time and costs associated with certifying products considered strategic.	FAA created four expedited certification pathways: for drugs tackling rare diseases, diseases for which there is no treatment, or cases where new drugs demonstrate the potential to be substantially better than existing ones. These pathways have special post-market surveillance mechanisms, gathering data on drug performance and previously undetected side effects.	AGATE has developed a new method that can qualify any composite materials. It reduces time and certification costs by more than half. Thanks to its success, the new qualification process has been extended to commercial aircraft.
	As existing rules might not be appropriate, regulatory agencies need to collaborate with industry members to ensure the proposed rules are appropriate for assessing the safety of innovations and new technology, avoiding rules that impose an excessive burden on firms' operations and the technology's overall potential.	Rules to qualify drugs and medical devices were inappropriate for computer models. Given that these tools can accelerate substantially the development of novel drugs, FDA created a Fit-For-Purpose initiative to validate tools and models beyond the scope of traditional rules.	Rules for navigation systems in general aviation were based on commercial aircraft requirements. This made the adoption of newer and safer technologies too expensive. FAA developed a new set of rules to foster the adoption of advanced navigation systems, better adapted to the reality of smaller aircraft.

5 Discussion

5.1 Theory-building: how regulatory uncertainty shapes the VoD

Studies about the VoD focused on overcoming existing financial barriers and establishing long-term policies to create a safer environment for firms' investments (McIntyre, 2014; NRC, 2004; Weyant, 2011), often failing to highlight the diverse actions which could reduce regulatory uncertainty. Based on our comparison of AGATE and CPI, summarized in Table 4, we propose a theory for how the three types of regulatory uncertainty in our analysis can alter the shape of the VoD (Figure 1).

The first type of regulatory uncertainty we consider, rule content, arises when firms believe that existing rules could change, but they lack enough information to assess the impact of those changes on their business. In our CPI and AGATE cases, we see two mechanisms that can reduce this uncertainty. Firstly, agencies establish new communication channels with the private sector. As a result, firms access regulatory knowledge which might be critical for commercializing their innovations, and what is more, they have the opportunity to influence policymaking. Agencies in turn acquire knowledge about firms' commercialization plans, and can respond more proactively to industry's needs (McCray et al., 2010). These interactions take place at maturation stages close to commercialization. Thus, we argue that a reduced rule content uncertainty can help increase private investment in technologies *from the right side* of the VoD (see Figure 1).

Secondly, agencies may design incentives such as SBIR grants, or disease-specific programs in C-Path, to fund innovations in areas which the government considers strategic, but the private sector does not necessarily find attractive. The lack of interest is probably because the technologies are not in a mature stage. Agencies may want to attract more innovative, young firms, in or outside their industry, to develop these strategic solutions. Consequently, we expect this lower rule content uncertainty, requiring public funding and focusing on immature technologies, would increase investment *from the left side* of the VoD (Figure 1).

The second type of regulatory uncertainty, final compliance, arises when firms cannot predict whether a product will comply with existing rules until very late in the development process,

sometimes after commercialization. With both CPI and AGATE, the agencies have tried to reduce this uncertainty by funding technology infrastructure such as simulation tools, or risk assessment models, which improve the information available to designers and managers about the potential success of a new product in its early development stages. These tools are perceived as legitimate as they have received the formal endorsement of regulatory agencies. In this way, pharma companies can discover that a new molecule is likely to fail, without having to spend millions of dollars and years of R&D on three phases of clinical trials; aircraft manufacturers will have better knowledge of what can go wrong with a new navigation system, already in the design phase. Thanks to this improved knowledge, firms should be able to detect the most promising products within their research portfolios and improve their allocation of financial resources. We anticipate that this reduced final compliance uncertainty translates into higher private investment in the early phases of product development (Figure 1).

The third type of regulatory uncertainty, qualification method, occurs where firms might be interested in commercializing a certain technology, but existing qualification methods are too costly, or existing rules are insufficient to assess the safety of the new technology. In the case of AGATE, the FAA approved new methods for qualifying composite materials and avionics systems, both of which could improve aircraft performance and system safety levels. Similarly, FDA has created specific regulatory pathways for data tools under their Fit-For-Purpose Initiative, and expedited certification processes in areas where there might not yet be an effective solution. Issuing these rules appears to have had a reactive (rather than proactive) effect on innovations which were ready, or almost ready, to be commercialized. New rules allow for a substantial reduction in the time and costs required to certify a new product, also enabling new products to reach the market. Once the new rules and certification processes were in place, industry responded with higher investments in those areas. Thus, we expect less qualification method uncertainty to foster private investments in technologies at the late stages of maturity (Figure 1).

Figure 1 illustrates how reductions in each type of regulatory uncertainty can impact the shape of the VoD. We expect the weight of each type of uncertainty to differ depending on the industrial context and application. In some cases, one uncertainty may dominate the rest. In

other cases, the three types of uncertainty may carry equal weight, creating a need for higher institutional coordination. It is therefore paramount that agencies, rather than having 'canned' solutions which can be applied to any case, tailor their policies to the sources of uncertainty specific to each case.

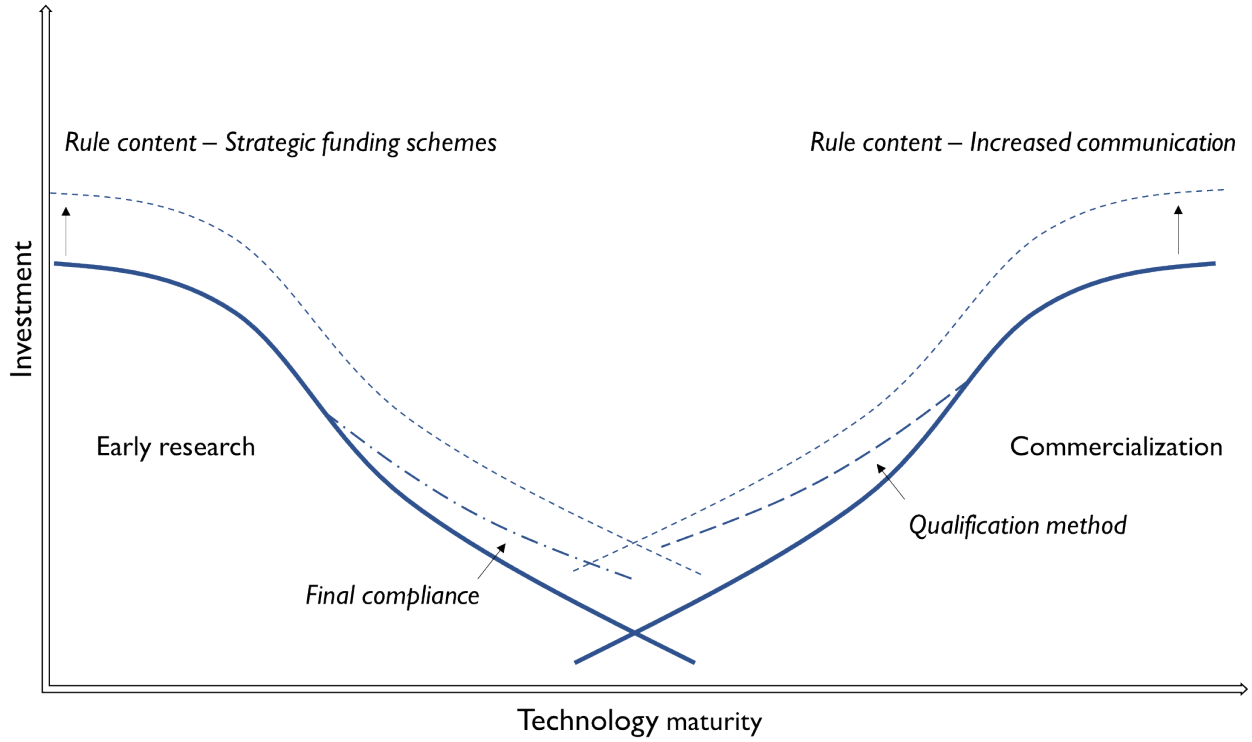

Figure 1 A reduction in the three different types of regulatory uncertainty can affect the shape of the VoD, depending on the technology's stage of maturation

5.2 Implications for practice

Regulatory agencies are typically well-established organizations whose main mission is to promote safety rather than innovation, and in many cases are associated with hindering private investment plans and technology adoption (Isaac, 2002; Olsen, 2017; Oster and Quigley, 1977; Thomas, 1990b). Our findings suggest, however, that regulators are not only gatekeepers, but also enablers of innovation. Their interaction with industry goes beyond just acquiring technical knowledge (Bonnín Roca et al., 2017; McCray et al., 2010; Oye, 2012), or funding the development of engineering tools in a semi-public context (Link and Metcalfe, 2008; Schofield

et al., 2010; Tassey, 2004). Agencies can become the social glue which keeps competitors within an industry collaborating in innovation activities which could not be performed otherwise.

Agencies can aid innovation by aligning industry's data requirements with regulatory goals, influencing technology directions, and even devoting resources to projects which otherwise would not have happened. These important functions cannot be done internally–they are necessarily born from interactions with a wide range of stakeholders in academia, industry, other agencies and user groups. The aforementioned interactions might become more important for emerging technologies and complex products, such as nanotechnology (Becker, 2013), precision medicine (Breckenridge et al., 2016), or artificial intelligence (Scherer, 2015), where technological uncertainty is very high. In these cases, there are important knowledge asymmetries between regulators and the regulated, and traditional regulatory frameworks might not be readily applicable.

We anticipate that agencies will face two challenges when trying to secure funding for innovation-related activities. First, some may argue that the role of regulatory agencies is not to promote innovation, but to ensure that new products are safe before their commercialization. Based on our findings, we believe that those two roles are interconnected, and that agencies, due to their lack of technical knowledge, can only evaluate the safety of those innovations if they learn from external organizations. That knowledge is necessary to compile appropriate rules and technical guidance. Furthermore, participation in consortia can lead to completely new regulatory mechanisms, such as the AGATE composites database. These simultaneously lower the costs and time for certifying new products substantially, and improve safety thanks to standardization.

The second challenge is selecting appropriate metrics to evaluate the benefits to society of officers participating in programs such as AGATE and CPI. In industries with lengthy development times, the potential positive effect on innovation may suffer from time lags that last longer than the political cycle. Sometimes the effect might not even be easy to observe. For instance, simulation tools can help firms discard certain molecules which would otherwise have failed during clinical trials, saving firms large amounts of time and money, but only the firm

knows these effects. Firms might not be willing to share sensitive data about their investments and success levels in the R&D pipeline, because competitors could take advantage of this knowledge. Our conversations with regulators in both the United States and Europe suggest that agencies currently rely on qualitative, anecdotal evidence, and that they lack a consistent set of metrics to properly influence policymaking. Such metrics could, however, be critical for securing funding to continue existing programs and create new ones.

Our findings also provide insights for firm managers in highly regulated industries. The data suggests that the benefits firms gain from participating in collaborative arrangements such as AGATE or C-Path projects are likely to outweigh the costs. Despite their value, the types of tools and models developed under the auspices of CPI and AGATE, given their lack of appropriability and the need for large-scale data collection, are not a key focus for corporate R&D. Pre-competitive sharing is therefore probably the most efficient way to expand a firm's capabilities and substantially reduce uncertainty across the VoD. However, firms' attitude towards consortia might be hostile, especially in leading firms that are afraid to lose their competitive edge. While the research results are available to the public, active members of the consortium are entitled to access critical information and regulatory agencies, which would hardly be possible outside the consortia. We see that, in both CPI and AGATE, after an initial adaptation time, firms become increasingly aware of the value of pre-competitive sharing and participate more actively.

5.3 Limitations and suggestions for future work

This study has the typical limitations of qualitative research. Our analysis is limited to two specific consortia in the pharmaceutical and aeronautics industries. We opted for AGATE and CPI because of their illustrative character; other consortia, even within the same industries, might have not been so successful in reducing regulatory uncertainty. Information from our interviewees regarding AGATE is more sensitive to temporal biases because its inception was a long time ago. To avoid potential biases, we compared the information from our interviewees with extensive archival data sources. While we expect the lessons from our cases to apply to other highly regulated industries, the validity of our proposed framework can only be assessed

through quantitative theory-testing. Our objective is thus "to guide and inspire new ideas" (Hargadon and Sutton, 1997, p.745).

The framework proposed in Figure 2 conceptualizes a more complex reality, and more work is needed to understand why each individual dimension and task can may have a different effect on the VoD curve, depending on the technology-industry context. Future work needs to create reliable metrics to assess the amount and quality of interactions with industry, and their impact on firms' valuations of their R&D portfolio. While our data suggests that increased interaction between regulators and the firms they regulate has had a positive effect on innovation, we have not addressed the potential dangers of regulatory capture, which can negatively impact innovation and safety. Additional research is needed to better understand and model the tension between reducing regulatory uncertainty and increasing the chances of regulatory capture.

6 Conclusion

This paper presents two case studies, the Critical Path Initiative and the Advanced General Aviation Transportation Experiments, to analyze the role of regulators in facilitating the translation of promising emerging technologies by decreasing regulatory uncertainty across the VoD. We analyze how regulatory agencies have addressed three different types of regulatory uncertainty to incentivize private investment in emerging technologies. Our findings suggest that government technology innovation programs should incorporate the required technical expertise from regulatory agencies, industry and the research community more effectively. We present a theoretical framework which may help government identify which are the major sources of regulatory uncertainty for a given technology and industrial context. Agencies may adapt their policies accordingly, to ameliorate the barriers that inhibit firms from taking innovative ideas successfully to market.

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