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# Capture and passive predation in times of COVID-19 pandemic

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**Abstract**
In the midst of a health crisis, a drug in development and candidate for COVID-19 contagious disease was granted orphan-drug designation (ODD). This decision by the US Food and Drug Administration was immediately denounced as an abuse of the Orphan Drug Act (ODA). This paper outlines how this decision may be considered as the result of a complex case of capture along the regulatory process. Therefore, a case study of the remdesivir episode is conducted, combining the definition of a framework for the analysis of capture and the identification of stylized facts marking the trajectory of a repositioned drug and candidate for COVID-19. In doing so, arguments are put forward to show to what extent this granting of ODD can be described as the result of a series of captures, a case of weak capture however that calls for an amendment of the ODA to preclude drugs for contagious and communicable epidemic diseases from obtaining orphan status in the first place.

**Keywords** Predation · Capture · Regulation · Rent-seeking · Orphan drug · COVID-19

**JEL Classification** I18 · K23 · L12 · L65 · 032 · P14

## 1 Introduction

In the midst of a public health crisis, a drug in development and candidate for COVID-19 was granted orphan-drug designation (ODD), with the promise of seven years of market exclusivity once marketing approval will be obtained. This decision by the United States Food and Drug Administration (FDA), through its Office of Orphan Products Development (OOPD), was immediately denounced as an abuse of the Orphan Drug Act (ODA). This latter was put in place in the early 1980s to encourage pharmaceutical firms to develop drugs for rare diseases, i.e. diseases that affect few people and for which the prospects of profit from the drugs developed are limited. The firm was criticized for filing such an application for a drug designed to treat a contagious disease and the FDA for responding favorably at the onset of a pandemic.

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The aim of this article is to shed light on the circumstances under which a major player in the pharmaceutical industry (Gilead) was able to obtain ODD for a drug (remdesivir brand name Veklury) to treat a contagious disease during a public health crisis. Our hypothesis is that this decision can be described as the result of a complex case of capture along the regulatory process. To address this hypothesis, the research method chosen is qualitative and consists of a case study. On the one hand, a review of the literature is conducted on capture in order to define a framework for analyzing a concept which admits of degrees and forms. On the other hand, secondary data are collected from various documentary sources (scientific articles, press articles, reports, notes, official statements, firms' press releases, …), issued by different stakeholders (researchers in social sciences, firms, international organizations, non-governmental organizations, government agencies, websites, etc.[1]) on the basis of key words (COVID-19, pandemic, clinical trial, clinical research, medical research, pharmaceutical firms, Gilead, remdesivir, medicine, drug, treatment, patent, patent opposition, price, license, …). From these data, some stylized facts are drawn to retrace the important steps in the trajectory of remdesivir: a repositioned drug and candidate for COVID-19, from the basic research initiated in the 2000s to the granting of ODD in March 2020. Thus, an in-depth case study of the remdesivir episode will be conducted, combining the definition of a framework for the analysis of capture and the identification of stylized facts marking the trajectory of the drug.

The purpose of the article is to contribute to a literature that argues for a fertile rapprochement between the "predatory state" and "regulatory capture" approaches by emphasizing the regulatory role of the state and the risk of passive predation. If regulation is defined as "the public administrative policing of a private activity in relation to a rule prescribed in the public interest" (Mitnick, 1980, p. 7), it is crucial then to admit the capacity of the state to regulate not to serve the public interest but private interests. The state is not necessary this benevolent dictator serving the public interest, in accordance with the "contractual approach" to the state inspired by Hobbes' Leviathan, where individuals consent to abandon their natural rights and invest the state with power in order to avoid anarchy and private predation. The state is thus a wealth maximizer for society (North, 1981).[2] On the contrary, as suggested by theories of regulatory capture, economic actors may influence the state to put in place regulations that limit competition in markets and ultimately harm public welfare, as asserted by Stigler (1971). Finally, as proposed by Leeson et al. (2020), these theoretical approaches may be combined through "passive predation", to be distinguished from "active predation". The latter refers to a state that seeks to "suppress political competitors or expropriate citizens' property", using coercive means if necessary, while the former refers to "the state serving as a vehicle for the designs of private parties on each other" and "suppressing their competitors in the market or diverting the incomes of fellow citizens to their benefit" by means of regulation (p. 274).

In the following section, a review of the literature is undertaken on both the regulatory state and capture in order to define a framework for analyzing capture. Going beyond a first generation of works mainly devoted to "entry-barrier capture" à la Stigler (1971) and

[1] Such as the World Health Organization, South-Centre, Médecins sans Frontières, Knowlegde Ecology International, Public Citizen, USFDA, USPTO, WIPO, Patentoppositions.org, Medspal.org, Cinicaltrials.org, etc.

[2] A predatory state is "a state that would specify a set of property rights that maximized the revenue of the group in power, regardless of its impact on the wealth of the society as a whole" (North, 1981, p. 22, cited by Vahabi, 2016, 2020).

drawing on a second generation of works that enriches the study of capture, an analytical framework will be designed: to grasp the degree and forms of capture, to specify its ambivalent link to regulation as well as its nuanced relationship to passive predation. In a third section, tracing the trajectory of remdesivir on the basis of stylized facts and using our analytical framework, the hypothesis of a series of captures along the regulatory process will be considered through a case study of the remdesivir episode. In a last section, the argument is made that remdesivir finally suggests a weak capture, which calls for an amendment of the ODA: to prevent in the first place drugs for contagious and communicable (epidemic) diseases from obtaining ODD. Besides, the method defined and the case study carried out will be discussed: these do not claim to detect and measure capture as advocated by Carpenter (2014a). On the contrary, these show how capture is a complex concept that does not lend itself well to detection and measurement. However, is highlighted the urgent need to reform the ODA and its management by the FDA; given concerns about its misuse by an influential pharmaceutical industry driven by rent-seeking.

## 2 A framework for analyzing capture

The analysis of the regulatory state opposes two traditions: the "public interest theory of regulation" and the "private interest theory of regulation" (Den Hertog, 2010). These antagonistic approaches (generally associated with normative or positive approaches to the state) overlap with another distinction: the one between a protective state, serving the public interest, and a predatory state, serving private interests and thereby harming the public interest (Vahabi, 2016). Belonging to the latter tradition, theories of capture have developed over the decades to enrich the idea that regulation has to be apprehended as a predatory tool. A review of these theories will provide a framework to analyze capture in all its complexity.

### 2.1 Regulation as a predatory device

The economic study of state intervention starts from "market failures", "market inefficiencies" or "market inequities" recognition (Posner, 1974; Glaeser & Schleifer, 2003; Stiglitz, 2009). Beyond the uneasy functioning of markets when it comes to the presence of public goods or externalities, the public interest theory of regulation is concerned with the dynamics of markets. Left to their own devices, markets may produce oligopolistic and monopolistic structures in which firms adopt anti-competitive behaviors detrimental to the general welfare: supply rationing, high pricing, and quality cutting back for goods and services provided. Consequently, the state regulates to act on market structures and to prevent the noncompetitive behavior of economic actors, with a view to improving market efficiency and ultimately protecting the general interest.[3] The regulatory state is, in short, a protective state, whose action is dedicated to the maximization of general welfare (North, 1981).

[3] This echoes a distinction made by Kay and Vickers (1990) between "structural regulation" and "conduct regulation". Structural regulation concerns the regulation of the market structure, e.g. the implementation and enforcement of restrictions on entry or exit. Conduct regulation is used to control the behavior of producers and consumers on the market: price control or quality requirements for instance.

This vision of a regulatory and protective state was historically associated with the Progressive Era of the early twentieth century. During this period, the regulatory mission of the state was noteworthy in limiting the formation of trusts and monopolies in the markets and preventing harm to consumers. The regulatory state expanded through the creation of multiple commissions, the implementation of numerous regulations designed to control economic activities and the behavior of economic actors in various industries (transport, telecommunications, aeronautics, steel, meat, pharmaceuticals, etc.). Regulation was thus understood as a coercive tool mobilized by the state to protect the public interest (Glaeser & Schleifer, 2003; Novak, 2014; Holcombe, 2018),[4] mostly by preventing anticompetitive market structures.

In opposition to the conception of a regulatory and protective state, the private interest theory of regulation makes different hypotheses regarding the behavior of actors and tends towards a less idealized vision of the state's action on markets (Hanson & Yosifon, 2003; Peltzman, 1989). This approach rejects the hypothesis of an omniscient, benevolent and disinterested state acting exclusively to serve a public interest objective,[5] and moreover acting at zero cost. Instead, actors are assumed to take actions in markets at variable costs, both economic and political actors, and to be rational as their actions are guided by their self-interest satisfaction (Buchanan & Tullock, 1962).[6] Thus, regulation is described as the object and result of an exchange between political and economic actors, who behave as political and economic entrepreneurs, offering or acquiring regulation, following Stigler's (1971) statements.

From a first series of studies, inspired by Stigler's seminal article (1971), the "regulatory capture" refers to situations in which economic actors use their influence to obtain the implementation of a regulation that serves their private interests.[7] Based furthermore on the risk of free-riding inherent in collective action (Olson, 1965),[8] only small homogeneous groups with well-defined interests are able to influence political actors and obtain the implementation of regulations they can get benefit from. As "concentrated interests" or "special interests", these groups may enjoy anti-competitive market positions and benefit from rents (Krueger, 1976; Tullock, 1967),[9] thanks to a redistribution from the mass to themselves. Ultimately, a link is made between rent-seeking, capture and predation: the regulatory state, seized by rent-seeking interest groups, becomes a predatory state taking actions detrimental to the public interest (Holcombe, 2018; Vahabi, 2020).

In short, capture theories contrast "market failures" with "government failures" (Leight, 2009; Stiglitz, 2009). By regulating, the state does not conscientiously and virtuously serve

[4] Moreover, the political project cannot be ignored during this period, intended to limit the size of corporations to control their economic and political power (Novak, 2014). Beyond the possibility to undermine market efficiency and consumer welfare, large corporations have considerable resources and economic concentrated powers that are damaging to democracy (Zingales, 2017).

[5] A clear objective additionally: a peremptory assertion, as public choice theorists abundantly point out (for a review see Mueller, 2003; Butler, 2012).

[6] In other words, interest groups can influence the outcome of the regulatory process by providing financial or other support to politicians or regulators (Pelztman, 1989, p. 1).

[7] This definition refers so to what Dal Bo (2006) calls the broad conception of regulatory capture: "the process through which special interests affect state intervention in any of its forms". In contrast, under a narrow interpretation, "regulatory capture is specifically the process through which regulated monopolies end up manipulating the state agencies that are supposed to control them" (p. 203).

[8] Groups seek to exploit political processes for their own ends, but they are subject to the free-riding problem.

[9] For a literature survey on rent-seeking, see Tollison (2012).

the public interest but special interests, "as a rule" insists Sitgler.[10] State intervention as a cure (to market failures or market inefficiencies) is therefore even worse than the disease. Consequently, it is preferable that the state does not intervene and interfere with the functioning of markets, and that it refrains from regulating; at the risk of acting not in a protective way (serving the public interest) but in a predatory one (benefiting private interests) (Balleisen & Moss, 2010).

The regulatory and predatory state presented by the private interest theory of regulation was first associated with a revision of the historical reading of the Progressive Era. Following the works of Huntington (1952), Bernstein (1955), Kolko (1963) and Lowi (1969), the creation of commissions and the introduction of regulations are seen as the result of captures, the purpose of which for various industries is to create entry barriers to protect them from competition and to enable them to pocket rents; in short, "entry-barrier captures" that generate "regulatory benefits" (Holcombe, 2018). Regulation is captured by industries that are now regulated with the very specific aim of reducing the number of competitors and increasing prices (Peltzman, 1976; Posner, 1974; Stigler, 1971; Stigler & Friedland, 1962). So regulation set up favorable conditions for the emergence and consolidation of anticompetitive market structures. As asserted by Mitnick (1981), "companies preferred to pay the substantial costs of regulation rather than pay the uncertain and potentially large costs of operating in an unregulated market" (p. 72).

This conception of the state has inspired, from the 1970s and 1980s onwards, the politics of withdrawal from a state deemed responsible for inefficiencies and latent failures on the markets. It has ultimately prompted a massive deregulation process in whole areas of the economic system with the aim of dismantling non-competitive market positions.[11]

The influence of capture theories was then significant for decades in the field of research on regulatory politics. However, these initial investigations were not always able to apprehend the complexity of the concept of capture, which will be the project of a second generation of works.

### 2.2 Capture, a complex concept to define

The first generation of studies, following those conducted by Stigler, Posner and Peltzman,[12] implicitly or explicitly considered capture as a prevalent phenomenon in society, mostly associated with the implementation of regulations oriented towards the erection of entry-barriers. Subsequently, other approaches have intended to grasp the complexity of the concept, to deepen the study and understanding of the capture phenomenon. This second generation of works has shown, in particular since the 2000s, that capture admits degrees and forms that go well beyond "entry-barrier capture," and has as well an ambivalent relationship with regulation and deregulation processes observed during the twentieth century and the beginning of the twenty-first century (Balleisen & Moss, 2010; Braithwaite &

[10] "As a rule, regulation is acquired by the industry and is designed and operated primarily for its benefits" (Stigler, 1971, p. 4).

[11] What Peltzman (1989) calls "the most notable changes have meant a reduction or substantial elimination of regulatory constraints whose scope is unprecedented in modern American history" (p. 2).

[12] Works that propose more or less sophisticated mathematical models as noted by Posner (2014), with a particular reference to the imposing contribution of Laffont and Tirole (1993).

Drahos, 2000; Carpenter & Moss, 2014; Drahos, 2017; Jordana & Levi-Faur, 2003; Mattli & Woods, 2009).[13] To end with, these studies add to the idea of a passive predatory state.

### 2.2.1 Degree of regulatory capture

There is no present or missing capture according to a binary and narrow approach to the concept. There are degrees of capture, i.e. situations ranging from low to high levels of capture, which indicates symmetrically low or high levels of predation. As indicated by arrows in Fig. 1 below, the degree of capture determines the degree of predation, which in turn indicates the recommendations to be followed in order to put an end to a more or less severe damage to the public interest (Carpenter & Moss, 2014, pp. 11–12).[14] At one extreme, in a situation of "weak capture", the influence of special interests compromises the capacity of regulation to protect the public interest. The gap between the expected and observed outcomes of regulation is considered to be moderate, which also means by symmetry that predation has been moderated. In this case, the regulation will be amended to better serve the public interest (by adjusting the levels of subsidies or taxation applied in an industry for example). In this way, the regulatory action of the state is refined to reduce the effects of predation, to better align regulation with the public interest objectives. At the other extreme, in a situation of "strong capture", regulation has been extremely detrimental to the public interest. Predation has been strong and the social cost has been high. The regulation was put in place to produce specific policy outcomes, but the gap between expected and achieved outcomes can be viewed as huge; as a measure of the high level of predation that has taken place. In this case, the only possible option is to repeal the regulation, which is deemed to be extremely and irreparably harmful to the public interest; compared to an initial situation where there was no regulation (e.g. dismantling a regulated monopoly).

### 2.2.2 Types of regulatory capture

Capture cannot be summed up under the term "regulatory capture", which would be tantamount to admitting a single type of capture. In contrast, starting from the complexity of the "regulatory process", a useful typology of capture must be built up.

The "regulatory process" covers different steps: formulation, application and enforcement as described in the figure above. Each step involves the possibility of capture, as indicated by an arrow that associates the different steps of the regulatory process with various types of capture. As a result, different forms of capture inevitably exist, first of all legislative/statutory and agency captures (Carpenter, 2014a). The former identifies the upstream influence of interest groups on legislators in formulating regulation, while the latter recognizes their downstream influence on regulators in implementing regulation in the market. One does not exclude the other and these two types of capture may obviously coexist: a

[13] A second generation of works which, in the context of a globalized economy where the rising of regulations at national and international levels are significant, leads to the analysis of the dynamic of a "regulatory capitalism" (Levi-Faure, 2017; Braithwaite, 2011) or a "political capitalism", where capture is a determining ingredient (Holcombe, 2018). These studies are mainly conducted in the field of political science or international political economy.

[14] The literature also distinguishes "shallow and deep capture" (Hanson & Yosifon, 2003). The idea is that Stigler's seminal contribution refers to a "shallow capture" that underestimates the "potential depth of capture", and overlooks a critical degree of capture at work in society.

group may use its influence both to induce legislators to adopt a regulation favorable to its interests and to encourage regulators to administer it in its best interests, with more or less permissiveness for instance.

### 2.2.3 Intention and awareness of actors, and other types of capture

The first studies on capture are dedicated to the analysis of those economic situations where interest groups use their influence to obtain the formulation and implementation of regulation that erect entry-barriers; thereby sheltering incumbent firms from the competition of potential entrants. In this initial framework, these studies emphasize the awareness of public actors whose behavior is aimed, in exchange for personal gain, at formulating and implementing regulation that will serve particular interests at the expense of the general interest, in response to concentrated economic power. Thus, political and economic entrepreneurs become "rent creators" and "rent recipients" respectively (Holcombe, 2018). This is the case when an interest group offers a bribe to a legislator or regulator to induce him or her to formulate or implement regulation that serve its interests. Especially, regulation can be designed to limit the number of firms in a market, promoting non-competitive market structures conducive to rents. As indicated in Fig. 1, the existence of a bribe establishes so the awareness and intent of the recipient (over and above that of the giver), demonstrating a case of statutory or agency capture based on an illegal and condemnable practice. This is finally a "classic case of passive predation" described by Leeson et al. (2020), where public actors serve deliberately and selfishly private interests through the formulation or application of regulation (see below).[15]

However, there are more complex situations where the awareness and intent of public actors cannot be so clearly established, as highlighted by recent studies on "cultural capture", "social capture" or "cognitive capture" (Baxter, 2011; Buiter, 2008; Carpenter, 2014b; Kwak, 2014). Due to repeated interactions and proximity to economic actors, public actors may act under the more diffuse influence of interest groups. They internalize "the objectives, interests and perceptions of reality of the vested interests they are meant to regulate" (Kwak, 2014, pp. 78–79). Gradually, "their conception of the public interest has been colonized by industry", so that "the regulated industry can shape policy outcomes" (Idem). As indicated in the figure above, legislators and regulators may therefore act to the detriment of the public interest and for the benefit of private interests, without being aware of it, let alone intending to do so for personal gain. This is far from a "classic case of passive predation" à la Leeson et al. (2020) (see below).

As a matter of fact, revolving doors are at the heart of an informal, subtle and diffuse exchange between political and economic actors.[16] They offer the prospect of better paid future positions in the private sector for public actors who today formulate and apply regulation that may benefit an industry as a result of legislative or agency capture. In these situations, it is tricky to say whether there is compromise or corruption as in the case of a

[15] In Leeson et al. (2020), there is no such explicit and clear discussion of this in their study of the regulation of medicine (quack medicine) in the nineteenth century in England. Individuals are considered rational and act in pursuit of self-interest.

[16] "Revolving doors" through which the actors in charge of formulating or applying a regulation in an industry make available valuable "bureaucratic capital", made up of specific knowledge and special relationships capable of generating a substantial profit for firms able to offer jobs and high salaries (Brezis & Cariolle, 2019).

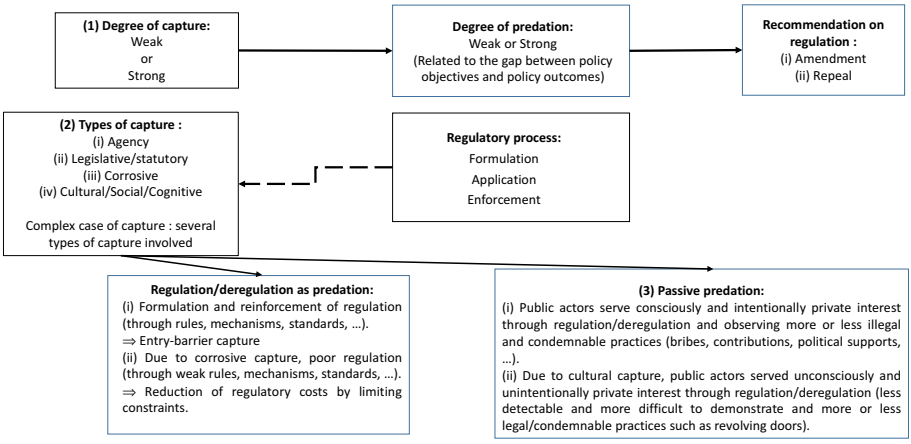


**Fig. 1** A framework for analyzing capture

bribe, since going through these doors is a legal option for public actors.[17] Therefore, even taking into account the existence of revolving doors, public actors may feel (or pretend) that they are acting in good faith, with integrity and honesty in order to protect the public interest to the best of their ability; while at the same time admitting the possibility of later taking up a position in the industry. In the absence of proven awareness and intent on the part of the public actor, it is hard to prove that capture has occurred.

To put it differently, on the one hand there is so "traditional materialist capture", also designed as "financial capture" with reference to situations of bribery, where the legislator or the regulator captured by concentrated economic powers is motived by his or her material self-interest rather than the public interest and acts in favor of private interests. On the other hand, there is "non-traditional non-materialist capture" (also called social, cognitive or cultural capture), in which the legislator or the regulator starts to think like the regulated industry and serves its benefit (Kwak, 2014). In the latter case, there are not necessarily bribes, financial contributions received or revolving doors passed through. Therefore, it is not easy to establish the awareness and intent of public actors, to detect and demonstrate capture as public actors may be convinced that they are acting with probity in the public interest and yet under the influence of concentrated economic powers.

### 2.2.4 Capture through regulation and deregulation processes

Studies make it possible to put into perspective the idea that capture implies a univocal orientation of state action towards the implementation and reinforcement of regulation to erect and consolidate entry barriers for the benefit of private interests.

There are situations where capture results in less regulation, i.e. the relaxation of regulatory constraints on economic actors, which reduces the costs incurred and increases rents. The concept of "corrosive capture" means that interest groups use their influence to

[17] Accordingly, public actors may act with impunity for the reason that revolving doors are neither illegal nor condemnable.

"render regulation less robust than intended in legislation or than what the public interest would recommend" (Carpenter & Moss, 2014, pp. 16–17).[18]

As specified in Fig. 1, the types of capture give rise to regulation and deregulation, both of which result from predation. So, regulation and deregulation may be two sides of the same coin, that of the capture of legislators by economic actors to obtain: (1) a strengthening of regulation to increase entry-barriers, to limit competition and favor rent-seeking; and/or (2) a relaxation of regulation to reduce regulatory costs for incumbents and to avoid the erosion of rents.

In sum, "deregulation, like regulation, may also be sought and/or manipulated strategically" (Mitnick, 1981, p. 80). The analysis of state action and the demonstration of capture become even more difficult since regulation is an ambivalent set of rules, norms, procedures, mechanisms, sanctions, etc. These are designed to both proscribe or prescribe economic behaviors, and may be used for the benefit of special interests.[19] This set is therefore made up of institutions that are more or less flexible or, on the contrary, more or less restrictive, which makes it difficult to examine and detect capture.

### 2.2.5 Passive predation

As stated in the introduction, our approach is based on a detailed analysis of capture that builds upon a second generation of works to go beyond "entry-barrier capture" à la Stigler. In doing so, the understanding of predation, in particular passive predation, is enriched.

Indeed, the identification of various forms of capture deepens the idea of passive predation. Predation can be passive in the sense that the state's regulatory action is designed to serve particular interests (Leeson et al., 2020). However, this understanding needs to be appreciated in terms of awareness and intention of public actors as discussed above. In a situation of cultural, social or cognitive capture, the legislator or regulator is not inevitably aware that he or she is acting in favor of private interests and to the detriment of the public interest, as the proximity to the regulated industries is strong. In short, state agents may, not necessarily deliberately but under the impetus of an influential interest group, operate a transfer of wealth from the mass to a group; so much since their way of thinking and their behavior have been colonized by the objectives, interests and perceptions of reality of the vested interests (Kwak, 2014).[20] As described in the figure above, predation may then be defined as passive in a variety of situations where the state serves as a vehicle for private parties' interests, with or without being aware of acting in favor of such interests and at the expense of the public interest, with or without intending to profit personally.

The concept of passive predation proposed here is finally different from that defined by Leeson et al. (2020). A critical distinction is made between public actors serving as vehicle to satisfy private interests and public actors serving more or less conscientiously and intentionally private interests. In other words, Leeson et al.'s approach to passive predation is an

[18] As Etzioni (2009) states capture may occur to "dilute existing regulations" (…) "weaken enforcement of existing regulations", or even "repeal existing regulations" (p. 323).

[19] As sums up by North (1991a), rules, norms, procedures, habits, customs, … are institutions, that is *"human devised constraints that shape human interaction"* (p. 3). As such, they reduce uncertainty and enable transactions to take place (North, 1991b).

[20] There is a reason widely highlighted in the public choice literature. Industry will not say, when trying to influence political actors, that the adoption of a law will serve its sole interest, but that it will primarily satisfy public interest objectives: domestic security, public health, national competitiveness or sustainable development.

intentionalist (or deontological) morality, whereas our approach is consequentialist (or teleological). According to our approach, and contrary to the intentionalist approach, the act is not judged according to the intentions of the individual who would seek to gain personal benefit from it, by serving particular interests and deliberately harming the general interest. To understand the full richness of the concept of capture and, by symmetry, that of passive predation, any action undertaken by an individual is considered immoral and condemnable if the consequences on the general welfare are deleterious for the reason that it benefits private interests. This is the useful distinction between the passive predation proposed by Leeson et al. and our own, starting from a thorough analysis of capture and then progressing to that of predation.

Besides, the purpose of a broader view of passive predation is, first, to insist on the complexity of capture as has been widely discussed above. Public actors may serve special interests while feeling that they are acting with integrity and honesty, putting forward if necessary the legality of their actions. Second, the purpose is to underline the difficulty to detect and measure capture, for the reason that public actors whose compromise or corruption is suspected, may insist on their probity by claiming the legality of their actions. Especially if they later get some personal benefit from their actions through, for instance, legal but morally reprehensible practices of revolving doors.

At the end of a selective literature survey on the theories of the regulatory state and particularly on the theories of capture, a framework for analyzing capture is defined and summarized in Fig. 1. In each situation, this framework allows to specify the degree of capture (weak or strong), by symmetry the degree of predation (weak or strong) and the recommendation to be followed for solving the predation (amending or repealing a regulation). It helps also to stipulate the form(s) of capture involved and their relationship with the processes of regulation or deregulation, through the concepts of legislative, statutory, agency and corrosive capture. This framework indicates furthermore the extent of passive predation: more or less awareness and intent of public actors to serve private interests when formulation or implementing a regulation (in the light of cultural, social or cognitive capture), and so to damage public interest, from a consequentialist moral approach to predation. It enables to conduct an in-depth examination of the FDA's decision to grant ODD to a firm for a drug candidate for a contagious disease in the midst of a public health crisis. The investigation of this decision will be conducted in order to highlight the possibility of a complex capture described as the result of a passive predation.

## 3 A COVID-19 drug candidate: A complex case of capture?

The trajectory of remdesivir has not been a smooth one. Initially in development for Ebola, then repositioned as a drug candidate for COVID-19, it has been the subject of much controversy in March 2020 at the start of a pandemic. On that date, the granting of a second ODD by the FDA raised suspicions of capture by a major player in the pharmaceutical industry. On the basis of data collected,[21] some stylized facts are drawn and, using the analytical framework designed previously, the complex capture hypothesis is examined.

[21] On websites: USPTO, USFDA, WHO, Clinicaltrials, Medspal and Patentoppositions.

### 3.1 The chaotic course of a drug candidate for COVID-19

Remedivir has successively been a drug in development, repositioned, contested, licensed, authorized and finally registered as retraced in the Fig. 2 below.

Initially, remdesivir was a molecule in development to cure coronaviruses (Ebola, then SARS and MERS), during basic and preclinical research largely paid with public funds (Ardizzone, 2020; Eastman et al., 2020; Kiplin et al., 2020). While this research did not lead to the commercialization of remdesivir, Gilead filed a provisional patent in 2008, obtained secondary patents from 2011 and gained a first ODD in 2015.

Later, remdesivir became a repositioned drug. On 4 February 2020, a public health emergency due to COVID-19 was determined in the United States and the urgency was to provide drugs as quickly as possible to treat infected patients, massively hospitalized. There was so a rush to drug repurposing, that is the recycling of existing drugs to treat the new coronavirus in a shorter time to avoid mass deaths (Dotolo et al., 2021).[22] Worldwide a large clinical trial was exploring drug repurposing, especially the Solidarity Clinical Trial for COVID-19 treatments launched by the World Health Organization (WHO) in March 2020 (WHO, 2020a). Like a few other molecules, remdesivir became a drug candidate, undergoing large clinical trials, mostly paid with public funds (see below).

Remdesivir then turned into a contested drug. Gilead had to face criticism regarding the management of its property rights and the associated monopolies (Médecins Sans Frontières, 2020). Legal opposition to its patents were raised in countries in the global South, concerned about access to medicine for COVID-19.[23] To face it, the firm signed non-exclusive voluntary licensing agreements on May: with nine generic producers based in Egypt, India and Pakistan, with the aim of providing the drug in 127 countries (Gilead, 2020a).

Meanwhile, remdesivir became a highly disputable orphan drug when Gilead was granted a new ODD in March 2020 for the molecule to treat COVID-19. Immediately, the announcement was followed by an outcry: the granting was considered as an unconscionable abuse of the ODA (Public Citizen, 2020).[24]

The ODA was first passed in 1983 to promote the development of drugs for rare diseases that affect limited populations. Today, more than 7000 rare diseases affect each a small number of patients and the total number of Americans living with such a disease is between 25 and 30 million.[25]The potential market for each rare disease is small and

[22] More precisely, whether repositioning, repurposing, reprofiling, redirecting, retasking, rediscovery or rescuing, these terms refer to the search for new uses or new indications for a known drug: a drug that is already marketed, withdrawn from the market (for health or commercial reasons), or never reached the market (remained in the development stage for lack of proof of safety or efficacy for a first indication). Drug repurposing therefore covers "drug candidates", "abandoned drugs", "approved drugs" and "old drugs" (Langedijk et al., 2015). In all these cases, drug repurposing makes it possible to reduce the costs and development time as well as the risk of failure. These drugs have often passed several stages of clinical development and therefore have demonstrated a known safety or even efficacy profile, and have been marketed for a first indication (Ashburn & Thor, 2004).

[23] A post-grant opposition and a pre-grant opposition were filed respectively in India in April and in Argentina in May as indicated in Fig. 2 (Medspal website).

[24] Immediately, Gilead requested the agency to rescind the status, and so renounced all the advantages that came with it (Gilead, 2020b).

[25] The number of people worldwide living with a rare disease is estimated at 300 million (www.rarediseasesinternational.org).

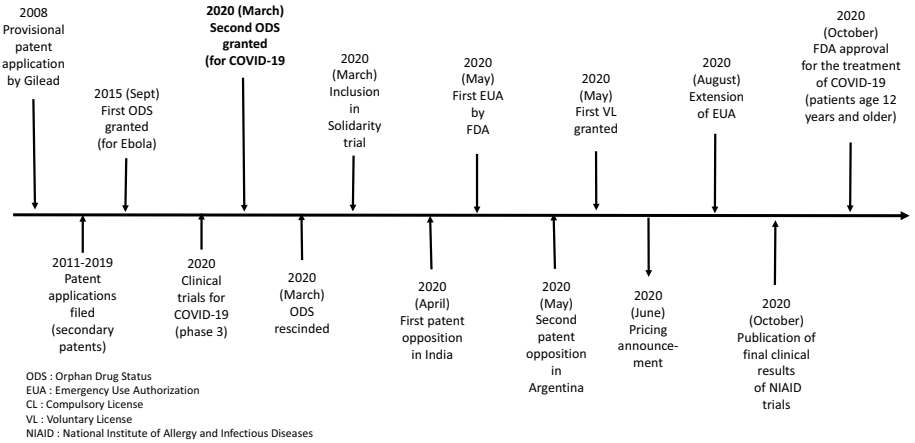


**Fig. 2** The trajectory of remdesivir: some stylized facts

unprofitable for pharmaceuticals firms.[26] To address this issue, economic incentives were designed to support the development of drugs needed by rare diseases patients. Once the orphan designation is granted for a specific product indication, the firm is qualified for seven-years of market exclusivity for the approved use of a drug: the so-called orphan drug exclusivity. During this period, the FDA cannot approve a new drug application or a generic drug for the same drug and for the same rare disease.[27]This post-approval incentive begins on the date of FDA approval for the designated orphan indication.[28] The OOPD gives also a 25% tax credit and grants for incurred clinical trials costs. In addition, a fast-track procedure is provided for the evaluation of registration files by the FDA for marketing approval,[29] as well as a waiver for the user fees the firms must pay to the federal agency for new drugs (Arno et al., 1995; Seoane-Vasquez et al., 2008; Kesselheim, 2010; Reardon, 2014; Haffner, 2016; Thomas & Caplan, 2019). Last but not least, ODD may be granted when the disease "affects less than 200,000 persons in the United States, or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or

[26] Especially due to the US Kefauver-Harris amendments to the Food, Drug and Cosmetic Act (or "Drug Efficacy Amendment") passed in 1962. These amendments required drug manufacturers to demonstrate the effectiveness of their drugs for its intended use prior to the FDA approval and marketing. Consequently, the costs of drug development significantly increased due to higher safety and efficacy standards put in place (Haffner, 2016).

[27] The FDA can approve a second application for the same drug for a different disease indication. This explains why Gilead was entitled to apply for a second ODD for remdesivir and obtained it.

[28] Initially, this market exclusivity was designed to address the limited opportunities to recoup R&D costs for drug without patent protection since the ODA required that marketing exclusivity could only be granted on non-patentable drugs (biotechnology ones). An amendment removed this requirement in 1985 (Arno et al., 1995).

[29] The procedure is faster compared to a new drug approval. The registration files provided are lighter for the reason that safety and efficacy standards applied are lower.

condition will be recovered from sales in the United States of such drug" (Department of Health and Human Services, 2001).[30]

Unsurprisingly, the federal agency was questioned for its handling of the application filed by Gilead and its decision to concede exclusive marketing rights for a drug candidate for COVID-19; a contagious disease that was declared "a national emergency" on March 13 in the United States, and "a pandemic" by the WHO two days earlier. The agency was criticized for failing to scrupulously respect the ODA, which stipulates the need to take into account "the facts and circumstances as of the date the request for designation of the drug" (Cassedy, 2020; Department of Health and Human Services, 2001).

The FDA's decision was described as setting a risky monopoly situation during a health crisis. By obtaining ODD for remdesivir, Gilead was about to enjoy a monopoly for seven years. This situation was all the more vivid that an orphan drug exclusivity cannot be lifted (compared to a patent exclusivity that can be suspended by the US government). The FDA may not authorize the marketing of other drugs; expressly those that could be produced under compulsory license.[31] Further, orphan market exclusivity is stronger than patent exclusivity since it may not be interrupted by a competitor, even if the underlying patent has expired (Kesselheim, 2010). Thus, Gilead had more leeway to set a high price for the molecule under a robust monopoly position (Cassedy, 2020; Lazonick et al., 2019).

In June 2020, remdesivir was announced to be an expensive and very lucrative drug. After the FDA issued an Emergency Use Authorization[32] for the drug, the firm announced that a 5-day treatment would cost 3120 dollars for private insurance and 390 dollars for US public health programs. The expected turnover was so estimated at one billion dollars for the US market, and even more than two billion dollars worldwide by the year 2020 (Mancini et al., 2020). As aforementioned, the drug was developed with significant public funding, from basic research to preclinical research and finally clinical research: from 2014 to 2019, 76 million dollars were funded by the NIH to prove that remdesivir was a broad-spectrum antiviral (Ardizzone, 2020; Eastman et al., 2020).[33]

In the end, Gilead demonstrated a very offensive management of the life-cycle of remdesivir. The firm tried to obtain market exclusivity and to make profits, through a second ODD for a drug not yet approved for a contagious disease during a health crisis, and developed with public funds. But was this ODD the result of a capture?

[30] Arno et al. (1995) recalls that in the first place the act covered "any disease condition that occurs so infrequently in the United States that the there is no reasonable expectation that the cost of developing and making available a drug for such disease or condition will be recovered from sales in the United States of such drug". So to qualify for tax credits, firms were required to submit financial data documenting limited profitability. So rather than be subject to such a financial scrutiny, the pharmaceutical industry sought to base the definition of orphan disease on the size of the affected patient population rather than on profits levels. Accordingly, the ODA was amended in 1984 to modify the definition of a rare disease or condition with a threshold of 200 000 persons arbitrary determined (pp. 233–234).

[31] This is a legal provision authorizing the temporary suspension of intellectual property rights and the production of generic drugs, in compliance with the TRIPS agreement, and in case notably of health crisis.

[32] FDA may authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases when there are no adequate, approved, and available alternatives (www.fda.gov).

[33] Likewise, a global mapping of clinical research on remdesivir shows that this research was widely public. According to the data collected at the end of June 2020 on ClinicalTrials.gov and taking the drug candidates selected by the WHO for clinical research, there were 204 clinical trials conducted in phase 3. Among these, remdesivir was subject to 17.1% of clinical trials in phase 3 of the selected drugs and public research represented nearly 66% for these trials.

### 3.2 Remdesivir, a complex case of capture?

From the framework for analyzing capture defined and the stylized facts retracing the trajectory of a drug candidate for COVID-19, the remdesivir case does not suggest a simple capture. It rather puts forward a series of captures or what may be defined as a complex capture architecture.

First, the remdesivir case suggests an "agency capture". The goals considered to be in the public interest are expressed in the regulation, but their achievement is "distorted, corrupted, watered down, or otherwise turned to an industry's advantage" (Carpenter, 2014a, p. 59). The application of the regulation, entrusted to the FDA, has been distorted, corrupted to benefit special interests. Actually, Gilead should never have received ODD for a drug in development to treat a contagious disease at the start of a pandemic. The highly contagious nature of the disease predicted large numbers of COVID-19 cases in the population and huge profit for any firm developing and marketing a treatment for the new coronavirus. This decision highlights a failure in the management of the ODA and reveals the influence of the firm and more largely of the pharmaceutical industry on the federal agency.

Indeed, since the ODA came into force, the FDA had granted on several occasions ODD to firms for drugs to treat a contagious or communicable disease during a health crisis. Until the 1980s, AZT was a failed drug, never marketed to treat cancer and repositioned to treat HIV/AIDS. In 1985, it was given ODD as a treatment for a communicable disease at the beginning of what was expected to be a pandemic (Ackiron, 1991; Arno et al., 1995). In 1988, another antiviral, ddC, also received ODD as a treatment for HIV/AIDS. Thus, the repeated and unfortunate granting of ODD makes evident that the formulation of the ODA needs to be questioned upstream and not merely its implementation downstream by the FDA.

Upstream, a "statutory or legislative capture" may to be lamented, "before the administrator ever acts" (Carpenter, 2014a, p. 59). A regulation should be designed for public interest, but in a context featured by a conflict between public and private interests. In this instance, the former relies in having access to drugs, that is the availability of quality drugs at reasonable prices so that patients can be treated. The industry's interest is to obtain the longest market exclusivity and to sell a drug at the highest price, free of competition to maximize rents. Thus, the ODA may have been formulated by the legislator to serve the industry's interests more than those of the public, through a limited "institutional supply" and a closed "institutional context of regulation" (Mattli & Woods, 2009, pp. 16–17).

Indeed, a "corrosive capture" may be raised to acknowledge the pharmaceutical industry's ability to lobby in order "not to build up new regulations, but rather to weaken current regulations and forestall new ones" (Carpenter, 2014b, p. 70). In particular, the industry may have influence the legislator to design a deficient regulation to serve its interests. The regulation may be deficient to the extent that essential safeguard mechanisms are not provided to limit capture and mismanagement of ODA. The industry may have lobbied to weaken laws, rules, standards, procedures, and mechanisms for serving its interests, to the detriment of the public interest.[34] Thus, deregulation and poor regulation may

[34] The phenomenon is not new and specific to ODA as reported by Nik-Khah (2014), Carpenter (2010) or Braithwaite and Drahos (2000). Since the beginning of the twentieth century, the pharmaceutical industry had constantly worked to limit the scope of regulation in the pharmaceutical sector on key issues such as patent protection, product safety and efficacy, price control and consumer advertising. This struggle to limit the scope of regulation and implement a poor regulation was especially intensified following the enactment of the 1962 Kefauver-Harris Amendments, which extended the FDA's powers following a health scandal. From that date and the enactment of these amendments, the industry had tirelessly sought to influence legislators through various means not to disband the FDA, but to limit its missions and powers.

be the sign of a “corrosive capture” operated by an influent industry on the legislator as aforementioned.

As a matter of fact, regulation is a social construction, in which a variety of stakeholders with different powers in time and space intervene (Braithwaite & Drahos, 2000; Drahos, 2017; Mattli & Woods, 2009). Therefore, regulation may be more or less stringent, reinforced or relaxed depending on the interplay of stakeholders (Carpenter & Moss, 2014). So in every institutional context, regulation may be the result of a capture. As previously stated, capture does not solely refer to situations where regulation is set-up and reinforced under the influence of an industry defending its interests, through for instance the implementation and the strengthening of property rights to limit generic competition on the market. Capture also refers to situations where regulation is implemented in a less restrictive manner under the influence of an industry, for example through the design of weak price control mechanisms to content firms’ rent-seeking behaviors.

In this case, a limited institutional supply and so the formulation of a deficient regulation may be regretted. In practice, safeguards are lacking to guarantee transparency in the application of ODA. The Act does not provide for mechanisms to publicize ODD applications filed by firms. This only requires the FDA to publish every month “all drugs designated as orphan drug”, “the date of the granting of orphan-drug designation” and “the designated use in the rare disease or condition” (Department of Health and Human Services, 2001). Unsurprisingly, when a NGO (Knowledge Ecology International) wrote to the federal agency on March 25 asking when Gilead filed an application for ODD, the agency answered "it was unable to share that information as it’s considered commercially confidential"(Cassedy, 2020). An orphan drug application, which entitles the applicant to government grants and other benefits intended to encourage the marketing of orphan drugs, does not require complete transparency while being filed and reviewed. Yet, advertising of patent filings exists within the USPTO and the extension of such a procedure could have been introduced in the Act regarding applications for orphan status received by the FDA.

Moreover, no procedure is laid down to monitor the follow-up of applications, to possibly oppose ex-ante or ex-post an application or the granting of ODD by stakeholders. Once more, such procedures are stipulated for patent applications in some legislations. These applications are advertised and can be contested, before or after a favorable decision is made by the patent office, as required for instance by Brazilian or Indian legislation (Shadlen et al., 2011). Firms or the civil society can oppose the granting of a patent or request the withdrawal of a granted patent. The US law only provides for the re-examination of granted patents at the request of a third party. Inopportunely, the ODA does not offer a more inclusive, transparent and fair review process. In this regard, the "institutional context of regulation" is limited: the implementation, monitoring and enforcement of the rules are entrusted to a "more exclusive and secretive agency" (Mattli & Woods, 2009, p. 17).[35]

Worse, no formal pricing mechanism is provided by the ODA, despite the proposals submitted and rejected over the years (Arno et al., 1995; Gamie et al., 2015; Picavet et al., 2014). But inflation has been observed over the years in the price of drugs marketed under orphan status (under a seven-year monopoly), which raises concerns.[36] A price control

[35] For instance, key stakeholders (above all civil society) are not involved in the review process for orphan drug applications to ensure that the public interest is best served.

[36] Between 1998 and 2017, the average annual cost of orphan drugs increased 26-fold, while the cost of specialized and traditional drugs doubled (Luzzato et al., 2018). In 2017, the average annual cost of an

mechanism is needed for orphan drugs, whose development costs are partly borne by taxpayers.[37] To date, the institutional supply remains poor in terms of pricing mechanisms for drugs in general and orphan drugs in particular. The risk is then that drugs are eventually marketed at high prices under monopolies, whereas the institutional demand is strong for price control mechanisms. This is confirmed by the involvement of civil society in the social issue of access to medicines and the call for legislators to enact accordingly; for the most part, since the HIV/AIDS epidemic and prohibitive pricing of antiretroviral marketed under monopoly because of ODD or patent (Trullen & Stevenson, 2006).

Finally, the ODA does not envisage the revocation of ODD when sales exceed a certain threshold. In contrast, in the European Union, the ten years of exclusivity granted to orphan drugs can be reduced to six years if a drug is sufficiently profitable after five years on the market. This mechanism limits the rent-seeking behavior of firms or makes it possible to rectify a judgment error (afterwards a larger population may be prescribed the orphan drug). Alike, the ODA does not require firms to repay the tax credits and research grants they received for developing orphan drugs when revenue from a drug exceeded a certain level (Thoene, 1991; Arno et al., 1995; Sarpatwari & Kesselheim, 2019; Thomas & Caplan, 2019; Kesselheim, 2010; Haffner, 2016).[38]

These shortcomings in designing safeguard mechanisms to ensure better protection of the public interest (public health issues) can be interpreted as the result of statutory or legislative capture and furthermore of a corrosive capture: the industry may have used its influence to obtain a favorable regulation, featured by blatant institutional deficiencies. These have not been addressed over the years despite the controversial episodes of AZT, ddC, amifampridine, ivacaftor, pirfenidone, nusinersen, entamidin or erythropoietin: all orphan drugs marketed at high prices and having generated millions or billions of revenues (Thoene, 1991; Sarpatwari & Kesselheim, 2019).

Finally, whether statutory, legislative, agency or corrosive, capture may above all be cultural for the reason that the way in which the federal agency is funded and operates has changed radically. The Prescription Drug User Fee Act (PDUFA) of 1992 transformed the FDA from an agency funded entirely by taxpayers to one funded in large part by user fees paid by pharmaceutical firms. In return, there is greater industry involvement in the operation of the federal agency, more direct involvement in the management and timeliness of the review of new drug application (Lazonick et al., 2019; Nik-Khah, 2014). Today, out of a total budget of 6.1 billion dollars, 46% is paid for by industry user fees (USFDA, 2021).[39] Firms pay fees when submitting applications to the FDA for drug review and annual fees

Footnote 36 (continued)
orphan drug was 124,000 dollars compared to 5000 dollars for a traditional drug (America's Health Insurance Plans, 2019).

[37] Most of all, when drugs are repurposed and R&D costs are much less expensive than those incurred for the development of new chemical entities.

[38] Different proposals have been submitted over the years to reform the ODA and prevent the marketing of orphan drugs at high prices, drugs then capable of generating large sales and huge revenues. In particular, proposals have been made with the aim of "precluding drugs for contagious epidemic diseases like HIV/AIDS from obtaining orphan status" (Arno et al., 1995). Proposals have been made to introduce price ceilings, a windfall profits tax on orphan drugs during the seven-year period of market exclusivity, or the revocation of ODD when sales exceed a certain threshold (Sarpatwari & Kesselheim, 2019; Thomas & Caplan, 2019; Kesselheim, 2010; Haffner, 2016). All these proposals have successively been rejected.

[39] The agency's resources have not evolved favorably in relation to the missions entrusted (mostly compared to the resources allocated to other federal agencies such as the NIH or the CDC). In addition, these resources have increasingly been dependent on the industry that the FDA is supposed to regulate (USFDA, 2021; Institute of Medicine Forum on Drug Discovery, Development, and Translation, 2007).

according to the number of approved drugs they have on the market. But the PDUFA is much more than user fees as noted by Mitchell et al. (2022). The FDA and the firms negotiate the user fees and performance measures that the federal agency has to meet to collect them, and proposed changes in FDA processes.[40] As a result, whereas it took 29 months for the FDA in 1987 to decide whether to grant a firm marketing approval for a drug, this time frame has been reduced to 10 months in 2018.[41] In addition, as shown by Mitchell et al. (2022), "the need for PDUFA reauthorization every 5 years has created a recurring legislative vehicle through which far-ranging changes to FDA have been enacted, reshaping the agency's interactions and relationship with the regulated industry" (p. 287), a process which may advantage the industry.[42] Consequently, the reform of the FDA's financing and operating rules in the 1990s effectively encourages repeated interactions and close proximity between the agency's administrators and the industry. This is likely to reinforce the phenomenon of revolving doors and professional mobility between positions as legislators, regulators or employees in the pharmaceutical industry. The permeability between the public and private spheres in the health sector is therefore real and reinforce a process by which the industry builds and strengthens the defense of its interests through repeated interactions and regular meetings. Specifically, on negotiation rounds that take place when the PDUFA is re-authorized every five-years.

For that reason, cultural capture operates insofar as legislators and regulators are more receptive to the arguments of the pharmaceutical industry: namely increased research and development (R&D) costs, longer lead times for developing innovative drugs, or length of review time for marketing approval application. The industry "may consciously seek to encourage its regulators to identify with [industry] members and their interests" (Kwak, 2014, p. 79), thus regulators may act more or less consciously and intentionally to serve the interests of the industry as aforementioned. Whether their conception of the public interest has been colonized by the industry, they then act without the awareness and intention of serving private interests, without seeking personal gain. They may act with a sense of serving the public interest. On the other hand, if they expect personal gain (getting a better paid job in the private sector in exchange for services rendered), then they act consciously and intentionally, but legally to serve private interests. In both cases, the passive predation of legislators and regulators is evident; being understood that passive predation does not necessarily include awareness and intent of public actors to serve special interests and damage public interest as discussed above, through the lens of a consequentialist view.

In the case of remdesivir, the FDA improperly granted ODD to Gilead for its drug to treat a contagious disease at the beginning of a public health crisis. This clearly suggests a case of agency capture, which can then be explained by cultural capture; where the federal agency, financially dependent on an influential industry (a huge concentrated economic power), can make decisions contrary to the public interest, more or less consciously and more or less intentionally. The fact remains that awareness and intentionality of the actors are difficult to establish in this case and so is the capture. It is also challenging to show

[40] The FDA is in a vulnerable position as judge and party in the marketing approval of drugs. As it speeds up the time to market a drug and increases the number of drugs marketed each year, its resources are increasing.

[41] This has consequences: Franck et al. (2014) found that before the user fee act was approved, 21.2% of medications were withdrawn or had new black box warnings as compared to 26.7% afterwards.

[42] The authors assert that "the majority of policy changes enacted through PDUFA legislation have favored industry through decreasing regulatory standards, shortening approval times, and increasing industry involvement in FDA decision-making" (p. 287).

whether public actors act consciously or not, intentionality or not when capture is cultural, social or cognitive.

To sum up, there may be a complex architecture where multiple cases of capture are revealed to furthermore understand the extent of passive predation. Under the influence of the pharmaceutical industry, it may be deplored that the Congress passed a regulation that still presents flaws to properly encourage R&D and marketing of orphan drugs under socially acceptable conditions. Notably, it neglected to put in place more consequent safeguard mechanisms to avoid capture and mismanagement of the ODA; in the first place by preventing drugs for contagious epidemic diseases from obtaining orphan status and monopoly. The content of the ODA still seems sensitive to the interests of pharmaceutical firms and its application by the federal agency may lead to decisions that, against all expectations, may harm the public interest by serving firms' rent-seeking; chiefly in the presence of failed drugs, in development and never marketed, like remdesivir at the time of the event.[43] The offensive strategies of firms can then go as far as trying to obtain undue exclusive marketing and to make unfair profits from drug developed in part with public funds.

## 4 Discussion

The case of a molecule repositioned and candidate for COVID-19 which was granted ODD in March 2020 can be interpreted as the result of agency capture: a firm was able to obtain ODD for a treatment to cure a contagious disease at the onset of a pandemic. But more than that, a complex case of capture was described. A firm was able to obtain ODD improperly because the ODA may have been the subject of statutory capture, or even more of corrosive capture and cultural capture. The lack of essential safeguard mechanisms is evident despite several amendments, which limits the scope of an act that should above all preclude the marketing of orphan drugs at prohibitive prices, which can then generate high profits. Moreover, the absence of such mechanisms can be explained essentially by major changes in the way the FDA is funded and operates. More dependent on funding from the pharmaceutical industry, which plays a greater role in setting its objectives, particularly performance targets, the federal agency is in fact under the perceptible influence of the industry.

Although complex, the remdesivir case suggests a "weak capture". Over the years, the ODA has enabled the marketing of drugs to treat orphan diseases. To date, more than 500 orphan drugs have been approved for sale in the US (IQVIA Institute, 2018). In 2018, 58% of new drugs approved were for a rare disease indication. Clearly, the marketing of orphan drugs at high prices and as a source of significant profits for pharmaceutical firms is to be deplored.[44] One can condemn the fact that orphan drugs become blockbusters: once marketed to treat an orphan disease, they are then prescribed for other therapeutic indications covering much larger populations without the ODD status being withdrawn.[45] However,

[43] It is rightly pointed out that the introduction of the ODA was not intended to change the pharmaceutical R&D model. As a matter of fact, firms are increasingly seeking to obtain ODD in order to enjoy all the benefits that go with it: notably lower R&D costs, exemption from user fees and a temporary monopoly (Thomas & Caplan, 2019).

[44] Another concern is that the large number of drugs marketed under ODD means more exemptions from user fees for firms and a loss of revenue for the FDA.

[45] Firms can artificially target a drug to a disease sub-population and thus try to obtain ODD and all the benefits associated (Reardon, 2014).

the remdesivir case is not the sign of "strong capture" that would require the repeal of the ODA. This puts forward a "weak capture" that calls for a modification of the Act to avoid passive predation, that is the influence of an industry on the legislators and regulators so that more or less consciously and deliberately regulation is designed and applied to serve private interests: firms' rent-seeking at the expense of public interest. Therefore, at the very least, provisions should be introduced to regulate the prices to be charged and the profits to be made, as well as to provide for the revocation of the ODD under certain conditions. More essentially, there is an urgent need to review the way the FDA is funded and operated in order to drastically reduce the influence of the pharmaceutical industry on a federal agency that ensures the safety and efficacy of products representing 20% of all consumer spending (USFDA, 2021).

Yet, the demonstration is still delicate when it comes to capture, a fortiori multiple captures as suggested here. The FDA's decision to grant ODD for a drug in development to treat a contagious disease in the midst of a public health crisis is a far cry from the objectives of the ODA: to ensure the marketing of drugs to treat orphan diseases, and obviously to preclude the marketing under ODD of drugs for communicable or contagious epidemic diseases, such as HIV/AIDS yesterday or COVID-19 today. This decision must be condemned for the reason that it consisted in granting a monopoly to a firm for a drug whose advertised price far exceeded the cost recovery. As mentioned above, a few weeks after the ODD was granted, Gilead announced high prices and expected huge profits. To justify these prices, the firm claimed that it had spent a lot of money on R&D: one billion dollars on clinical trials to make remdesivir a drug for COVID-19 (Institute for Clinical and Economic Review, 2020). However, other sources put development costs at 150 million dollars (Brown, 2020), while production costs are reported to be less than one dollar per treatment day (Hill et al., 2020). The ICER (2020) estimates that Gilead's price is 10 times higher than the cost-effective benchmark price.[46] This is questionable considering the fact that no mortality benefit has been demonstrated for remdesivir and that public funds were allocated to support the development of the molecule.[47] In other words, the price of the drug under ODD had to be all the higher at the time of its marketing as the therapeutic benefit linked to its use had not been clearly established. All of these elements fuel the hypothesis of a complex capture, intended to serve private interests and to damage the public interest.

However, the qualitative research method defined and used here does not intend to demonstrate capture in the sense of detecting and measuring capture as Carpenter (2014a) advocates. On the contrary, it highlights the difficulty of demonstrating capture, so complex is the concept. Capture admits degrees and forms that are more or less detectable and quantifiable, like especially social, cognitive or cultural capture. On the other hand, the method used does suggest a complex case of capture that really questions the content and management of the ODA with regard to the granting of ODD to a drug developed to treat a contagious disease at the onset of a pandemic. This case study conducted by crossing a framework for analyzing capture and stylized facts marking the trajectory of a repositioned

[46] It should be mentioned here that the way pharmaceutical firms set prices has changed drastically over the last decades. Whereas in the past it was a matter of setting a price to cover R&D costs, today it is a matter of claiming a significant share of the savings generated by the use of pharmaceutical products in the health care system. Besides, billions of dollars dedicated to R&D are claimed by the pharmaceutical industry (DiMasi et al., 2016), but also contested (Avorn, 2015; Light & Warburton, 2011).

[47] Remdesivir shortens time to improvement, but has no significant mortality effect and causes significant side effects (Beigel et al., 2020; WHO, 2020b). However, the drug received an EUA in May 2020, extended in August 2020 and was finally approved for patients age 12 years and older as reported in Fig. 2.

drug candidate for COVID-19 puts forward a complex case of capture in the sense that it crystallizes several types of capture. Even complex, the capture remains minor and so requires a reform of the content of the ODA and its management by the FDA, advocating the introduction of safeguard mechanisms to promote a better use of the Act. More broadly and upstream, it stresses the urgency of reforming the way the FDA is funded and operated to limit the influence of the pharmaceutical industry on the federal agency. These are the key contributions or our case study.

## 5 Conclusion

The starting point of this article was the identification of a disputed situation: a major player in a highly regulated industry having obtained ODD for a drug repositioned and candidate to treat a contagious disease at the very beginning of a pandemic. The purpose was to analyze the remdesivir episode through the prism of capture and contribute to a fertile rapprochement between capture and predation, by insisting on passive predation.

The case study has described a complex case of capture, characterized by a range of captures from agency capture to cultural capture (on downstream regulators) to legislative or statutory capture (on upstream legislators). This broadens the definition of passive predation proposed by Leeson et al. (2020). If capture can be cultural, cognitive or social (to borrow from a second generation of works largely explored in this article), then it is appropriate to account for situations where the awareness and intention of the public actors in charge of formulating or administering a regulation raise questions. There is passive predation in the sense that public actors may deliberately serve private interests and prejudice the public interest, taking a personal benefit such as a bribe, a practice that is legally condemnable. But there is passive predation in the sense that public actors serve private interests, without intending to do so, or even necessarily being aware of it. In both cases, passive predation is part of a consequentialist vision, as the only thing that matters are the effects on the general interest of a decision taken by a public actor that tends to favor particular interests. The interest of such a nuance is furthermore to account for the difficulty of detecting and measuring capture, and finally to fully demonstrate capture.

This case study has allowed to defend the idea that the remdesivir episode does not reveal a simple capture in the sense of the influence that an industry exercises on the state to obtain the implementation of a regulation serving its interests to the detriment of the public interest as suggested by Stigler (1971). Moreover, the study has described a complex architecture of capture where legislators and regulators are passive predators in the service of firms' rent-seeking strategies, through the formulation and application of regulation that has been particularly deficient since its inception. However, it has been shown that this was a case of weak capture which requires a modification of the ODA. There is an urgent need to provide essential safeguard mechanisms to better serve the public interest, and to preclude above all drugs for contagious and communicable epidemic diseases from obtaining orphan status.

Beyond a probable capture episode and a strong call for amendments of the ODA to make it more effective in ensuring the development and marketing of drugs intended to treat orphan diseases under socially acceptable conditions, the issue is the power of an industry characterized for so many decades by an oligopolistic market structure. The economic power of the pharmaceutical industry has been transformed into political power in the context of what Kolko (1963) and Holcombe (2018) refer to as "political capitalism",

where the risk of collusion between political and economic elites is latent. The risk is that the public interest will be relentlessly attacked in the field of health and that the inaccessibility of medicines will become the rule, ultimately due to an unreasonable capitalism, to borrow from Commons (1934).

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