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Mechanisms of regulatory capture: Testing claims of industry influence in the case of *Vioxx*

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Abstract

This paper presents a systematic empirical study of the causal mechanisms of regulatory capture. It applies process-tracing methods to the *Vioxx* drug scandal that was widely regarded to be a result of capture. In doing so, this paper provides a robust empirical analysis of regulatory capture lacking in the current literature. The analysis focuses on the role of the UK drug regulator in licensing and monitoring a drug that caused hundreds of thousands of heart attacks before it was taken off the market in 2004. We develop and systemically operationalize three causal mechanisms of capture to study the evidence on regulatory decision-making on *Vioxx*. Through explicit theoretical and empirical evaluation of the evidence, we show that the degree of capture through the revolving door, information overload and shared cultural frameworks was limited. By opening the black-box of empirical capture research, the paper highlights the problematic consequences of (mis-)diagnosis of regulatory capture by scholars, the media, and policymakers.

Keywords: cultural capture, pharmaceuticals regulation, process-tracing, regulatory capture, revolving door.

1. Introduction

Regulatory agencies are frequently criticized for their openness to regulatory capture. Regulatory capture conceptualizes the idea that special interests excessively influence regulation, thereby diverting the government's ability to work in the public interest (Bernstein, 1955; Dal Bó, 2006; Huntington, 1952; Laffont & Tirole, 1991; Stigler, 1971; Wilson, 1980). This paper challenges notions of regulatory capture by focusing on how industry can influence regulatory agencies in decision-making processes. Although the literature has identified many potential causes of capture, such as the "revolving door" and industry-funding of regulatory agencies, mechanisms of capture are not well understood. Instead, these potential causes are often equated with regulatory capture. What remains unclear, theoretically and empirically, is what happens inside the black box of the regulatory process that enables industry to exert influence (cf. Rilinger, 2021; Young, 2012). This paper develops process-based theories of regulatory capture to enable systematic empirical study of how industry influence affects regulatory decision-making (cf. Beach & Pedersen, 2019).

Building on Carpenter and Moss (2014), this paper highlights the importance of adopting a clear and stringent definition of regulatory capture to avoid classifying any regulatory process that produces undesirable outcomes as "captured." Based on a conceptual discussion of how we can define "regulatory capture," we argue that we need to focus on capture as a process, instead of an outcome. The paper focuses on theorizing three prominent mechanisms of capture, namely the effects of the revolving door, information overload by the industry, and shared cultural frameworks between the industry and the regulator. Showing that the regulated industry had the opportunity to influence decision-making, that regulators have theoretical reasons to be receptive to industry interests, or that regulator decisions were in the industry's interest, is not enough to evidence capture.

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To develop this argument, we trace the process of a notorious case of regulatory decision-making accused of being captured, namely the regulation of the painkiller *Vioxx*. *Vioxx* was withdrawn from the market in 2004 after it was found to increase the risk of heart attacks and strokes. *Vioxx* caused one of the biggest drug scandals of all time, partly due to the high number of people who took the product. Merck & Co. marketed the painkiller to alleviate the symptoms of arthritis. As many as 88,000 to 140,000 people in the United States alone may have suffered heart attacks due to *Vioxx*, 30% to 40% of which may have been fatal (Graham et al., 2005). This paper focuses on the approach of the British pharmaceuticals regulator, the Medicines Control Agency (MCA), which became the Medicines and Healthcare Products Regulatory Agency (MHRA) in 2004. Public commentators, politicians and the media quickly branded *Vioxx* a result of regulatory capture once the product was withdrawn. Paul Flynn, Labour MP for Newport West at the time, for example, said that "the recent crises of *Seroxat* [an antidepressant] and *Vioxx* demonstrate that the regulators in their incestuous relationships with pharmaceutical companies have failed patients by not holding these companies to account" (The Independent, 2004). After *Vioxx* was withdrawn, Richard Horton, long-standing editor of the *Lancet*, put forward that decisions unbiased by the industry were impossible for pharmaceutical regulators (Horton, 2004; The Independent, 2004b). The press also investigated the influence of an advisory committee member who had close links to Merck (Sunday Times, 2005). But to what extent did *Vioxx* indeed represent a case of regulatory capture? Our detailed empirical process-tracing analysis of regulatory decision-making on *Vioxx* reveals that industry influence on regulatory decision-making alone cannot explain slow regulatory action. The evidence shows that there were elements of the revolving door, information overload and cultural capture in decision-making on *Vioxx*. However, none of them translated into a strong degree of capture, meaning that excessive industry influence alone does not explain why regulators approved the drug and did not restrict its use more stringently. Our analysis shows that the presence of regulatory capture becomes far more questionable when we study the causal mechanisms underlying industry influence on regulatory decision-making.

The paper thus makes several key contributions. Concerning theory development, it makes *causal mechanisms of capture* more explicit than existing literature. It also shows how to apply systematic process-tracing methods to the empirical study of capture. Process-tracing enables us to study if and how capture mechanisms lead to excessive industry influence on regulators. The operationalization of process theories developed here can be applied to other case studies. They also present an example for operationalizing other capture mechanisms. Empirically, the paper provides the first detailed social scientific case study of regulatory decision-making on *Vioxx*. More broadly, the paper helps develop a more nuanced account of bureaucratic government in the context of regulation. It contributes to an emerging understanding that regulatory authorities are less vulnerable to industry influence than is often assumed by focusing on regulatory processes' complex and contingent nature. This is far from a parochial addition to knowledge considering public confidence in bureaucratic government suffers if there is a widespread belief that regulators are unduly influenced by industry.

2. What is regulatory capture and how does it happen?

Although regulatory capture has been extensively theorized and ostensibly empirically documented, especially in the US context (e.g., Becker, 1983; Bernstein, 1955; Dal Bó, 2006; Huntington, 1952; Laffont & Tirole, 1991; Wilson, 1980), evidence of causal relationships between industry influence and regulatory outcomes is severely lacking (Carpenter & Moss, 2014). Indeed, empirical research has been restricted to demonstrating that industry had the opportunity to influence regulation or has focused on correlations between regulatory decisions and theorized interests of the regulated industry (e.g., Thomas, 1990). Daniel Carpenter and David Moss rightly seek to shift the regulatory capture debate away from theoretical and methodological approaches that make it too easy to interpret any regulatory outcome to be the result of capture (cf. Noll, 1989 as quoted in Carpenter & Moss, 2014, p. 8). In line with their approach, we define capture as industry influence that shifts regulatory decisions away from the public interest toward special interests (which is echoed in many scholarly contributions on capture, going back decades, e.g., Quirk, 1981; Stigler, 1971; for further discussion, see Carpenter & Moss, 2014b, p. 13).

Defining capture this way avoids the pitfall of simply equating a regulatory decision in line with industry interests with a captured decision-making process. This definition also provides a clear view of what makes industry influence "excessive," namely if regulation serves the interest of industry (or other special interests) at the

expense of wider societal interests. Carpenter and Moss argue that for capture to occur, the regulated industry must intentionally exert excessive influence on public decision-making bodies. However, we argue that capture can also happen without explicit industry intent. For example, if cultural capture mechanisms are at work (discussed further below): regulators may take decisions that favor the regulated industry and harm the public interest because of their shared identities and social networks with the regulated industry. Here, we focus on capture mechanisms at the level of regulatory agency decision-making. As such, we exclusively focus on which role industry influence plays in agency decision-making rather than studying the actions and intentions of the regulated industry. In this respect, we suggest that understanding the motivations of bureaucratic decision-making within regulatory processes is a key part of studying regulatory capture (cf. Levine & Florrence, 1990).

Our definition of capture requires researchers to evidence if and how special interests influence regulatory decision-making excessively. What, then, does academic literature tell us about capture mechanisms? Of course, there are capture mechanisms related to corruption and blackmail. Economists also frequently focus on rent-seeking dynamics and have discussed capture by threat (e.g., Dal Bó & Di Tella, 2003). In literature about the capture of regulators in established democracies, however, "softer" capture mechanisms play a greater role. This literature has identified industry funding of regulators, the "revolving door," "cultural capture" and capture through information as conduits for capture. Related to information capture, industry influence through consultation procedures has been identified as another crucial avenue of capture (Shapiro, 2012; Yackee, 2006). Bernstein (1955), on the other hand, focused on the lack of political and public attention and staff enthusiasm that beset agencies in "old age" as mechanism of capture. Here, we are focusing on three of the most likely culprits of capture in pharmaceutical approvals and supervision: the revolving door, capture through information, and cultural capture. These three mechanisms span prominent assumptions about regulator motivation. The rational choice version of the "revolving door" highlights people's propensity to seek personal gain over benefits to the larger community. Information capture is grounded in assumptions of bounded rationality, highlighting that regulators possess limited time and attention, even if they wish to work for the public good. Cultural capture instead draws on sociological assumptions around the importance of group behavior and people's propensity to respond to social norms while highlighting cognitive limitations. Exploring this set of mechanisms thus allows us to reflect on the relative importance of these different drivers of behaviors. Pharmaceutical regulation is a fruitful area within which to explore these three mechanisms of capture: Pharmaceutical companies effectively control all the information on any drugs in development. In the UK context, it is common for regulatory staff to come from industry and leave the regulator for the industry. There are often close research links between scientific advisers and pharmaceutical companies. Moreover, scientists on both sides share a set of scientific norms. We discuss each mechanism below before turning to a discussion of how they relate to each other.

The most prominent capture mechanism in media coverage and public imagination is the "revolving door": regulatory officials may be tempted by lucrative jobs in private industry, thus acting in the industry's interests to secure a well-numerated job offer. Few good studies gauge the effect of the revolving door, and those that do, show minimal evidence that revolving doors result in excessive industry influence on regulators (Cohen, 1986; Gormley, 1979; Makkai & Braithwaite, 1992; Quirk, 1981). We thus require a clear theoretical proposition about how capture may occur when the revolving door is present (as outlined in Table 1).

The mechanism focuses on a rational choice conception of the revolving door, that is, that officials can benefit from favoring the regulated entities in regulatory decision-making. The theorization of the mechanism focuses on

TABLE 1 Revolving door capture mechanism

Cause	Part 1	Part 2	Part 3	Outcome
"Revolving door" dynamics (i.e., regulatory officials/executive move from regulator to the regulated industry	Regulatory official(s) stands to gain a personal advantage from aiding industry interests in the decision-making process	Regulatory official gains/has access to key decision-making process and plays active role in decision-making process and advocates industry position	Regulatory official(s) successfully shift(s) final decision to the advantage of regulated entity/entities directly affected by this decision and away from the public interest	Regulatory capture

obtaining evidence that officials stood to gain a personal advantage due to the revolving door, they had access to regulatory decision-making, and could influence decision-making in favor of the regulated industry. This goes beyond the notion of a conflict of interest, as the presence of a conflict of interest does not necessarily result in the individual realizing this benefit. This scenario overlaps with some forms of legal corruption as the individual uses their position of influence to derive a private gain. However, we include dynamics in which an individual takes advantage of their position for professional gain (such as getting a research grant or a lucrative job in the industry), which goes beyond some definitions of private gains used concerning corruption. Moreover, no explicit quid pro quo may be evident in revolving door dynamics. However, the revolving door is often conceptualized in its "softer" sociological version, which emphasizes that people may spend their careers alternating between the private sector and the regulator, thus losing relational distance to the regulated industry (Seabrooke & Tsingou, 2020). This paper incorporates this conceptualization under the umbrella of the "cultural capture" mechanism discussed below. The analysis section provides a detailed overview of how we operationalized the revolving door capture mechanism.

Next, we turn to capture by information overload, where the regulated industry's information monopoly allows it to influence regulators excessively. This has been evidenced in administrative rule-making procedures of American regulators, where the industry essentially battles the regulator into submission by overloading it with information (Wagner, 2010) or benefits from having far greater expertise than the regulator (McCarty, 2014). See Table 2 for a theoretical proposition of how capture can occur through information overload by the industry. Information capture is present when the regulator lacks the resources to properly allocate attention to process information from industry and third-party sources. Consequently, regulatory decisions are based on information provided by the industry, leading to capture. The threshold to capture in this scenario does not relate to a particular amount or degree of complexity of industry information. It also does not signify that the use of industry information necessarily equals capture, as regulators usually require access to this type of information to regulate effectively. Instead, information overload is conceptualized in relation to the resources available to a regulator and how it allocates resources amidst competing priorities. We outline detailed observable manifestations for this mechanism in the Supplemental Material.

Cultural capture focuses on how shared mindsets and worldviews foster regulatory decision-making that favors industry interests due to an inability of regulators to think in frames of reference other than the ones they share with people working in the industry (Kwak, 2014). Kwak suggests this may result from shared identities between regulators and the regulated; officials' perception that people working in the industry are of a higher status than them, and (or) shared social networks and personal relationships between officials and industry staff. Shared frames of reference may be fostered and perpetuated through the revolving door, attendance at the same educational establishments, or the intellectual dominance of certain schools of thought in a particular field. In Table 3, we suggest a theoretical proposition about the mechanism through which shared cognitive frameworks may result in capture. The theoretical causal mechanism explains the effect of shared frames of reference on regulatory officials' ability to question industry views and information. In this scenario, officials dismiss anyone or any information overly critical of the industry's position and sideline them. Consequently, regulators base their decisions on the industry's positions, expertise and information, resulting in capture. We outline observable manifestations of each part of this mechanism in the Supplemental Material.

TABLE 2 Information capture mechanism

Cause	Part 1	Part 2	Part 3	Outcome
Regulated entity/ entities provide excessive amounts/excessively complex information to the regulator during the regulatory process	Regulatory official(s) are reaching the limits of their capacity in processing this information	Regulatory official(s) do not consider third party/alternative sources of information due to lack of resources	Regulatory decision is solely/ overwhelmingly based on information provided by regulated entity as evidence-base and conforms with interest of regulated entity at the expense of the public interest	Regulatory capture

TABLE 3 Cultural capture mechanism

Cause	Part 1	Part 2	Part 3	Outcome
Shared cognitive frameworks or worldviews between regulatory officials and people working in the regulated industry (e.g., through shared education, professional norms, revolving door dynamics etc.)	Regulatory official(s) does not question the information/ opinions provided by regulated entity/ entities as part of the regulatory process	Regulatory official(s) ignore, side-line and/or actively dismiss outlier/third party information/ opinions	Industry information/ opinions form sole/ overwhelming evidence-base for regulatory decisions, which conforms with interests of regulated entity at the expense of the public interest	("Cultural") regulatory capture

The three mechanisms presented here are not mutually exclusive or competing: they may operate in isolation or work simultaneously and reinforce each other. For example, an individual may be incentivized by the benefits of the revolving door but not regard this as problematic because of shared worldviews with people working in the industry. An organization may channel resources and attention in a particular way because of priorities set by shared frames of reference with the regulated industry. Alternatively, a regulator under pressure from, for example, too much information from the industry, falls back on heuristics because this happens when we do not have time for close consideration (Kwak, 2014, p. 93; also see Bagley, 2010). Our analytical distinction of these mechanisms enables us to take different routes to capture seriously. The main benefit of doing so is that we can only get better at preventing capture if we understand, rather than assume, how industry influence comes to bear on regulators' behavior.

3. Methodology and case study selection

Process-tracing analysis is uniquely suited to the identification of causal mechanisms of capture (Beach & Pedersen, 2019; Bennett & Checkel, 2015). Researching what happens inside the "black-box" of regulatory capture is currently lacking in the field. Indeed, this is symptomatic of research on politics, public policy, and public administration in general. Scholars have increasingly called for a greater focus on mechanistic causal explanation in these fields (ibid.).

We suggest that capture research must show that regulatory decision-making shifted to protect private interests at the expense of public interests to evidence capture. This paper provides a fresh methodological approach by studying a set of regulatory decisions widely regarded as against the public interest: the approval and continuous supervision of a pharmaceutical product that caused severe physical harm or death. This research design allows us to study to what extent decisions on the market approval and safety monitoring of a product, *Vioxx*, resulted from regulatory capture. This research design differs from the conventional understanding of a "typical case" in process-tracing. Instead of trying to unpack the causal process in a typical case of capture, we argue that we need to study the process of decision-making to understand whether capture occurred (cf. Beach & Pedersen, 2019, p. 97ff).

The two core features of process-tracing are the theoretical unpacking of a process and tracing it empirically (Beach & Pedersen, 2019, pp. 1–9). This requires careful operationalization through the development of observable manifestations (or "fingerprints") of the activities associated with each mechanism. For example, consider the evaluation of information capture: one part of the information capture mechanism is that regulatory officials reach their capacity limit while processing industry information. One fingerprint of this mechanism is that the industry gives a large amount of information and (or) supplies exceedingly complex information to the regulator. The fingerprints we have developed (see Section 5 and Supplemental Material) are of a general nature (e.g., whether regulatory officials moved to a regulated company soon after a key regulatory decision, in case of the revolving door mechanism). As such, researchers can apply them to other case studies of regulatory decision-

making, especially in the field of product approvals and safety monitoring. Equally, other researchers can modify our fingerprints to make them as relevant as possible to the regulatory decision-making process they are studying, or they can use our approach as a template to develop their own detailed observable manifestations of capture mechanisms.

The development of theoretical observable manifestations is followed by empirical study of the process. Empirical analysis in process-tracing entails theoretical and empirical evaluation of evidence. Theoretical evaluation entails the assessment of *theoretical certainty* and *theoretical uniqueness*. *Theoretical certainty* refers to reasoned speculation about the empirical fingerprints we expect each part of the causal mechanism to leave. For instance, we need to find evidence of regulators struggling to process the amount or complexity of industry information to evidence information capture. This means we attach *high theoretical certainty* to this observable manifestation because information capture does not exist without the industry providing a large amount/highly complex material to the regulator. *Theoretical certainty is low or medium* if finding evidence for a particular fingerprint does not (or only somewhat) indicate that a particular mechanism is at play. For example, one fingerprint related to information capture is that regulators mention that they were too overstretched to consider nonindustry submissions (such as reports from consumer advocacy groups). However, we attach low theoretical certainty to this fingerprint because captured regulators may be too busy with digesting industry information to even think about their inability to process third party information. *Theoretical uniqueness* relates to the analysis of whether there are alternative explanations for finding evidence for each fingerprint. For example, the industry providing a large amount of information to the regulator has *low theoretical uniqueness* because the industry may simply be complying with regulatory requirements or wish to submit all its high-quality information for consideration by the regulator, so finding evidence for this fingerprint does not necessarily mean that capture is at play. *Theoretical uniqueness is medium or high* if there are few or no alternative explanations for finding evidence of a particular fingerprint. For example, we attach high theoretical uniqueness to regulators repeating the industry's position as if it were fact without critical engagement and dismissing contradictory views without justification (a fingerprint of cultural capture) because alternative explanations to capture for this dynamic are relatively unlikely. The empirical evaluation entails assessment of *empirical certainty* and *empirical uniqueness*. *Empirical certainty* refers to the assessment of whether we had full access to the empirical record, which is particularly important if we do not find evidence for a theorized empirical fingerprint. Empirical certainty is *high* when we have full access to the empirical record, *medium* if we have very good, albeit not full access to the record. It is *low* if we do not have access to some key sources. *Empirical uniqueness* relates to an evaluation of whether we can trust the evidence. Empirical uniqueness is *high* when sources are highly trustworthy (e.g., court case documents, official records etc.). It is *medium* or *low* when less trustworthy sources are concerned, such as an account of an interviewee with a clear agenda to mislead the researcher (Beach & Pedersen, 2019, p. 155ff). The analysis section and the Supplemental Material provide a detailed insight into the theoretical and empirical evaluation of evidence conducted for the *Vioxx* case study.

To conduct the analysis, we collected all relevant available documentation of regulatory decision-making on *Vioxx* in the UK. We analyzed this material chronologically to avoid interpreting material based on the eventual problems associated with *Vioxx*. We first focused on the chronological analysis of UK media and trade press coverage of *Vioxx* (1680 articles accessed via Nexis search). The next step was the analysis of 68 regulatory decision-making documents of the MCA (after 2004, the MHRA) and its scientific advisory bodies, the Committee on Safety of Medicines (CSM) and the Sub-Committee on Pharmacovigilance (SCOP). This also included documents from the European Medicines Agency. Many documents were publicly available, but we obtained some key documents through freedom of information requests. This was complemented by an analysis of 42 official documents of other British governmental bodies that expressed opinions on the *Vioxx* case (e.g., the health technology assessment agency NICE and discussions in parliament). Except for documents obtained through freedom of information requests, we obtained the documents through keyword searches for "*Vioxx*" and "rofecoxib" in the web archive of the UK government. In the last step, we analyzed 59 documents of official inquiries, court documents, discussions in medical journals and secondary literature. We identified these through the documents mentioned above and a keyword search for "*Vioxx*" and "rofecoxib" on Google Scholar.

4. The Vioxx case study

Merck marketed *Vioxx* to alleviate the symptoms of osteoarthritis and rheumatoid arthritis. Millions of people took it globally, including approximately 400,000 people in the UK. Like many other painkillers, such as ibuprofen, *Vioxx* (or rofecoxib) is a non-steroidal anti-inflammatory drug (NSAID). However, unlike conventional NSAIDs, it is a COX-2 inhibitor, or coxib, meaning that it fights pain by selectively targeting COX-2, an enzyme responsible for pain and inflammation. In contrast, non-selective NSAIDs inhibit COX-1 and COX-2. Since COX-1 helps protect the stomach lining, non-selective NSAIDs have long been known to carry a risk of gastrointestinal bleeding, including fatal and debilitating peptic ulcers. Coxibs were developed with the promise of carrying lower risks of such gastrointestinal side effects. When Merck withdrew *Vioxx* voluntarily from the market in 2004, it had been marketed for 5 years and was authorized in 84 countries. UK authorities never released estimates of the number of British victims of the drug. However, there is no doubt that *Vioxx* harmed British patients who suffered heart attacks and strokes due to taking the product.

The withdrawal of *Vioxx* caused a huge backlash in the media, and editors of medical journals, scientists, politicians and journalists alike accused regulators of being captured by the pharmaceutical industry. A large public inquiry in the US investigated industry influence on the Food and Drug Administration (FDA) in the case of *Vioxx* (US Senate Finance Committee, 2004). The UK House of Commons Health Select Committee also discussed the *Vioxx* case in its inquiry into pharmaceutical industry influence in the UK context (Health Select Committee, 2005a). However, no detailed social scientific case study of the regulatory decision-making on *Vioxx* in Britain (or the United States) has been published. Table 4 below provides an overview of the key regulatory decisions taken in the UK regarding *Vioxx* (coded D1-D13, which we refer to in the analysis). The overview shows that the regulator and its scientific advice committees continuously discussed safety concerns relating to

TABLE 4 UK regulatory decision-making on Vioxx

February 1999: MCA assessment report concludes that the risk-benefit balance of *Vioxx* at 25 mg dose is positive (D1)
April 1999: CSM evaluates MCA report and recommends approval of *Vioxx* (D2)
June 1999: MCA approves *Vioxx* to the market as first European country to do so; approval for osteoarthritis at a 25 mg maximum dose (D3)
April 2000: Preliminary results of Merck's VIGOR trial raise questions about whether Vioxx increases the risk of heart attacks
June 2000: CSM Sub-Committee on Pharmacovigilance (SCOP) discusses the VIGOR trial at their meeting and decides that no regulatory action is required; the CSM endorses this recommendation (D4)
November 2000: SCOP discusses the safety of *Vioxx* again but does not change its position (D5)
August 2001: An article in the Journal of the American Medical Association publishes a meta-analysis that highlights cardiovascular risks of Vioxx
Autumn 2001: MCA carries out a safety review of *Vioxx* after new concerns were raised in the medical literature (D6)
December 2001: Following the MCA review, the CSM recommends labeling changes to warn doctors of prescribing *Vioxx* to patients with cardiovascular risk factors (D7)
June 2002: The MCA reviews *Vioxx* safety update from MSD (D8)
September 2002: SCOP discusses the safety of *Vioxx* at its meeting amidst ongoing safety concerns (D9)
Autumn 2002: The MCA implements the labeling changes recommended by the CSM (D10)
December 2002: The MCA reviews *Vioxx* safety update from MSD (D11)
5 October 2002: The Lancet publishes a review article that raises doubts about the cardiovascular safety of Vioxx at doses of greater than 25 mg
April and September 2003: SCOP discusses the safety of *Vioxx*, again noting the lack of conclusive evidence about the cardiovascular risks of *Vioxx*, and recommends no further regulatory action (D12)
January and July 2004: The MCA reviews *Vioxx* safety update from MSD. The regulator's position now is that *Vioxx* is likely associated with increased rates of heart attacks. However, since stronger warnings of this risk were already included in the label, it recommends no further regulatory action (D13)
25 August 2004: An FDA study by Dr David Graham presented at a conference finds that Vioxx is more likely to cause heart attacks than ibuprofen
30 September 2004: Merck announces worldwide voluntary withdrawal of Vioxx due to results of its APPROVe trial that tested Vioxx for colon cancer and showed increased heart attack risks after 18 months of Vioxx use

Vioxx over the years. However, they did not take decisive action on restricting the availability or use of the product because they did not find the evidence on these risks conclusive enough. Nevertheless, they enforced labeling changes for *Vioxx* to highlight that the product may carry cardiovascular risks. Merck eventually withdrew the product voluntarily when one of its clinical trials provided strong evidence of the cardiovascular risks associated with the product.

So, to what extent, if any, was UK regulatory decision-making on *Vioxx* a case of regulatory capture? And if capture did occur, how did it happen? The next section discusses the evidence for capture through our three mechanisms. The Supplemental Material provides a more detailed, chronological summary of UK regulatory decision-making and the scientific controversy regarding *Vioxx*. The material offers a detailed discussion of these regulatory decisions and provides a contextual understanding of the case study.

5. Analysis

In this section, we present our empirical analysis for each of the three capture mechanisms. We conducted a full analysis of theoretical and empirical certainty and uniqueness for all observable manifestations linked to these mechanisms. We provide a full overview of this evaluation for the revolving door mechanism in the text below. The same process of analysis was followed for the information and cultural capture mechanisms, but for reasons of space the relevant analytical tables can be found in the Supplemental Material. Throughout the analysis section, we refer to the codes for regulatory decisions developed in the previous section (D1–D13).

5.1. Revolving door mechanism

In regulatory decision-making on *Vioxx*, a revolving door relationship was evident in the close collaboration between Prof Langman, a CSM member, and Merck/MSD. Langman, an expert on NSAIDs, had been a committee member since 1987. He was impressed when he heard that Merck was working on a safer drug for the gastrointestinal tract than conventional painkillers, and Merck recruited him as a consultant on *Vioxx* (Sunday Times, 2005). In this context, he was appointed to lead a UK-based clinical trial of *Vioxx*, called VICTOR. VICTOR investigated whether *Vioxx* could prevent colon polyps in patients at risk of colon cancer. This provides evidence for the first causal part of the revolving door mechanism as a key expert advisor in this case had an ongoing contractual relationship with the company that stood to lose or gain from regulatory decision-making on *Vioxx*. Langman also published on coxibs in the medical literature as a proponent of this class of drugs. He stood to lose from tough regulatory action against MSD, due to his involvement in the VICTOR study and his public advocacy of coxibs. Prof Langman left the room during the discussion about licensing (D2) due to his conflict of interest (CSM, 1999). However, the Chair asked him to stay in the room during a key discussion about new safety concerns (D7) due to his expertise in the field. This is evidence that the second part of our causal mechanism—that an advisor or official that stands to lose or gain directly from regulatory decisions has access to decision-making—was also at play. Based on the evidence we had access to, we cannot exclude the possibility that Langman's voice as a prominent expert on NSAIDs might have been influential in these settings. However, the committee chair and committee members were aware of this conflict of interest during relevant discussions, and he had to recuse himself from the decision-making about a labeling change (D7) (CSM, 2001). Furthermore, Langman was only one of many members of a large advisory committee, licensing and safety concerns were discussed by scientific sub-committees without Langman, and discussions about decisions involved regulatory officials too. This provided checks and balances on the influence any individual. Scientific committee meetings and confidential regulatory action documents show consistency in the approach taken in the wide consultation and deliberation about the available evidence on *Vioxx* over time and do not appear to be decisively influenced by Prof Langman (the third part of the mechanism). Hence, capture through his influence was ultimately limited.

There is no evidence that broader revolving door mechanisms were operating in this case when we consider key advisory committee members and key MCA staff. The MCA/MHRA came under scrutiny over Ian Hudson, who headed the agency's licensing division from 2001 to 2013. He was the Director and Vice President of Clinical Safety at Smith Kline Beecham from January 1999 to January 2001 and held other roles in industry between 1989 and 1999. His industry roles could indicate general trust toward the industry (see section on cultural capture) but are

unlikely to have specifically affected the licensing of *Vioxx*, since SBK did not market it. This would be more likely in the case of the MCA executive Keith Jones, whom MSD employed before joining the MCA. There is no evidence that he played any direct role in decision-making on *Vioxx*. However, as with Ian Hudson, this career path could indicate a positive attitude toward the industry. Moreover, other key figures did not have similar conflicts of interest during the timeline under scrutiny. Rather, June Raine, head of post-marketing at the time, did not come to the agency from industry and has remained at the agency ever since (she is its Chief Executive at the time of writing). Professor Sir Alasdair Breckenridge, Chair of the CSM from 1994 to 2003, and Chair of the MHRA from 2003 to 2013 spent his much-lauded career as a medical practitioner and independent scientist. Professor Sir Gordon Duff, Chair of the CSM from 2003 to 2005 (and Chair of the subsequent Committee for Human Medicines from 2005 to 2012 and Chair of the MHRA from 2013 to 2014), has spent his highly distinguished career in academic research institutions. As such, industry influence through key personnel is unlikely to have played a significant causal role, but we could not evaluate the career trajectories of all involved regulatory staff.

Table 5 provides a full evaluation of the evidence for the revolving door mechanism, especially concerning the role played by Prof Langman. It showcases how to develop observable manifestations and evaluate theoretical and empirical certainty and uniqueness in capture research (equivalent tables for the information overload and cultural capture mechanisms can be found in the Supplemental Material). The detailed theoretical and empirical evaluation of the evidence outlined in the table confirms that a degree of revolving door dynamics were present concerning Part 1 and Part 2 of the causal mechanism. There were key decision-makers with links to the involved company that stood to gain or lose directly from regulatory decisions. However, the evidence suggests that capture through the revolving door was limited as decisions were ultimately not decisively influenced by said decision-maker. While we had full access to advisory committee meeting minutes and key confidential regulatory information (e.g., Periodic Safety Update Reports), there were no full transcripts of meetings and we could not evaluate informal exchanges between committee members and regulatory staff. This means we had high uniqueness but medium certainty of empirical evidence for this mechanism, which gives us confidence in our analysis, but also highlights the limits of the evidence base (Table 5).

5.2. Information overload capture mechanism

A degree of information capture dynamics is inherent in the initial assessment and approvals of drugs: to protect intellectual property rights, all data on a new product come from the manufacturer. As is required, MSD supplied many complex studies (270 volumes in total) to the MCA for approval. However, this was the only indication of information overload. We found disconfirming evidence for other key observable manifestations, such as regulators being unable to process industry information adequately. Indeed, the review documents show that MCA staff could evaluate the application dossier of MSD competently, contextualizing it in existing knowledge and pushing MSD for further information, especially on adverse events (D1). This means that when the initial approval of the drug was concerned, information capture was only present in relation to MSD's general monopoly on data about *Vioxx* at this stage of development, but the regulator was not overloaded or overwhelmed by this.

Even more crucially, the MCA, CSM and SCOP did not fail to discuss the cardiovascular safety of *Vioxx* over the years. Once the drug was on the market, regulators and advisory bodies were able to draw on third party information about the safety of *Vioxx*. Independent studies and new clinical trials run by Merck both flagged possible safety concerns. The regulator and the advisory bodies discussed the issue comprehensively, considering the studies provided by MSD (D1, D8, D11, D13), but also the available evidence published in the medical literature, spontaneous adverse drug reaction reports (Yellow Card data) (D2, D4, D5, D7, D9, D12) and internal analyses (D6, D7) (e.g., CSM, 2001; MCA, 2002a, 2002b; SCOP, 2001). This points against the presence of the second part of our "capture by information" mechanism since the regulatory bodies explicitly considered a broad range of information and were able to study, evaluate and discuss them in detail. However, this was not straightforward as the complexity of establishing whether the cardiovascular safety of *Vioxx* was considerable. The cardiovascular risks of *Vioxx* were difficult to detect because heart attacks and strokes are a relatively common occurrence in the age group that was primarily taking the painkiller. Equally, many studies compared *Vioxx* to other NSAIDs, which later emerged to carry similar cardiovascular risks when used at high doses and for long-term treatment (CHM, 2006). This large complexity in degree of scientific uncertainty made it difficult for regulators to assess

TABLE 5 Operationalization and evaluation of evidence – revolving door mechanism

	Observable manifestations	Theoretical certainty and uniqueness	Empirical evaluation of evidence
P1 Regulatory official(s) stands to gain a personal advantage from aiding industry interests in the decision-making process	1. Key official(s) moves to a more lucrative job with an industry player that gains from regulatory decision soon after decision under scrutiny	*Medium to high certainty*: There can be other ways of gaining an advantage from industry, but the relevant literature focuses most heavily on this route *Medium to high uniqueness*: Although alternative explanations are possible (e.g., official is hired for competence), close temporal proximity between decision and job change/repeated advocacy in favor of the industry before job move make alternative explanations less likely	*Medium certainty*, *high uniqueness*: Disconfirming evidence, key MCA staff and CSM committee members had long-time career trajectories in the regulator and in university/research positions, with the exception of a Head of Licensing who moved from a regulated company (but not Merck), and agency executive who moved from MSD; recorded in public-facing websites and official documents; access to records of all higher-ranking staff and all committee members, but not all involved staff
	2. Key official(s) have ongoing contractual relationship with industry (e.g., research grants, advisory roles in companies, consulting contracts etc.) that gains from regulatory decision under scrutiny	*Medium to high certainty*: There can be other ways of gaining an advantage from industry (see above and below), but it represents one of the key mechanisms for doing so *Medium uniqueness*: Ongoing relationship of this kind make alternative explanations for advocacy in of industry relatively unlikely, but not impossible (e.g., official has already gained advantage from the ongoing relationship and will not gain further related benefits in the future)	*High certainty*, *high uniqueness*: Confirming evidence, a key expert on CSM (Prof Langman, an expert on painkillers) was working closely with Merck on trials of *Vioxx* and received funding from Merck to lead a *Vioxx* trial in the UK (the VICTOR trial); confirmed in multiple media stories, and official documents; committee membership was tightly scrutinized by investigative journalists, all media coverage of *Vioxx* was analyzed
	3. Key official(s) has received/is due to receive give-aways, presents or other indirect benefits from an industry player that gains from regulatory decision	*Medium certainty*: There can be other ways of gaining an advantage from industry (see above), but this represents a key mechanism for doing so *Low to medium uniqueness*: Present/benefit may not be of high enough value to influence officials' views/may	*Low certainty*, *high uniqueness*: No evidence, but no full insight into existing conflicts of interests (see below) and general level of these types of give-aways from pharmaceutical industry is high; CSM and SCOP

(*Continues*)

TABLE 5 Continued

	Observable manifestations	Theoretical certainty and uniqueness	Empirical evaluation of evidence
		receive similar benefits from different regulated companies (uniqueness is higher depending on the value/ frequency of benefits)	members need to declare conflicts of interests, which happened for a small number of committee members, but the nature of the conflict of interest (with the exception of Prof Langman) is unknown; recorded in official, and published minutes and CSM Annual reports
P2 Regulatory official gains/has access to key decision-making process and plays active role in decision-making process and advocates industry position	1. Key official(s) has official role/membership in unit/ committee responsible for decision(s) under consideration and advocates position that benefits the industry during meetings	*High certainty*: We must find evidence of active participation or other routes to influence of key official and advocacy and industry-friendly position *Low uniqueness*: Key official may happen to be a regular member of decision-making body and position may be informed by other motivations (e.g., evidence speaking in favor of industry-friendly position)	*Medium certainty*, *high uniqueness*: Confirming evidence, Prof Langman (see above) left room during licensing decision (D2) but was allowed to stay in the room during discussion of new safety concerns that resulted in labeling changes due to his expertise and despite his known conflict of interest, but had to recuse himself from decision-making (D7); we do not have access to full transcripts of discussions, so cannot exclude some influence on committee's decision due to persuasive argument; however, at meeting in question (D7), more restrictive labeling for *Vioxx* was agreed; recorded in official and public meeting minutes
	2. Key official(s) participates in decision-making in advisory capacity or through ad hoc interventions (e.g., position papers, presence at particular meetings) and advocates position that benefits the industry	*High certainty*: We must find evidence of active participation or other routes to influence of key official and advocacy and industry-friendly position *Medium uniqueness*: Official could give advice based on expertise or insights that would otherwise be lacking but unsolicited interventions	*High certainty*, *high uniqueness*: Disconfirming evidence, no external scientific advisors with Merck-friendly positions consulted by SCOP and CSM in the process (D2, D4, D5, D7, D9, D12); committee attendance of is officially recorded in public meeting minutes;

(*Continues*)

TABLE 5 Continued

	Observable manifestations	Theoretical certainty and uniqueness	Empirical evaluation of evidence
		are less likely to be explainable by such alternative explanations	interventions of this type with MCA staff highly unlikely since consulted sources of information about *Vioxx* safety were all recorded in Periodic Safety Update Reports (confidential official documents retrieved through FOI) (D8, D11, D13)
	3. Key official(s) do not have access to decision-making but relay their position in favor of the industry to influential members of the decision-making body (e.g., in one-on-one-meetings, or written communication)	*High certainty*: We must find evidence of key official seeking to influence decision-making through formal or informal participation *High uniqueness*: Behind-the-scenes attempts to influence, especially if unsolicited, are difficult to explain through alternative explanations	*Medium certainty*, *high uniqueness*: No evidence, existence of informal exchanges between external individuals or Prof Langman and SCOP, CSM or MCA staff cannot be fully excluded on the basis of the available record, but critical new evidence or pieces that were important for decision-making would usually be cited in committee meeting minutes and Periodic Safety Update reports (public and confidential official documents) (D2, D4, D5, D7, D8, D9, D11, D12, D13)
P3 Regulatory official(s) successfully shift(s) final decision to the advantage of regulated entity/ entities directly affected by this decision (and away from the public interest)	1. After presenting different views at first, other officials change their view to align with the view of key official(s) *after* the latter have represented their views	*Medium certainty*: Although we must find evidence of influence of "revolving-door" officials, the shift in position can happen over long periods of time, rather than through sudden shifts in opinion *Medium uniqueness*: There are possible alternative explanations, e.g., committee members consumed other pieces of information in the meantime and thus changed their mind (degree of uniqueness depends on how many other officials change	*Medium certainty*, *high uniqueness*: No evidence: Scientific committee meetings and confidential regulatory action documents show consistency in the approach taken in the wide consultation and deliberation about the available evidence on *Vioxx* over time and do not appear to be decisively influenced by Prof Langman (D1-D13); however, we do not have

(*Continues*)

TABLE 5 Continued

	Observable manifestations	Theoretical certainty and uniqueness	Empirical evaluation of evidence
		their view and how quickly they do so after key official presents his view)	access to full transcripts of meeting minutes or informal exchanges
	2. After no clear contributions are made by other officials or after an array of different views is presented, the final decision closely resembles the views of the key official	*Medium certainty*: We have to find evidence of influence by the "revolving door official," but the effect of this influence could manifest more subtly (e.g., over long periods of time). *Low uniqueness*: There are alternative explanations, e.g., if the key official's position also resembles a compromise position or is the most evidence-based position	*Medium certainty*, *high uniqueness*: No evidence, scientific committee meetings (D2, D4, D5, D8, D9, D12) and confidential regulatory documents (D1, D6, D8, D10, D11, D13) show clear and consistent approach taken in the comprehensive consultation and deliberation about the available evidence on *Vioxx*; they do not appear to be decisively influenced by Prof Langman; however, we do not have access to full transcripts of meeting minutes or informal exchanges

safety. While *Vioxx* was on the market, the CSM and MCA were cautious in taking regulatory action due to a relative paucity of "hard and fast" evidence of the cardiovascular risks of *Vioxx*. Nevertheless, the MCA introduced more restrictive label warnings in 2002 (D7, D10) following an internal review conducted in 2001 (D6), which were largely a result of evidence from nonindustry studies (CSM, 2001). This shows that regulators not only considered these sources but took restrictive action because of them, pointing against the presence of the third part of our causal mechanism.

As is often the case with high profile regulatory failures, capture allegations were primarily leveled at regulators after *Vioxx* was withdrawn from the market. In doing so, the critiques significantly downplayed the degree of scientific uncertainty surrounding the safety of *Vioxx* prior to its withdrawal. While the cardiovascular risks of *Vioxx* were suddenly presented as a clear-cut issue once Merck withdrew the product, there was a relative lack of clear evidence of the risks of *Vioxx* while it was on the market. A full overview of observable manifestations, and the theoretical and empirical assessment of the empirical evidence for this mechanism is presented in Table 1 of the Supplemental Material. It shows that there is limited evidence for the first part, and disconfirming evidence for the second and third parts of the mechanism. We had full access to key regulatory documents, advisory committee meetings and all scientific publications on *Vio*xx, meaning there is high uniqueness and certainty of our empirical material on this mechanism. This means we can have a very high degree of confidence in our analysis and the conclusion that information overload did not significantly contribute to capture in this case.

5.3. Cultural capture mechanism

As discussed above, the advisory committees and the regulator seriously considered all available evidence on *Vioxx* and always maintained an open mind that Merck/MSD's interpretation of the data could be wrong. For example, the regulator and the CSM probed MSD vigorously about their data and amended product characteristics during their

approval process (D1) (e.g., MCA, 1999a, 1999b). This speaks against some of the observable manifestations associated with cultural capture, such as a lack of effort by regulators to seek out evidence that contradicts the industry view or repeating the data or view presented by the industry as a fact. However, we found evidence that conforms with another observable manifestation of cultural capture, namely a lack of criticism leveled at the industry view or data. Our evidence shows that the MCA/MHRA operated with a clear "hierarchy of evidence" that prioritized evidence from clinical trials (i.e., randomized controlled trials [RCTs]) over observational and epidemiological studies when assessing the safety of *Vioxx*. The regulator's arguments were very similar to Merck's defence of *Vioxx* in this respect. The evidence on interactions between MSD and the MCA post-marketing division shows that MSD decisively and continuously argued that all observational studies of *Vioxx* pointing to an increased cardiovascular risk were inherently limited by their research design (MCA, 2002a, 2002b, 2004a, 2004b). Simultaneously, the company continuously defended the results of one of its clinical trials (the VIGOR trial), which pointed to an increased cardiovascular risk of *Vioxx*. The study compared patients taking *Vioxx* with a control group who took the painkiller naproxen. According to Merck, the study showed that *Vioxx* did not increase patients' risk of suffering from a heart attack; rather, taking naproxen provided some protection against heart attacks. This would later be referred to as Merck's "naproxen hypothesis." The MCA/MHRA and CSM closely considered all independent observational studies on this question but also continuously argued that RCT data was needed to reach firm conclusions about possible cardiovascular risks. This means that the advisory committees and the agency largely agreed with Merck/MSD's interpretation of the available evidence. Observational studies in favor of Merck's "naproxen hypothesis" were questioned less vigorously than observational studies showing cardiovascular risks of *Vioxx* (D2, D4, D8, D11, D13). The regulator also had a significant degree of trust in the studies supplied by MSD and did not consider the possibility that the company may be withholding data. Suspicions of this emerged after the withdrawal of the drug but they could not be substantiated.

While the similar lines of argumentation used by the regulatory bodies and the company suggests industry influence linked to the first causal part of our mechanism, namely a lack of critical questioning of the industry position, this picture is complicated by the presence of shared scientific norms about what constitutes good evidence. RCTs are regarded as the gold standard of medical research in the broader scientific community. Moreover, risk-benefit assessments of drugs are complex. Regulators considered trade-offs between different kinds of adverse effects, such as the risks of gastrointestinal risks of conventional NSAIDs compared to cardiovascular risks of coxibs. In this context, the possibility that Merck/MSD were wrong about the "naproxen hypothesis" was actively and consistently entertained by the regulators and the advisory committees (D2, D4-D9, D11-D13). This means that the focus of the advisory bodies and the regulator was on the quality of data, instead of representing a simply repeating the company's arguments. Moreover, our evidence did not match the observable manifestations related to the second and third parts of the cultural capture mechanism, namely the side-lining and active dismissal of evidence critical of the industry view, and subsequent decision-taking that conforms to industry views. When safety concerns relating to *Vioxx* emerged, the regulator conducted a major review study in which independent studies were (D6, D7). This speaks against observable implications of the second part of the mechanism, such as that views contradictory to the industry's position are not sought out or adequately represented in regulatory decisions. Moreover, independent studies were the rationale for restrictive regulatory action (product labeling changes) (D6, D7, D10). This means that shared frameworks of what constitutes good evidence and a partial overlap between lines of argumentation between regulatory bodies and Merck/MSD did not translate into unequivocal influence of the company over decision-making. The limited degree of cultural capture is further supported in Table 2 of the Supplemental Material, which provides a full overview of the observable manifestations, and our theoretical and empirical evaluation of evidence. The table also highlights high uniqueness and certainty of the empirical material, enabling us to have a very high degree of confidence in our analysis.

6. Discussion

Discussions about capture are often dominated by the dichotomy of regulation either being captured or not. However, capture most likely operates in shades of gray rather than black-and-white (Carpenter & Moss, 2014). This is also true for the case of regulatory decision-making on *Vioxx*. The empirical evidence does not suggest that decision-making shifted from the public interest to the interests of Merck or MSD due to excessive influence by the company. Instead, the evidence demonstrates scientific uncertainty that made clear-cut decisions difficult,

where regulators thought that *Vioxx's* risks were small if managed appropriately. Therefore, the analysis showcases the importance of theorizing causal mechanisms explicitly and studying them empirically. For instance, in the case of *Vioxx*, the media equated Prof Langman's conflict of interest with capture. But while these types of conflicts of interest are undoubtedly problematic, our empirical analysis shows that we need to carefully consider if and how these translate to capture. Based on our analysis, it seems unlikely that Prof Langman was able to influence adecisions on *Vioxx* to a significant degree.

Moreover, our observable manifestations for an information overload and cultural capture mechanism enabled us to study fine differences between these mechanisms. For example, at no point did the regulatory bodies neglect to consider all available evidence. However, regulators shared Merck's view that findings from RCTs would provide the most conclusive evidence on the cardiovascular risks of Vioxx, which means their decisions were relatively slow. Our process-tracing approach shows that it is difficult to disentangle causality in this respect. After all, it is an established scientific norm that RCTs provide the most conclusive evidence. Although Merck/MSD tried to discredit observational studies that highlighted the cardiovascular risks of *Vioxx*, the direct impact this rhetoric had on the regulatory bodies is difficult to discern. Ultimately, the empirical material suggests that regulators took different types of studies seriously and always entertained the possibility that Merck's interpretation of the data was wrong. Capture was incomplete since regulators explicitly and carefully considered independent sources of information. The impact of shared scientific norms on decision-making highlights that to the degree that capture was present, it was not providing specific benefits to MSD/Merck because of the company's influence. Instead, these operated on a systemic level. Our approach highlights these problematic sources of influence and shows that regulatory bodies were not defenceless against them. It also indicates that these different avenues of capture are likely to be at work simultaneously, especially in areas of regulation with high information asymmetry between industry and regulator.

Our theoretical and empirical evaluation of evidence provides a transparent evaluation of the strength of the evidence. The evaluation provided higher certainty in the empirical sources for information overload and cultural capture mechanisms compared to the revolving door, since we did not have access to records of informal discussions or full transcripts of meetings. Studying all three mechanisms also allowed us to reflect on the different behavioral motivations of regulators: incentives for private personal gain, organizational capacities and shared norms all played a role in decision-making. Research on capture needs to remain mindful of the complexity of the motivations underpinning organizational and individual behavior.

Is it possible that capture occurred through different mechanisms altogether? Our in-depth empirical approach safeguarded us from missing significant routes of industry influence. However, two further mechanisms deserve discussion: influence through industry funding and influence through implied or implicit threats. Industry-funding of a regulator is often invoked as a source of undue industry influence, and the MCA/MHRA have been accused of being captured for this reason (cf. Abraham & Davis, 2009). This question deserves greater consideration than we can devote to it here, but we did not find any evidence or indication that decision-making on Vioxx was driven by concerns over industry fees and the regulator was not under unusual resource pressure at the time (also see NAO, 2003). However, influence of this kind may manifest in how decision-making is structured, rather than in individual decision-making processes. Further research with clear theorization and operationalization of how industry funding results in capture is needed. We found no direct evidence that implicit threats of industry litigation played a role in decision-making on Vioxx. However, there is limited evidence that the MCA/MHRA's concern over litigation by the industry played a role in other cases (House of Commons, 2005a, p. 85; House of Commons, 2005b, Eva 84). One indication that implicit threats or behind-the-scenes pressure exerted by MSD may have played a role was that more than 6 months passed between the CSM recommending new safety warnings on the label and the MCA implementing these changes. Drug companies are notorious for trying to avert and tone down such changes and delaying them in the process.

The relative weakness of capture dynamics in this case cannot be equated with the absence of excessive influence of the pharmaceuticals industry more broadly. *Vioxx* brought to light a long list of unethical practices employed by Merck and spotlighted the industry's problematic behavior. Moreover, the case showed a gulf between regulators' and societal perceptions of what constitutes adequate regulatory action when product risks emerge. The MCA considered changes to the label of *Vioxx* to be sufficient to safeguard patients. However, a

considerable body of evidence shows that changes to the Summary of Product Characteristics (SPCs) do not impact the prescription behavior of doctors (e.g., Uhl & Honig, 2001; Van Groothest & Edwards, 2002). Hence, MCA warnings about the cardiovascular risks of *Vioxx* did not resonate with the public and prescribing doctors (Health Select Committee, 2005a). Indeed, doctors received promotional materials from MSD that deliberately steered doctors' attention away from the cardiovascular risks of the product (Health Select Committee, 2005b, also see Lyon, 2007), making it more difficult for regulatory messages to come through. However, rightly or wrongly, regulators ascribe high autonomy to health care professionals' judgment in selecting which products to prescribe and warning their patients adequately of the risks stated in the SPC (Abraham & Davis, 2009). This highlights that systemic industry influence played a role in causing harm, which is most likely what the commentators mentioned in the Introduction were alluding to. However, it remains important to distinguish this from capture of *regulatory decision-making*. This is a crucial reminder that we need to be careful in attributing scandals of this kind to individual causes, rather than a complex web of issues. When *Vioxx* is concerned, the interaction between the complexity of scientific uncertainty, the industry's control over RCT data and the dominant shared scientific belief in the superiority of these types of studies played a crucial role in the cautious approach to restrictive regulatory action.

Our findings contradict existing literature in some key respects. Literature on drug approvals and safety withdrawals in the UK is limited, but has highlighted the importance of capture and corporate bias as an explanation for safety-related withdrawals (Abraham & Davis, 2009, 2020). This literature has also indicated a high tolerance of drug risks in UK drug regulation, which gets reinforced through closure between regulators, doctors and the industry (Abraham & Davis, 2005, 2009). Our study shows the limits of using capture as an explanation for drug safety withdrawals, which is in line with studies of FDA drug safety withdrawals: through the use of game theoretic and decision-theoretic models, this literature has highlighted that time pressure for approval, firm size, experimentation times of the new drug, whether a drug is the first in its class, and a regulators' familiarity with an applicant firm can all play a role in explaining why the FDA approved drugs that were later withdrawn (Carpenter, 2004; Carpenter & Ting, 2007; Carpenter et al., 2010, 2012). This points to the important role of bounded rationality in explaining regulatory errors. The *Vioxx* case indeed shared these features: in the scheme of new drug approvals, experimentation time was short and it was made by an experienced firm with whom regulators were very familiar (and who happened to be one of the most trusted pharmaceutical companies in the world) (also see Carpenter & Ting, 2005, p.32f). While the MCA/MHRA does not have FDA-like deadlines for drug approval, it has a long tradition of fast drug approvals (Abraham & Davis, 2020), and *Vioxx*, together with Pfizer's *Celebrex*, were the first Cox-2 inhibitors to come to the market.

However, the regulation of *Vioxx* has been primarily criticized for how regulators handled safety problems after approval. The FDA's discussions of *Vioxx*, just like the debates in its UK counterpart, were ultimately about the relative value of RCTs versus observational studies, and of pharmacology versus epidemiology in drug regulation (with the difference that the FDA's post-marketing arm carries out its own observational studies, pitting different parts of the organization against each other in a more dramatic fashion than is the case in the UK) (Carpenter, 2010, p. 737ff). It shows that expert drug regulators share the challenge of evaluating different types of evidence under conditions of uncertainty. They need to keep drugs with severe side effects off the market, but they must be careful not to deny patients access to effective, novel treatments. Ultimately, we can interpret the UK regulator's decisions on *Vioxx* as those of an organization with a relatively high tolerance of drug risks, as previous studies, which have been critical of the agency, have done (Abraham & Davis, 2005; Abraham & Davis, 2009). However, in the case of *Vioxx* that may be too simple: regulators thought Cox-2 inhibitors were highly effective in reducing pain of arthritis suffers at lower gastrointestinal side effects than other painkillers, and they did not know at the time that other Cox-2 inhibitors were less risky than *Vioxx*. Rather, the main explanation for not restricting the product more stringently was a dominant belief in the superiority of RCT evidence over observational studies, which initially provided for a seemingly less risky profile of the drug. *Vioxx* thus highlighted the need for a greater openness to observational studies, which the MHRA pledged it would develop. *Vioxx* resulted in reforms at the EU level that enabled regulators to demand very specific post-marketing RCTs to assess safety, however, the success of this has been patchy as regulators lose the ultimate "carrot" once market approval has been granted.

7. Conclusion

Regulatory capture is frequently "misdiagnosed" because research lacks conceptual clarity, often sets a low empirical standard for evidencing capture, and has rarely tried to shed light on how capture happens (Carpenter & Moss, 2014). The presence of *opportunities* for the industry to influence regulatory decision-making is too often equated with excessive, harmful levels of industry influence. Commonly, the existence of the potential *causes* of capture, such as the "revolving door" or industry funding, are seen as direct evidence of captured regulatory *outcomes*. Using process-tracing methods can shift this debate by shedding light on how (and *if*) opportunities for influence are translated into actual influence. Distinguishing more accurately between situations in which regulatory decision-making was or was not captured is crucial for understanding how to prevent undue industry influence. Likewise, tracing causal mechanisms of regulatory capture presents a vital step in understanding how to break chains of harmful influence. Ultimately, capture research needs a far more nuanced understanding of what capture is, how we identify it, and how it occurs. This, in turn, can enable relevant research to develop a more precise understanding of the conditions under which capture is likely to occur.

This paper takes a crucial step by using systematic process-tracing methods (cf. Beach & Pedersen, 2019) to study the case of regulatory decision-making on *Vioxx*, which has been widely regarded as a case of regulatory capture. *Vioxx* caused one of the biggest drug scandals of all time, not least because so many people took the painkiller, resulting in a high number of people who suffered heart attacks or strokes due to taking the product. Observers quickly identified excessive industry influence on pharmaceutical regulators as the cause of this drug scandal. However, when we scrutinize regulatory decision-making on *Vioxx* in detail, it looks far from a straightforward case of regulatory capture. Using process-tracing to dissect the causal mechanisms at play, we find that such influence is not substantiated empirically. Crucial parts of how industry influence translates into capture were not present in this case. At the same time, the analysis highlighted the importance of more systemic sources of industry influence. UK regulatory bodies displayed a clear tendency to favor evidence from RCTs over observational studies. The industry usually dominates RCTs on the efficacy and safety of drugs. Thus, industry evidence was influential in decision-making due to shared scientific norms of what constitutes "the best science" and the industry's' systemic control of this type of evidence. More systemic influence was also crucial in *Vioxx* concerning regulators' inability to communicate their safety warnings effectively to doctors due to the sheer amount of engagement with industry information that doctors are exposed to compared to regulatory information. This is a pointed reminder that it is problematic to construe expertise as exogenous to political processes (Weinkle, 2020), while also raising the question of which types of experts to include in decision-making processes in the first place (Slayton & Clark-Ginsberg, 2018).

This paper, and the wider research agenda it calls for, thus do not aim at negating widespread industry influence on our economic and political institutions. Instead, it calls for more willingness to dissect avenues of influence more precisely. In this respect, the findings of this paper also do not aim to draw broad conclusions about the infallibility of regulators when it comes to excessive industry influence. Rather, by studying if and how capture occurred in a notorious case of regulatory failure (or what has at least been widely perceived as such), the paper seeks to highlight the need to develop a more nuanced understanding of regulatory capture and through which mechanisms it occurs. Captured regulators need to be reformed, but equally, we must highlight the limits of industry influence on regulatory decision-making. If regulators are portrayed as captured by the media, politicians and scholars, public trust in expert decision-making and bureaucratic government is eroded. Thus, capture allegations must only be made if they are truly warranted. Recently, the Covid-19 pandemic and public disagreements about vaccine safety and efficacy have reminded us that public trust in regulatory decision-making can be much more important than we often believe. Thus, we must ensure that research applies clear evidentiary standards to study whether capture occurred in given cases. To do so, we need to pay more attention to studying *how* industry influence translates into capture.

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Conflict of interest statement

The authors declare no conflicts of interest.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are available in the public domain but cannot be shared via a data repository scheme since the authors do not hold the copyright to the material.

References

Abraham, J., & Davis, C. (2005). Risking public safety: Experts, the medical profession and 'acceptable' drug injury. *Health, Risk & Society*, 7(4), 379–395.

Abraham, J., & Davis, C. (2009). Drug evaluation and the permissive principle: Continuities and contradictions between standards and practices in antidepressant regulation. *Social Studies of Science*, 39(4), 569–598. https://doi.org/10.1177/0306312709103480

Abraham, J., & Davis, C. (2020). International and temporal comparative analysis of UK and US drug safety regulation in changing political contexts. *Social Science & Medicine*, 255, 113005. https://doi.org/10.1016/j.socscimed.2020.113005

Bagley, N. (2010). Agency hygiene. *Texas Law Review*, 89, 1–14.

Beach, D., & Pedersen, R. B. (2019). *Process-tracing methods: Foundations and guidelines*. University of Michigan Press.

Becker, G. S. (1983). A theory of competition among pressure groups for political influence. *Quarterly Journal of Economics*, 98(3), 371–400.

Bennett, A., & Checkel, J. T. (Eds.). (2015). *Process tracing: From metaphor to analytical tool*. Cambridge University Press.

Bernstein, M. H. (1955). *Regulating business by independent commission*. Princeton.

Carpenter, D. (2004). Protection without capture: Product approval by a politically responsive, learning regulator. *American Political Science Review*, 98(4), 613–631.

Carpenter, D. (2010). *Reputation and power: Organizational image and pharmaceutical regulation at the FDA*. Princeton University Press.

Carpenter, D., Chattopadhyay, J., Moffitt, S., & Nall, C. (2012). The complications of controlling agency time discretion: FDA review deadlines and postmarket drug safety. *American Journal of Political Science*, 56(1), 98–114.

Carpenter, D., Moffitt, S. I., Moore, C. D., Rynbrandt, R. T., Ting, M. M., Yohai, I., & Zucker, E. A. (2010). Early entrant protection in approval regulation: Theory and evidence from FDA drug review. *Journal of Law, Economics, & Organization*, 26(3), 515–545.

Carpenter, D., & Moss, D. A. (Eds.). (2014). *Preventing regulatory capture: Special interest influence and how to limit it*. Cambridge University Press.

Carpenter, D., & Moss, D. A. (2014b). Introduction. In D. Carpenter & D. A. Moss (Eds.), *Preventing regulatory capture: Special interest influence and how to limit it* (pp. 1–22). Cambridge University Press.

Carpenter, D., & Ting, M. M. (2005). Regulatory errors under two-sided uncertainty: Or, The Political Economy of Vioxx. Discussion Paper.

Carpenter, D., & Ting, M. M. (2007). Regulatory errors with endogenous agendas. *American Journal of Political Science*, 51(4), 835–852.

CHM. (2006). Safety of Selective and non-selective NSAIDs. London: CHM, 24 October 2006.

Cohen, J. E. (1986). The dynamics of the "Revolving Door" on the FCC. *American Journal of Political Science*, 30(4), 689–708.

CSM. (1999). Summary of the Committee on Safety of Medicines meeting held on 29 April 1999. Date of Summary: April 2001.

CSM. (2001). Summary of the Committee on Safety of Medicines meeting held on 12 December 2001. Date of Updated Summary: November 2004.

Dal Bó, E. (2006). Regulatory capture: A review. *Oxford Review of Economic Policy*, 22(2), 203–225.

Dal Bó, E., & Di Tella, R. (2003). Capture by threat. *Journal of Political Economy*, 111(5), 1123–1154.

Gormley, W. T. (1979). A test of the revolving door hypothesis at the FCC. *American Journal of Political Science*, 23(4), 665–683.

Graham, D. J., Campen, D., Hui, R., Spence, M., Cheetham, C., Levy, G., Shoor, S., & Ray, W. A. (2005). Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal antiinflammatory drugs: Nested control study. *Lancet*, 365, 475–481.

Health Select Committee. (2005a). *The influence of the pharmaceutical industry: Volume I*. House of Commons.

Health Select Committee. (2005b). *The influence of the pharmaceutical industry: Volume II, formal minutes, oral and written evidence*. House of Commons.

Horton, R. (2004). Comment: Vioxx, the implosion of Merck, and the aftershocks at the FDA. *The Lancet*, 364(9450), 1995–1996.

Huntington, S. (1952). The marasmus of the ICC: The commission, the railroads and the public interest. *Yale Law Journal*, 61(4), 467–509.

Kwak, J. (2014). Cultural capture and the financial crisis. In D. Carpenter & D. A. Moss (Eds.), *Preventing regulatory capture: Special interest influence and how to limit it* (pp. 71–98). Cambridge University Press.
Laffont, J. J., & Tirole, J. (1991). The politics of government decision making: A theory of regulatory capture. *Quarterly Journal of Economics*, 106(4), 1089–1127.
Levine, M. E., & Florrence, J. L. (1990). Regulatory capture, public interest, and the public agenda: Toward a synthesis. *Journal of Law, Economics, & Organization*, 6, 167–198.
Lyon, A. (2007). "Putting patients first": Systematically distorted communication and Merck's marketing of Vioxx. *Journal of Applied Communication Research*, 35(4), 376–398. https://doi.org/10.1080/00909880701611052
Makkai, T., & Braithwaite, J. (1992). In and out of the revolving door: Making sense of regulatory capture. *Journal of Public Policy*, 12(1), 61–78.
MCA. (1999a). *Preclinical assessment report of rofecoxib*. MCA (FOI 20/388).
MCA. (1999b). *Clinical assessment report of rofecoxib*. MCA (FOI 20/388).
MCA. (2002a). *Periodic safety update report 7 June 2002: Preliminary assessment report for Vioxx/Rofecoxib*. MCA (FOI 20/388).
MCA. (2002b). *Periodic Safety Update Report December 2002: Final Assessment Report for Vioxx/Rofecoxib*. MCA (FOI 20/388).
MCA (2004a). Periodic Safety Update Report January 2004: Preliminary Assessment Report for Vioxx/Rofecoxib. London: MCA (FOI 20/388).
MCA (2004b). Periodic Safety Update Report July 2004: Preliminary Assessment Report for Vioxx/Rofecoxib. London: MCA (FOI 20/388).
McCarty, N. (2014). Complexity, capacity, and capture. In D. Carpenter & D. A. Moss (Eds.), *Preventing regulatory capture: Special interest influence and how to limit it* (pp. 99–123). Cambridge University Press.
NAO [National Audit Office]. (2003). *Safety, quality, efficacy: Regulating medicines in the UK*. NAO.
Noll, R. G. (1989). Economic perspectives on the politics of regulation. In R. Schmalensee & R. D. Willig (Eds.), *Handbook of industrial organization* (pp. 1276–1277). North Holland.
Quirk, P. J. (1981). *Industry influence in Federal Regulatory Agencies*. Princeton University Press.
Rilinger, G. (2021). Who captures whom? Regulatory misperceptions and the timing of cognitive capture. *Regulation & Governance*, 17, 43–60. https://doi.org/10.1111/rego.12438
SCOP. (2001). Summary of the Meeting of the Committee On Safety of Medicines Sub-committee on Pharmacovigilance held on Tuesday 27 November 2001. Date of Summary: November 2001.
Seabrooke, L., & Tsingou, E. (2020). Revolving doors in international financial governance. *Global Networks*, 21(2), 294–319.
Shapiro, S. (2012). The complexity of regulatory capture: Diagnosis, causality and remediation. *Roger Williams University Law Review*, 102(1), 101–172.
Slayton, R., & Clark-Ginsberg, A. (2018). Beyond regulatory capture: Coproducing expertise for critical infrastructure protection. *Regulation & Governance*, 12, 115–130.
Stigler, G. (1971). The theory of economic regulation. *Bell Journal of Economics and Management Science*, 2(1), 3–21.
Sunday Times. (2005). Victims of drug that took a hidden toll. By Brian Deer, 21 August 2005.
The Independent. (2004). Letter: Drug regulation. By Paul Flynn, MP, 20 October 2004.
The Independent. (2004b). *Drug giants ignored dangers of painkiller in pursuit of profits*. Jeremy Laurance, 8 October 2004.
Thomas, L. C. (1990). Regulation and firm size: FDA impacts on innovation. *The Rand Journal of Economics*, 21(4), 497–515.
Uhl, K., & Honig, P. (2001). Risk management of marketed drugs: FDA and the interface with the practice of medicine. *Pharmacoepidemiology and Drug Safety*, 10, 205–208.
US Senate Finance Committee. (2004). *FDA, Merck, and Vioxx: Putting patient safety first?* US Senate Finance Committee.
Van Groothest, A. C., & Edwards, I. R. (2002). Labelling and 'Dear Doctor' letters: Are they noncommittal? *Drug Safety*, 25(15), 1051–1055.
Wagner, W. E. (2010). Administrative law, filter failure, and information capture. *Duke Law Journal*, 59, 1321–1432.
Weinkle, J. (2020). Experts, regulatory capture, and the "governor's dilemma": The politics of hurricane risk science and insurance. *Regulation & Governance*, 14(4), 637–652.
Wilson, J. Q. (Ed.). (1980). *The politics of regulation*. Basic Books.
Yackee, S. (2006). Sweet-talking the fourth branch: The influence of interest group comments on Federal Agency Rulemaking. *J Public Adm Res Theory*, 16(1), 103–124.
Young, K. L. (2012). Transnational regulatory capture? An empirical examination of the transnational lobbying of the Basel committee on banking regulation. *Review of International Economy*, 19(4), 663–688.

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Data S1: Supporting Information

