Organizational Reputations and the Observability of Public Warnings in 10 Pharmaceutical Markets*

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ABSTRACT

How does a regulator's reputation affect its willingness to make catastrophic errors public? To address this question, I draw on recent developments in institutional political science that view regulators as generally rational agents, and also as politically conscious organizations interested in protecting their reputations. I present a model in the policy domain of drug safety, which suggests that if a regulator is able and willing to develop a predominant basis of reputation, media coverage of the regulator's catastrophic errors will be a function of the regulator's predominant basis of reputation: media coverage will be lowest when the regulator maximizes its reputation for expertise, and highest when it maximizes its reputation as a guarantor of public safety. Empirical tests of the model – in the form of an analysis of procedures regulating the issue of public warnings following safety-based drug withdrawals in the US, UK, Germany, Canada, South Africa, Australia, New Zealand, Ireland, Israel, and Switzerland between 1975-2004, combined with an analysis of the media coverage of these warnings – support the model's prediction.
The abrupt voluntary withdrawal of the arthritis drug Vioxx on September 30, 2004 by Merck & Co made the headlines in almost every newspaper worldwide. With more than 2 million Americans taking Vioxx at the time it was pulled and more than 84 million prescriptions written worldwide, the event was the largest voluntary recall in pharmaceutical history. The massive media attention that followed conjured up images of strong and well-publicized public warnings, issued when drugs are voluntarily pulled off the market for safety reasons, and an opportunity to pin blame on the FDA for allowing such products to remain in the market as long as they did. This study calls attention to the veracity of these images in a comparative perspective by positing the following question: why do some regulators make safety warnings more publicly observable than other regulators performing similar tasks?

The withdrawal of Vioxx has brought the issue of regulatory error to the fore (Carpenter and Ting 2005a). Prior research suggests that three general factors – the protections of the agency's reputation, the familiarity and credibility of pharmaceutical manufacturers, and the political clout of disease victims – all affect regulatory error (Carpenter 2002, 2004; Carpenter and Ting 2005b). However, largely overlooked in the discussion of regulatory error is how a regulator's reputation affects the public observability of its catastrophic errors.¹ At its core, choosing a reputation protection strategy following catastrophic regulatory errors presents the regulator with an observability problem: it must decide whether or not to encourage large media coverage of its errors. To illustrate this problem, consider a decision by a regulator to withdraw a truly dangerous drug from the market. When this decision is reached and the supplier is unable to identify and contact each customer, the need to communicate the warning directly to the public arises. This need is independent of all imaginable public relations factors, which are also in play, because of the moral responsibility to notify users of the serious side effects, as well as the risk of death, associated with the use of the drug. While the moral imperative to communicate warnings to the public is obvious, the regulator’s willingness to do so is not. A primary reason for this

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¹ The term "catastrophic" is used here in the sense of the impact on the health of patients.
dynamic is that public consideration of a given issue as a catastrophic regulatory error largely depends on the perception of regulator’s degree of expertise. Bureaucratic expertise, argue Rourke (1984) and Bawn (1995), is central to determining whether politicians or administrative agencies are responsible for policy directives. This implies that a catastrophic regulatory error is only likely to tarnish the reputation of a regulator that has maximized its reputation for expertise. This insight highlights the potential calculus underlying the decision of whether or not to encourage large scale media coverage of a regulator's error: when a catastrophic error occurs, agency leaders must carefully weigh the costs and risks associated with the visibility of their error relative to the predominant basis of the reputation they build for their organization — reputations for expertise; efficiency, uniqueness of service; neutrality; protection of public morality; protection of public safety, and so on. It also implies that any research on the topic must be undertaken in a context that offers a clear-cut understanding of the expertise that the regulatory agency seeks (e.g., in the policy domain of drug safety, "expertise" refers to the ability to detect post-approval risks).

In order to understand the relationship between organizational reputation and media coverage of an agency’s catastrophic errors, I draw on recent developments in institutional political science that view regulators as generally rational agents, and also as politically conscious organizations interested to protect their reputations. I develop a model of rational reputation building, which offers several interesting and counterintuitive predictions. The model distinguishes between two types of reputations — reputation for expertise in detecting drug risks and reputation as a guarantor of public safety in the pharmaceutical market. I suggest that, if drug safety regulators are able and willing to develop a predominant basis of reputation, the same catastrophic error (e.g., approving a particular drug which is truly dangerous) may not be considered a failure for some regulators, while it may be for others depending upon the predominant basis of reputation of the regulators involved. Regulators that are able and willing to develop a reputation for technical expertise will naturally be blamed for technically-related errors and, at the same time, will not be able lay the blame at any other door. They, therefore, are most likely to opt for low public observability of their...
catastrophic errors. For regulators operating in a context that inhibits the development of technical expertise, high public observability of catastrophic errors offers a greater opportunity to promote their reputation as the guarantor of the public safety in the pharmaceutical market. Such regulators may therefore go either way: they can either lay the blame at the experts' door and opt for high observability of public warnings or else they can opt for low public observability of such warnings.

I analyze the procedures regulating the issue of public warnings following safety-based drug withdrawals in the US, UK, Canada, Germany, South Africa, Australia, New Zealand, Ireland, Israel, and Switzerland during the period 1975-2004. I find that the procedures enacted to protect a reputation of expertise include, at best, a required press release regarding the (mostly) “voluntary” withdrawal, which may or may not be picked up by the general media. These procedures were recorded in the US, Germany and UK where a reputation for expertise is deliberately cultivated. Similar procedures were recorded in Canada, Switzerland, Israel and South Africa, where regulators have proved unable to develop a reputation for expertise in detecting drug risks and at the same time unwilling to develop an alternative basis of reputation or unable to enlist political support to do so. This may be, for example, because politicians who play the blame game (Hood 2002) prefer to place all the blame at the door of the domestic regulator instead of pinning it, for example, on the FDA. Whatever the reason, these regulators formulate procedures that limit public access to meaningful information or shadow similar procedures formulated by regulators who enjoy technical expertise.

In contrast, procedures enacted to protect an agency’s reputation as the guarantor of the public safety in the pharmaceutical market impose a requirement on manufacturers to advertise public warnings in daily national and regional newspapers, and in some cases, even forbid the inclusion of the word “voluntary” in the text of the public warnings. Furthermore, sanctions for non-compliance with public notification requirements are anchored in legislation. These procedures were recorded in Australia, New Zealand and Ireland.
The article also analyzes the media coverage of public warnings following safety-based drug withdrawals in the aforementioned countries during the period 1975-2004. I find that, if a drug-safety regulator is able and willing to develop a predominant basis of reputation, media coverage of safety-based drug withdrawal will be a function of that reputation. Specifically, media coverage will be lowest when the regulator maximizes its reputation for expertise, and highest when it maximizes its reputation as the guarantor of public safety in the pharmaceutical market.

This research carries important implications for public health. Regulators that opt for low public observability of their catastrophic errors, by communicating their decisions primarily to health professionals, effectively fulfill the bureaucratic requirement of communicating safety information. However, they only contribute minimally to protecting the public health mainly because their risk communication strategy is based on the naive assumption that most physicians read "Dear Health Professional" letters and/or notifications posted on the regulators’ web pages. The problem here is that some health professionals do indeed read and act, while others do not (Schiff et al. 2002; Smalley et al. 2000; Graham et al. 2001; Seligman 2003). The low public observability of safety-based drug withdrawals recorded in the US, Germany and the UK, as well as in Canada, Switzerland, Israel, and South Africa implies that patients are often unaware of the risks associated with their medication, and therefore continue to take dangerous drugs until they require a new prescription.

This research also carries important implications for regulators operating in a context that inhibits the development of technical expertise. These regulators can successfully practice the politics of legitimacy by opting for another predominant type of reputation, for example, as guarantors of the public safety in the market in which they operate. They can also persuasively imply that their “errors” (i.e., their approval of what is later shown to be a truly dangerous product) were mainly based on approval decisions by regulators with international reputations for expertise. While some regulators may subsequently survive, as in New Zealand’s case of the Medicines and Medical Devices Safety Authority (Medsafe),
others may gain substantial autonomy, as the Australian's Therapeutic Goods Agency (TGA) and the Irish Medicines Board (IMB) have demonstrated.

The plan of the article is as follows. The first section considers the observability problem from two perspectives: the behavior of bureaucratic organizations and agenda setting. The second section outlines the model and the derived hypothesis, the third section elaborates the methodology employed, and the fourth section presents the empirical analysis. The fifth section presents the article’s conclusions.

RELATED LITERATURE

Why do some regulators make safety warnings more publicly observable than other regulators performing similar tasks? This should have been a central theme in the literature on bureaucratic politics, especially with regard to agencies that manage and regulate risky technologies. Yet, despite two decades of illuminating research in this area, students of political science have said little about the question: What happens when public observability itself is the variable of bureaucratic choice?

Most studies on the behavior of bureaucratic agencies have focused mainly on two themes. The first is the study of political control of bureaucratic agencies and the mechanisms with which politicians can influence agency behavior, the second is a line of research, grounded in organizational theory, which has analyzed the internal behavior of agencies. These studies have explored the tension between elected authorities and bureaucrats by analyzing the content of bureaucratic choices. However, none have placed alternative parameters of choice at the center of analysis. A recent advance in the study of bureaucratic politics has demonstrated very elegantly that, in the policy area of drug approval, many of the

most significant decisions made by bureaucratic organizations involve choices of timing. The critical problem is not what to choose but when to choose (Carpenter 2002, 2003). This view suggests that at its core, drug approval is an optimal stopping problem. The agency learns about a drug during the course of a review in order to reduce uncertainty about key parameters (e.g., efficacy and safety), “stopping the learning process to approve the drug if and when the benefits of waiting are exceeded by the costs of further delay” (Carpenter 2002, 491).

The assumption underlying Carpenter’s (2002; 2003) arguments is that the regulator protects its reputation (Quirk 1980; Heimann 1997; Carpenter 2001; Krause and Douglas 2005). Bureaucratic reputations “are valuable political assets – they can be used to generate public support, to achieve delegated autonomy and discretion from politicians, to protect the agency from political attack, and to recruit and retain valued employees” (Carpenter 2002, 491). While I take no issue with Carpenter and other scholars regarding the importance of bureaucratic reputation (Rourke 1984; Whitford 2002; Wilson 1989), I do provide a political and bureaucratic rationale to suggest that when a regulator outweighs the costs and risks associated with its catastrophic error, the public observability of a decision will be equally, if not more, important than the content or timing of the decision. This is because “Visibility is a factor in the expanding of the scope of conflict” (Schattschneider 1960, 16). It expands the “audience” of an agency decision beyond self-interested pressure groups, to include the general public (Schattschneider 1960). Once the general public participates in a policy dispute, it can change the definition of the policy problem (Fritschler and Hoefler 1995) and increase the saliency for a policy issue amongst the myriad issues in the political process (Baumgartner and Jones 1993; Baumgartner and Leech 1998), thus influencing which policy is ultimately successful. Precisely because of this potential influence, actors in the political process are likely to attempt to push issues either towards or away from the public agenda (Schattschneider 1960; Elder and Cobb 1983; Riker 1982, 1986; Kingdom 1995). To capture the regularities in the way bureaucratic agencies solve their observability problem, I have developed a simple model of rational reputation building in drug safety.
RATIONAL REPUTATION BUILDING

How does a predominant type of bureaucratic reputation emerge? To answer this question, I focus on safety regulators in the pharmaceutical sector with the premise that a decision to approve what later turns out to be a truly dangerous drug is reputationally irreversible (Carpenter 2002, 492). With the use of any medication comes the possibility of adverse drug reactions (ADRs). Prior to approval, drugs are studied in selected populations for limited periods in what is known as pre-marketing drug trials. These trials are undertaken in controlled conditions under direct medical supervision without necessarily significant exposure to other drugs and underlying diseases. Consequently, the trials are often insufficient to detect the full range of ADRs as some important reactions may take an extremely long time to develop, occur infrequently, or occur at rates of 1 in 10,000 or fewer drug exposures (Brewer and Colditz 1999; Lasser et al. 2002). They are also insufficient to detect ADRs, which appear in special populations such as pregnant women or children who often do not participate in these trials (Brewer and Colditz 1999). These limitations in pre-marketing trials mean that a new drug may bring with it the possibility of immediate ADRs, as well as rare but serious ADRs, or common, delayed ADRs.

A number of methods have been used to identify previously unknown detrimental outcomes that may be attributable to the use of medications. The effectiveness of these detection mechanisms is determined primarily by both the availability of the raw material for analyses, namely ADRs data, and the existence of an effective system designed to collect the data. The availability of ADRs data is dependent on the extent of patient exposure to new drugs with yet unknown toxic effects and to conventional drugs with rare adverse reactions.

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3 Most common methods include spontaneous case reports; aggregate population-based data sources; computerized collection of data from organized medical care programs; postmarketing cohort studies and meta-analysis.

4 Additional safety data is derived from the medical literature, on-going clinical trials, and epidemiological studies.
The higher the patient exposure to new and old drugs, the greater the chances of revealing the side effects of drugs. This is especially true for common side-effects, which numerically inflict suffering on the majority of patients experiencing ADRs. The importance of mass medication use (i.e., large population size and large number of drugs) for generating ADRs data is further intensified by the lack of scientific gold standard in the area of methodology for adverse drug reaction monitoring (Edwards and Biriell 2001, 93); the problem of causality in detecting ADRs [i.e., an adverse outcome does not establish the drug as the cause of the injury (Brewer and Colditz 1999, 827)], and the problem of reliability in detecting ADRs [i.e., “there is still no reliable method for identifying potential ADRs that occurred widely separated in time from the original use of a drug, occur with measurable frequency in the unexposed population, and have no predictable relationship to the major effects of the drug” (Brewer and Colditz 1999, 827)].

Although agencies that regulate risky technologies exist to bring needed expertise to difficult policy decisions, some are better placed than others to develop their reputation for expertise. Drug safety regulators operating in pharmaceutical markets characterized by mass medication use and an effective system for collecting ADRs data enjoy favorable conditions for developing a reputation for expertise. Mass medication use provides the regulator with numerous reports of ADRs that occur after the initial use of the medication and after long-term use. This information has an advantage in that it allows the agency to develop a pool of expertise in this policy area and devise new detection methodologies, leading to a more accurate evaluation of the risks associated with drug use. However, just because mass medication exists does not mean that the agency will always have such a pool of expertise or that it will always devise new detection methodologies. The capacity to develop a reputation for expertise may be significantly jeopardized if the regulator lacks various capabilities, such

5 At the global level there is another source for ADRs data – namely, the World Health Organization’s Collaborating Centre for Drug Monitoring – whose exclusive function is to identify rare ADRs (below 1/1000).
as, a clear and effective process for making decisions about postmarket drug safety issues; clarity about how decisions are made; oversight by management, and criteria for determining what safety actions to take and when to take them. Insufficient communication between divisions, data constraints, limited authority to demand certain studies from industry, and limited resources for obtaining data may also contribute towards such an outcome.

By contrast, regulators operating in markets characterized by low level patient exposure to new and conventional drugs will find it very difficult to develop a reputation for expertise. Such regulators are likely to seek active international collaboration to support their efforts to determine with reasonable certainty which adverse events are caused by drugs. To successfully practice a politics of legitimacy, they are likely to develop an alternative predominant basis of reputations, such as, a reputation as guarantors of public safety in the pharmaceutical market.

RATIONAL REPUTATION PROTECTION

At its core, choosing a reputation protection strategy following safety-based drug withdrawals presents the regulator with an observability problem: it must decide whether or not to encourage large media coverage of its catastrophic errors. Given that bureaucratic expertise is central to determining whether politicians or administrative agencies are responsible for policy directives (e.g., Bawn 1995; Rourke 1984), the regulator must outweigh the costs and risks associated with the visibility of its error in relation to its predominant basis of reputation. For a drug safety regulator whose predominant reputation basis is for expertise, the approval of a truly dangerous drug is a catastrophic error that can tarnish its reputation. The danger of politicized failure may culminate in opponents calling attention to lethal weaknesses and deep-rooted problems in the agency’s regulatory oversight (e.g., that licensing of new drugs supersedes safety evaluation), signaling that “something is rotten” (Kingdon 1995, 98; Brändström and Kuipers 2003, 281).

Given that citizens are not likely to have “traceability” constraints when it comes to tracking safety-based drug defects (Arnold 1990; Ellis 1994), an agency should never be seen committing any visible errors (Heimann 1997, 18). Political executives in charge of health
affairs are well aware of this danger, and thus face strong incentives to design procedures that
direct the agency’s risk communication strategy mainly towards the professional community
(e.g., “Dear Health Professional” letters, fax/email communications; bulletin/newsletter
announcements, etc.). This strategy meets the bureaucratic requirement of communicating
safety information and although it can possibly lead to criticism in professional journals, most
importantly for political executives, coverage of the errors in the general media will be
suppressed.

There is always the risk of information leaking from health professionals to the
general media, but the agency could counteract the effect of this by promising a more
aggressive response over the tracking of safety-based drug defects. For example, the agency
can establish an internal program to ensure that the views of dissenting scientists are heard;
submit a formal request to an academic body to study the regulator’s safety monitoring
procedures, and replace the director of the drug safety division. A classic example of this last
line of defense against political and public pressures was the FDA’s initiatives following the
Vioxx episode to improve the postmarket decision making process by (i) establishing a Drug
Safety Oversight Board, (ii) drawing up a draft policy on major postmarket decision making
and holding regular meetings between the Office of New Drugs and the Office of Drug
Safety, and (iii) identifying new data sources (GAO 2006). The first initiative did "not address
the lack of systemic tracking of safety issues and their resolution" (GAO 2006, 5-6); the
second initiative was not fully implemented, and the third was limited due to data constraints
(GAO 2006). The point here is not that agency officials could, at any time, by-pass the public
notification procedures and put public safety first and public relations second. Rather, it is that
scientific and technocratic information cannot answer all the agency's questions, and that even
(and especially) technocratic regulators find it necessary and worthwhile to manage their
public image.

By contrast, the costs and risks faced by drug safety regulators whose predominant
reputation basis is as guarantors of the public safety in the pharmaceutical market may be
completely different. Such regulators can persuasively hint that the “error” (i.e., approving
what is later revealed as a truly dangerous drug) was mainly based on the approval decisions made by drug safety regulators who enjoy international reputations for expertise. Thus, to protect their reputation as guarantor of public safety, it would be rational for them to facilitate high observability of public warnings following safety-based drug withdrawal. Political executives in charge of health affairs are well aware of the benefits of large media coverage aimed at protecting public safety by advertising the deadly side effects of hazardous products that have been withdrawn, and thus face strong incentives to design procedures that direct agency response towards the public at large, along with communication strategies directed at the professional community.

The theoretical discussion so far points to a process in which the same event — withdrawing a dangerous drug from the market — elicits a blame-avoidance reaction (Weaver 1986) for expertise-based agencies and provides an opportunity for credit claiming (Weaver 1986) for guardian of safety-based agencies. In the first case, the expectation of the agency is for approvals of safe drugs – thus when a dangerous drug is found the agency faces potential blame for approving it. In the latter case, the agency is expected to provide timely and effective warning about drug-related dangers and therefore finding a dangerous drug will elicit strong and immediate public warning. The fear of such an agency is to appear as if it failed to provide timely, sufficient, and effective warning– since that is what it is expected to do.

Using the intuition laid out above and with media coverage as a proxy for public observability, I seek to test the following claim: Media coverage of safety-based drug withdrawals is a function of the regulator’s predominant basis of reputation: media coverage will be lowest when the regulator maximizes its reputation for expertise, and highest when it

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6 A classic example is the FDA, which is “the best resourced in the world, and is renowned for subjecting the pharmaceutical industry to stringent regulatory checks […]” (Abraham 2002, 1498).
maximizes its reputation as guarantor of public safety. Below I discuss data and measurements for the variables under consideration.

**DATA AND MEASUREMENTS**

The first and most intractable problem was one of country selection. Ten countries were selected for this analysis and divided into three groups. Between-group variance reflects the varying contexts within which different predominant types of reputations are likely to emerge. Within-group variance reflects the varying therapeutic culture of the countries under examination, that is, "the relationships among the state (including legislatures and regulatory agencies), the pharmaceutical industry, the medical profession, and disease-based organizations" (Daemmrich 2004, 4). Because the aforementioned cultural differences have been discussed elsewhere [for Germany and the US, see Daemmrich (2004); for the US, UK and Canada, see Hughes Tuohy (1999)], attention now turns to the varying contexts within which different predominant types of reputations are likely to emerge.

The first group comprised the US, Germany and the UK. 7 These countries have been among the top ten pharmaceutical markets in the world in 1976 (18.4%, 7.9% and 2.4% respectively); 1985 (28.1%, 6.4% and 2.5% respectively), and 2000 (52.9%, 5.7% and 3.9% respectively) (WHO 2004, 34). Regarding population exposure to new and conventional drugs, a recent study has estimated that insofar as prescription drugs are concerned, half of US adults take at least one drug during a week, and 7% of them take at least five drugs (Kaufman et al. 2002). Data on medication use in the other countries selected is not available,8 but it is reasonable to use the number of prescription-only drugs in the market as a

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7 Drug safety regulators in all the countries selected, except of Germany, are in charge of both drug approval and post-marketing surveillance. In Germany, both roles are undertaken by two independent agencies, with no intervention by the drug approval agency in decisions regarding safety-based drug withdrawals [Ulrich Hagemann, Phone interview with Nadine Zielinsky, 27 May 2006].

8 The available data only covers patterns of medicine use for a specific disease.
proxy for population exposure to new and conventional drugs (although the data is only available for the mid-1990s). Thus, in Germany in the mid-1990s, around 82 million patients were exposed to 20,000 prescription-only drugs whereas in the UK, around 58 million patients were exposed to 10,624 prescription-only drugs (Olsson 1999). Regarding the effectiveness of the system designed to gather ADRs data, average annual reports of ADRs in the US, Germany, and the UK in the mid-1990s were approximately 102,000, 18,400, and 18,000, respectively (Olsson 1999). These figures are proportional to the population size in the three countries cited.

The second group consists of Canada, Australia, New Zealand, Israel, Ireland, and Switzerland. Although population size in these countries ranges from 3.5 million (Ireland) to 29 million (Canada), the number of prescription-only drugs available to the public was less than 5,000 in the mid-1990s, for example, 1,500 in New Zealand; 3,330 in Israel; 5,000 in Australia; 4,605 in Canada, and 4,005 in Switzerland (Olsson 1999). Although in this group of countries Canada is the largest in terms of population size, it sits squarely in this group, as reflected in its own admission: “Health products are used worldwide and it is more difficult for a relatively small country (e.g., Canada) […] to generate and evaluate signals for rare adverse reactions” (Health Canada 2004, 5). Regarding the effectiveness of the system designed to collect ADRs data, average annual ADRs reports in the countries of the second group during the mid-1990s range from approximately 900 (Switzerland) to around 8100

Switzerland is among the world's leading pharmaceutical producers of brand-name drugs (WHO 2004). The pharmaceutical sector is among the largest export sectors in Ireland (brand-name drugs) (Egeraat 2006) and Israel (generic drugs) (Blay 2002). The Australian pharmaceutical manufacturing industry is small by global standards (Faunce 2005). Pharmaceutical production in New Zealand is almost non-existent.

There is no corresponding figure, from the same source or other sources, for Ireland, although it is known that in the mid-1990s, there was a total of 7,500 drugs which includes prescription-only drugs, pharmacy-only drugs, and general sales drugs (Olsson 1999).
(Australia). The third group consists solely of South Africa, which has a population of 38.7 million; 7,308 registered drugs (i.e., prescription-only drugs, pharmacy-only drugs, and general sales drugs), and a very weak and ineffective adverse reaction monitoring system, which collected an average of 260 ADRs reports annually during 1993-1997 (Olsson 1999).

To test H1, I have employed an institutional analysis of procedures governing the issue of public warnings following safety-based drug withdrawals in the countries selected during the period 1975-2004. A drug is categorized as “withdrawn for safety reasons” if the drug removal was initiated by the drug safety regulator for safety reasons or if the manufacturer voluntarily withdrew it from the market following the identification of life-threatening adverse drug reactions (ADRs). “Drug removal” refers to a removal of all the batches of the drug for safety-reasons, whether the problems were inherent in the product itself or due to manufacturing deficiencies. The analysis focuses on public warning procedures either under the umbrella of drug “withdrawal” or “consumer-level recall”, when the public health is seriously jeopardized (i.e., when there is a strong likelihood that a product will cause serious ADRs or death). The study period 1975-2004 was chosen because it corresponds with the modern era of drug surveillance (Merrill 1999).

The analysis of media coverage aims at capturing the extent to which public warnings are picked up by any major media. To this end, I have relied on lists of safety-based drug withdrawals, which were either maintained by the regulator or obtained from the medical literature. The lists refer to pharmaceutical drugs containing new active substances. Drugs

11 I recognize that there are two distinct types of withdrawal, namely permanent removal and temporary removal for product correction. Yet, this distinction is irrelevant in the model advanced here.

12 I call attention to the fact that all drug safety regulators nowadays post public warnings on their websites. Because there were no websites during the 1970s, 1980s and, most of the 1990s, the methodology employed here focuses on the traditional forms of public warning advertisement (i.e., the written press and the broadcast media).
that, although approved, were not commercialized in the country under examination, were omitted from the study. Also omitted from this study were drugs restricted to hospital use, drugs prescribed solely by specialists, and drugs approved with rigorously restricted indications. Overall, 172 cases of safety-based drug withdrawals in 8 countries were examined. In countries where such lists do not exist in the medical literature and were not held by the respective drug safety regulators (namely, Australia and New Zealand), senior officials employed in the corresponding recall coordination sections were approached to obtain information regarding the level of compliance with public warning regulations.

To test H2, media coverage during the ten days following the withdrawal announcement was tallied and the number of news items specifically mentioning the fact that the drug had been withdrawn from the domestic market was tabulated. The period of ten days was chosen to allow journalists to align their priorities following the withdrawal of a dangerous drug from the market and bring the event before the public. In cases where the actual withdrawal of the drug took place a few weeks after the announcement of withdrawal (i.e., to provide an opportunity for users to be assessed and to obtain special permission to continue taking the drug), media coverage was searched for ten days after the announcement was made as well as ten days after the actual withdrawal. To measure print coverage, I consulted the electronic archives of elite and mass newspapers. To measure broadcast news coverage, I consulted the Vanderbilt TV News Archive in the US, which is searchable

13 The relatively large number of cases examined enables me to overcome a problem related to two types of events, which are not taken into account in this study. First, a company may suspend marketing before suspension is imposed by the regulatory authority. Second, there are cases, in which a series of restrictions are imposed and a drug is withdrawn only after several years (for example, Terfenadine, Astemizole). In such cases, what may generate the publicity are the earlier restrictions as opposed to the withdrawals, which occur later when the drug is no longer in frequent use and the media attention has abated.
electronically (I found no TV archives in the remaining countries for the period under investigation).

**EMPIRICAL ANALYSIS**

Table 1 outlines the institutional framework that regulates the issue of public notification following safety-based drug withdrawals. It shows that the existence of a rigorous policy regarding public notification, or its lack thereof, clearly splits drug safety regulators into two groups: the US, Germany, the UK, Canada, South Africa, Switzerland and Israel, on the one hand, and Ireland, Australia and New Zealand, on the other. In the former group, a press release is issued to daily newspapers if the regulator decides that there is a strong likelihood that a product will cause serious side effects or death, with the exception of Germany where a press release, if issued at all, is directed at professional journals only. In the US, for example, if necessary the FDA requires manufacturers to issue a press release. No such requirement exists in Canada and the UK. In Canada, the Health Protection Branch of Health Canada issues a press release only if necessary and if required to do so by the Assistant Deputy Secretary. In the UK, the Medicines Control Agency (MCA), which was replaced in 2003 by the Medicines and Healthcare Products Regulatory Agency (MHRA), will do so, if necessary, and if ministerial approval in high profile cases is granted.\(^{14}\) Recent developments in the European Union have formally underlined the fact that in the UK there is no requirement to recall drugs from the public. In conjunction with the *EU Guidance on Good Distribution Practice of Medicinal Products for Human Use* (94/C 63/03, paragraph 29), recall only goes as far as wholesale dealers, retail or hospital pharmacists, and persons entitled to sell medicinal products to the public.

[Table 1 about here]

\(^{14}\) Email correspondence with MHRA, 8 March 2005.
By contrast, in Australia, New Zealand and Ireland, when there is strong likelihood that a drug will cause serious ADRs or death, rigorous procedures require manufacturers to place public notification advertisements in leading daily newspapers. In Australia, “if the depth of recall is to consumer level or for retail level recall in which all retail outlets cannot be identified […], advertisement paid by the sponsor are to be inserted in the daily print media of each State/Territory” (TGA 2001, 19).\(^{15}\) In some cases, two newspapers are identified as is the case in New South Wales, Victoria, and Tasmania.\(^{16}\) Rigorous procedures regulate the format and content of the advertisement. In the case of urgent consumer level recall, “it may be necessary to issue a media release” (TGA 2001, 20). In such cases, the text of the media release is jointly developed by the drug sponsor and the Australian Recall Coordinator.\(^{17}\) Where drug sponsors have been reluctant to undertake advertising, the Therapeutic Goods Administration (TGA) has the option to mandate recall under Section 30 EA of the Therapeutic Goods Act 1989. Sanctions for non-compliance are specified in the Therapeutic Goods Act 1989 (2003 amendment). The 2003 amendment was initiated following the recall of medicines manufactured by Pan Pharmaceuticals Pty Ltd. The recall covered over 1,600 products domestically and a similar number of exported products. Given the enormity of the product list associated with this recall and the fact that there were over 250 drug sponsors in Australia, special arrangements were introduced whereby paid advertisements were placed by the Australian government in national newspapers and all regional newspapers nationwide, listing the products subject to recall. The major changes introduced in the amendment included mandatory recall powers entrusted with the Therapeutic Goods Administration (TGA) in cases of products not manufactured in

\(^{15}\) One exception to this is where a supplier can identify and contact each customer. In these cases, paid advertisements may not be required.

\(^{16}\) Email correspondence with Australia's TGA, 27 October 2004.

\(^{17}\) A drug sponsor is someone who imports or manufactures therapeutic goods, or has therapeutic goods imported or manufactured on their behalf.
accordance with good pharmaceutical manufacturing practices, as well as the power entrusted in the TGA by the Secretary to impose public notification requirements on manufacturers (Section 30EA, 2b).

The procedures regulating consumer level recall in New Zealand also combined “an appropriate paid advertisement and/or press statement” (Ministry of Health 1995, 24), depending on the seriousness of the safety problem and the ease with which all retail outlet could be identified. However, in serious cases, New Zealand has a much more rigorous approach to recalls than Australia. In such cases, drug sponsors must place paid advertisements in all 23 regional daily newspapers, and meet patient and other costs associated with the recall (e.g., couriers). In addition, the Ministry of Health demands a higher response rate from pharmacies; recall letters have a more structured format, and a toll free number is strongly encouraged (Oceania Health Consulting 2004, 25). Ministerial response following non-compliance with the aforementioned regulation — in the form of a public statement issued by the Director General of the Ministry of Health — is anchored in section 98 of the Medicines Act (1981). Equally important is whether the word “voluntary” appears in the public notification advertisements. When public notification is required, the word “voluntary” in the public warning text implies that the withdrawal is optional (i.e., the firm can do it or not as it wishes). In New Zealand, for example, the manufacturer is not allowed to insert the word “voluntary” into public notification advertisements (Oceania Health 2004, 14).

The procedures regulating consumer level recall in Ireland are also clear-cut. “Recall of the product/batch(es) to patient or user level may be necessary. If so, this can be done via announcements by the Product Authorisation Holder on the radio and television and/or by newspaper notifications.” (Irish Medicines Board 2004, 11).

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18 Email correspondences with the Ministry of Health, 18-19 November 2004.

19 Interestingly enough, in 1978, the Regional Health Branch (Tel-Aviv) of the Israeli Ministry of Health published guidelines for public notification following safety-based drug withdrawals. These guidelines are similar to those found in Australia, New Zealand and
These significant differences in procedures regulating public notification in cases of safety-based drug withdrawals, support the earlier conclusion in the theoretical section regarding the link between the contexts within which regulators operate and the emergence and maintenance of reputations. The fact that regulators in Canada, Switzerland, South Africa, and Israel have designed procedures that are not in line with our theoretical prediction may be easily explained: Regulators may be unable to develop a reputation for expertise in detecting drug risks and, at the same time, they may not wish to develop an alternative basis for a reputation, or may be unable to enlist political support to do this. For example, politicians who play the blame avoidance game may prefer to place all the blame at the door of the domestic regulator instead of pinning blame on the FDA. Politicians may prefer a weak or passive regulator for political and economic reasons and may therefore opt for shadowing the procedures and policies adopted by drug safety regulators with an international reputation for expertise, leaving them ample room for maneuver when required. Politicians may also wish to protect the economic interests of drug manufacturers and may therefore discourage public access to meaningful information and, thence, will dampen the regulator's hope of developing a reputation as a guarantor of public health. Three examples suffice to illustrate the myriad of causes for the lack of a predominant basis of reputation. A senior official in the Pharmaceutical Section of the Israeli Ministry of Health admitted that: "Israel lacks the appropriate infrastructure for a thorough pre-clinical assessment of toxicity of a drug containing a new molecule, hence the reliance, in this specific area, on the FDA and European Ireland, and read as follows: "The text of the press release will be determine by the Regional Pharmacist and the publication of the notification in the press will be undertaken by, and be the responsibility of, the product registration holder or product sponsor […]." (Tel Aviv Regional Health Branch, the Ministry of Health 1987, 2). These guidelines were replaced in 1989 (Ministry of Health 1989) by national guidelines similar to those applied in the US and the UK.
Medicines Agency (EMEA)”. A similar consideration was recorded in Switzerland. As Rudolf Stoller, Head of Pharmacovigilance Center at Swissmedic, noted: "[…] it is true that the European Union, or the American FDA, of course have much larger resources and can do a more detailed review. We also take into consideration decisions of these regulatory agencies". The South Africa's case provides a different consideration, namely, a preference for international harmonization. As Joey Gouws, Director of Inspectorate and Law Enforcement at the Medicines Control Council, noted: "[…] We do have the necessary infrastructure and competence for a thorough pre-clinical assessment of toxicity of a drug containing a new molecule. Our recall procedure were designed over the past 40 years however, as we have applied for membership of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) we have fine tuned our recall procedure to be in line with the requirements of PIC/S". Note that the PIC/S guidelines contain requirements regarding inter-agency communication of warnings rather than procedures that regulate public warnings.

By contrast, government ministers and regulators in Ireland, Australia and New Zealand have been willing and able to develop a predominant basis of reputation. This willingness may be derived from the potential public demand for the regulators to be abolished (because they consume public resources whilst lacking a reputation for expertise), and be replaced by a policy of, say, shadowing the FDA. To show patients how crucial their agency’s role is, they design public warning procedures, involving spectacular signaling displays in cases of safety-based drug withdrawals. These signals — which may be accompanied by news stories — are reliable because they are costly to produce and because they are designed to amplify the regulators’ reputation as guarantors of the public health. They are cost-free (to the agency) because the advertisements are paid for by drug sponsors,


21 Email Correspondence, 3 August 2006.

22 Email correspondence, 14 July 2006.
and they contain multiple safety cues (e.g., advert size, border design, etc.), making them markers of the regulator’s predominant basis of reputation.

[Table 2 about here]

Next, we turn to Table 2 which reports media coverage of safety-based drug withdrawals in the countries under examination (with the exception of Australia and New Zealand, where the absence of lists of drugs withdrawn for safety reasons inhibits any systematic search of print and broadcast media). The lowest level of public observability of safety-based drug withdrawals in the print media – between 9% and 14% – was recorded in the country characterized during the mid-1990s by the weakest adverse reactions monitoring system, South Africa. This result seems reasonable given that the South African Medicines Control Council operated during most of the period under examination in a context inhibiting the development of a reputation for expertise. Despite this handicap, it is nevertheless eager to protect its reputation as the most expert drug safety regulator in Africa.

Low to medium levels of public observability of safety-based drug withdrawals were found in countries with regulators characterized by a predominant basis of reputation for expertise (the US, Germany, and UK), and also in countries whose regulators are unable or unwilling to develop a predominant basis of reputation [i.e., Canada, Switzerland, and Israel]. Only between 43% and 47% of safety-based drug withdrawals in the US were found to receive print media coverage; between 13% and 33% in Germany; between 33% and 38% in the UK; between 34% and 42% in Canada; between 33% to 50% in Israel, and between 20% and 35% in Switzerland. Recorded coverage [with the exception of Vioxx and, in the US, the two anti-obesity (i.e., diet) drugs, Fenfluramine and Dexfenfluramine] includes mostly one or two articles with less than one hundred to a few thousand words. In the broadcast media, between 26% and 48% of safety-based drug withdrawals in the US received any coverage at all. Recorded coverage (with the exception of Vioxx) included mostly one or two news items ranging from less than one minute to a few minutes. Overall in the US, 9 out of 21 safety-
based drug withdrawals (43%) did not receive coverage either in print or in the broadcast media during the period 1985-2004.

A striking 100% of all safety-based drug withdrawals received media coverage in Australia, New Zealand, and Ireland. Regarding Australia and New Zealand, given that drug sponsors operating in these countries are obliged to place paid advertisements in the daily newspapers where the drug has been distributed, it is reasonable to rely on compliance data obtained from senior officials employed at the recall coordination units, as a proxy for media coverage data. In Australia, for the period 2001-2004, “there is approaching 100 percent compliance with the requirement to place paid advertisement for consumable recalls where required”. 23 Given the cooperative nature of safety-based drug withdrawals, it is reasonable to assume that a very high compliance rate with the aforementioned requirement was also evident throughout the 1980s and 1990s. In New Zealand, “over the time of my involvement with recalls in Clinical Services Division and later Therapeutics section (i.e., from about 1981 until Medsafe was formed) I cannot recall any occasion where we had difficulty persuading a company to place paid adverts for consumer level recalls”. 24 For the period 1999-2004, “we have not had an instance where we have had a company not comply with our requirements in this regard, so compliance would be 100%”. 25

Overall, the near-perfect compliance with public warning regulations in Australia, New Zealand, and Ireland indicates observable, costly action (Lupia and McCubbins 1998, 54; 2000, 58-9) by drug sponsors. This, in turn, reveals the intensity of the issue of public safety in the corresponding pharmaceutical markets, and provides a benchmark for how

23 Email correspondence with a senior official employed in Australia’s TGA, 11 April 2005.

24 Email correspondence with a senior official employed in the NZ Ministry of Health, 18 April 2005.

25 Email correspondence with a senior official in New Zealand's Medsafe, 12 April 2005.
citizens learn what they need to know. At a more theoretical level, although some data was more readily available than others, Tables 1 and 2 offer results that are consistent with the analytical framework outlined here, namely that, if drug safety regulators are able and willing to develop a predominant basis of reputation, media coverage of safety-based drug withdrawal is a function of the regulator’s predominant basis of reputation. Public observability may therefore be an asset (i.e., when reputation is solidified) and a choice (i.e., when reputation is protected) in a way that current models in political science fail to recognize. If low public observability is the goal, procedures are put in place by political executives during the design of the agency to guarantee precisely that; and if high public observability is the goal, procedures are put in place to guarantee this too. Not surprisingly, drug safety regulators whose predominant basis of reputation is technical expertise are least likely to encourage media coverage precisely when the analytical framework suggests (i.e., when drugs they approved are withdrawn from the market for safety reasons). By contrast, drug safety regulators whose predominant basis of reputation is as guarantors of the public safety in the pharmaceutical sector, act exactly the opposite way in the same circumstances.

CONCLUSION

Much of the existing empirical work on reputation does not consider reputation effects separately from the increased autonomy that improved efficacy, uniqueness of service, moral protection, and expertise bring. This is easy to understand because reputation is the key prerequisite of an agency’s autonomy: “Autonomy prevails when agencies can establish political legitimacy — a reputation for expertise, efficiency, or moral protection and a uniquely diverse complex of ties to organized interests and the media — and induce politicians to defer to the wishes of the agency even when they prefer otherwise” (Carpenter 2001, 4). However, embedded in Carpenter’s argument is the notion that the basis of reputation may vary. This variation, I claim, is crucial for understanding the relationship between a regulator’s reputation and the public observability of its catastrophic errors.

This study confirms that, if drug safety regulators are able and willing to develop a predominant basis of reputation, the same catastrophic error (e.g., approving a particular drug
which is truly dangerous) may not be considered a failure for some regulators, while it may be for others. For regulators operating in a context which inhibits the development of technical expertise, high public observability of catastrophic errors means a greater opportunity to promote their reputation as a guarantor of the public safety in the pharmaceutical sector. By contrast, regulators operating in a context which facilitates the development of technical expertise respected worldwide are most likely to opt for low public observability of their catastrophic errors, and instead, communicate their decisions primarily to health professionals. From a regulatory perspective, this strategy effectively fulfils the bureaucratic requirement of communicating safety information. However, it only provides a minimal contribution to the protection of public health mainly because it is based on the naive assumption that most physicians read "Dear Health Professional" letters and/or notifications posted on the regulators’ web pages. The problem arises because some indeed do read and act, while others do not.\textsuperscript{26} The low public observability of safety-based drug withdrawals recorded in the US, Germany and the UK, as well as in Canada, Switzerland, Israel and South Africa implies that many patients will be unaware of the risks associated with the medication they use, and therefore continue to take the dangerous drugs until they require a new prescription.

Focusing on organizational reputation is therefore to marry bureaucracy and politics. It conceives politics as a process of building mechanisms that protect the predominant aspect of reputation enjoyed by an agency. In this process, politicians are successful in creating the bureaucracy they want by imposing a particular type of procedural design. The model outlined here suggests that procedural politics plays an important role in protecting the choices relating to the methods and processes entrained by politicians and the interests to which they respond. None of the drug safety regulators examined here have ceased to exist,\textsuperscript{26} See, for example, the failure of physicians to respond to repeated warnings about drug-related health risks (Schiff et al. 2002; Smalley et al. 2000; Graham et al. 2001; Seligman 2003).
nor have they been subject to any significant reforms. Instead, all have triumphed at regulatory decision making, giving rise to the argument that it is the predominant type of reputation – and the capacities and coalitions that support it (Carpenter 2001, 354) – to which autonomous agencies owe their survival.

Before delving into the ways this research may be improved it is important to point out that the model developed here faces two formidable obstacles. First, it may be more difficult for regulators to pay for and develop expertise, which they then have to preserve and protect, than for them to simply act as an alarm system. Why wouldn’t regulators take the easier road of relying on reputation as guarantor of public safety in the pharmaceutical market? To answer this question, one must recognize that reputation accumulates gradually as a result of repeated success and high-quality performance (Mailath and Samuelson 2001, 416). Regulators have numerous opportunities every year for repeated success in drug approvals, but very few, sometimes none, in drug safety. Furthermore, approval decisions generate wide and highly-favorable media coverage along with political support from organized disease advocates, which all serve to advance the regulator’s reputation. The resulting reputation improvement guarantees the regulator increased autonomy (Carpenter 2001) as well as sufficiently high future revenue both with respect to current expenditure and future revenue in case of failure. The regulator may fail to approve beneficial drugs, but this will not result in strong demand for greater accountability or harsh consequences for the regulator (Olson 2002, 619).

The second obstacle is the argument that the empirical basis for assuming that agency reputations must be dichotomized into reputation predominantly for expertise or reputation predominantly as guarantor of public safety is either non-existent or very weak. A related argument is that a reputation for expertise and a reputation for consumer (patient) protection

27 Even after Vioxx was pulled from the market, the FDA, for example, initiated reforms that did not address the lack of systematic tracking of ongoing safety issues (GAO 2006).
may overlap or even co-vary to some degree. To bypass this theoretical obstacle, I rely on Prat (2005) who distinguishes between three kinds of information that can be observed by the regulator’s principals (e.g., political executives; the general public): (i) information regarding the action that the regulator takes (e.g., communication strategy); (ii) information regarding the content of the regulator’s decisions (e.g., assignment of blame to the manufacturer), and (iii) information regarding the consequence of the regulator’s action (e.g., agency reputation following the removal of a drug from the market). To by-pass the aforementioned theoretical obstacle, the model developed here focuses solely on regulatory actions, that is, on when regulatory agencies take steps to make their mistakes more or less visible, or more or less traceable. Once a decision has been reached to remove a drug from the market for safety reasons, the action taken by the regulator to communicate warnings to the general public in fact exposes the predominant reputation basis, which is the prime target of reputation protection efforts made by the regulator when it makes a mistake.

Future research in this field of study can be expanded by thoroughly analyzing the value of media coverage, which, in turn, depends upon the worth of the information aired to the public. The most damaging outcomes or effects for regulators is when a whistleblower airs disturbing information that shows, for example, that risks were evident years before the drug was finally withdrawn from the market by its manufacturer. The weakest links may be regulators’ external advisors or former employees from the manufacturer’s internal system of post-marketing surveillance or at the regulator’s oversight unit. Going public and disclosing their views regarding the seriousness of the ADR data may not be a useful strategy because the regulator will always be able to defend its reputation by presenting the reverse expert opinion. Alternatively, whistleblowers can resign and go public by disclosing flaws in clinical trial designs (e.g., small sample, etc.) or a lack of sufficient public safety information. To keep this option hypothetical, political executives tend to approve legislation according to which pre-marketing data, if not published, may be considered proprietary and thus unavailable to inform post-approval research. Whatever strategy the whistleblowers choose,
the regulator may find it very difficult to shore up its reputation when faced with constant challenges and the consequent erosion of public trust.

This research can also be expanded upon by taking into consideration the uniqueness of the regulatory context insofar as it creates a much more efficient market for managers compared to the private sector context. This is because it is easier for those outside a regulatory agency to distinguish between the performance of the organization as a whole and the performance of individual staff members (Fama 1980). The relative ease with which private sector professionals can assess the performance of their public sector colleagues, implies that “Regulatory administrators’ professional reputations are […] likely to be closely linked to other professionals’ observations of their performance in the public sector. This reputation determines their chances of moving to higher-paid private sector jobs and, therefore, higher expected lifetime income” (Horn 1995, 56). Future research should therefore move away from analysis of agency reputation towards analysis of regulatory administrators’ reputations in order to gauge whether public observability considerations in cases of safety-based drug withdrawals are influenced by considerations related to their reputations. A convenient starting point may be an analysis of the move by individual staff members employed at drug safety regulators to private sector jobs in firms which were previously regulated by these individuals.

To conclude, I call attention to the fact that the analytical framework developed here helps to explain several empirical regularities in media coverage of safety-based drug withdrawals. The crucial difference between the analytical model developed here and standard models of bureaucratic choice is the incorporation of the insight that observability of public warnings has value and is an object of choice. Regulators can still opt for decisive and visible actions directed at drugs with low market share, thereby avoiding significant impact upon the cash flow of larger firms. They can also opt for decisive and visible actions directed at products in parallel markets (e.g., homeopathic/herbal products), which are regulated by the same agency that regulates pharmaceutical drugs. All this being said, when it comes to the
most significant decisions faced by bureaucrats when a catastrophic error occurs, the variance in public observability ultimately depends on the regulator’s predominant basis of reputation.
REFERENCES


Tel-Aviv Regional Health Branch. 1987. *A Procedure for a Recall of a Medical Product from the Market. Tel Aviv: Regional Health Branch.*


### Table 1. The Regulation of Public Notification following Safety-based Drug Withdrawal*

<table>
<thead>
<tr>
<th></th>
<th>Legal Basis</th>
<th>Notification Issuer</th>
<th>Communication Strategy</th>
<th>Wording Restrictions</th>
<th>Sanctions for Non-Compliance</th>
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</thead>
<tbody>
<tr>
<td><strong>U.S.A</strong></td>
<td>Guidelines &amp; Regulations</td>
<td>Manufacturer, upon consultation, or jointly, with the FDA</td>
<td>- Press Release&lt;br&gt;- Talk Paper/website posting&lt;br&gt;- Letters to health professionals</td>
<td>Manufacturers are advised to follow a model press release</td>
<td>The FDA will issue a press release</td>
</tr>
<tr>
<td><strong>U.K.</strong></td>
<td>Procedures</td>
<td>The MCA/MHRA will issue a press release in high profile cases following ministerial approval</td>
<td>- Press Release&lt;br&gt;- Bulletin an website announcements&lt;br&gt;- Letters/fax/email to health professionals</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>Procedures &amp; Law</td>
<td>Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)</td>
<td>- Press Release to weakly professional journals, such as, &quot;Pharmazeutische Zeitung&quot; and &quot;Deutsches Ärzteblatt.&quot;&lt;br&gt;- In case 50 or more companies are concerned, publication in the German Federal Gazette (Bundesanzeiger)&lt;br&gt;- Letters/Webpage posting</td>
<td>The text of the letters should be discussed with the BfArM</td>
<td>No</td>
</tr>
<tr>
<td><strong>Canada</strong></td>
<td>Procedures</td>
<td>The Assistant Deputy Minister decides whether a public announcement is mandatory, and whether it will be issued by the Health Protection Branch</td>
<td>- Press Release&lt;br&gt;- Website posting and an announcement in Health Canada's newsletter&lt;br&gt;- Letters to health professionals</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>South Africa</strong></td>
<td>Guidelines</td>
<td>The holder of a certificate of registration.</td>
<td>- Press Release&lt;br&gt;- Letters to the distribution chain</td>
<td>Text of media release issued jointly with the Medicines Regulatory Affairs (MRA)</td>
<td>The Medicines Control Council (MCC) issue a press release</td>
</tr>
<tr>
<td><strong>Aus.</strong></td>
<td>Procedures &amp; Law (2003) for Non-compliance</td>
<td>Drug sponsor, upon consultation with the regulator (Australian Recall Coordinator, TGA)</td>
<td>- Paid and approved advertisements in the daily print media&lt;br&gt;- Press Release/letters/website posting</td>
<td>- A set recall letter text&lt;br&gt;- A set recall envelopes&lt;br&gt;- A set advertisement text</td>
<td>- The Minister of Health can impose requirements on the firm to inform the public&lt;br&gt;- Up to 60 penalty units</td>
</tr>
<tr>
<td>Legal Basis</td>
<td>Notification Issuer</td>
<td>Communication Strategy</td>
<td>Wording Restrictions</td>
<td>Sanctions for Non-Compliance</td>
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<tr>
<td>N.Z.</td>
<td>Procedures Drug sponsor, upon consultation with Medsafe</td>
<td><strong>Paid and approved advertisements</strong> in each of the 23 regional daily newspapers, <strong>Press release</strong>/letters/website posting</td>
<td>The word “voluntary” may be mentioned in the ad.</td>
<td>A public statement is released by the Dir. Gen. of the Ministry of Health</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td>Guidelines Product Authorization holder in consultation with the Inspectorate Department of the Irish Medicines Board (IMB)</td>
<td><strong>Announcement on the radio and TV and/or newspaper notification</strong> <strong>Press release</strong>/letters</td>
<td>Letter text must be agreed by the IMB Inspectorate Department</td>
<td>In rare circumstances, suspension/revocation of a wholesale/manufacturing license, or product authorization.</td>
<td></td>
</tr>
<tr>
<td>Israel</td>
<td>Procedures - The Ministry of Health (MOH) - In special cases, the license holder may be required to issue a public notice within a time to be defined</td>
<td><strong>Press Release</strong> in Hebrew and additional languages as required - <strong>Letters</strong> to health professionals</td>
<td>- License holders must gain prior approval of the content of the public notice by the Director of Pharmaceutical Administration</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Switz.</td>
<td>Regulations Manufacturer, upon IKS recommendation and subsequent decision by the relevant authority in each canton</td>
<td><strong>In exceptional circumstances,</strong> - <strong>Press release in canton and inter-canton daily newspapers</strong> - <strong>Press release</strong> to professional journals - <strong>Letters/webpage posting</strong></td>
<td>Depending on the policy applied by the relevant authority in each canton</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

* I refer to cases where there is a strong likelihood that a product will cause serious side effects or death (Class I recall; consumer level recall).

### Table 2. Media Coverage of Safety-Based Drug Withdrawals

<table>
<thead>
<tr>
<th>Region</th>
<th>No. of withdrawals (Year-Range)</th>
<th>Withdrawals reported in the print media</th>
<th>Withdrawals reported in the broadcast media</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>21 (1997-2004)</td>
<td>Washington Post (9 (43%))</td>
<td>ABC (8 (38%))</td>
</tr>
<tr>
<td></td>
<td>17 (1984-2004)</td>
<td>USA Today (8 (47%))</td>
<td>CBS 10 (48%)</td>
</tr>
<tr>
<td></td>
<td>17 (1985-2004)</td>
<td>Newsday (NY) (8 (47%))</td>
<td>NBC 7 (33%)</td>
</tr>
<tr>
<td></td>
<td>21 (1977-2004)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>21 (1977-2004)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>21 (1977-2004)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19 (1980-2004)</td>
<td></td>
<td>CNN 5 (26%)</td>
</tr>
<tr>
<td></td>
<td>22 (1984-2004)</td>
<td>Toronto Star (9 (41%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27 (1985-2004)</td>
<td>Financial Times (9 (33%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27 (1985-2004)</td>
<td>Daily Mail (10 (37%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 (1992-2004)</td>
<td>Süddeutsche Zeitung (1 (13%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (1986-2004)</td>
<td>Handelsblatt (2 (20%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11 (1998-2004)</td>
<td>Cape Times (1 (9%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31 (1986-2004)</td>
<td>Basler Zeitung (11 (35%))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (1998-2004)</td>
<td>Le Temps (2 (20%))</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>No list of drug withdrawals</td>
<td>(100%)*</td>
<td>n.a.</td>
</tr>
<tr>
<td>New Zealand</td>
<td>No list of drug withdrawals</td>
<td>(100%)**</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

* Email correspondence with a senior official at TGA, 11 April 2005.
** Email correspondence with a senior official at the NZ Ministry of Health, 18 April 2005.
*** Irish list is based on world-wide recalls, UN (2003); Irish Medicines Board's Drug Safety Newsletter 1995-2004, and Email correspondence with the IMB, 23 February 2006.

**Media Sources:** Television News Archive Collection at Vanderbilt University; Washington Post, National Post, Newsday (e-archive); The Times (e-archive and digital archive); Globe & Mail (e-archive and CD-ROM); Toronto Star, Daily Mail, Financial Times (LexisNexis archive); Die Burger, Cape Times (e-archive); Frankfurter Allgemeine and Süddeutsche Zeitung (e-archive and archive service); Handelsblatt (e-archive); The Irish Times (e-archive); Haaretz (e-archive+microfilms); Yedioth Hchronoth (digital archive); Neue Zürcher Zeitung and Basler Zeitung (e-archive and archive service); Le Temps and Der Bund (e-archive).
Appendix: Lists of Drug Withdrawals

Drugs withdrawn in the U.S.A: Azaribine (Triazure); Ticrynafen (Selacryn); Zomepirac sodium (Zomax); Benoxaprofen (Oraflex); Suprofen (Suprol); Nomifensine maleate (Merital); Terfenadine (Seldane & Seldane-D); Encainide hydrochloride (Enkaid); Astemizole (Hismanal); Temafloxacin hydro. (Omniflox); Flosequinn (Manoplax); Cisapride (Propulsid); Troglitazone (Rezulin); Cerivastatin (Baycol); Mibefradil dihydrochloride (Posicor); Bromfenac sodium (Duract); Grepafloracin hydrochloride (Raxar); Rapacuronium; (Raplon); Vioxx (Rofecoxib)

Source: Lasser et al. (2002); UN (2003); CDER (2004).

Drugs withdrawn in the U.K.: Polidexide (Secholex); Practolol (Eraldin); Benoxaprofen (Opren); Clomacran Phosphate (Devryl); Brotilzolam; Indoprofen (Flosint); Zomepirac (Zomax); Osmosin (Indomethacin – modified release; Zimeldine (Zelmid); Fenclofenac (Flenc); Feprazone (Methrazzone); Alphaxolone±Alphadolone (Althesin); Perhexilene (Pexid); Suprofen (Suprol); Nomifensine (Merital); Brotilzolam; Dilevalol (Unicard); Glaaline eye drops; Triazolam (Halcion); Terodiline (Micturin); Temafloxacin (Teflox); Nebucumab (Centoxin); Flosequinn (Manoplax); Remoxipride (Roxiam); Pemolin (Volutal); Troglitazone (Romazin); Ponderax; Adifax; Sertindole (Serdolect); Tolcapone (Tasmur); Mibefradil (Posicor); Trovafloxacins (Trovan); Grepafloracin (Raxar); Fenfluramine; Dextfenfluramine (Redux); Cisapride (Prepulsid); Pumactant (Alec); Amfoteric agents (Amfepramone, Phentermine; Cerivastatin (Lipobay); Doperidol (Droleptan); Refocoxib (Vioxx).

Sources: Jefferys (1998); UN (2003); Email communication with the Post-Licensing Department, MHRA, 4 June 2004.

Drugs withdrawn in Canada: Chlorizemone; Astemizole (Hismanal); Cerivastatin (Baycol); Cisapride (Propulsid); Clioquino; Danthon (Dantron); Dextfenfluramine (Redux); Etretinate (Tegison); Fenfluramine (Pondimin); Grepafloracin (Raxar); Methapyriline; Mefazodone; Neomycin (injectible); Nomifensine; Oxeladin; Oxyphencyclazone; Oxyphenisatin; Pemoline (Cylert); Phenformin; Phenolphthalain; Phenylpropanolamine (PPA); Phenylamine; Remoxipride; Sulfamethoxypyridazin; Terfenadine (Seldane); Tolcapone (Tasmur); Trovafloxacins (Trovan); Zomepirac; Vioxx (Rofecoxib)

Source: Lexchin (2005)

Drugs withdrawn in Germany: Benoxaprofen (Coxigon); Feprazone; Indoprofen; Toradol (Ketrolac); Mesna (Urometixan); Nomifensin (Alival; Psyton); Orgotein; Prenylamine (Segontin); Sulcotidil; Omeprazole (Nuclosina); Terfenadin (Teldane); Miberfradil (Posicor); Barbiturat; Anoractic agents (Amfepramone, Phentermine); Vioxx (Rofecoxib).

Source: Email communication with Bundesinstitut für Arzneimittel und Medizinprodukte, 3 Aaugust 2005; UN (2003).

Drugs withdrawn in Israel: Phenacetin; Practol (Practolol); Alphaxolone and Alphadolone (Althesin); Phenformin (Diaboral); Shigroin (Phenylbutazone); Choloramphenicol (Tablets) (Syntomytecin); Lipogis (Cerivastatin Sodium; Hismanal (Astemizole; Terfenadine (Ternalin); Cisapride (Propulsid); Terodiline (Mictrol); Doperidol (Neuloridol); Raxar (Grepafloracin Hydro.); Ponderax (Fenfluramine Hydrochloride); Vioxx (Rofecoxib).

Drugs withdrawn in South Africa: Astemizole (Hismanal); Cerivastatin (Baycol); Chlormezanone; Cisapride (Prepulsid); Fenfluramine/dexfenfluramine; Nefazodone (Serzone); Oxyphenbutazone; Pemoline; Phenolphthalein; Regibloc; Rofecoxib (Vioxx); Terfenadine (Seldane & Seldane-D); Thioridazine; Miberfradil (Posicor); Barbiturates.

Source: Email communication with the Medicines Control Council, 16 September 2005; Email communications with the Medicines Information Center, University of Cape Town, 21 October 2005 and 3 January 2006.

Drugs withdrawn in Switzerland: Nomifensin (Alival); Phenacetin; Muzolimin (Edrul); Suprofen (Suprol); Heparinoid (Arteparon); Prenylamin (Segontin); Catergen; Sicc-cell; Barbiturates; I-Tryptophan; Beclobrate (Turec & Beclipur); Pirpofen; Terodilin (Mictrol); Glafenin (Glifanan); Benzaron (Fragivix); Ketanserin (Sufrexal); Rumalon; Cumarin (Venium & Lymphex); Chlormezanon; Dexfenfluramine (Isomeride); Fenfluramine (Ponflural); Miberfradil (Posicor); Grepaflloxacin (Raxar); Trovafloxacin/Alatrofloxacin (Trovan); Astemizole (Hismanal); Cisapride (Prepulsid); Terfenadine (Teldane); Cerivastatin (Lipobay); Benzbromarone (Desuric); Nefazodone (Nefadar); Rofecoxib (Vioxx).

Source: Email communication with Rudolf Stoller of Swissmedic, 17 March 2006.