

# **TENDERING GENERIC DRUGS:**



## **WHAT ARE THE RISKS?**

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## EXECUTIVE SUMMARY

At their meeting of July 26 – 27, 2012 Canada's Premiers announced that they will identify three to five generic drugs to include in a national competitive bidding process, or "tender", by Fall 2012 and that lower prices would take effect by April 1, 2013. This paper evaluates the risks of this proposal.

Publicly funded drug plans in Canada typically reimburse pharmacies for the cost of generic drugs at some percentage of the equivalent brand drug price. This percentage has declined sharply over the last six years; for many years it was 70%, while now it is as low as 25%. As a result of these cuts, generic drug reimbursement rates in Canada are comparable to prices paid elsewhere. Some countries, however, have achieved particularly low prices by the use of tenders. The tendering system used to procure prescription drugs in New Zealand is often held as a model that Canada should emulate.

If implemented in Canada, tendering will have a substantial impact on the market. At present, generic drug reimbursement rates often exceed the lowest price that generics can sell at. Generic pharmaceutical manufacturers are thus able to sell for less and, indeed, do so to compete for the pharmacy's business. With tendering, generic firms would compete, likely quite aggressively, for the drug plan's business. Pharmacies would have no choice but to stock the product of the winning firm. Thus the drug plan would directly reap the benefits of price competition among manufacturers. As such, tendering may, at least in the short term, generate lower per unit prices for some drug products compared to the current system.

***Tendering may, however, result in some undesirable consequences, such as:***

- Potential drug shortages because of less redundancy in the drug supply system
- Less patent litigation by generic manufacturers resulting in delayed availability of lower-cost generic drugs
- Less manufacturing of generic drugs in Canada
- The closure of some generic drug manufacturing plants in Canada
- Less competition in generic drug markets in Canada
- Less customer service offered by generic suppliers to pharmacies
- The closure of some pharmacies
- Less "free" customer service in the remaining pharmacies

Tendering removes the incentive for generic pharmaceutical manufacturers to mount legal challenges to the patents on branded drugs. Brand drug firms normally have several patents on their drugs. Some of these patents effectively bar generic entry until they expire. Other patents may be invalid or not actually infringed by a generic version of the drug. If a generic firm wishes to enter the market, it must notify the brand firm why existing patents are invalid or not infringed. The brand firm, should it disagree, then has the option of initiating a judicial review in which the merits of the generic's claims are assessed. If the generic prevails in these proceedings, and also satisfies other regulatory requirements, the generic may receive Health Canada approval to enter the market.

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These legal challenges are expensive but the increase in market share the generic receives from being first to market can make it profitable for the generic firm to invest in such litigation. Payers for prescription drugs in Canada, whether they are government – or employer-sponsored drug plans, or uninsured patients, are the chief beneficiaries from early generic entry enabled by litigation. We estimate that early generic entry on five of the top-selling drugs results in billions of dollars of savings to drug plans and consumers. Tendering will reduce margins and hence the advantages of early entry. It will also expose the early entrant to additional damages in the event that a brand firm successfully sues a generic firm for patent infringement. We thus predict that tendering will result in the delayed arrival of lower-cost generic drugs. The New Zealand tendering system provides some corroborating evidence. Many important drugs are genericized much later in New Zealand than in Canada. For example, the top-selling drug Atorvastatin was genericized only in February 2012 in New Zealand, almost two years later than in Canada. Olanzapine and Venlafaxine became generically available in New Zealand approximately four years later than in Canada.

The competition amongst generic firms results in another valuable benefit to consumers. In particular, it leads to multiple generic firms producing medium to high-volume drugs, which in turn affords some redundancy in the system: Should one manufacturer be unable to supply, others can normally fill the gap. This redundancy is unavailable in single-source tenders. Another related benefit is that competition for margins results in companies producing a wide range of low-volume drugs, not because they are particularly profitable, but rather to offer pharmacies a wide range of products and the convenience of “one stop shopping”. Firms that offer this service may have an advantage in marketing the more profitable high-volume drugs to pharmacies. But if most high-volume drugs are procured via tender, then offering a large product catalog is less advantageous. As a result, some low-volume or high cost drugs may no longer be produced.

We also note that tendering, if applied on a large scale, will lead to consolidation in the domestic generic industry. Many existing suppliers of high-volume drugs would either be unable to bid (given that they lack the manufacturing capacity) or would merge with other firms. Thus, there is a legitimate question of whether it is possible to sustain low prices over the long-term. Tenders can only be successful if there are enough competitors bidding, but by their nature, tendering systems tend to reduce the number of active, effective competitors. The international experience with tendering indicates that, over time, tendering reduces the number of domestic manufacturers and increases the supply of foreign produced generic drugs. In New Zealand, for example, almost all tenders are sourced by foreign manufacturers; there is only one domestic generic manufacturer remaining.

It is obviously important for provinces to explore these issues carefully, since tendering has important implications for overall costs, patients, generic manufacturers and pharmacies. Tendering is but one of the approaches that can be used to procure generic drugs. We believe that there are other approaches that could be used to control prescription drug costs in Canada that are better aligned with Canada’s existing systems of patent litigation, generic manufacturing and distribution. These deserve serious consideration.

# 1 INTRODUCTION

The provincial and territorial premiers recently announced that they intend to explore tendering as a means of procuring generic drugs for their public drug plans. Tendering is akin to an auction: The drug plan or plans solicit bids from different producers and the firm that offers the lowest price wins the exclusive right to coverage. In this paper, we explore the implications of tendering for overall costs, patients, generic manufacturers and pharmacies.

At present, publicly funded drug plans in Canada set the maximum reimbursement for generic drugs at a fixed percentage, such as 35%, of the price of the equivalent branded (i.e., originator) drug. This percentage has declined sharply over the last six years; in Ontario the allowed percentage has dropped from 75% to 70% to 50% to 25%.<sup>1</sup> As a result of these cuts, generic drug reimbursement prices in Canada are comparable to prices paid elsewhere. Some countries, however, are able to achieve particularly low prices by the use of tenders. It is understandable that public payers would like to achieve the same low prices. However, tendering may lead to some undesirable consequences. In order to understand why, it is helpful to consider the outcomes of the existing system of generic drug procurement.

As we mentioned above, the public plans have set generic drug reimbursement prices at some fraction of the price of the equivalent brand drug. These reimbursement prices are arbitrarily chosen, and thus bear no relation to the costs of producing generic drugs. As a result, the reimbursement price will either be above or below the generic manufacturer's "reservation price" – the lowest price the manufacturer can sell at. If the rate is above the reservation price, then pharmacies and generic drug manufacturers will share the proceeds. If the rate is below the reservation price, the drug will not be produced unless the drug plan grants an exception. One result of the reductions in the reimbursement percentage is that the provincial drug plans have granted hundreds of exceptions. The exceptions essentially create a system of cost-based regulation in a competitive market, an outcome that is both intrusive and highly inefficient. From the point of view of the drug plan, then, under the current system, prices are either too high or are determined through cost-based regulation.

Despite these inefficiencies, the existing system does have some desirable outcomes. As mentioned, when the generic drug reimbursement price exceeds the generic manufacturers' reservation price – the difference or "margin" – accrues to pharmacies and manufacturers. (The portion accruing to pharmacies is called the "rebate" or "professional allowance.") No doubt, some portion of these margins represent pure profits; likely the majority, however, gets competed away. That is, pharmacies and manufacturers spend money in an attempt to earn market share and the margins that come with it. The competition is valuable to drug plans and consumers.

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*...If the rate is below the reservation price, the drug will not be produced unless the drug plan grants an exception...*

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The *raison d'être* of tendering is to eliminate the margins so that the drug plans pay the generic manufacturers' reservation price. This will reduce generic drug prices, but it will also eliminate the competition for the margins. In this paper, we ask the following question: If tendering is successful in reducing prices, what is the cost? In a competitive environment, excess profits typically don't exist for long; they get competed away. So if we reduce the amount of money being divided by generic drug manufacturers and pharmacies, this would result in a reduction or elimination of some activities undertaken by those firms. Most likely, tendering will result in:

- Potential drug shortages because of less redundancy in the drug supply system
- Less patent litigation by generic manufacturers resulting in delayed availability of lower-cost generic drugs
- Less manufacturing of generic drugs in Canada
- The closure of some generic drug manufacturing plants in Canada
- Less competition in generic drug markets in Canada
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It is obviously important for provinces to explore these issues carefully, since the costs imposed by tendering have important implications for budgets, patient services, investors, and jobs. We believe that there are other approaches to obtaining lower prices that are better aligned with Canada's existing systems of manufacturing and distribution. So far, however, no provinces have explored using such approaches.

## 2 THE IMPORTANCE OF LITIGATION

A common misconception is that generic drugs become available following “the expiry of the patent” on the brand drug. The reality is more complex. Most brand drugs are protected by a number of different patents. Innovators have strong incentives to try to obtain the most protection possible for their products, and they use the patent system for this purpose. In particular, they seek to file patents on all the potentially patentable features of their products. Indeed, blockbuster drugs typically have patents that, left unchallenged, extend market exclusivity for many years. This is simply a good business decision that reflects the financial importance to these firms of retaining their monopoly positions for as long as possible. A generic drug company, however, may challenge some of these patents in Federal Court if the company deems these patents invalid or not infringed by its product. As an example, a brand firm might obtain a patent for a particularly efficient means of producing a drug. A generic manufacturer would be able to produce the product without infringing the patent if it used a different manufacturing method. Other patents that appear to be sufficient to prevent generic competition may actually be invalid. This would be the case if the subject matter disclosed in the patent had already been described elsewhere or if the invention was thought to be “obvious” given the existing state of knowledge.

The rules governing generic challenges of brand name patents are set out in the *Patented Medicines (Notice of Compliance) Regulations*, or the “NOC Regulations,” for short. Briefly, brand drug firms may list certain types of patents on a Patent Register. A generic manufacturer cannot market its product until it has successfully addressed the patents listed on the Patent Register against the brand drug. To address these patents, the generic firm first issues to the brand firm a Notice of Allegation (NOA) that the listed patents will not be infringed or are invalid. The brand firm then can accept the NOA or, if it disagrees, it can commence a judicial proceeding during which the merits of the NOA are assessed. This judicial review is called a “NOC Proceeding.” If the generic prevails in these proceedings, and also satisfies bioequivalence and other regulatory requirements, the generic receives Health Canada approval to enter the market, by way of a Notice of Compliance, or “NOC.”

Legal challenges by generic drug companies to brand drug patents confer a spillover benefit to drug plans and consumers. That is, if the generic drug manufacturer is successful in litigation, lower priced generic drugs are available sooner than they would otherwise be. However, generic firms incur the costs and risks of patent challenges, not as a public service, but in the pursuit of profits: Getting into the market before other firms normally results in a permanent increase in market share.

Drug plan generic reimbursement prices directly affect the profits from patent challenges for two reasons. First, reductions in reimbursement prices reduce revenues accruing to generic manufacturers and this reduces the benefit of entering early. Second, early generic entry entails some financial risk and reductions in generic reimbursement prices increase this risk. The reason is that the NOC proceedings do not settle claims of patent

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invalidity or infringement. Instead, they serve the more limited purpose of determining, on the basis of a summary review of the evidence, whether a generic firm is allowed to enter the market. As a result a generic firm that prevails in a NOC proceeding, and launches its product, can still be sued for patent infringement under the Patent Act. An early generic entrant is thus potentially liable for the brand firm's damages. The financial risk faced by an early entrant depends on the difference between the brand and generic reimbursement prices: Generic drugs sell at a fraction of the brand drug price, but damages are calculated at the full price of the brand drug. Thus, financial risk increases as the price of the generic drug decreases. Drug tenders, should they reduce generic drug prices, would inadvertently increase the financial risk to generic drug firms that challenge patents.

Therefore, tendering would immediately reduce the profits and increase the risk from patent challenges. This would likely result in fewer patent challenges, longer periods of exclusivity of brand drugs, and commensurately higher drug costs to payers. Moreover, it is unclear if any generic firms would participate in a tender if patents deemed relevant by the brand firm are still in effect, even if the generic firms had been successful in an NOC proceeding. Given the uncertainty of the outcomes of infringement suits, and the relatively low profits earned on the tender, the financial risk may be deemed to be unacceptably high.

Evidently, drug plans could minimize their downside risk by delaying the tender for products that only recently became genericized. But it is unclear exactly when it would be safe to issue the tender. The would-be generic entrant would presumably make its decision to challenge patents on the basis of the increase in its anticipated share of the market from being one of the first to enter, the total size of the market, both in the current year and into the future, expected litigation costs and expected damages from patent infringement suits. The drug plan would not be particularly well informed on these matters and thus may lack the information to optimally time the tender.

To examine the spillover benefits of patent challenges to drug plans and consumers, we worked through the litigation histories of the top five-grossing generic drugs: Amlodipine, Atorvastatin, Pantoprazole, Ramipril, and Venlafaxine. The Ramipril case history follows immediately and the other four histories are in the appendix to the paper. It is worth noting that these drugs, because of their commercial importance, have attracted the greatest amount of patenting and the greatest amount of litigation. These products are also the drugs most likely to be tendered, because of their budgetary importance, and because, being high-volume drugs, they have many generic competitors.

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## RAMIPRIL

Ramipril is an angiotensin-converting enzyme inhibitor, used to treat a variety of cardiovascular conditions. In 2011, over 426 million Ramipril pills were dispensed in Canada. The product (marketed as “Altace”) was brought to market in Canada by Sanofi-Aventis in 1995 (four years after its US introduction). Even after the product was marketed, Sanofi continued to list new patents on the Patent Register, including in 2001, 2002, 2003, and 2005, all of which it alleged would be infringed if any generic were to produce Ramipril. As a result, according to the recent decision by Justice Snider, “Between July 2003 and May 2008, Apotex was continuously engaged in litigation under the NOC Regulations with respect to Ramipril.”<sup>2</sup> However, as Justice Snider remarks, ultimately Sanofi was only successful in one proceeding, with respect to whether generic firm Apotex would infringe the ‘457 patent. This success, however, was irrelevant because in a later proceeding the ‘457 patent was found invalid on the basis of obviousness.

Apotex was granted an NOC in December 2006 and launched its generic immediately. In response, Sanofi sued Apotex for patent infringement under the Patent Act. A decision was reached in 2009 that Apotex was not infringing because the relevant patent was invalid; Sanofi then appealed, unsuccessfully, with a decision handed down in November 2011. Finally, Sanofi applied to the Supreme Court, which denied leave to appeal in July 2012. The net result is that there was uncertainty about whether Apotex was infringing Sanofi’s patents for over five years following Apotex’s entry.

In addition, in May 2012, Apotex obtained a decision about the damages for which it was eligible because it was kept out of the market by Sanofi during the period April 2004 – December 2006 by virtue of Sanofi’s commencement of its unsuccessful NOC proceeding in response to Apotex’s patent challenge. These damages were intended to compensate Apotex for its lost profits during that time, and hence were set based on the expected volume Apotex was likely to have sold multiplied by its assumed margin on every unit sold.<sup>3</sup>

It is important to note that Apotex was involved in NOC litigation for approximately five years on an at-risk basis since, if it lost, it would obtain no benefit and would have to pay Sanofi’s and its own legal costs. Once it entered the market, it incurred a significant financial risk: If Apotex took half the market and was found to infringe Sanofi’s patent, it would be liable for Sanofi’s lost profits, which were hundreds of millions of dollars. Further, Apotex’s profits would only have been a fraction of its liability. After it had entered the market, Apotex faced lawsuits for patent infringement for over five additional years. At all stages, Apotex was at risk either of not being successful in getting a NOC from Health Canada, or of paying large damage claims to Sanofi once it had entered.

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## A TENDERING COUNTERFACTUAL: RAMIPRIL

Suppose that provinces in Canada had decided to tender Ramipril as soon as there were five manufacturers in the market. That would have occurred in July 2007, seven months after Apotex was granted a NOC. Let's also assume that Apotex had a one-fifth chance of winning the tender, but to do so, it would have had to trim its margins very finely. In effect, its profits would have been extremely small: let's generously assume 10% of the price of the branded drug. If it had won, it would still have been facing a patent infringement suit from Sanofi for which it would have been responsible for paying Sanofi's margins, equal to about 90% of the price of the branded drug.<sup>4</sup> This doesn't sound like a good deal for Apotex or any other generic firm. Indeed, the only firm that would have been safe from concerns about infringement liability is Sanofi, which would likely have been able to win the tender as a result. Thus, one could realistically expect that Apotex, following five years of litigation in NOC Proceedings, would have found that it enjoyed about six months of sales. When considering the damages to Apotex caused by Sanofi's invalid patents during the period April 2004 – December 2006, Sanofi would argue that the damages to Apotex were extremely small, because the potential profits to be earned by Apotex would have been limited by the use of tendering.

Looking forward, it seems improbable that Apotex would have found it worthwhile to mount a patent challenge. It would likely have waited to enter in 2020, when the last patent listed on the Patent Register would have expired. Tendering would have commenced then, with payers getting very low prices, given that Ramipril would have been in generic production all over the world for many years. Manufacturing would naturally be located in an overseas plant since all the expertise and the existing production capacity would be overseas.

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***The Appendix shows the litigation histories for the other top-selling generic drugs.***



## THE IMPORTANCE OF LITIGATION, BY THE NUMBERS

For each of these five top-selling drugs, we estimate the savings to drug plans and consumers attributable to early generic entry in the tables below. The calculations are straightforward. Suppose that generic firms did not challenge patents, knowing that the benefits of doing so would be rapidly eroded by competitive tendering. Then generic entry would have been substantially delayed, in some cases by years. The following table shows the dates on which the last patents on the Patent Register would have expired for our five drugs, compared to the actual date of generic entry.<sup>5</sup> ***The average delay if generic firms simply waited for the expiry of the last patent on the Register would have been 4,250 days for these five drugs, or about 12 years.***

TABLE 1: DELAYS AVOIDED BY GENERIC LITIGATION

Drug Name	Date of Generic Entry	Date of Expiry of Last Patent on Patent Register	Delay in Competition if No Litigation (Days)
RAMIPRIL	12 DEC. 2006	20 AUG. 2020	5000
ATORVASTATIN	19 MAY 2010	21 MAY 2022	4385
AMLODIPINE	9 JULY 2009	21 AUG. 2021	4426
PANTOPRAZOLE	5 MARCH 2008	8 DEC. 2018	3930
VENLAFAXINE	2 AUG. 2007	12 MARCH 2017	3510
<b>AVERAGE DELAY</b>			<b>4250</b>

We estimate the savings created by generic litigation below, assuming that the average price following generic entry is 50% of the brand price.<sup>6</sup> Obviously, if the generic price were lower, there would be even larger savings for payers, so these calculations are intended only to illustrate the potential magnitude of the savings.

What is striking is that for these five drugs alone, the savings calculated are roughly three times the entire annual spending on generic drugs for Canada. The potential savings from tendering are much, much smaller than this on an annual basis. One should obviously proceed carefully in this context.

**TABLE 2: SAVINGS ACHIEVED BECAUSE OF GENERIC LITIGATION**

<b>Drug Name</b>	<b>Total Savings Because Of Generic Litigation</b>
<b>RAMIPRIL</b>	<b>\$2.6 BILLION</b>
<b>ATORVASTATIN</b>	<b>\$7.5 BILLION</b>
<b>AMLODIPINE</b>	<b>\$2.8 BILLION</b>
<b>PANTOPRAZOLE</b>	<b>\$1.8 BILLION</b>
<b>VENLAFAXINE</b>	<b>\$1,6 BILLION</b>
<b>TOTAL SAVINGS</b>	<b>\$16.3 BILLION</b>

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The preceding analysis estimates the spillover benefits to payers actually achieved by early generic entry. One could also estimate the cost to payers of delayed generic entry. These are the actual delays in entry attributable to the time required to litigate patents that were ultimately found to not inhibit generic entry. It is apparent that if generic incentives for entry are further weakened, then generic competition will be delayed.

To assess these costs, we adopt the date on which generic manufacturers claim they could have entered if not for the use of the NOC Regulations as the counterfactual.<sup>7</sup> This date is the date of expiry of the final valid patent, i.e., the patent that was neither invalidated in an NOC proceeding nor could be worked around. Essentially, in this exercise we are taking away the barrier to entry caused by patents later shown to not prevent entry. When we do this, we obtain for the drugs the following feasible dates of entry:

**TABLE 3: DELAYS TO GENERIC ENTRY CAUSED BY PATENTS SHOWN IN THE NOC PROCEEDINGS TO BE INVALID OR NOT INFRINGED**

Drug Name	Generic	Earliest Feasible Date Generic Could Have Received NOC	Date Of Generic Entry	Days Delay
RAMIPRIL	APOTEX	26 APR., 2004	12 DEC., 2006	960
ATORVASTATIN	APOTEX	MAY 15, 2007	MAY 19, 2010	1,100
AMLODIPINE	TEVA	20 OCT., 2004	9 JULY, 2009	1,723
PANTOPRAZOLE	APOTEX	26 APRIL, 2004	5 MARCH, 2008	362
VENLAFAXINE	TEVA	10 JAN., 2006	2 AUG., 2007	569

During the delay period, the patentee enjoyed exclusivity based on patents that were ultimately found invalid or not infringed. Thus payers paid the brand price instead of a competitive generic price during this period. The additional cost to payers is uncertain and depends on both the generic price and the share of sales that would have been generic. Typically generic prices have been in the range of 25% to 50% in the last few years. To give a sense of the magnitudes involved, we offer some rough estimates of how much extra payers spent on these five drugs because of invalid and non-infringed patents. To construct our estimate, we assume that payers would have saved 50% off the brand price had the products been generically available.<sup>8</sup> This assumption is most likely a significant underestimate of the unrealized savings, but it serves as an indication of the scale of the expenditures. Given this assumption, the excess payments actually made by payers for these five drugs in Canada are more than \$3.5 billion.<sup>9</sup> If we were to consider a larger set of drugs, we would obtain larger total excess costs.

*...the excess payments actually made by payers for these five drugs in Canada are more than \$3.5 billion. If we were to consider a larger set of drugs, we would obtain larger total excess costs.*

**TABLE 4: EXCESS COSTS CAUSED BY INVALID PATENTS**

<b>Drug Name</b>	<b>Savings not Achieved Because of Delayed Generic Entry</b>
<b>RAMIPRIL</b>	<b>\$0.5 BILLION</b>
<b>ATORVASTATIN</b>	<b>\$1.8 BILLION</b>
<b>AMLODIPINE</b>	<b>\$1.0 BILLION</b>
<b>PANTOPRAZOLE</b>	<b>\$0.2 BILLION</b>
<b>VENLAFAXINE</b>	<b>\$0.3 BILLION</b>
<b>TOTAL</b>	<b>\$3.6 BILLION</b>

## **POLICY TRADEOFFS**

Drug plans contemplating the use of tendering face a dilemma. Tendering, if generic firms actually participate, will almost certainly reduce the per-unit cost of generic drugs already on the market. But tendering will also reduce the incentive for generic firms to challenge the patents of brand drugs that have yet to be genericized. As we noted earlier, there are already substantial unrealized savings because patentees are able to delay competition by asserting invalid or non-infringed patents. Tendering will only exacerbate this problem and may increase costs to payers. It is unclear whether the savings to payers from the use of tendering outweighs the higher costs associated with a delay in the availability of generic competitors to branded drugs.

One way to assess this trade-off is to ask how much additional delay in getting generic competition one could accept for a given reduction in generic prices. Suppose, for example, that the public drug plan wishes to tender a top-selling branded drug once generics become available. Ontario already reimburses these drugs at 25% of the brand price. Suppose that, with tendering, the price would fall by half, to 12.5% of the brand price. We will assume that the province has a twelve-year planning horizon. This might be because very distant expenditures are hard to predict, because use of the drug might fall off in the distant future, or because of other contingencies. We will also assume a 4% discount rate for the future, so that a reduction of expenditure today is worth more than the reduction of expenditure in the future.

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A simple calculation shows that, given these assumptions, payers are worse off given a 12.5% generic price if generic competition is further delayed by 15 months or more. If the delay in generic competition is shorter than 15 months, payers will be better off (ignoring all the other costs of tendering). Is there reason to think that tendering might cause such a delay? As Table 3 shows, there are already much longer delays than 15 months in generic competition because of the strategic use of patents that are ultimately found invalid or not infringed. And as Table 1 shows, patentees are making an effort to delay generic entry much more: indeed, if not for litigation, generic competition would have been delayed on the top five generic products by a further twelve years. If tendering is really effective in reducing generic prices and limiting the benefits of patent challenges, we can reliably predict that generic firms will respond by investing less in patent challenges.

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## ARE TENDERS IN NEW ZEALAND A MODEL FOR CANADA?

New Zealand's national public drug plan Pharmac has used tendering since 1996. Because New Zealand pays relatively low prices for generic drugs, it is often touted as a model for tendering in Canada. Canada could likely obtain the same low prices provided that there are generics on the market. The problem is that a would-be generic entrant faces higher entry costs in Canada than it does in New Zealand, and tendering provides little to no reward to cover these entry costs. As a result, if Canada adopts tendering as a method for procurement, generic entry will likely be delayed, perhaps significantly.

The difference in entry costs in the two countries stems from differences in their pharmaceutical markets and intellectual property regimes. Canada's NOC Regulations require would-be generic entrants to address patents listed on the Patent Register as a condition for entry. In effect this creates a "linkage" between regulatory approval and patent status.<sup>10</sup> This exercise is costly (perhaps in the range of \$2 million to \$4 million per NOC proceeding, whether successful or not) and time-consuming. There is no equivalent to the NOC Regulations in New Zealand, so generic firms can enter freely if they believe that there are no outstanding valid patents that would be infringed.

Not only does New Zealand have a different regime, without the same obstacles to generic competition as Canada, it also has much less aggressive patenting by innovator companies. There are likely three reasons for this: First, as discussed above, Canada's NOC Regulations inadvertently encourage brand patenting as a means to delay generic entry. Second, New Zealand has a small market and has aggressive brand drug price controls, so that it is not as attractive for brands to try to extend monopoly positions by engaging in costly patent strategies. Third, with almost no drug manufacturing capacity in New Zealand, there is little need to list patents that relate to production methods.

*Not only does New Zealand have a different regime, without the same obstacles to generic competition as Canada, it also has much less aggressive patenting by innovator companies*

We examined the patent portfolios for a few drugs available in both Canada and New Zealand, looking at the patent databases in both countries. In New Zealand, Pfizer and its subsidiary Warner Lambert have 17 patents

on Atorvastatin (the active ingredient in Lipitor); in Canada, there are 99 patents. In New Zealand, 15 patents contain the word “rosuvastatin” (the active ingredient in Crestor); in Canada, there are 376. There are 5 patents containing the word “bevacizumab” (the active ingredient in Avastin) in New Zealand; in Canada, there are 353.

One outcome of the New Zealand regime is that there is very little patent litigation relating to generic entry in that country, while in Canada litigation between brand and generic firms costs well in excess of \$100 million per annum.

It is clear that there are significant differences between the jurisdictions that must lead one to be cautious about assuming that New Zealand’s experience can be transplanted to Canada. New Zealand is generally successful in having timely entry of generic competition despite its aggressive policies concerning the pricing of generic drugs, however; it seems certain that implementing similar policies in Canada would lead to significant delays in generic entry as generic firms reduce or entirely stop investing in litigation.

Despite the obstacles created by the extensive patenting in Canada and the NOC Regulations, this does not lead in every case to later generic entry in Canada than in New Zealand. Generic firms in Canada have a motivation to try to enter, while in New Zealand they lack incentives to litigate. No generic firm wants to take a risk of being sued for infringement when the profits from being the sole supplier are rather slim. Possibly as a result, many important drugs are genericized much later in New Zealand than in Canada. For example, Atorvastatin was genericized only in February 2012 in New Zealand, almost two years later than in Canada. Olanzapine became available generically in June 2011 in New Zealand, four years later than in Canada.<sup>11</sup> Venlafaxine became generically available in August 2011 in New Zealand, four years later than in Canada.<sup>12</sup>

## ARE TENDERS IN GERMANY AND THE NETHERLANDS A MODEL FOR CANADA?

Germany and the Netherlands, as described below, have been using tendering for generics in recent years. Again, the ratio of risk to reward for generic entry is higher in Canada than in these countries. There are three reasons. First, like New Zealand, Germany and the Netherlands do not have an equivalent to Canada’s NOC Regulations. In other words, they do not make regulatory approval contingent on first addressing brand patents. Thus, generics can enter if they believe that they will not infringe any valid patents, though, of course, they take the risk of being sued. Second, generic firms enter to serve the entire European Union and are not dependent only on tendering markets. (All EU member states recognize the safety and efficacy review of the European Medicines Agency. Once this agency approves a generic drug, it grants marketing authorization for all markets within the European Union.<sup>13</sup>) Third, the European Union is a very large and attractive market.

*In New Zealand, 15 patents contain the word “rosuvastatin” (the active ingredient in Crestor); in Canada, there are 376.*

*it seems certain that implementing similar policies in Canada would lead to significant delays in generic entry as generic firms reduce or entirely stop investing in litigation.*

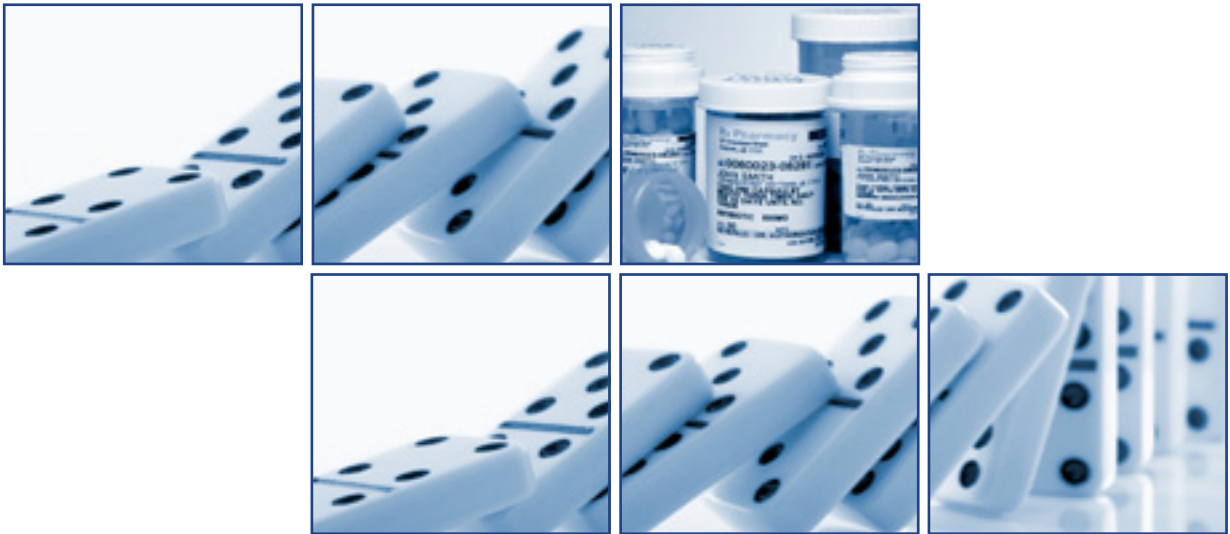
*...the ratio of risk to reward for generic entry is higher in Canada than in these countries. There are three reasons.*



## IS THE UNITED STATES A MODEL FOR CANADA?

How timely is generic entry and how low are generic drug prices in the United States, a country that, like Canada, links regulatory approval to having first addressed brand patents? While there are important differences, the US offers a model of a jurisdiction with lower generic drug prices that is still able to attract generic entry. Does this prove that low prices are consistent with a linkage system where firms are effectively required to litigate to enter? We have some reservations about this assessment, owing to three key differences between the US and Canada: First, the US is a very large market that is attractive to enter, with much higher rates of generic utilization than in Canada. Second, the US has a system that rewards firms for challenging patents.<sup>14</sup> While imperfect, this system provides very substantial incentives to generics to try to overcome invalid or non-infringed patents. Canada has no such system. Third, the nature of competition in the retail pharmacy sector is different in the US. Canadian pharmacies compete primarily on the basis of quality, not price. In the US, pharmacies are forced to compete on generic drug prices (i.e. charge drug plans an amount closer to their actual acquisition cost) because of much more aggressive price negotiations with drug plans (or with pharmacy benefit managers acting as their agents). Moreover, the size of the uninsured population in the US is larger than in Canada and pharmacies naturally use low prices to attract their business.

*US is a very large market which is attractive to enter, with much higher rates of generic utilization than in Canada. ...the US has a system that rewards firms for challenging patents.*



### 3 SUPPLY SECURITY

In our current system, most commonly-prescribed drugs are manufactured by multiple generic drug companies. Indeed, some high-volume drugs, like Amlodipine, are produced by more than 20 companies. With multiple suppliers, the total market supply – the amount produced by all manufacturers – is less susceptible to disruptions than if there were just one supplier. Having multiple suppliers affords some redundancy in the system: Should one manufacturer be unable to supply others can fill the gap unless all manufacturers are affected by the same supply shock. This redundancy is obviously unavailable in single-source tenders.

A drug shortage caused by having a single supplier is not just a theoretical risk. The recent disruptions in the Sandoz plant in Quebec created shortages of dozens of injectable drugs commonly used in hospital settings.<sup>15</sup> One possible reason that there was only one manufacturer of these injectable drugs is that hospitals acquire their drugs through group purchasing organizations (GPOs). GPOs are known to negotiate aggressively. Given this, and the relatively small size of the market, other firms may not have found it profitable to set up productive capacity for these specialized pharmaceuticals.<sup>16</sup>

What is the evidence on the effect of tendering on the supply of conventional oral solid drugs? There have not been any reports of serious supply disruptions in the European Union countries that use tendering. This could be due to the fact that tendering has been practiced there for only a few years, so that the longer-term effects have yet to be realized. Another possible reason that supply appears to be stable is that the tenders in Germany and the Netherlands do not encompass the entire national market so that there are likely alternative suppliers able to fill in any gaps. Even if the German and Dutch tenders encompassed their respective national markets, there would probably still be a large number of alternative suppliers owing to the EU's mutual recognition system. Thus, while the EU does not show that tendering will induce supply shortages, it doesn't offer any evidence that tendering cannot create shortages in Canada.

The New Zealand tendering system has been in operation for longer – since 1996 – and we encountered reports of potentially serious supply disruptions in this jurisdiction.<sup>17</sup> Shortages were ultimately resolved by rationing demand, switching patients to different drugs, and sourcing the product from alternative suppliers.

*With multiple suppliers, the total market supply – the amount produced by all manufacturers – is less susceptible to disruptions than if there were just one supplier.*

*... tendering has been practiced there for only a few years, so that the longer-term effects have yet to be realized.*

Awarding the tender to the two lowest bidders can mitigate the risk of shortages of tendered drugs, but this requires a way to split the market between them. Suppose that firms A and B win the contract, with B bidding the higher price. B will then be in a position to gain market share from A by offering larger rebates to pharmacies. Generic drug companies will be aware of this when formulating their bids, so bids will be inflated to pay pharmacy rebates. The drug plan can address this by announcing an allocation rule in advance of the bidding. For example, the tender might be designed so that the lowest-price firm gets one geographic region, and the runner-up gets another, smaller geographic region. Under such an arrangement, the tender winners wouldn't have to compete for pharmacy business post tender.

Having two suppliers substantially resolves the security of supply of the tendered drugs. However, splitting the tender is likely to undermine its purpose. First, it reduces the extent to which manufacturers can exploit economies of scale in production; this means higher prices than what would be available in a single source tender. Second, it means that it is impossible to expect the lowest price, since the second lowest bidder has not offered to supply at that price. New Zealand's Pharmac reports that dividing the tendering process in two increased prices on average by 17%.<sup>18</sup>

*Having two suppliers substantially resolves the security of supply of the tendered drugs. However, splitting the tender is likely to undermine its purpose.*



## 4 MANUFACTURING

A tender system, should it be applied on a large scale in Canada, would have profound effects on the domestic generic manufacturing sector. The most likely outcome is a reduction over time in the number of Canadian manufactured products being bid in the tenders.

Consider the market for Atorvastatin in Canada. Currently, we have many suppliers, each producing a share of the market. Should Atorvastatin be put up for tender, only a subset of existing suppliers would be in a position to mass produce the drug. Many are simply not set up to do so. Such firms could presumably raise the capital needed to create the infrastructure to mass produce and bid in future tenders but it is not clear that this would be particularly profitable. Suppliers excluded from the market become less likely to bid competitively in the future: First, they lose experience in the technology of producing Atorvastatin en masse. (This is particularly important because the firms that are winners of the contract are of course gaining substantial experience in producing large volumes of the drug and thus reducing their costs.) Second, the appeal of re-entering the market is less if the expected margins are too thin. Most current suppliers of Atorvastatin therefore would likely turn their attention to other drugs and other markets.

The existing generic firms that are equipped to mass-produce Atorvastatin and the other drugs put up for tender would also need to adapt. The tender system increases the variability of earnings and rewards large and flexible manufacturing capacity. Existing firms would also likely face competition from foreign firms that operate manufacturing at a scale sufficiently large to supply international markets. This would put pressure on domestic firms to achieve comparable scale economies. The requirements for large, flexible and low-cost manufacturing capacity are precisely the conditions that lead to industry consolidation.

Thus, there is a legitimate question of whether it is possible to sustain really low prices over the long-term. Tenders can only be successful if there are enough competitors bidding, but by their nature, tendering systems tend to reduce the number of active, effective competitors. Thus, tendering systems are likely to start off with considerable success because they take advantage of the existing competitive market; but over time they undermine that competitive market, leading to higher prices in the future. This is not to say that, in the long run, prices would be higher than those currently paid. If prices rise too high then additional foreign generic manufacturers would find it worthwhile to seek regulatory approval to sell their product in the Canadian market and begin bidding on the tenders, putting downwards pressure on prices. Instead, the lesson is that prices that are very close to the variable costs of production may not be sustainable over the long term.

*...Should Atorvastatin be put up for tender, only a subset of existing manufacturers would be in a position to mass produce....*

*Tenders can only be successful if there are enough competitors bidding...tendering systems tend to reduce the number of active, effective competitors...*

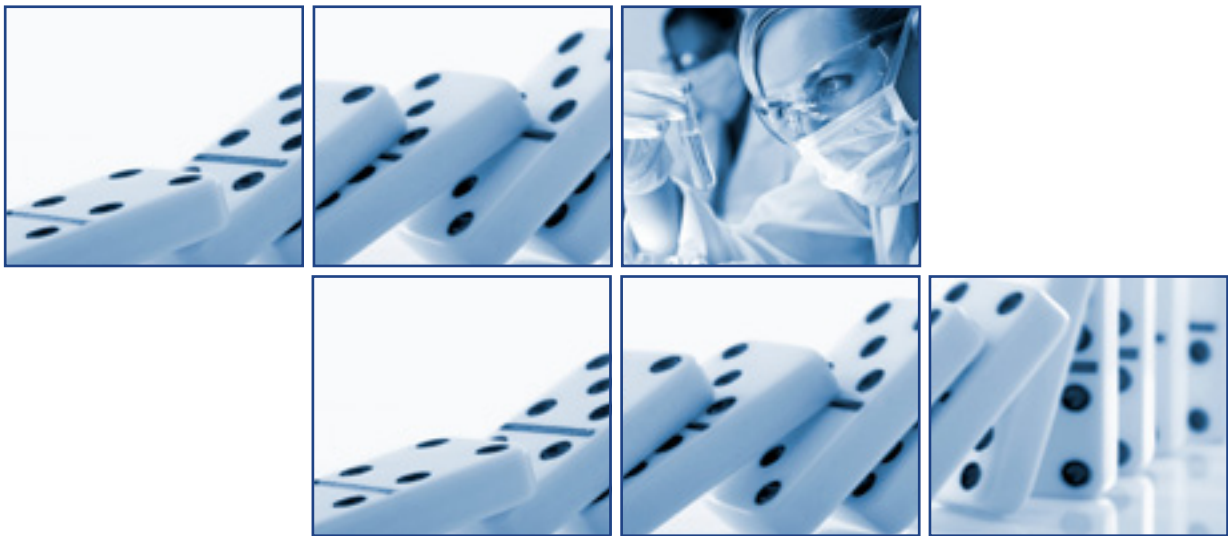
The international experience with tendering does indicate that, over time, tendering reduces the number of domestic manufacturers and increases the supply of foreign produced generic drugs. In New Zealand, there is only one domestic generic manufacturer remaining, Douglas, which produces only 29 prescription medicines.<sup>19</sup> Another domestic firm, Pacific, closed all of its New Zealand manufacturing operations in 2008.<sup>20</sup> Predictably, foreign manufacturers source virtually all of the New Zealand tenders.

*...international experience with tendering does indicate that, over time, tendering reduces the number of domestic manufacturers...*

The European Union countries that have used large-scale tenders provide corroborating evidence. After tendering was initiated in the Netherlands, Apotex withdrew 15 products from the market and ratiopharm closed its production plant.<sup>21</sup> In Germany, tendering has resulted in manufacturing relocating to “low-wage countries.”<sup>22</sup> The United States vaccine supply, which is procured primarily through tenders, is also illustrative. Danzon, Pereira and Tejawani (2005) note that between 1967 and 2002, the number of licensed vaccine suppliers for the US had fallen from 26 to only 12, and that five of the eight recommended pediatric vaccines had only a single supplier.<sup>23</sup>

*...between 1967 and 2002, the number of licensed vaccine suppliers for the US had fallen from 26 to only 12, and that five of the eight recommended pediatric vaccines had only a single supplier.*

Tendering may also harm competition even in drug markets in which it is not used. Some companies produce a range of low-volume drugs, not because they are particularly profitable, but rather to be able to offer pharmacies a large catalogue of different products and the convenience of “one stop shopping”. Firms that offer this service may have an advantage marketing the more profitable high-volume drugs. But if most high-volume drugs are procured via tender, then offering a large product catalog is less advantageous. As a result, some low-volume drugs may no longer be produced or may be produced by a smaller number of firms.



## 5 INTERACTIONS BETWEEN MANUFACTURERS AND PHARMACIES

A move to tendering will also have implications for the level of service provided by generic manufacturers to pharmacies. In normal competitive interactions, suppliers use customer service to attract and retain clients. In the pharmacy sector, good customer service involves supplying the pharmacy with adequate supplies of the drug in a timely manner, in amounts requested, with sufficiently long expiry dates, all invoiced correctly. Customer service is responsive. Manufacturers may provide ancillary services such as anti-counterfeiting guarantees, training, or patient compliance programs. Generic manufacturers who fail to provide good service are likely to find that pharmacies turn to other manufacturers. The same is not true, of course, when the product is sole-sourced, since the pharmacy has no alternative. In sole-sourced supply situations, especially where margins are tight, the supplier has little incentive to be responsive to pharmacy demands. If a pharmacy finds itself short of stock because of unexpectedly high demand, in a competitive situation it will normally be able to replenish its stocks rapidly. But with a monopoly supplier, the incentives to assist the pharmacy are weak.

Higher margins help to pay for this customer service to pharmacies. This does not in itself justify high margins, of course. But elimination of margins will reduce the level of service that manufacturers provide to pharmacies. Such customer service matters to pharmacies and their customers, since both care whether pharmacies have stock.

There is the possibility that the manufacturer that wins the tender will voluntarily provide good levels of customer service. The reason is that the tender will not normally encompass the entire national generics market. Certain provinces may be excluded from the tender. Also, the tender may include just the largest volume generic drugs. Presumably the manufacturer that wins the tender would want to maintain a good reputation with pharmacies if it wishes to provide them with generic drugs that are procured outside of the tender. It may be difficult, however, for such a generic manufacturer to win the contract. The reason is that good customer service is costly and these costs need to be incorporated into the bid submitted to the tender. It may lose the contract to a manufacturer that is not concerned about its reputation with pharmacies in the non-tendered market. This would happen, for instance, if a foreign manufacturer with no existing domestic presence were to win the tender.

The drug plan could attempt to include the level of customer service as an element to be considered, alongside price, when deciding who wins the tender. But this may be difficult to do in practice. First, the contract would need to specify the desired levels of each element of customer service that the winning firm is expected to provide. But it may be hard to specify all of these elements in advance given that “good customer service” can take many forms. Second, enforcement may be a challenge. Suppose that pharmacies complain to the drug plan that customer service provided by the contractor is poor. The drug plan would therefore need the capacity to determine whether the allegations are true and also the extent to which pharmacies are to blame.

*...In sole-sourced supply situations, especially where margins are tight, the supplier has little incentive to be responsive to pharmacy demands...*

*customer service is costly and these costs need to be incorporated into the bid submitted to the tender. It may lose the contract to a manufacturer that is not concerned about its reputation...*



## 6 THE IMPACT ON PHARMACIES AND CUSTOMER SERVICE

Rebates have constituted an important source of pharmacy revenues since the provincial drug plans were first launched in the early 1970s. Not surprisingly, they have fundamentally affected the economics of community pharmacy in Canada.<sup>24</sup> Rebates have increased the revenue earned by the pharmacies per prescription dispensed and this increase in gross margins has likely attracted additional pharmacies into the industry or sustained “marginal” pharmacies. These marginal pharmacies have sufficiently high average dispensing costs such that they would not be viable—and hence would not have entered or remained in the market—without the rebate income. There are substantial economies of scale in pharmacy, so these marginal pharmacies tend to be smaller operations. The high gross margins have also caused pharmacies to attract and retain customers by offering them high levels of customer service, including convenient store hours, short wait times, patient counseling services, disease management, and general responsiveness to their patients’ needs.

Rebate income has already declined during the last six years as a result of the cuts to generic reimbursement rates. A move to large scale tendering will eliminate them entirely for tendered drugs.

The reduction in rebates will induce marginal pharmacies to exit the industry. The reduction in the number of pharmacies will have various secondary effects. First, surviving pharmacies will absorb the dispensing volumes of pharmacies that close. Surviving pharmacies might be able to exploit some scale economies, i.e., their average fixed dispensing costs will decline as their dispensing volume grows. Second, pharmacy closures might increase the travel time for some residents of rural areas, where pharmacy density is relatively low. Most individuals, however, will notice little impact on pharmacy access, since most patients have several pharmacies within a reasonable distance. Indeed, Law et al. (2011) show that a 30% reduction in pharmacies in Ontario would for most individuals have only “a small impact on geographic access to pharmacies.”<sup>25</sup>

More importantly for patients, a reduction in gross margins and the reduction in the number of competing pharmacies will also reduce the incentive (and likely the resources) among surviving pharmacies to compete for market share by offering ancillary patient services and other dimensions of quality. Patients with particularly complex medication regimens, who make relatively heavy use of pharmacy services, would feel this reduction most acutely.

The airline industry provides a useful analog to understand the likely effects of the elimination of rebates. Prior to the early 1980s, airline ticket prices were regulated; airlines could not use low prices to compete for customers. Instead they competed on quality: customer service, flexibility in changing reservations, the quality of meals served on board, legroom, generous baggage allowances, and so on. The deregulation of the 1980s changed the nature of competition. Now airlines compete primarily on ticket prices, not customer service. We get lower prices but lower levels of service. It is still possible for the customer to acquire higher levels of service, but this

*...Rebate income has already declined during the last six years as a result of the cuts to generic reimbursement rates...*

*Patients with particularly complex medication regimens, who make relatively heavy use of pharmacy services, would feel this reduction most acutely.*

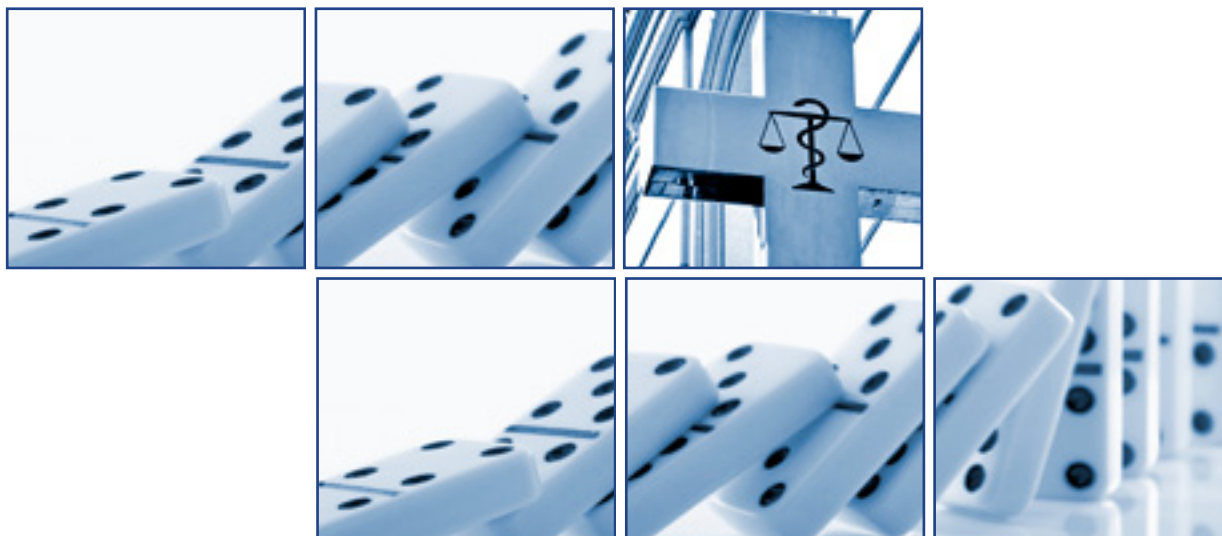
requires that the customer pay a premium (such as an upgrade to a business class ticket). The airline industry also consolidated following the price drops that followed deregulation. This consolidation increased the market power of survivors, which in turn appears to have moderated some of the price reductions.<sup>26</sup>

By casting the likely effects of tendering in a pharmacy profit competition model, we do not mean to imply that pharmacies are purely profit-maximizing firms. Pharmacists are bound by a professional obligation to help their patients. The quid pro quo for this is that they receive adequate compensation so that they can focus on their patients' health. Rebate income provided the cushion needed for pharmacists to do exactly that.<sup>27</sup>

The lesson we draw is that the margins in a competitive industry like retail pharmacy are competed away in the form of service. Elimination of these margins (via tendering) will result in fewer locations to choose from and a reduction in the patient services that were previously offered at no charge.

The Ontario public drug plan, which has had the deepest cuts to generic reimbursement levels, has taken some steps to address these issues. Professional (i.e. dispensing) fees are modestly higher for rural pharmacies to help ensure that they remain viable. Ontario has also introduced the MedsCheck program. This program offers pharmacies a payment for the provision of several services, including medication reconciliation.<sup>28</sup> Whether this program will offset the reduction in patient services that will attend the elimination of rebates is unclear. The services paid for by MedsCheck are but several of the services that pharmacies provide, so these other services will not be compensated by rebate income.<sup>29</sup>

*...The lesson we draw is that the margins in a competitive industry like retail pharmacy are competed away in the form of quality...*





## 7 SUMMARY

Retail or reimbursed prices of generic drugs in Canada, while comparable to or lower than those in many countries, are above the lowest prices paid internationally. These relatively higher prices are not the result of a lack of competition amongst generic manufacturers in the Canadian market. Indeed, there are over 20 generic competitors in Canada; the Competition Bureau's study of the generic industry found it highly competitive for high-volume drugs.<sup>30</sup> Instead the high prices are due to the way that generic drugs are procured. Drug plans set reimbursement prices at some arbitrarily chosen fraction of the brand drug price. Historically, this price has been above the lowest price that generic manufacturers are willing to sell at. The difference in the reimbursement price and generic manufacturers' reservation price – the margin – accrues to pharmacies and manufacturers. (The portion accruing to pharmacies is called the “rebate” or “professional allowance”.) No doubt, some portion of these margins represent pure profits; likely the majority, however, get competed away. That is, pharmacies and manufacturers spend money in an attempt to earn market share and the margins that come with it. The competition is valuable to drug plans and consumers.

Pharmacies engage in service competition by offering convenient locations, operating hours and patient services. Generic manufacturers compete in a variety of ways. The margin provides an incentive for manufacturers to mount legal challenges to the patents on branded drug. These challenges are expensive, and if successful, entering the market entails the risk of a patent infringement suit, but the increase in market share the generic receives from being first to market makes it worthwhile. Drug plans benefit tremendously from the early generic entry. As long as the NOC Regulations force generic firms to engage in litigation to enable generic entry, tendering as practiced in other jurisdictions is likely to result in significantly delayed entry and ultimately higher, not lower, drug costs. The margin also invites entry by multiple generic firms and this provides some insurance against drug shortages and has supported a vibrant domestic manufacturing sector. Competition among manufacturers for the pharmacy's business results in responsive customer service.

The *raison d'être* of tendering is to eliminate the margins so that the drug plans pay the generic manufacturers' reservation price. This will reduce generic drug prices, but it will also eliminate the competition for the margins. As a result, pharmacies will offer fewer patient services, drug plans will wait longer for the arrival of lower priced generic drugs, and drug supply will be less secure. Given these considerations policy makers need to carefully weigh the advantages and disadvantages of tendering.

## APPENDIX:

### FOUR DRUG LITIGATION CASE STUDIES

#### ATORVASTATIN<sup>31</sup>

Atorvastatin is a lipid metabolism regulator that lowers blood cholesterol. Pfizer started marketing and distributing Atorvastatin in Canada in 1997 under the brand name Lipitor. When Pfizer first began distributing Lipitor in Canada it had two Lipitor patents listed on the Patent Register. As Lipitor's sales grew, and it became the largest selling drug in the world, Pfizer pursued an aggressive patenting strategy listing eighteen more patents on the Patent Register. Pfizer asserted that these patents would be infringed if a generic manufacturer began to market Atorvastatin in Canada.

In order to get approval for its product, Apotex was involved in litigation about these patents from January 2006 to May 2010, and was eventually successful. Its generic version of Atorvastatin was approved on May 19, 2010. As a result, Apotex was able to market and distribute its Atorvastatin product years before Pfizer's patents expired.

Apotex has also claimed damages for being kept off the market from May 15, 2007 to May 19, 2010.

Apotex's successful litigation and "at risk" entry of a less expensive generic Atorvastatin product in the marketplace has saved Canadians at least \$7.5 billion dollars, as shown in Table 2 above.

#### A TENDERING COUNTERFACTUAL: ATORVASTATIN

If there had been a tendering process in place when Apotex was considering whether to invest in challenging the patents in order to bring its generic to market, Apotex would have known that it might not win the tendering process, and even if it did win and get the business, its margins would have been thin. Apotex also would have been aware that it might face many years of expensive litigation, and a huge risk of damages if it were eventually found to infringe one or more of the patents.

In these circumstances, Apotex would very likely have decided not to challenge the Atorvastatin patents. Rather than Apotex's product coming to market in May 2010, there would have been no generic product until the last of the twenty or so Pfizer patents expired in 2022. A helpful observation is that Atorvastatin became generic in the United States much later in November 2011, following a settlement between Pfizer and Ranbaxy. Ranbaxy not only did not face the threat of tendering, but also captured a 180-day exclusivity period during which other generic firms could not compete. In other countries, such as the UK, generic Atorvastatin did not become available until May 2012. In New Zealand, it became available in February 2012.<sup>32</sup>

*...entry of a less expensive generic Atorvastatin product in the marketplace has saved Canadians \$7.5 billion dollars...*

*Rather than Apotex's product coming to market in May 2010, there would have been no generic product until the last of the twenty or so Pfizer patents expired in 2022.*

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## AMLODIPINE

Amlodipine is a calcium ion antagonist that is used to treat mild to moderate hypertension and to manage chronic stable angina. Pfizer started marketing and distributing Amlodipine in Canada in 1997 under the brand name Norvasc. At that time Pfizer had two patents listed on the Patent Register relating to Norvasc. Several years later, Pfizer listed two additional patents. It asserted a generic product would infringe these patents.

In order to bring a generic version to market, ratiopharm (acquired by Teva in August 2010) was in litigation against Pfizer regarding these patents for five years from July 2004 to July 2009. For procedural reasons, it had to litigate one of the patents at issue twice. The court also determined that one Pfizer patent had been worded in such a way that it contained an intentionally misleading misstatement at its core and the patent was impeached.

*to bring a generic version to market, ratiopharm (acquired by Teva in August 2010) was in litigation against Pfizer regarding these patents for five years*

## A TENDERING COUNTERFACTUAL: AMLODIPINE

If there had been a tendering process in place when ratiopharm was considering whether to invest in challenging the patents in order to bring its generic version of Amlodipine to market, ratiopharm would have known that it might not win the tendering process, and even if it did win and get the business, its margins would be razor thin. It would have known that it faced many years of expensive litigation.

In these circumstances, ratiopharm would very likely have decided not to challenge the Amlodipine patents. Rather than bringing its generic product to market in July 2009, there would have been no generic product until the last of the four Pfizer patents expired in 2021.

In fact, Saskatchewan immediately tendered Amlodipine as soon as the product was genericized. Ironically, a Pfizer subsidiary, GenMed, won the tender to become the sole provider of Amlodipine in Saskatchewan. Thus Pfizer, which likely had invested several million dollars in litigation with the goal of delaying generic competition (based on patents that were eventually found invalid), became the only firm to supply generic Amlodipine to Saskatchewan. ratiopharm, which had invested so much to enable competition and low prices, and which was shown to be correct in its assertions, earned nothing in Saskatchewan. If such a system were more broadly implemented, it is obvious what the outcome would be for patent litigation and the duration of exclusivity.

*Rather than bringing its generic product to market in July 2009, there would have been no generic product until the last of the four Pfizer patents expired in 2021.*

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## PANTOPRAZOLE

Pantoprazole is a proton pump inhibitor that is used to treat ulcers, reflux esophagitis, gastro-esophageal reflux disease and lesions induced by non-steroidal anti-inflammatory drugs. Nycomed (Solvay at the time) started marketing and distributing Pantoprazole in Canada in 1996 under the brand name Pantoloc. It had a patent which expired in 2006. Nycomed listed four other patents on the Patent Register in 2005 and 2006, which it argued would be infringed if a generic manufacturer began to market Pantoprazole in Canada.

In order to obtain its approval Apotex was in litigation on these patents from March 2006 to March 2008. It was successful, and received approval to enter the market on March 5, 2008.

Apotex has claimed damages for being kept off the market from March 9, 2007 to March 5, 2008. Nycomed has filed a patent infringement suit and continues to assert that its patents are infringed. If Nycomed's suit is successful, Apotex will be liable for the lost profits of Nycomed, which may exceed the profits Apotex has been able to earn.

*In order to obtain its approval Apotex was in litigation on these patents from March 2006 to March 2008.*

## A TENDERING COUNTERFACTUAL: PANTOPRAZOLE

It is difficult to imagine that a tendering process would have worked successfully for this product, given the continued assertion of patent infringement. Certainly, it would have been relatively unattractive for any generic firm to invest in litigation knowing that winning the tender would earn it very thin margins and a potential infringement liability. Presumably, no firm would have challenged the Pantoprazole patents. Instead of the Apotex generic product coming to market in March 2008, there would have been no generic product until the last of the four Nycomed patents expired in 2018.

*...with very thin margins and a potential infringement liability... Presumably, no firm would have challenged the Pantoprazole patents...*

## VENLAFAXINE

Venlafaxine is an antidepressant/anxiolytic used to treat depression, generalized anxiety disorder, social anxiety disorder and panic disorder. Wyeth began marketing and distributing Venlafaxine in Canada in 1994 under the brand name Effexor, and introduced an extended-release version in 1998 under the brand name Effexor XR. Wyeth's principal patent on Effexor XR expired in 2006, but it was granted two other patents in 2005 and 2006, which it listed on the Patent Register. Naturally, it argued that these patents would be infringed if a generic manufacturer began to market a Venlafaxine extended release product in Canada.

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In order to get approval to enter the market, ratiopharm, (now Teva) was in litigation from February 2006 to August 2007. ratiopharm was ultimately successful and received approval on August 2, 2007.

As a result, ratiopharm (sold to Teva in August 2010) was able to sell its generic product, but it did so at risk; Wyeth sued, and asserted that its patents were valid and infringed by Teva. In September 2011, Wyeth discontinued its patent infringement claims. Had the Court found Teva infringed either of these patents, Teva would have had to pay significant damages.

### A TENDERING COUNTERFACTUAL: **VENLAFAXINE**

For this product as for the others, the difficulty of tendering is very apparent. With an infringement suit extending years beyond entry, ratiopharm had to accept very considerable risks after entry, even beyond the risky investment in litigation it absorbed before entry. If the reward for taking on these risks is merely a chance at earning a slim profit, it is hard to see how a generic firm could make a business case for challenging patents or even competing after entry.

In these circumstances, ratiopharm very likely would have decided not to challenge the Venlafaxine patents. Instead of the ratiopharm generic product coming to market in March 2007, there would have been no generic product until the last of the Venlafaxine patents expired in 2017

*In these circumstances, ratiopharm very likely would have decided not to challenge the Venlafaxine patents.*



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## END NOTES

1. Anis A, Harvard S, Marra C. Ontario's plunging price-caps on generics: deeper dives may drown some drugs. *Open Medicine*, 2011; 5(3). <http://www.openmedicine.ca/article/view/454/427>
2. *Apotex v. Sanofi-Aventis*, 2012 FC 553, paragraph 29.
3. We don't know the amounts that were set by the court, but it is clear that Sanofi made substantial additional profits for the period April 2004 – December 2006, even after paying damages, since the amount per unit paid to Apotex was much less than the profits per unit earned by Sanofi.
4. This assumption about Sanofi's costs of production is speculative.
5. The dates on which the last patent on the Register expired were supplied to us by the law firm Hazzard and Hore.
6. A few details on the calculations: The CGPA provided us with data from IMS Health Canada, which collects drug sales data. The data was total sales of the branded products using the CDH Audit for the relevant years. We assumed that the brand would have had the same sales in each year as it actually had during the last full year before generic competition. First and last year savings are scaled according to the number of days in which the generic was on the market. Savings are assumed to be half the total assumed brand revenue, which is probably an underestimate given current pricing of generic drugs. Our goal here is to convey the magnitude of the savings attributable to generic litigation. Precision can be gained by incorporating additional elements that are not considered here.
7. The dates on which generic manufacturers claim they could have entered were supplied to us by the law firm Hazzard and Hore.
8. This isn't a precise estimate and the pricing assumption is of course crude. We are simply trying to deliver an idea of the magnitude of the importance of litigation for payers.
9. A few details on calculations: For the initial year, we scaled the total sales for the year by the number of days of delay. For the final year, we used the penultimate year and then scaled by the number of days delay in the final year. For example: for Amlodipine, we used 2008 sales as a proxy for 2009 sales, and we scaled the number down to reflect that the delay in 2009 was only 189 days. The projected savings are then calculated by adding up total estimated brand sales during the time of delay and multiplying by 50%.
10. Canada's system is relatively unusual; see: Bouchard, Ron A., Daniel R. Cahoy, Bengt Domeij, Graham Dufield, Tom Faunce, Aidan Hollis, Paul Jones, Feroz Ali Khader, Joel Lexchin, Heesob Nam and Juan Luis Serrano, "Structure-Function Analysis of Global Pharmaceutical Linkage Regulations". *Minnesota Journal of Law, Science & Technology* 12(2): 391-457, 2011.
11. See Pharmaceutical Management Agency GP Newsletter, June 2011, available at <http://www.pharmac.govt.nz/2011/06/01/ClinNewsletter.pdf>
12. See Pharmac Consultation 5 April 2011, available at <http://www.pharmac.govt.nz/2011/04/05/2011-04-05%20PHARMAC%20consultation%20on%20proposal%20to%20fund%20generic%20Venlafaxine.pdf>
13. See European Commission, VOLUME 2A Procedures for marketing authorization, CHAPTER 4, Centralised Procedure, April 2006, available at [http://ec.europa.eu/health/files/eudralex/vol-2/a/chap4rev200604\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-2/a/chap4rev200604_en.pdf)
14. The US rules offer the successful generic litigant a 180-day exclusivity period during which no other generics are permitted to enter. This opportunity to become established as the generic supplier, and to enjoy relatively weak competition and high prices for a full half year, can be worth tens or even hundreds of millions of dollars to a successful generic firm. See: Federal Trade Commission, "Authorized Generic Drugs: Short-Term Effects and Long-Term Impact" August 2011, Available at <http://www.ftc.gov/os/2011/08/2011genericdrugreport.pdf>.
15. See: Gagnon Marc-Andre "Drug Shortages: Searching for a Cure". *Healthcare Policy* (2012) 7;4 pp.10-17. (available at: <http://www.longwoods.com/content/22887>) Production in the Sandoz plant slowed for some time as Sandoz attempted to address FDA concerns over its facilities. Then a fire in the plant shut down production for a week, causing substantial havoc for hospitals and their patients.
16. See: Dhalla, Irfan., Karen Born and Jeremy Petch "Medication shortages: how Ontario came to rely on one manufacturer" accessed October 1st, 2012.  
Available at:  
<http://healthydebate.ca/2012/04/topic/politics-of-health-care/medication-shortages-how-ontario-came-to-rely-on-one-manufacturer>
17. According to MacKay (2005), the first drug shortage was resolved when the brand drug company that originally produced the drug stepped in to fill the shortfall. The second incident, which involved a disruption in the supply of a tendered drug produced by the Canadian manufacturer Apotex, was resolved by "Temporarily listing new brands; Using Close Control to ration stock; Sourcing alternative brands through the PHARMAC tender; and Providing advice to clinicians on potential alternatives." See: MacKay P, Is PHARMAC's sole supply tendering policy harming the health of New Zealanders? *J N Z Med Assoc* (2005) 118;1214 Available at: <http://journal.nzma.org.nz/journal/118-1214/1433/>; and the Pharmaceutical Management Agency Annual Report For the year ended 30 June 2010. Available at: <http://www.pharmac.govt.nz/AnnualReport>
18. Pharmaceutical Management Agency, "Sole Supply - it's all about competition" (2009) pp.1 Available at: <http://pharmac.govt.nz/2009/11/19/Inpharmation%20November%202009.pdf>

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## END NOTES

19. See: Douglas, "Prescription products" last accessed Oct 1, 2012, <http://www.douglas.co.nz/prescription-products-a-z/>
20. See: Pacific Pharmaceuticals, "Company Profile" last accessed Oct 1, 2012, [http://www.pacificpharmaceuticals.co.nz/company\\_profile.html](http://www.pacificpharmaceuticals.co.nz/company_profile.html)
21. Kanavos Panos, Liz Seeley, Sotiri Vadoros, "Tender systems for outpatient pharmaceuticals in the European Union: Evidence from the Netherlands, Germany and Belgium" European Commission. (2009) pp. 31. Available at: [http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/study\\_pricing\\_2007/tendering\\_systems\\_en.pdf](http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/study_pricing_2007/tendering_systems_en.pdf)
22. Bretthauer, B., "The generic medicines market in Germany." *Journal of Generic Medicines* (2012) 9;9 pp. 10.
23. Danzon Patricia M., Nuno Sousa Pereira, Sapna S. Tejwani., "Vaccine Supply: A Cross-National Perspective." *Health Affairs* (2005) 24;3 pp.706-717
24. Grootendorst P, Rocchi M, Segal H, An economic analysis of the impact of reductions in generic drug rebates on community pharmacy in Canada. Report for the Competition Bureau, 2008. Available at: [http://individual.utoronto.ca/grootendorst/pdf/Grootendorst\\_et\\_al\\_Pharmacy\\_Rebates\\_Report\\_Final.pdf](http://individual.utoronto.ca/grootendorst/pdf/Grootendorst_et_al_Pharmacy_Rebates_Report_Final.pdf)
25. Law Michael R., Anna Dijkstra, Jay A. Douillard, Steven G. Morgan., "Geographic Accessibility of Community Pharmacies in Ontario." *Healthcare Policy* (2011) 6;3 pp.36.
26. Maynard Micheline. "Did Ending Regulation Help Fliers?" *The New York Times*. 17 April 2008. Available at: [http://www.nytimes.com/2008/04/17/business/17air.html?pagewanted=all&\\_r=0](http://www.nytimes.com/2008/04/17/business/17air.html?pagewanted=all&_r=0). We are not suggesting here that pharmacies would reduce service quality in a way that would harm patient safety, just as deregulated airlines did not reduce their focus on safety. However, patient convenience could suffer if there are fewer pharmacies and pharmacists; there could be fewer pharmacies; shorter times of opening; longer queues; and other services that encourage patients to use one pharmacy rather than another.
27. See: Committee Transcripts: Standing Committee on Social Policy - May 30, 2006 - Bill 102, Transparent Drug System for Patients Act, 2006 for some evidence on the issue. Available at: [http://www.ontla.on.ca/web/committee-proceedings/committee\\_transcripts\\_details.do?locale=en&Date=2006-05-30&ParlCommID=7430&BillID=412&Business=Bill+102%2C+Transparent+Drug+System+for+Patients+Act%2C+2006&DocumentID=20450](http://www.ontla.on.ca/web/committee-proceedings/committee_transcripts_details.do?locale=en&Date=2006-05-30&ParlCommID=7430&BillID=412&Business=Bill+102%2C+Transparent+Drug+System+for+Patients+Act%2C+2006&DocumentID=20450)
28. Ontario Pharmacists' Association., "MedsCheck". Last accessed Oct 1, 2012 <http://www.opatoday.com/index.php/resources/medscheck>
29. Of course, pharmacies could always charge for these services, in the same way that airlines charge passengers to upgrade to business class. The services provided by pharmacists for their patients are so varied that it may be difficult to devise a fee schedule. An annual fee that covers the entire range of services may be more likely.
30. Competition Bureau, Canadian Generic Drug Sector Study, (2007) p. 20. Last accessed Oct 1, 2012. <http://www.competitionbureau.gc.ca/eic/site/cb-bc.nsf/eng/02495.html>
31. The details of litigation for the following cases were provided by the law firm Hazzard and Hore.
32. There is an interesting history around generic Atorvastatin in New Zealand. According to Pharmac, the patent on Lipitor expired in mid-2010, and a generic tender was awarded. Nevertheless, no generic supply was forthcoming, and Pfizer continued to supply the market until August 2012. Dr Reddy started shipping some generic Atorvastatin into the market from February 2012.  
See: Pharmac., "Sole Supply and Removal of the Special Authority (text extract)" last accessed Oct 1, 2012, <http://www.pharmac.govt.nz/2010/06/17/2010-06-04%20Atorvastatin%20notification.pdf/text>; Pharmac text extract for Atorvastatin listing changes, 13 August 2010, last accessed Oct 1 2012 at <http://www.pharmac.govt.nz/2010/08/13/Notification%20of%20Atorvastatin%20listing%20changes.pdf/text>; and Rapley L, 1 February 2012, "Dr Reddy's generic Atorvastatin enters market." *Pharmacy Today*, last accessed Oct 1 2012 at <http://www.pharmacytoday.co.nz/in-print/2012/february-2012/01-february-2012/dr-reddy-s-generic-Atorvastatin-enters-market.aspx>