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AMERICANS ARE AFTER OUR DRUGS AGAIN

Why and what can we do about it?

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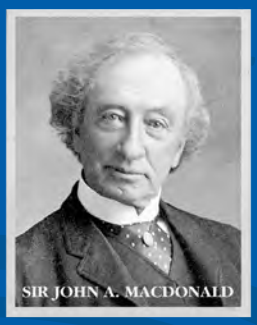
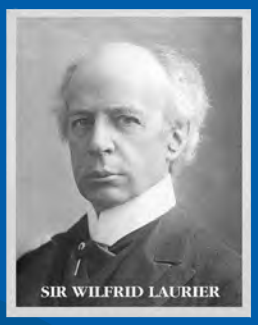
10 MLI
A DECADE OF TRUE NORTH IN CANADIAN PUBLIC POLICY





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Executive Summary

While Canadians have watched with fascination the drama of the American election in recent weeks, a particular issue that could have a serious impact on Canadians' own health and wellbeing has gone largely unnoticed. Championed by President Donald Trump and legislators in a number of states, but also supported by Democrats Bernie Sanders and presidential nominee Joe Biden, an old idea for addressing America's perceived problem of high-priced prescription drugs is back in a big way. During the campaign, Trump promised that new regulations would allow US states to import medicines from Canada, "at a fraction of the price" paid in the US.

The resurgence of this idea has been prompted by drastic increases in the prices of longstanding generics, and from issues around the pricing and profitability of small market, or orphan, drugs. The last time this idea surfaced, the focus was on letting individual Americans buy drugs from Canadian online pharmacies. Today's focus is on plans by individual states to institute large-scale bulk buying from Canadian suppliers, and on moves in Washington, DC, to permit bulk importation nationally.

Given the size of the American market, this sort of move would seriously disrupt the Canadian supply of pharmaceuticals. One widely cited study has estimated that if 20 percent of US prescriptions were filled from Canadian re-imports, the Canadian supply would be exhausted in 155 days. More recent research has found that many individual drugs would run out much sooner.

Drug reimportation will also have little benefit to the US. For example, parallel import of drugs among EU countries (from low-price countries such as Greece and Spain to high-price countries such as Germany and the UK) became a significant issue at about the same time as the possibility first arose between Canada and the United States, around 20 years ago. But the European evidence is that the bulk of the financial benefit from parallel imports accrues to the wholesaler, not to the national health system of the importing country, and especially not to individual consumers in those countries.

In many ways, re-importation as a cure is typical of the American approach to health care issues – a quick fix that engenders a range of collateral problems,

each of which is also thought to be amenable to a quick fix. The sponsors of the various US bills seem to believe that they will be able to legislate away all the obstacles to accessing as many drugs via Canada as the American market might demand.

American politicians who see re-importation as a cure are not looking at the root causes of their pricing problem. They are likely to see any attempt by Canada to block re-exports as decidedly unfriendly. Canadians, therefore, not only have to convince Americans that their proposals would be harmful to us; we also have to explain to them the source of their price problem.

But we can take steps to protect ourselves. The Canadian government should revive a proposal made by then federal minister of health Ujjal Dosanjh when proposals for parallel importation first arose. The Canadian minister of health should be given the authority to block, and indeed should be required to approve, the large-scale export of drugs from Canada. Such a power was included in Canada's emergency COVID legislation but is now expired. A similar permanent measure seems achievable. This could be combined with an extension of the policy, currently in place, that drug companies should notify the federal government of impending drug shortages.

These measures would not stop individual Americans from buying their drugs in Canada nor would it need be an obstacle to Canadian generic manufacturers exporting into the US market.

Canada must not be complacent about our supply of medicines, particularly during the COVID-19 pandemic. Whether we are talking about excessive re-exportation of drugs from Canada or about restrictions on the volume flowing through the supply chain into Canada, we are looking at the risk of serious disruption to the Canadian market. We need to look at making our supply chains more robust, specifically by ending our reliance on just one or two countries for supply. The most straightforward way of tackling geographic dispersal of production in the case of generic drugs might be to form a consortium of countries, all of which commit to maintaining high quality standards and to undertaking the level of inspection necessary to ensure quality.

At its core, the Canadian government needs to make it plain to Americans that re-importation is not a cure for their drug price problems. Canada's argument has to go beyond simply objecting that it will harm Canadians. We have to make it plain to the US that the proposed re-importation policy will not work – for either country.

Sommaire

Au cours des dernières semaines, pendant que les Canadiens suivaient avec fascination la comédie de l'élection américaine, un problème particulier susceptible d'avoir de graves répercussions sur leur santé et leur bien-être est passé sous le radar. Défendue par le président Donald Trump et les législateurs de certains États, mais également soutenue par les démocrates Bernie Sanders et le candidat à la présidentielle Joe Biden, une vieille idée pour résoudre le problème de l'apparent coût élevé des médicaments sur ordonnance a refait surface avec force. Durant la campagne, Trump a promis que de nouvelles réglementations permettraient aux États américains d'importer des médicaments du Canada « à une fraction du prix » payé aux États-Unis.

La résurgence de cette idée s'explique par les augmentations draconiennes du prix des médicaments génériques de longue date et par certains problèmes de prix et de rentabilité liés aux marchés restreints ou orphelins. La dernière fois qu'elle a fait surface, on s'est surtout intéressés à la possibilité que les Américains puissent faire leurs achats dans les pharmacies en ligne canadiennes. Ces derniers temps, l'intérêt a porté plutôt sur les projets d'achats de gros à grande échelle de divers États auprès des fournisseurs canadiens et sur les intentions de Washington, D.C., visant à permettre l'importation de gros à l'échelle nationale.

Compte tenu de la taille du marché américain, ce genre de mesure perturberait gravement l'approvisionnement canadien en produits pharmaceutiques. Selon une étude largement citée, l'approvisionnement canadien serait épuisé en 155 jours si 20 pour cent des ordonnances étaient remplies par les réimportations en provenance du Canada. Des recherches plus récentes ont montré que de nombreux médicaments particuliers seraient épuisés beaucoup plus tôt.

En outre, la réimportation de médicaments ne bénéficiera que très peu aux États-Unis. Les importations parallèles relatives aux médicaments des pays de l'UE (à partir des pays à prix faibles – par exemple la Grèce et l'Espagne – vers les pays à prix élevés – par exemple l'Allemagne et le Royaume-Uni) sont dev-

enues un enjeu important tout comme ce fut le cas lorsque la possibilité s'est présentée pour la première fois entre le Canada et les États-Unis il y a environ 20 ans. Or, les données probantes européennes montrent que les avantages financiers découlant des importations parallèles reviennent aux grossistes, et non pas au système de santé national des pays importateurs, et encore moins aux consommateurs de ces pays.

À bien des égards, la réimportation est typique de l'approche américaine aux problèmes de santé – une solution rapide qui engendre une variété de problèmes collatéraux, chacun de ces derniers pouvant être à son tour réglé rapidement. Les parrains des divers projets de loi américains semblent croire qu'ils pourront légiférer pour éliminer tous les obstacles en matière d'accès à autant de médicaments canadiens que le marché américain risque d'exiger.

> *La réimportation est typique de l'approche américaine aux problèmes de santé.*

Les politiciens américains qui envisagent la réimportation comme solution de rechange ne cherchent pas à cerner les causes profondes de leur problème de prix. Vraisemblablement, ils verront toute tentative du Canada visant à bloquer les réexportations comme un geste résolument hostile. Les Canadiens ne doivent donc pas seulement démontrer aux Américains que leurs propositions leur nuiraient; il faut aussi clarifier la source de leur problème de prix.

Toutefois, le pays peut prendre des mesures pour assurer sa protection. Le gouvernement canadien devrait réexaminer la proposition présentée par Ujjal Dosanjh, ministre fédéral de la Santé lorsque sont apparues les premières propositions relatives aux importations parallèles. En outre, le ministre canadien de la Santé devrait être investi du pouvoir de bloquer et, en fait, être tenu d'approuver l'exportation à grande échelle de médicaments en provenance du Canada. La *Loi sur les mesures d'urgence visant la COVID-19* prévoyait un tel pouvoir, mais ce dernier s'est terminé. Une mesure permanente similaire semble réalisable. Elle pourrait être combinée à un prolongement de la politique, déjà en place, qui demande aux sociétés pharmaceutiques d'informer le gouvernement fédéral sur les pénuries imminentes de médicaments.

Ces mesures n'empêcheraient pas les particuliers américains d'acheter leurs médicaments au Canada ni n'auraient à devenir un obstacle empêchant les

fabricants canadiens de médicaments génériques d'exporter vers le marché américain.

Le Canada se doit de demeurer vigilant quant à son approvisionnement en médicaments, en particulier pendant la pandémie de COVID-19. Que ce soit en matière de réexportations excessives de médicaments provenant du Canada ou de restrictions sur le nombre de produits qui circulent le long de la chaîne d'approvisionnement vers le Canada, il s'agit d'examiner le risque de perturbation grave du marché canadien. Le pays doit chercher à rendre ses chaînes d'approvisionnement plus robustes, tout particulièrement en mettant fin à la dépendance de l'approvisionnement à l'égard d'un ou de deux pays seulement. La formation d'un consortium de pays assurant le maintien de normes élevées de qualité et le niveau d'inspection nécessaire pour garantir la qualité serait le moyen le plus simple de contrer la dispersion géographique de la production de médicaments génériques.

Fondamentalement, le gouvernement canadien doit faire comprendre aux Américains que la réimportation ne permet pas de remédier au problème du prix des médicaments. L'argument du Canada doit aller au-delà de la simple prétention qu'elle nuira aux Canadiens. Nous devons faire comprendre aux Américains que la politique de réimportation proposée ne fonctionnera pas – pour l'un ou l'autre des deux pays.

"For every complex problem there is an answer that is clear, simple, and wrong."

—H.L. Menken

Introduction

Almost missed in the flood of COVID-19 news stories was a late-April 2020 Gallup Poll release on the American public's perception of the cost of prescription drugs. According to Gallup, 35 percent of US adults surveyed believed that prescription drug prices had increased significantly since 2017, 36 percent of adults believed that the Trump administration had not made very much progress on tackling rising drug costs, and 29 percent believed that the administration had made no progress at all.[1] Perhaps most importantly, at least from the perspective of political strategists, was the fact that 30 percent of US adults (and 12 percent of Republicans) ranked a political candidate's position on drug prices as among the most important factors in determining how they would vote in the 2020 elections.

Perceptions, of course, are tricky things. Perceptions of drug price increases are going to depend on things like the type of drugs the respondent takes (generics or brand name), the nature of insurance cover, and the structure of the out-of-pocket price each individual faces. A well insured individual, most of whose prescriptions are for generics, would tend to have a different perception even than that of their employer, who could be expected to be aware of the impact of rising drug prices on the cost of employer-based insurance and of the impact of the cost of insurance on their labour costs of doing business. Still, the view that Americans are paying too much for prescription drugs is widely held and longstanding.

What the US should be doing about drug prices is a matter on which there is no consensus. There seems to be a fair degree of support for the idea that US government drug plans should be given more freedom to negotiate with drug companies over prices, even though most of the proposed bills incorporating such a provision would affect only a small share of prescription drugs. Another idea that has recently resurfaced is to allow Americans, including US states, to buy their drugs from Canada.[2]

History

Re-importation[3] of drugs from Canada as a way of reducing costs to American consumers is an idea that has been around for quite some time. It got considerable attention from the press and politicians about 20 years ago[4] and then died away. It has recently returned in a form that a number of Democratic presidential aspirants adopted, and a version of it has been endorsed by the Trump White House (Associated Press 2019). The obvious questions are why the idea went away and why it is back, what it would do to the Canadian market if it were adopted, whether it really makes sense as a way of tackling the US health care costs, and how Canada should respond to it.

The basic idea behind the various American proposals seems to be that patented drugs sold in Canada, whether produced here or not, are subject to the pricing regulations of the Patented Medicine Prices Review Board (PMPRB) and, importantly, that those regulated prices would continue to apply when the drugs were re-exported to the United States, so their prices would stay at Canadian levels rather than rising to US levels.[5]

The first time re-importation became an issue in the US, the focus was on allowing individual Americans to buy their drugs from Canadian-based Internet pharmacies. The earlier push for importation died away fairly quickly, in part because of opposition from the Food and Drug Administration (FDA), which made the point that just because an Internet drugstore had a Canadian web address didn't mean that it had any physical presence in Canada, and hence wouldn't be subject to any kind of Canadian regulations on drug quality. Another factor might well have been that at the beginning of the previous episode the Canadian dollar was at about US$0.60 – as the loonie appreciated, much of the appeal of Canadian prices faded.

In that first episode, sales of drugs imported from Canada into the US reached an estimated US$700 million by 2003, of which US$408 million was from Internet pharmacies and US$287 million was from foot traffic sales (HHS Task Force on Drug Reimportation 2004). Sales levelled off in 2002-2003 then dropped rapidly – in 2005 they were down to US$420 million and US$211 million in 2006. Canadian online pharmacies were reported to have made sales worth US$121 million in the first quarter of 2005, but by the fourth quarter of 2006 their sales were down to US$40 million.[6]

To some degree the decline in re-exportation from Canada was illusory. According to Industry Canada trade data,[7] while Canada's overall deficit in pharmaceutical trade has been growing pretty steadily since the 1990s, our trade with the US moved from deficit in the 1990s into surplus in the 2000s, and re-exports[8] rose from accounting for less than 1 percent of our exports to the US by value in the 1990s to being over 10 percent today. Apparently, the decline in re-exportation by online pharmacies was only part of the story.

The resurgence among American politicians of the idea of re-importation caught Canadians by surprise. The general sense in Canadian policy circles had been that interest in the policy had died away at about the same time as re-exportation from Canada seemed to have died away. In any event, the fact that leading American politicians from both parties are again touting re-importation as a cure for the US drug price problem is something that has to concern Canadians. We should also be concerned by the fact that those same US politicians are ignoring our concerns.

The current episode

This time the focus is on plans by individual states to institute large-scale bulk buying from Canadian suppliers, and on moves in Washington, DC to permit bulk re-importation nationally. Not surprisingly, possible implications of the recent US proposals for the Canadian market have caught Canadian attention. The United States has a population almost ten times Canada's – California alone is more populous than Canada, and Texas and Florida are not far behind Canada in numbers.[9] One widely cited study (Shepherd 2010) estimated that if 20 percent of US prescriptions were filled from Canadian re-imports, the Canadian supply would be exhausted in 155 days. Shepherd (2018) found a similar impact in a recent update of the earlier study and Skinner (2019) has recently looked in more detail at how quickly Canadian supplies of individual drugs would be exhausted, concluding that many would be exhausted much sooner than Shepherd's broad figure suggests.

Among state-level initiatives, Florida's probably caught Canada's attention first. It involves the state taking advantage of the fact that in 2003 the US Secretary of Health and Human Services (HHS) was given the authority to approve large-scale importation from Canadian wholesalers who satisfied certain criteria, even though to date, no Secretary of HHS has certified any suppliers.[10]

Florida's state law[11] requires the state to enter into a contract with a Canadian wholesaler to supply drugs that the state would identify as particularly high cost to a specified wholesaler in Florida. While it would presumably be easier to monitor a single wholesaler than to monitor a whole slew of Internet pharmacies, Florida's law still requires the cooperation of HHS and the FDA. Its proponents say that it will use FDA-registered wholesalers and follow a reliable supply chain, but this still amounts to assuming that the FDA is in a position to certify that supply chain.

From the Canadian perspective, the more ominous proposal has come from the White House. The Trump administration proposal involves using its existing authority to authorize "demonstration projects" of importation from Can-

ada. States, wholesalers, and pharmacists would be able to propose projects explaining how they would import Health Canada-approved drugs that are in compliance with the US *Food, Drug and Cosmetic Act* (FD&C).

Under what is termed Pathway One of the administration's proposal:

> drugs eligible for importation must be drugs authorized for sale in Canada that are versions of FDA-approved prescription drugs. Specifically, such drugs would be eligible for importation if they contain only active pharmaceutical ingredients (API) manufactured at facilities that also manufacture API for the FDA-approved version, and if they are formulated using processes, specifications, and facilities that are used in accordance with the approved new drug application for the FDA-approved version. The NPRM would require attestation and supporting documentation regarding the authenticity and eligibility of a drug. (US Food and Drug Administration undated)

Further, applicants would be required to show that the drugs meet all of the FDA's labelling requirements and demonstrate how they will trace the drugs from manufacture to pharmacy, how they will ensure that the foreign sellers are properly registered, how they will satisfy importation entry requirements for drugs, and how they will handle adverse event reporting for the imported drugs. In addition, applicants would have to be able to demonstrate that their proposal would result in a significant reduction in the cost of drugs to Americans.

A second pathway in the administration's proposal would extend beyond re-importation from Canada and allow manufacturers of FDA-approved drugs to import into the US the versions of these drugs that they sell in other countries. "To use this pathway, the manufacturer or person authorized by the manufacturer would need to establish with FDA that the foreign version is the same as the US version (such as through manufacturing records)" (US Food and Drug Administration undated). The White House's proposal, then, puts the onus on the state or the manufacturer[12] to establish that the drugs they are proposing to import are not counterfeit or adulterated and satisfy FDA conditions for sale in the US.

The most detailed American proposal seems to have been that put forward by Senator Bernie Sanders, who at one time was among the leading contenders to be the Democratic presidential nominee in 2020 and whose ideas still resonate strongly with a significant segment of the American population. In 2017 Sen. Sanders proposed legislation (S.469) to amend the FD&C act "to allow for the importation of affordable and safe drugs by wholesale distributors, pharmacies, and individuals" (*Affordable and Safe Prescription Drug Importation Act*, S. 97).

The proposed legislation stated that legally imported drugs would have to be purchased from an FDA-certified foreign seller and have the same active ingredient, the same route of administration, and the same strength as drugs approved in the US. It would also have prohibited a manufacturer to, "except with respect to a prescription drug on the drug shortage list under section 506E, discriminate by denying restricting, or delaying supplies of a prescription drug to a certified foreign seller, on account of such a seller's status as a certified foreign seller, that sells such a drug to an importer in accordance with this section, or by publicly, privately or otherwise refusing to do business with such a foreign seller on account of such seller's status as a certified foreign seller" (*Affordable and Safe Prescription Drug Importation Act*, S. 97). In other words, it would be illegal for a manufacturer to refuse to supply a Canadian wholesaler simply because that wholesaler was known to be re-exporting drugs from Canada to the USA.[13]

> *"The most detailed American proposal seems to have been that put forward by Senator Bernie Sanders.*

Sen. Sanders' proposal[14] went into considerable detail in how it plans to block measures that drug companies might take to discourage re-importation. It specifies, for example, that it would be unlawful for a drug manufacturer to charge "a higher price for a prescription drug sold to a certified foreign seller that sells such a drug to an importer in accordance with this section than the price that is charged, inclusive of rebates or other incentives to the country from which the drug is exported, to another person that is in the same country and that does not import such a drug into the United States in accordance with this section" (*Affordable and Safe Prescription Drug Importation Act*, S. 97).

And, interestingly, under the Sanders bill, it would be unlawful to "cause there to be a difference (including a difference in active ingredient, route of administration, bioequivalence, strength, formulation, manufacturing establishment, manufacturing process, or person that manufactures the drug) between a prescription drug for distribution in the United States and the drug for distribution in Canada or another permitted country, subject to subsection (e), for the purpose of avoiding sales by certified foreign sellers" (*Affordable and Safe Prescription Drug Importation Act*, S. 97). Whether any of this would be effective depends on such things as: how would one prove that a difference in strength, formulation, or manufacturing establishment between the version of a prescription drug intended for distribution in the

US and that intended for distribution in Canada was indeed for purposes of avoiding sales into the US.

The Sanders proposal went into considerably more detail than do the Florida or the White House proposals. Florida's approach basically punts the more difficult problems to the federal department of Health and Human Services to deal with[15] and the White House's proposal, while on the surface directing HHS to support demonstration projects of proposals such as Florida's, basically (judging from the FDA release) puts the onus on the proposer of the demonstration project to show how it would satisfy the regulatory requirements that are already in place.

While Sen. Sanders is no longer in the running for the Presidency, the fact that both the Trump and Biden[16] campaigns favour importation strongly suggests that Canadian policy-makers should be trying to get ahead of the issue.

The European experience

The amount of detail that Sen. Sanders' proposed legislation included about what drug companies would not be permitted to do seems to have been inspired by consideration of the European Union's (EU) experience with re-exportation among its member nations, and with drug companies' responses to it.

Under EU law, a manufacturer loses any claim over its product the first time it is sold anywhere in the EU. That means that as soon as a drug is sold to a wholesaler in any EU country, that wholesaler is free to re-sell it into any other EU country. Parallel import of drugs among EU countries became a significant issue at about the same time, or a bit before, as the possibility first arose between Canada and the United States. However, by the nature of the single market and because of the attitude of various EU member country governments, the issue did not die down as it did in North America.

A number of countries, most notably Greece and Spain, use price control regulation to keep the price of drugs low.[17] This has made them natural sources of supply for higher-price EU countries, notably Germany, Sweden, and the UK.[18] In 2003, parallel imports accounted for 17 percent of the UK market and 10 percent of the Swedish market (Scheuermann 2006). In 2001, when parallel imports accounted for 9 percent of the Swedish market and 5 percent of the German market, just under 25 percent of Greek drugs were parallel exports to other EU countries. Clearly this is the kind of situation that Canadian policy-makers fear will arise here under the various American proposals.

The strategies that drug companies have implemented in Europe to discourage parallel trade would almost certainly be under consideration here. Drugs, even when manufactured by the same firm for sale in the two countries, will not necessarily be in the same form (pill, capsule, caplet, etc.) in the two countries, nor will one physical unit (one pill, for example) necessarily contain the same dosage of the active ingredient in the two countries. There can be a range of reasons for this, often coming down to what the local regulators were willing (or asked) to approve, but drugs that are being parallel imported must be basically identical across the two countries. It must never be the case that the dosage a patient takes depends on where the latest box of pills that patient bought happened to be produced.

> *Parallel trade flourishes only to the extent that it is profitable for wholesalers.*

One possible option for drug manufacturers would be for the Canadian market to be supplied in the presentations (referring to the form of the medicine delivered)[19] and from the production plants (since production sites would have to be approved by each country) that supply some of the European countries. The US market, which is probably large enough to support separate production runs, would then be supplied from a separate site. It would be costly for brand-name drug companies to switch presentations of existing drugs, especially ones that were nearing the end of their period of market exclusivity (i.e., the period when the drug is protected from generic competition) in Canada, but it is an approach that could be introduced for new drugs.[20]

A second approach that drug companies have adopted in Europe has been dual pricing, that is, invoicing wholesalers different prices depending on where the wholesalers will be selling the drugs. In Spain, for example, the practice was to invoice wholesalers for drugs that were to be sold in Spain on the basis of Spanish government drug pricing regulations, and to invoice those same wholesalers at a higher price if those drugs were to be sold outside Spain. In cases where the manufacturer suspected, but was not able to prove, that the drugs were to be sold outside Spain, the entire shipment was invoiced at the export price, and it was up to the wholesaler to prove that they had been sold within Spain, in which case they would receive a rebate from the manufacturer.

The European Union's experience of parallel trade has been quite extensively studied[21] and, besides being instructive about the range of possible producer responses to such a policy, is instructive for what it tells us about who gains from this sort of policy. Clearly the original manufacturers of pharmaceuticals are not going to engage in parallel trade. In the drug sector, parallel trade is done by wholesalers and, as the experience of the European Union shows clearly, wholesalers are profit maximizers and will price accordingly.

The bulk of the literature (Kanavos and Costa-Font 2005, Vandoros and Kanavos 2014) indicates that parallel traders price their drugs below the domestic price in the importing country, but well above the price in the country in which they were purchased. The price in the importing country is set at a level that gives the government of a high-price country an incentive to defend the practice, but no lower than that.

The European evidence, then, is that the bulk of the financial benefit from parallel trade accrues to the wholesaler, not to the national health system of the importing country, and especially not to individual consumers in those countries (since the importing countries have universal drug insurance and patients only pay a co-pay amount, which is at best very loosely related to the price of the drug). It is true that the national health systems in the importing countries do benefit from parallel trade, but parallel trade flourishes only to the extent that it is profitable for wholesalers.

There is no reason to believe that Canadian wholesalers would be intrinsically any less profit oriented in their dealing with the US than Spanish wholesalers are in their dealings with Sweden.[22]

What prompted the revival?

So, what prompted the revival of the idea of Americans re-importing cheap drugs from Canada? It didn't come out of a clear sky – it was almost certainly prompted by recent concerns by some in the US over high drug prices. We can assign many of these concerns to two broad categories, neither of which can be tackled by re-importation. The first of these involves drastic increases in the prices of longstanding generics, and the second arises from issues around the pricing and profitability of small market, or orphan, drugs.

Generic drugs

The initial trigger for the revival of interest in re-importation probably lay in the generics market, particularly the case of Martin Shkreli of Turing Pharmaceuticals, and the drug Daraprim (Pyrimethamine), the price of which was increased, after its acquisition by Turing, from US$13.50 to US$750.00 a pill.

This was not the first drastic price increase for a generic drug, but the sheer magnitude of the increase caught headlines. Much of the news coverage was unhelpful to anyone wanting to understand the cause of high US drug prices, fostering the impression that the increase was simply an addition to the list of sins of Big Pharma. In fact, the economic structure underlying the Daraprim case was different in many key ways from that of Big Pharma.

Daraprim, which had originally been approved by the FDA in the 1950s, was long off patent. The key to the price increase was that the market for Daraprim in the US was small (the drug is used in the treatment of HIV/AIDS), so there had been no incentive for many generic manufacturers to enter the market when the original patent expired. In addition, the process of gaining FDA approval for a new generic competitor is expensive and time consuming, so that even if a generic producer decided to enter the market Turing would still have had a monopoly for about four years according to some estimates. This barrier to entry applied not only to new American producers but also to producers supplying Daraprim to other markets. In the UK, GlaxoSmith-Klein (GSK) was supplying pyrimethamine (Daraprim) at a price of roughly US$0.66 a tablet, but GSK's product could not be imported into the US (it could be imported into Canada at a price of US$2.20 a tablet).

> *"The Daraprim episode, then, was an example of a producer taking advantage of a monopoly situation.*

The Daraprim episode, then, was an example of a producer taking advantage of a monopoly situation to convert what economists term "consumer surplus" – the value that consumers derive from a product in excess of the price they pay for it – into what is called "producer surplus." In simpler terms, Turing Pharmaceuticals spotted a situation in which a monopoly existed but was not being exploited to its full potential and took advantage of it. Turing seems to have assumed that the profit generated by raising the price to its monopoly level would attract competition. At the price Turing set, the barriers that had previously kept competitors out would be irrelevant.

Turing was by no means the only firm that recognized an under-exploited monopoly situation. At the time, it shared the headlines, most notably, with Canadian-based Valeant Pharmaceuticals. Valeant's business plan, at the time, was essentially Turing's writ large. Valeant made a policy of buying up firms that had under-exploited monopolies and raising the prices of their products. Some defenders of Valeant argued that the price increases were necessary to

fund research into new drugs. This argument assumed that Valeant was part of the research-based drug sector, whose research is funded out of profits earned on current drugs. It was weakened by the perception that Valeant's first move on acquiring any drug company that did engage in research was to eliminate its research division.[23]

These are by no means the only cases in which generic drug pricing changes have prompted public ire in the US. The case of Mylan's pricing strategy after it acquired US rights to the EpiPen autoinjector for epinephrine made headlines at roughly the same time.[24] When Mylan acquired the US rights to the EpiPen from Merck, the device was priced (in 2007) at about US$100; by 2016 it was priced at about US$600. The price in Canada, where it is distributed by Pfizer, remained at about $100. In this case, it is worth noting that the drug itself is a generic – market exclusivity relates to the autoinjector, which is critical to the self-administration of the drug in emergency situations. Mylan has also launched what is often referred to in the press as a generic version of its own product, which it priced at US$300 – when Teva pharmaceuticals obtained FDA approval for its own version of the EpiPen it priced it, in classic duopoly fashion, at about US$300.

> *Drugs have always been commodities, supplied by commercial enterprises in markets.*

Much of the anger that has been directed at firms that have raised prices in the market for generic drugs arises out of a failure to understand the economics of the generic drug market, which engenders a sense that the drug companies are somehow not playing by the rules. Commentators sometimes refer to suppliers coming to treat drugs as commodities, with the implication that this is somehow new. To be clear, drugs have always been commodities, supplied by commercial enterprises in markets that differ from the markets for other commodities primarily because of the combination of insurance and very particular government regulation.

The common perception has been that generic drugs would intrinsically be cheaper than brand name drugs because generic manufacturers do not have to put their products through the full range of clinical trials that the brand name originals went through.[26] This definitely reduces the fixed cost of supplying the drug to market and therefore reduces the minimum price that would have to be charged per pill for the drug to cover its costs, fixed and variable. But, above that minimum cost-covering level, the price that is

actually charged will depend on the conditions in the market, specifically the elasticity of demand for the product as a category, and the number of generic firms supplying that market.

The fundamental problem in the generics market is the steady decline in the degree of competition in the generics sector, exacerbated by national restrictions on imports. This is an issue that Canada is also facing and which could be tackled by international agreements and increased freedom of trade.

Orphan drugs

The second group of drugs that has been making pricing headlines in the US is what is generally referred to as orphan drugs. The definition of an orphan drug, if indeed there is one, varies from country to country, but the basic idea is that it refers to a drug that can treat a condition the number of sufferers of which is too small to make the drug commercially viable. This is especially the case given that small-market drugs would normally have to go through the same process of clinical trials as would a large-market drug, with a smaller market over which to spread those research costs once the drug reaches the market.

In the US, the *Orphan Drug Act* of 1983 was aimed at encouraging research into drugs that would treat conditions faced by small populations of patients, specifically, those afflicting fewer than 200,000 Americans. The act created special categories and support for things like clinical trial regulations for drugs that were granted orphan status – tax credits equal to half of the development costs of the drug, for example. The most important of these incentives is probably the grant of seven years market exclusivity, beginning at the point of FDA marketing approval and continuing to apply even if the drug goes off patent. The act also sets a high hurdle for the entry of potential competitors – as Cheung et al. (2004) put it, the intent is to create a monopoly for firms considering doing research into drugs for small market diseases. The idea is that the monopoly pricing power which would go along with the period of exclusivity would outweigh the small size of the market when brand-name drug companies were weighing up where to focus their research.

In one sense, the *Orphan Drug Act* has been extremely successful; the number of drugs under development that have been granted orphan status has grown steadily over time. The issue here is whether too many drugs have been granted orphan status with the associated monopoly pricing power. There is a growing sense (Danzon 2018, Herder 2016) that a remarkable number of orphan drugs have turned out to be financial blockbusters, which probably should not have been possible, even under monopoly pricing, giving the presumed size of the market. There seem to have been cases in which the same drug has been granted orphan status for a number of different conditions, suggesting that producers were finding ways to game the wording of the reg-

ulations. There has been a suggestion that this seems particularly to be the case for cancer drugs, where there is a growing sense that cancer diagnoses can be sliced thinly, perhaps by relying on genetic subtypes that are not in fact relevant to the function of the drug. The suggestion is that once a genetic element has been accepted as part of the definition of the disease, it becomes possible to define disease subgroups as different small populations, each of which is amenable to treatment by the same drug.[27]

Even if we assume that there is no gaming going on, the grant of monopoly position beyond that which a new drug would normally receive will translate into monopoly pricing.[28] To the extent that prices are higher and exclusivity is extended, the success of the *Orphan Drug Act* could well ratchet US drug prices upward in the long-run.

The FDA is in a delicate position as far as orphan drugs are concerned. On the one hand it is clearly desirable to encourage research into small-market drugs, especially when a small market can amount to 200,000 people. It is also in the interest of patient populations in other, smaller countries like Canada to have the US supporting research into orphan diseases – it is unlikely that the Canadian government could devise incentives sufficient to encourage research into drugs aimed at Canadian-sized small markets.[29] But if it does prove to be the case that orphan status is being granted on the basis of subdividing disease populations according to factors that make no difference to the effectiveness of a drug as a treatment for the disease population as a whole, the long-run effects of the *Orphan Drug Act* might prove to be undesirable – contributing to increased unproductive monopolization[30] and higher drug prices.

Possible Canadian solutions

In many ways, re-importation as a cure is absolutely typical of the American approach to health care issues – a quick fix that engenders a range of collateral problems, each of which is also thought to be amenable to a quick fix. The only real difference between this legislation and earlier US legislation is that this time some of the undesired consequences have been thought of in advance. There remains the assumption that these consequences can be dealt with by a few lines of legislation.[31] What this legislation does not do is tackle the realities of the US drug price problem.

Take Canadian concerns about the exhaustion of our supplies of drugs. Many American supporters of re-importation do not see this as a legitimate concern because they assume that Canadian wholesalers could simply re-stock by increasing their orders from the producers of the drugs. The assumption that Canadian wholesalers would be able to restock without limit assumes, of course, that the producing companies would fulfil those orders. Again, Amer-

ican politicians seem to believe that they have covered that eventuality when their proposed bills specify that should a producer restrict supply to Canadian wholesalers (typically they would restrict it to a quantity normally just sufficient to satisfy the Canadian market) the producer would be deemed to be acting in restraint of trade in the US and in violation of anti-trust laws. Thus, the sponsors of the US bills believe that they will be able to legislate away all of the obstacles to accessing as many drugs via Canada as the American market might demand.

This leaves Canadian policy-makers in an awkward position. American politicians who see re-importation as a cure for their problems are not looking at the root causes of their pricing problem and believe that the only problem their proposals could cause for Canadians – exhaustion of supply – has been neutralized. As a result, they are likely to see any attempt by Canada to block re-exports as decidedly unfriendly. Canadians, therefore, not only have to convince Americans that their proposals would be harmful to us; we also have to explain to them the source of their price problem.

> *"Re-importation as a cure is absolutely typical of the American approach to health care issues.*

Clearly, at this point, we need to give some attention to possible solutions, including things that Canada should do as well as policies that the US should consider which would be more likely than re-importation to be effective cures.

Considering the problem from a purely Canadian perspective, the Canadian government should pull out of whichever filing cabinet drawer it languishes in the legislation that was proposed by then federal minister of health Ujjal Dosanjh back when proposals for parallel importation first arose.

Dosanjh as Minister of Health took the re-importation issue very seriously:[32] Krauss (2005) quotes him as saying that "Canada cannot be the drugstore of the United States of America." Ultimately, nothing came of his efforts but the issue has once again arisen since then. In 2006, Carolyn Bennett, then an opposition MP and today Minister of Crown-Indigenous Relations, introduced a Private Member's bill on the same topic.[33] That bill did not become law, but in March of 2020, Part 9 of Bill C-13, Canada's COVID-19 emergency legislation, included a provision (Subsection 33(3)) to the effect that "the Governor in Council may make any regulations that the Governor in Council considers

necessary for the purpose of preventing shortages of therapeutic products in Canada or alleviating those shortages or their effects, in order to protect human health" (see *COVID-19 Emergency Response Act*). This authorization appears to have expired, automatically, on October 1, 2020, when Subsection 33(4) of the emergency response act came into effect. Subsection 33(4) simply states "Subsection 30(1.4) of the Act is repealed," and Section 35 says that the 33(4) comes into effect October 1, 2020.

It is clearly not beyond the bounds of reason to suggest that a similar, more targeted measure could be implemented on a more permanent basis. The government should announce that it will initiate a process, based on the Dosanjh proposal, of identifying shortages which will emerge as a result of re-exportation, and granting the minister the power to suspend exports for some period of time as necessary.

The Canadian minister of health should be given the authority to block, and indeed should be required to approve, the large-scale export of drugs from Canada.[34] This would not need to prevent individual Americans from buying their drugs in Canada nor would it need to be an obstacle to Canadian generic manufacturers exporting into the US market since a mechanism could be developed to give them routine approval.

It is worth remembering that earlier proposals for parallel imports into the US had a strong base of support in Canada mainly among the companies that expected to be doing the exporting. Brand name drug companies opposed the proposals and threats by manufacturers to cut off supplies to exporting firms probably helped dampen the enthusiasm for the idea.

It needs to be made clear that this is not simply an issue of trade protectionism. The estimates that suggest Canadian supplies (meaning the supplies that would otherwise be available for Canadian patients to buy) would be wiped out in about six months should be seen primarily as stark illustrations of the difference in size between the two markets (and probably should be taken more seriously by Americans than by Canadians, since they really serve to emphasize the point that importation from Canada is not a serious solution to a serious home-grown American problem). But there is no doubt that large-scale institutional imports into the US from Canada, while being profitable for the wholesalers involved, would seriously disrupt Canadian supply chains.[35]

One issue that might arise if this option were to be invoked might be Canada's obligations under international trade agreements. Article XI of the General Agreement on Tariffs and Trade (GATT) generally forbids the imposition of quantitative restrictions on trade, exports as well as imports. However, the same article specifies that:

> The provisions of paragraph 1 of this Article shall not extend to the following:
> (a) Export prohibitions or restrictions temporarily applied to prevent or relieve critical shortages of foodstuffs or other products essential to the exporting contracting party. (World Trade Organization Undated)

Since the type of pharmaceuticals involved in this case are clearly essential and the measure would be intended to prevent a critical shortage, a revival of the Dosanjh proposal seems to fall under this provision.

Canada (and the US) should learn from the EU experience that the financial benefit of this kind of trade goes primarily to the wholesalers. While no one should object, on principle, to wholesalers making a profit, the experience of Greece and Spain suggests that the cost to the Canadian population would be significant.

Drug companies have a definite interest in maintaining the separation between the Canadian and US markets.

It is fairly certain that a revival of the Dosanjh proposal to give the minister of health the authority to prohibit exports would be well received by drug companies. However, their support would really be in gratitude for the political cover Canadian legislation would give them.

Drug companies have a definite interest in maintaining the separation between the Canadian and US markets. The ability to price discriminate is remunerative, especially at the level of the prices of many US drugs. While it is undoubtedly true that current revenues finance future drug development, this fact does not of itself mean that US drug prices are optimal. Drug development is a risky business, but it is also a profitable one. It should not be taken for granted, even by the most market-oriented economists, that the current balance is optimal.

The proposed US legislation focuses directly on brand name drug companies as the ones most likely to be the primary obstacles to US parallel importation. Passage of revived Canadian legislation would allow the drug companies to say that, while they would love to comply with American wishes, Canadian law prohibits their so doing. That has the potential of shifting the focus of American ire from drug companies to the Canadian government, and would do so regardless of who wins the 2020 presidential election since the leading

candidates from both parties support re-importation. Hence the need for a Canadian government to be politically courageous by reviving (as it should) the Dosanjh legislation or by using the COVID-19 emergency legislation as a starting point for policy development.

Revival of the earlier legislation would basically be a defensive move on Canada's part and would not do anything to resolve the more fundamental, underlying pharmaceutical policy issue that both countries face.

Policy options

Canadians tend to regard the problem of high prescription drug prices as a peculiarly American one. We should not allow ourselves to become complacent. In recent years, shortages of fundamental generic drugs have become increasingly pressing in Canada, although the nature of the drugs involved – specialty drugs for cancer treatment, for example – has militated against it becoming the same kind of major political issue as has the issue of drug prices in the US. One consequence of the COVID-19 pandemic has been to draw attention to the reliability of supply chains for essential commodities, including drugs. Our ultimate reliance on a very small number of suppliers of the ingredients for essential medications became quite clear when certain countries moved to restrict their export in order to ensure that their own populations were well supplied.

Whether we are talking about excessive re-exportation of drugs from Canada or about restrictions on the volume flowing through the supply chain that brings the drugs into Canada in the first place, we are looking at the risk of serious disruption to the Canadian market. Some commentators have suggested that we should be looking at options for domestic production of the drugs we need, but for a great many of those drugs, for which our domestic market is relatively small, autarkic production of the quantities we need would jack our own drug costs up to unreasonable levels.

Looking at the options open to us, it seems clear that the Dosanjh proposal needs to be revived and retained even after the COVID-19 emergency ends. This is not because it is some kind of a first-best solution to the issue of excessive re-exportation, but because it should be available as a last resort. It could be combined with an extension of the policy, currently in place, that drug companies should notify the federal government of impending drug shortages so that, should there be the risk of a shortage of an essential drug due to demands from other countries, quantitative export restrictions could be imposed.

From a broader perspective, though, the COVID-19 pandemic has shown that

when the primary supplier of an essential ingredient imposes quantitative export restrictions, while it might be beneficial for that country in the short-run, the world-wide implications are negative. COVID-19 has shown us that we need to look at making our supply chains more robust, not only for drugs but for a range of essential commodities.

The most important element of that policy would involve ensuring that there is a much greater geographic dispersal of the sources of essential items. Instead of relying on one or two countries, so that the world supply of key drugs will be interrupted the next time an epidemic or an untreatable new disease arises, production facilities should be dispersed in the hope that some will remain open even if others are forced to close for some period of time. A geographic dispersal of production would mean losing the cost advantages of economies of scale that arise from more concentrated production, which will in turn raise everybody's drug prices, but the COVID-19 episode suggests that it's probably worth paying higher everyday drug prices in order to guarantee the resiliency of supply.

"Production facilities should be dispersed in the hope that some will remain open even if others are forced to close.

The most straightforward way of tackling geographic dispersal of production in the case of generic drugs might be to form a consortium of countries, all of which commit to maintaining high quality standards and to undertaking the level of inspection necessary to ensure quality. They would agree to accept each other's inspections as equivalent to their own and open their markets to supplies from other member countries, and would also agree not to impose unbalanced quantitative export restrictions in the case of their suddenly becoming the world's primary supplier of a particular drug. This sort of agreement could be implemented relatively quickly in the case of traditional small molecule generic drugs and could be extended over time to biosimilars – the counterparts of generics for the new drug category of biologicals.

Issues are more complicated for orphan drugs. On the one hand, incentives for the development of orphan drugs in the US seem to have been very successful, although as a number of analysts have noted there is concern that what has really been happening has been that drug companies have become adept at gaming the regulatory system – at finding ways of obtaining orphan

status for drugs that would in fact have large markets. The criticism attached to the announcement that Gilead Pharmaceuticals had applied for orphan status for Remdesivir (an application that was withdrawn by Gilead almost as soon as it was granted (Mahase 2020)) can probably be taken as an indication that orphan status will be scrutinized more closely in the future.

This is an area that could prove extremely damaging to Canada. A drug with a very small market in the US will have a much smaller market in Canada. If the PMPRB puts a tight cap on the price of such a drug, and if the US were to proceed with any of the proposals for drug re-importation, the obvious remedy for a drug company to adopt would simply be not to release the drug in Canada at all. While Canada cannot play a direct role in resolving the issue of whether the US orphan drug system is open to gaming, we certainly have enough of an interest in the matter that collaboration with the US on broad issues related to defining and regulating orphan drugs would be to our benefit.

> *A drug with a very small market in the US will have a much smaller market in Canada.*

There are other measures that Canada could take. Since the various proposed US plans require that any drugs re-imported from Canada be of a dose and in a presentation already approved by the FDA for American use, it would presumably be feasible for Canada to indicate that, if the drug were being made available in some European countries in a different presentation – caplet rather than pill, for example – we would prefer to use that form in Canada. The American market is generally large enough to support its own production runs and while our market probably isn't, it might be feasible to combine our production runs with other countries. The Sanders proposal specified that anti-trust action would be taken against any company that changed the delivery form of a medication with an eye to getting out from under the legislation; differentiating it at the behest of the Canadian government would, one hopes, be a different matter. On the other hand, such a change could be very inconvenient for Canadians who spend a lot of time in the US.

Overall, though, it must be acknowledged that, beyond the blunt instrument of quantitative export restrictions, Canada's options are limited. Passage of such legislation might best be seen as a device to catch American attention.[36] Ultimately our best hope is to try and convince the US that its problems are home grown and that they need to be addressed at home.

Taken as a whole, the US importation proposals would do very little to tackle the problem of American drug prices and would almost certainly cause significant disruption to Canadian drug supplies. It would be nice to think that the US proposals are designed solely for domestic political consumption and are not intended actually to be implemented, but that seems less and less likely.

Disruptions to the Canadian market could take a number of forms as drug companies respond to the particulars of whichever piece of legislation might be implemented. While reducing revenue from Canadian sales, delaying the release of new drugs in Canada would probably be acceptable to the drug companies if it prevented a much larger loss of American revenue. The various mechanisms that have been adopted in the EU would probably be seen here, adapted to the wording of US laws.

We could expect to see manufacturers moving to take more control of their distribution chains as they have in Europe. In Greece, for example, manufacturers basically set up their own wholesalers. While this would be a costly change to the industry structure, it would probably be seen as a cost worth bearing. Whether or not Canadian drug supplies were actually exhausted, we could expect to see significant disruption as manufacturers adopted defensive measures.

The Canadian government basically needs to make plain to Americans in general that re-importation is not a cure for their drug price problems. Canada's argument has to go beyond simply objecting that it will harm Canadians. We have to make it plain to the US that the proposed re-importation policy will not work. Doing so would require Canada to take the lead; too many Americans are convinced that because re-importation works for individuals, it will work for the country as a whole.

This is a delicate matter since, at present, launching the argument would amount to intervening in a US presidential election, but at the very least it could be done after November 2020, regardless of who takes the White House. Americans and their leaders need to be told in no uncertain terms that the proposed reimportation schemes would do next to nothing to address pricing issues in the US, create numerous issues for drug safety and drug supply chains, and could have serious negative consequences for the Canadian drug supply. Instead of trying to free-ride on our price control system, they should face up to the long and hard task of first trying to understand and then address the real issues affecting their own pricing system.

About the author

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Endnotes

1 While the result of the question about perception of price increases was reported by political affiliation – 45 percent of Democrats thought prices had increased a lot as compared to 22 percent of Republicans – the question about the performance of the Trump administration was not reported by affiliation.

2 According to a poll conducted by the Kaiser Family Foundation in October of 2019, 78 percent of Americans favoured "allowing Americans to buy drugs imported from licensed Canadian pharmacies." Broken down by political party affiliation, the proposal was favoured by 75 percent of Democrats, 75 percent of Republicans and 82 percent of Independents. See https://www.kff.org/medicare/issue-brief/10-faqs-on-prescription-drug-importation/.

3 In the academic economics literature this policy is generally referred to as "parallel trade." From the Canadian perspective, since most of the drugs involved are imported into Canada, the term re-exportation is apt. The American literature tends to use the term re-importation, which, strictly speaking, refers to drugs originally manufactured in the US and exported to Canada. See Bhosle and Balkrishnan (2007).

4 For a sense of the state of play at the time, see Gokcekus et al. (2006) and the references therein.

5 The US government's attitude to Canadian price controls is not consistent. While the White House has come out in favour of the importation of drugs from Canada as a cost-cutting measure, the Office of the US Trade Representative, in its April 2019 *Special 301 Report* dealing with whether US owners of intellectual property (IP) have "a full and fair opportunity to use and profit from their IP around the globe" Canada was placed on a Watch List because of concern about proposed changes to the Patent Medicine Price Review Board's procedures. According to the 2019 report, the United states urges Canada to "contribute fairly to re-

search and development for innovative treatments and cures." This sort of comment from the US is usually taken as a criticism of low Canadian drug prices.

6 FDANEWS Daily Drug Bulletin release, April 4, 2007, based on IMS Health Data. See https://www.fdanews.com/articles/91684-canada-s-internet-sales-to-the-u-s-fall-by-half. FDANEWS is not a publication of the FDA.

7 Obtained from Canada (2020).

8 Industry Canada defines re-exports as goods which had previously been imported into Canada and are leaving in the same condition as when first imported, or after having been minimally re-processed but not substantially enhanced in value.

9 As of 2020 the US has a population of 321.2 million compared to Canada's 35.8 million. California's population is 39.7 million, Texas 29 million and Florida 21.6 million, presumably not counting Canadian snowbirds. See https://worldpopulationreview.com/.

10 The view has been that it is virtually impossible for American regulators to guarantee that drugs being bought in Canada are in some sense Canadian drugs and not, as the current HHS Secretary once remarked, being routed through Canada from a counterfeit drugs factory in China.

11 Florida House of Representatives (2019), discussed by Simmons-Duffin (2019).

12 As a practical matter it seems unlikely that many manufacturers would be interested in making use of this pathway.

13 Presumably this applies to Swiss and Swedish drug companies and not just to American ones, and would subject their American operations to penalties.

14 Summary at https://www.sanders.senate.gov/download/final_-affordable-and-safe-prescription-drug-importation-act-of-2019---bill-summary?id=-3F55AA41-4A20-426D-8CEB-987A30F3A838&download=1&inline=file; complete bill at https://www.sanders.senate.gov/download/final_-affordable-and-safe-prescription-drug-importation-act-of-2019?id=3AC157ED-B4F5-4B7E-8B64-F980132A856C&download=1&inline=file.

15 Although it has been claimed that the passage of the state legislation has prompted some manufacturers to offer better deals on prices (see Simmons-Duffin 2019).

16 The Biden campaign has released the following statement as part of his health care proposal: "Allowing consumers to buy prescription drugs from other countries. To create more competition for U.S. drug corporations, Biden will allow consumers to import prescription drugs from other countries, as long as the U.S. Department of Health and Human Services has certified that those drugs are safe." See https://joebiden.com/healthcare/.

17 Under the EU principle of subsidiarity, this kind of price regulation is a matter for individual country's governments.

18 Many of the drugs parallel imported into Sweden were produced by AstraZeneca, a Swedish drug company. AstraZeneca basically found itself in competition with itself, and in some cases lost the Swedish market to parallel imports of its own products.

19 Presentation as used here refers to the form in which the medication is delivered, which may be a pill, a caplet, a tablet, etc.

20 Interestingly, Danzon et al. (2011) actually looked for matches for 609 different US presentations of drugs. Defining a match as a presentation that would be approved by the FDA for importation, they found that only 308 were available in Canada and only 166 were available in Canada with a lower price than in the US at the time (2008) of their data set. At that time, of course, Canadian prices for many generic drugs were higher than US prices.

21 See, for example, Dubois and Sæthre (2020) and the references therein.

22 Remember that Sen. Sanders' bill imposes penalties on manufacturers who charge higher prices to wholesalers in Canada who plan to re-export to the US. It does not seem to deal with the issue of the prices that those wholesalers choose to charge in the US.

23 Neither Valeant nor Turing seem to have believed that they could justify their actions by saying that they were trying to maximize their profit. In each case there seems to have been a belief that they had to make a corporate social responsibility argument. On the Valient episode, see Surowiecki (2016) and LaMattina (2015).

24 Epinephrine injections are critical treatment for anaphylactic shock.

25 According to a Reuters report (Paperny 2018), while Canada did not experience a similar price increase, it has experienced EpiPen shortages. The Reuters report indicates that all EpiPens are manufactured at a single Pfizer facility in Missouri, that Mylan, which has the US rights and

set the US price, decides how EpiPens are allocated to different countries, and that while there were shortages in other countries (including Canada), there was at that time no shortage in the US.

26 Generics have to be shown to be bioequivalent to the brand name originals, meaning that they have the same active ingredient and that that ingredient is released into the body at the same rate as it is in the case of the original drug. Since the nature of the active ingredient can be established from such sources as the patent on the brand name drug, the issue often comes down to the nature of the materials that hold the pill together and control the rate of release.

27 It should be pointed out that much of this speculation is to be found in sections of the health policy literature that regard drug companies as evil and assume them to be guilty until proven innocent. However, the accumulation of evidence on the profitability of designated orphan drugs suggests that gaming the system, without breaking any of the rules as written, is a not-implausible hypothesis.

28 Normally a brand name drug operates under patent protection. Patent protection lasts for 20 years from the data on which the firm files for a patent, but since drug companies generally file for patents very early in the drug development process, there tends to be no more than 10 years of patent life left by the time a drug receives marketing approval from the FDA (assuming that it is one of the 10 percent that does make it to market). Even when it is under patent protection, it can face competition from other drugs that are aimed at treating the same condition but whose mechanism of action is sufficiently different from that of the first drug that they do not violate the first drug's patent. On-patent competition can be quite significant (Lichtenberg and Philipson 2002). FDA market exclusivity is separate from (but often confused with) patent protection. The FDA can grant exclusivity which would preclude competition even from a drug that does not violate the first drug's patent. Presumably, then, a grant of orphan status early in the development phase doesn't just protect the firm that receives it from competitors who might be thinking of working on the same compound with the same mechanism of action, but could discourage research by firms whose notional drug, if it worked, would not violate the first firm's patent. If that were to be the case, the effective period of market exclusivity might well exceed the length of the formal seven years of exclusivity.

29 That doesn't mean that Canada gets a free ride on those drugs. Some of the most contentious cases before the PMPRB recently have involved the prices of small market drugs. See, for example, Blackwell (2015).

30 Unproductive monopolization is distinct from the monopolization resulting from a well-functioning patent system, which does encourage research. The patent system has its weaknesses and it is a second-best device for encouraging drug research, but none of the alternatives that have been proposed can really be seen as first-best.

31 Accompanied, one suspects, by hundreds of pages of regulations.

32 And he still does – see his recent comments in the *Globe and Mail* at Dosanjh (2020) as well as his comments at a Macdonald-Laurier event in 2019 (https://www.macdonaldlaurier.ca/video-photos-donald-trump-coming-canadians-medicines/).

33 This was *Bill C-378, An Act to amend the Food and Drugs Act and the Food and Drug Regulations (drug export restrictions).* For the debate on this Bill (which was defeated at Second Reading), see https://openparliament.ca/bills/39-2/C-378/ and, within that debate, https://openparliament.ca/debates/2007/11/27/ujjal-dosanjh-1/.

34 Drug companies almost certainly have no objection to uninsured Americans paying Canadian prices out of pocket, since it amounts to a form of price discrimination and brings them sales that they almost certainly would not have made otherwise.

35 The American move in June 2020 to pre-purchase the world's entire supply of remdesivir, a promising treatment for COVID-19, may well strengthen Canadian incentives to safeguard domestic drug supplies. See, for example, Boseley (2020).

36 Given the protectionist streak which has emerged from both parties during the NAFTA renegotiations it is not at all clear that the desire to be a good neighbour is particularly strong among leaders of either major US party.

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