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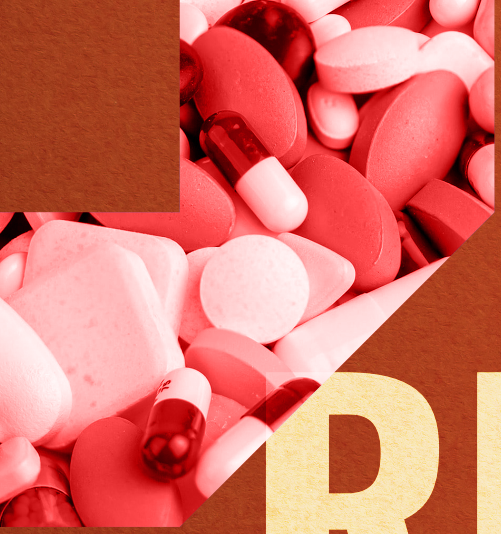

REALITY CHECK

Dispelling the myths around the benefits of drug price controls

TRUE NORTH IN CANADIAN PUBLIC POLICY

A BETTER PATH on Canadian drug prices

A NEW MLI SERIES

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Haya Sardar

TRUE NORTH
IN CANADIAN PUBLIC POLICY

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Executive Summary

Canada's Patented Medicine Prices Review Board (PMPRB) should be completely dismantled. Its relevance has been greatly reduced by large-scale price negotiations and its utility has been largely superseded by modern pharmaceutical science. Yet one of the PMPRB's most damaging effects is to enforce drug price controls, which is a topic that warrants a broader analysis and is the focus of this paper. This paper identifies – and debunks – 12 myths that circulate in support of drug price controls.

The first myth is at the root of most objections to pharmaceutical pricing: that a patient's "right" to have access to new medications competes with the rights of the patent owner and needs to be accommodated in pharmaceutical policy. A patented medicine belongs to its owners and may be shared on the terms chosen by them. Patients are the market. If their right to pharmaceutical inventions superseded the rights of the inventor, the industry would collapse.

It is unreasonable to expect that all new drugs could be made available to all patients at a low price. Pharmaceutical inventions are complex, risky, and expensive, and entail enormous potential liabilities and regulatory compliance costs. Studies have estimated that drug manufacturers spend from US $350 million to up to US$900 million to bring a small-molecule medicine to mar-ket. For biologics, this number rises to US$2.6 billion. This is only the tip of the iceberg and does not include the costs of failed drugs, risk, and opportu-nity costs.

Some observers allege that the pharmaceutical industry enjoys notoriously high-profit margins, particularly on patented drugs. Far from being too profitable, the pharmaceutical industry isn't profitable enough. Its return on capital is much lower than for many other industries like information technology, automobile production and financial services. Its profits are modest for industry risk levels. It would be in everybody's interest if the pharmaceutical industry were more profitable, because more valuable research would be funded.

Drug price controls delay or prevent access to drugs – and lead to fewer drugs being launched in that market. New medicines increase life expectancy as well as quality of life. The monetary gains can be calculated by the amount of money that is saved because of access to new drugs. According to Innovative Medicines Canada, in 2018 Canada saved $2.1 billion in costs to the health care system because of treatment through drug clinical trials. Such savings will be lost – and mortality costs will rise – if Canada's regulatory process limits or causes undue delays in access to life-saving drugs.

Canada, and in fact all countries, freeload on US drug innovation. The US "foots most of the bill for global life-sciences innovation." Although the US produces 22 percent of global GDP (while accounting for only 4 percent of the global population), it accounts for 44 percent of global pharmaceutical R&D expenditure. Canada relies on the US to innovate since we do not, then insists that the US consumer subsidize our access to those innovations. We are shifting the costs that we should rightfully bear onto the backs of others. All countries – Canada included – should promote and help pay their fair share for pharmaceutical innovation.

Through policies like those outlined in the PMPRB, Canada's approach to pharmaceutical access has been driven more by mistake and cynicism than by compassion. It is not, after all, companies that hinder access by expecting to be paid for their services and the enormous risks they take. It is absurd to think that they should subsidize their own products. Compassion does not authorize us to steal from them in order to save our own money. Expropriation is simply a cheap, expedient way to keep one's own pocketbook shut by dipping into someone else's.

It is past time to open our eyes and accept not only the great benefits of modern pharmaceutical science, but the responsibilities and opportunities that come with meaningful collaboration within the international life sciences industrial ecosystem. Without PMPRB controls, we would have wider and quicker access to new treatments, and, over time, greater wealth from a more robust life sciences industry, stronger economy, and improved health outcomes.

Sommaire

Le Conseil canadien d'examen du prix des médicaments brevetés (CEPMB) doit être démantelé en entier. Les négociations de prix à grande échelle diminuent grandement sa pertinence tandis que la science pharmaceutique moderne remet en question une bonne partie de sa raison d'être. Or, le contrôle des prix des médicaments est l'un de ses effets les plus néfastes, une situation qui mérite une analyse approfondie et constitue l'objet du présent document. Ce document recense –et déboulonne –douze mythes associés au contrôle des prix des médicaments.

Le premier mythe est au cœur de la plupart des objections à la fixation des prix des médicaments : c'est-à-dire que le « droit » des patients à l'accès à des nouveaux médicaments entre en concurrence avec celui des titulaires de brevets et doit être pris en compte dans la politique pharmaceutique. Un médicament breveté appartient à ses propriétaires et peut être partagé selon les modalités choisies par ces derniers. Les patients forment le marché. Si le droit des patients aux inventions pharmaceutiques supplantait celui des inventeurs, l'industrie s'effondrerait.

Il serait illogique de s'attendre à ce que tous les nouveaux médicaments soient mis à la disposition de tous les patients à bas prix. Les inventions pharmaceutiques sont issues d'opérations complexes, risquées et onéreuses qui supposent un régime de responsabilités et des coûts de conformité réglementaire considérables. Selon les études, les fabricants de médicaments dépensent entre 350 et 900 millions de dollars américains pour mettre en marché un médicament composé de petites molécules. Ce chiffre s'élève à 2,6 milliards pour les produits biologiques. Et ce n'est que la pointe de l'iceberg, car ces sommes ne tiennent pas compte des échecs, des risques encourus et des coûts d'opportunité.

Certains observateurs affirment que l'industrie pharmaceutique enregistre des marges bénéficiaires notoirement élevées, tout particulièrement en ce qui concerne les médicaments brevetés. Loin d'être trop rentable, l'industrie pharmaceutique ne l'est pas assez. Le rendement du capital de cette industrie est bien inférieur à celui de beaucoup d'autres : les technologies de l'information, la production automobile et les services financiers, notamment. Les

bénéfices réalisés sont modestes par rapport aux niveaux de risque. Tout le monde se porterait mieux si l'industrie pharmaceutique était plus rentable, car cela lui permettrait de financer des recherches plus précieuses.

Le contrôle des prix des médicaments retarde ou empêche l'accès aux médicaments –et réduit le nombre de nouveaux médicaments lancés sur ce marché. Les nouveaux médicaments relèvent l'espérance de vie ainsi que sa qualité. Les gains financiers en découlant peuvent être estimés en calculant les sommes d'argent économisées grâce à leur emploi. Selon Innovative Medicines Canada, en 2018, les essais cliniques ont permis au Canada d'économiser 2,1 milliards de dollars en coûts pour le système de santé. De telles économies seront perdues –et les coûts de la mortalité augmenteront –si le processus réglementaire canadien limite ou retarde indûment l'accès aux médicaments nécessaires à la survie.

Le Canada –comme la totalité des pays d'ailleurs –compte sur les innovations pharmaceutiques américaines. Alors que les États-Unis représentent 22 % du PIB mondial (mais 4 % de la population de la planète), ils contribuent à 44 % des dépenses engagées en R et D pharmaceutique dans le monde. Le Canada dépend des États-Unis pour les innovations, puisqu'il n'en réalise pas, puis insiste pour que le consommateur américain en subventionne l'accès. Nous refilons aux autres les coûts que nous devrions légitimement prendre à notre compte. Tous les pays –y compris le Canada –devraient inciter et veiller au paiement de leur juste part en matière d'innovation pharmaceutique.

L'approche du Canada en matière d'accès aux médicaments tient davantage de l'erreur et du cynisme que de la compassion. Après tout, ce ne sont pas les entreprises qui entravent l'accès parce qu'elles s'attendent à être rémunérées pour leurs services et les risques énormes qu'elles prennent. Il est absurde de s'attendre à ce que ces dernières subventionnent leurs propres produits. La compassion ne nous autorise pas à les piller afin d'économiser notre argent. L'expropriation n'est qu'un moyen bon marché et expéditif de renflouer son propre porte-monnaie en siphonnant celui d'un autre.

Il est grand temps d'ouvrir les yeux et de reconnaître non seulement les importants bénéfices apportés par la science pharmaceutique moderne, mais aussi les responsabilités et les possibilités qui découlent d'une collaboration notable au sein de l'écosystème industriel international des sciences de la vie. S'il n'en était des contrôles de prix du CEPMB, nous aurions un accès plus étendu et plus rapide aux nouveaux traitements et, à terme, à une plus grande prospérité amenée par une industrie des sciences de la vie plus robuste, une économie plus forte et de meilleurs résultats en santé.

Introduction

Canada's Patented Medicine Prices Review Board (PMPRB) has always sat on shaky historical and legal foundations; its relevance has been greatly reduced by large-scale price negotiations and its utility largely superseded by modern pharmaceutical science. The federal government's proposed New Regulations to govern its price controls would have only gravely worsened the overall impact of the PMPRB and increased its unconstitutionality, thereby increasing its dire impact on Canada's life sciences industry. While the 2022 budget eliminated key amendments of the New Regulations, the government's silence on what might replace them does not make one sanguine that this is the last that we've heard about updating this body.

As discussed in part one of this paper series (Owens, Rosenberg, and Sardar 2022), we advocate for the PMPRB to be completely dismantled. Yet the issue of drug price controls is a topic that is larger than the PMPRB itself. As such, this companion paper turns its focus to a broader analysis of the market for pharmaceuticals, pharmaceutical pricing, and trade regulation. Many myths circulate in support of drug price controls. We have identified 12 myths that support drug price controls. This paper dispels each in the hopes of providing a more informed and optimistic context for the evaluation of pharmaceutical development and commercialization.

Myth 1: Patients' rights to drugs are independent of and compete with inventor and owner rights

This myth may be the fundamental error at the root of most objections to pharmaceutical pricing. In correcting it, I'm making no attempt to diminish the needs of those who are ill or to attenuate compassion. Instead, we must look closely at legal and economic realities and affirm that those realities truly serve compassionate ends.

Those who decry price as a barrier to access to patented medicines err in an implicit assumption – that a patient's right of access to new medications competes with the rights of the patent owner and needs to be accommodated in pharmaceutical policy. To be an advocate for patients needing drugs is right and compassionate, but those who advocate methods and policies that lead to diminishing the supply of drugs for these same patients are misguided indeed. We must keep our heads cool about maintaining systems with incentives that best serve compassionate ends in the long-run, and about the appropriate socialization of costs.

Of course, medicines should get to people who benefit from them whenever possible. From a practical standpoint, it is almost always easy to get a medicine (subject to supply limitations and regulatory approvals): one seeks a prescription and buys the drug at a pharmacy. Yet objection to the transactional nature of drug acquisition is widespread. A buyer unable or unwilling to pay the stipulated price may take advantage of this sentiment and turn to politics, arguing the drug price is unjustified or their needs are special and therefore demand that someone else pay for or confiscate the drug. Or politicians may step in to do so on behalf of their constituents. There is no sound principle behind any of this conduct and considerable damage flows from it.

Law

A patented medicine belongs to its owners and may be shared on the terms chosen by them – that is, if sharing is permitted by the public authorities who are the real gatekeepers to pharmaceutical access. To supply medicines without marketing approvals risks penal sanctions (Canada 2020). Neither a patient's suffering nor a physician's eagerness to prescribe translates into title to any goods, or into any right to compel delivery or treatment. Governments rely on that fact to impose regulatory barriers to access; producers rely on it to continue to provide cures on a sustainable for-profit basis.

Consider how or when a right of access could crystallize, and its absence becomes clearer still. No entitlement can pre-exist the pharmaceutical invention since there is nothing to be entitled to. There is no right to force anyone to commit the massive amounts of time and resources to invent and commercialize a new drug. Nor could any right arise at the moment of invention, since at that time viability is uncertain – it is a possibility, not a therapy. A patent makes an invention known and understood when it is filed, but at that point the invention is still not proven clinically useful or made legally accessible. The law requires clinical trials, and a patient is not entitled to enrollment in a trial (National Institute on Aging 2020).

Finally, to suggest that a right arises once testing and approval is finally done is merely self-serving. It is like waiting until someone brings in the harvest before demanding he provide bread. And what would cause a right to crys-

tallize? What does a patient do to be deserving? Illness befalls her, but, while unfortunate, that does not argue for a right to someone else's property to deal with it. Indeed, by falling ill, she does not contribute to making the drug available and does not make any contribution that could be recognized, by natural right, as an entitlement. Instead, she falls into the very category of person targeted to pay for the drug – the only possible consumer. This may sound harsh, but it is simple market reality.

Economics

It is in the interest of patentholders to devise economically viable terms to get their inventions to patients. But that is an opportunity, not a duty (although unreasonable failure to make an invention available can qualify as patent abuse under the *Patent Act*) (Owens 2022). Pharmaceutical inventions are complex and risky and entail enormous potential liabilities and regulatory compliance costs. For all these reasons, it is unreasonable to expect that all new drugs could be made available to all patients at a low price.

From an economics perspective, patients are the source of demand that drives innovation and commercialization. It is precisely on keeping them from access to medicines except on payment of the stipulated price (and satisfaction of other terms, including a valid prescription) that the whole process of inventing and distributing medicines depends. The essential characteristics of the market, therefore, also militate against patient rights of access.

Patents drive new therapies. Delaying access to cheaper generic versions of a drug for the relatively brief period of the patent life is entirely reasonable compared to not benefiting from the invention at all, since but for the patent the invention would otherwise not exist, be disclosed, or commercialized. That is not to say no drugs would be created that were not patentable or patented – but the vast majority would not (Bodem Undated). The ability to profitably sell is the foundation of the whole risky, expensive, and complex process of drug development and discovery.

A further issue in the allocation of therapies is economic efficiency. This may not be our primary concern, but it is important when supply is constrained, as it often is with biologics and other therapies and devices, particularly early in the commercialization and marketing processes (see Appendix 1). Price signals will direct limited supply to the highest value uses and enable revenues to fund the scaling of supply. Employing the price signal is the quickest way to achieve greater supply and lower prices. Charitable generosity, including very often from drug companies themselves, and social schemes enhance access and allow the needy to be served.

How to be compassionate

While we need this structure of rights, we cannot ignore the fact that a patented drug may be a critical remedy for real people in need. That must be what motivates life scientists, after all. If they were motivated just by profit, they would choose another career – investment banking or computers or automobiles – all of which generate far more profit than pharmaceuticals (Damodaran 2021b). And indeed, rare is the pharmaceutical company, large or small, that does not go to great lengths to enhance both local and international access to its products, including providing products for free to those in need (Access to Medicines Foundation 2014). This mix of compassion and commerce makes for a complicated political economy of pharmaceuticals.

Through policy modalities like the PMPRB, Canada's approach to pharmaceutical access has been driven more by mistake and cynicism than by compassion. It is not, after all, companies that hinder access by expecting to be paid for their services and the enormous risks they take. Indeed, they are legally obligated to secure compensation, being bound by law to create profits for their shareholders. It is absurd to think that they should subsidize their own products. Compassion does not authorize us to steal from them in order to save our own money. Expropriation is simply a cheap, expedient way to keep one's own pocketbook shut by dipping into someone else's.

Another moral injunction applies: *pacta sunt servanda* – keep your promises. We promise pricing power to those who take on the long odds and years of exacting toil to bring a drug to market. Yet we perjure ourselves when we give in to temptation and confiscate the pricing power of pharmaceutical patents. Society benefits greatly from honest adherence to rules and principles; drug price controls are a dishonest way to take with one hand what we have given with the other. Public morality and critical incentive suffer alike.

Myth 2: Price controls are no worse than bulk purchases

Higher pharmaceutical prices lead to higher revenues that fund more research and development (R&D) of new drugs (CBO 2021). Of course, a willingness to pay excessive prices to get greater benefits of discovery does not necessarily follow from that. The combination of revenues and investment capital flowing into the pharmaceutical industry at any given time should be roughly optimal, given the availability of other factors of production and the opportunities for capital and expertise available both inside and outside the industry. Contributions of cash outside the normal structures of investment would have a much higher likelihood of being used inefficiently or wasted

(Catozzella and Vivarelli 2014) – a truth lost on all the advocates of innovation subsidies in Canada.

Unfortunately, this economic balancing is badly thrown off by worldwide price controls that constrain pharmaceutical company revenues below the levels required for optimal levels of drug discovery. But it is not only PMPRB price controls that constrain pharmaceutical revenues in Canada; bulk purchase negotiations by Canadian governments do, too. Should these negotiations be limited or done away with, along with PMRPB?

The case for doing so may not be as strong as with price controls. The first reason is moral: price controls are confiscatory, whereas negotiation (at least in theory) is an uncompelled exchange between free parties. Pharmaceutical providers should have all the benefits for their hard work and property, but we should not shield drug companies from the rigors of the marketplace. Government purchasers bring more to the table – minimum purchase levels, pharmacoeconomic data, liability limitations – that sellers value. Moreover, priority of supply can be negotiated. The buyer could explicitly accept supply delays (i.e., trading deaths for cash) in exchange for price relief. If, however, this were to occur in public sector negotiations, then a corollary must be transparency and immediate supply in the private market, at whatever price necessary. The alternative – blanket deprivation, with its cost in human lives – is immoral.

The limitations of bulk purchases should be transparent, to the extent possible, and commercially reasonable (Turner 2017). Governments should be answerable for refusing to buy any drug or therapy or delaying to do so. Not all new formulations will make sense for the public health care system, but those that do not might still make sense for individual cases. There must still be the option of fulfilling a doctor's prescription for a recommended cure privately. This will create inevitable political and even budgetary difficulties, but that is the outcome of a socialized health care system.

The argument could be raised that bulk purchases address the budgetary preferences of governments, whereas PMPRB price reductions benefit individual consumers. If we allow bulk purchase negotiations but abolish the PMPRB, the interests of that patient population are abandoned. This does not mean the PMPRB is necessary, however. Marginal increases in drug prices to consumers without the PMPRB could be managed by consumers, and most of them have private insurance coverage for their purchases (Brandt, Shearer, and Morgan 2018).

Some will suffer – those not young enough or old enough to be covered by provincial plans, or those in poverty. But it is far better to subsidize those people directly through a targeted pharmacare program rather than subsidize every consumer by price confiscation, which works against the interests of

consumers by limiting drug discovery. Without PMPRB controls, we would have wider and quicker access to new treatments, and, over time, greater wealth from a more robust life sciences industry, stronger economy, and improved health outcomes (Esmail and Barua Undated). Considered holistically, forcing drug prices lower does more harm than good, even on those it is meant to benefit.

Another critique of bulk purchases, which underscores the urgency of transparency, is that they will disproportionately affect expensive hospital-administered biologics and chemotherapy drugs, since those are purchased and paid for by the health care system. The price disincentives to public authorities of acquiring these products could result in less attention and fewer resources for rare disorders and life-threatening cancers (Voss 2020). Again, it is not reasonable for the public purse to bear the cost of any and every drug. But they must nonetheless be accessible, at least on commercial terms. To that end, the pace of drug approvals must also be increased, and we should accept reviews by other competent Organisation for Economic Co-operation and Development (OECD) regulators.

> *Forcing drug prices lower does more harm than good, even on those it is meant to benefit.*

While tolerating bulk-purchasing more than price controls, we must acknowledge that excessive exercise of monopsonistic power, as seems to be widespread internationally, may have profoundly deleterious effects on drug innovation. While legally different from legislated price controls, this is nonetheless economically indistinguishable from their effects. Indeed, price controls are morally indistinguishable from patent holders imposing excessively high prices for their drugs. If patent abuse is subject to legal consequence for its unconscionability, then its mirror image, price confiscation, implicates governments in behaviour no less unconscionable. Abuse of monopsonistic negotiating power does the same.

It is worth noting that the US has implemented "virtuous" limits on exercises of bulk purchasing power. US Medicare insures more than 60 million beneficiaries and should, in theory, have a large bargaining position to negotiate low drug prices (Wasik 2018). However, the government is banned from negotiating lower prices with drug manufacturers in accordance with the "non-interference clause." This is found in the US Social Security Laws, with a clause that stipulates the government "may not interfere with the negotiations between drug manufacturers and pharmacies and PDP sponsors,

and may not require a particular formulary or institute a price structure for the reimbursement of covered part D drugs" (United States, Social Security Administration 1935). Furthermore, the government may not institute a price structure that allows reimbursement of covered drugs (United States, Social Security Administration 1935). This means that the government can effectively have no role in either regulating or negotiating drug prices. However, as discussed below (see Myth 10), proposals under consideration in the United States would limit or undo these altruistic constraints.

Myth 3: Pharmaceuticals are priced arbitrarily high

Pricing is complex. It is formed within a nexus of production cost, development cost, demand, supply, and uniqueness. Pharmaceutical drugs are priced based on their estimated value in the market (Entis 2019), using evaluations of uniqueness, competition, effectiveness, and R&D (Hawley 2022) (see Appendix 2 for the effect of competition on drug prices). If a drug is priced too high, it will not sell. If a drug is priced too low, it may not generate sufficient revenue, and prescribing physicians may even conclude that it is less effective than more expensive alternatives that already exist (Hawley 2022).

A drug's price is ineluctably constrained by market value. Value will vary according to individual estimations, but it is averaged for public health care based on pharmacoeconomic calculations using populace-wide approximations for variables.

Unfortunately for producers, there is not necessarily any correlation between a drug's value in the market and its development and production costs. Where the costs of development, production, testing, and marketing exceed potential revenues based on the value of the resulting drug, then there will be no viable product; absent a humanitarian or political reason to subsidize it, the project will languish or fail. A patent creates exclusive rights, but it does not create demand or confer added value. Patent or no patent, the market will not demand a drug priced above its therapeutic value to that market. However, with most drug purchases paid for by insurers and government agencies, the impact of the price/value relationship is distorted. Still, it can hardly be said that government purchasers are price inelastic.

Uniqueness

The uniqueness of a drug influences its price because a saturated market will not accept a new, high-priced drug without an increase in effectiveness (Hawley 2022). Thus, uniqueness lifts a drug's price. This is why breakthrough and

first-in-class drugs are priced higher than alternative-treatment drugs, at least initially.

Effectiveness

Clinical trials are required to test the effectiveness and safety of a drug (Hawley 2022). If a drug is proven by trial to be as effective as treatments that already exist, it will likely be priced the same. Conversely, if a drug is more effective in treating the same condition, or prevents expenditure elsewhere, the drug can be priced higher because it has greater value to the patient. For example, if a drug can prevent the need for hospital trips, surgery, or other costly treatments, drug companies can increase a drug's price because of overall savings (Hawley 2022). Lastly, if a drug extends life, manufacturers can price it higher.

Research estimates that the overwhelmingly largest share of value gains through technological innovations is appropriated by consumers, not suppliers – as much as 96 percent (Ezell 2021). Assuming, as one reasonably would, that this share of values applies to pharmaceuticals, consumers get a fantastic bargain, whatever the price of the drug.

R&D

The pharmaceutical drug industry requires massive amounts of R&D to bring a drug to market. Over a decade ago, *Forbes* estimated that drug manufacturers spend around US$350 million for a successful small-molecule medicine to reach the market (Herper 2011). Other studies have calculated this base estimate as reaching up to US$900 million (Contoyannis et al. 2005). For biologics, this number rises even higher to US$2.6 billion (PhRMA 2015). Even still, this is only the tip of the iceberg. Pricing executives must consider the costs of failed drugs, risk, and opportunity costs before they can price a drug to make it profitable. If all these costs cannot be recovered, a manufacturer's operations will "cease" (Winegarden 2014).

Critics of the pharmaceutical industry often claim that the steep price reductions that may follow the end of a patent term are evidence that the patented drug price was too high (Winegarden 2014). If a company that develops patented medicines continues to produce a drug after losing patent protection, it is only evidence that the compound can be profitably produced at the same price as a generic or slightly higher (since name-brand drugs often command a premium, usually for reasons of quality, purity and patient toleration). Of course, that would be the case since generics are priced to make a profit. The generic establishes a new price floor; the drug is profitable over a much narrower cost base of production, it is free of R&D and clinical trials, and is also free of the initial liability risks of introducing a new compound and developing worldwide markets – all massive expenditures, and ones on which

the generic manufacturer happily free-rides.

Pharmaceutical manufacturers must also account for the money spent investigating drugs that never make it to market. The California Biomedical Research Association estimates that only five out of 5000 drugs that begin pre-clinical testing reach the stage of human testing. Only one out of those five is approved for use (Winegarden 2014). A drug manufacturer cannot simply recover the costs of inventing a successful drug; it must also recover the costs of failed drugs. Thus, *Forbes*' estimate of US$350 million in R&D costs per drug increases to US$5.0 to 5.9 billion for innovating companies (Herper 2013). Successful pharmaceutical innovation must be profitable not by product, as many activists would insist, but enterprise.

In addition to R&D costs, companies also have vast corporate overheads – head office, compliance, insurance, human resources management, legal, real estate, office management, and marketing costs.

The pharmaceutical industry is capital-intensive, and so must provide sufficient return on capital to continue to satisfy capital requirements. The Pharmaceutical Research Manufacturers Association (PhRMA 2013) estimates that drug development timelines run from 10 to 15 years (PhRMA 2013). This time has an opportunity cost; the next best alternatives are foregone. Shareholders could invest this money into the market at the average annual return of 9.9 percent (Winegarden 2014). Therefore, to give incentives for investment, the drug would have to recover its US$5.5 billion development cost, compounded by the 9.9 percent that investors could have earned elsewhere, for every year of development. Table 1 lists the opportunity cost during the drug development process.

TABLE 1: OPPORTUNITY COST (US$) DURING THE DRUG R&D DEVELOPMENT PROCESS

Year	Investment
0	$5.5 billion
10	$14.1 billion
15	$22.6 billion

On top of this astounding US$22.6 billion, there is also the question of risk, such as whether a drug will be approved or will be commercially successful. PhRMA estimates that only 20 percent of drugs that reach the market recover or exceed their R&D costs. This is unsurprising given the magnitude of the sum of R&D costs. And there are regulatory and liability risks, too. Riskier

industries require a greater rate of return to provide an incentive for investment or else investors would take a safer route and invest elsewhere. All these factors must be considered when determining a drug's price.

The impact of patent terms

A drug's patent and marketing exclusivity terms are not related to its development and commercialization costs. The average term of market exclusivity in the US is 14.4 years (Rome, Lee, and Kesselheim 2020), while in Canada it is 12.3 years (Lexchin 2017). For biologic drugs, average market exclusivity is greater: 21.5 years in the United States (Rome, Lee, and Kesselheim 2020), and between 9 and 18.3 years in Canada (Lexchin 2017). Whether a company must generate US$350 million, US$14.1 billion, or US$22.6 billion merely to recoup its initial investment, the term remains the same. Hence, innovative pharmaceutical companies must keep drug prices high because they are the ones that bear the burden of failed drug inventions.

Patents prioritize dynamic efficiency (developing new products) over static efficiency (distribution of existing products) to guarantee future investment in innovative drugs (Winegarden 2014). Critics of patents focus on static losses but the value of patent-driven innovation is dynamic. Any particular high-cost good makes a poor argument; it has already been invented. We pay not for that good, but for the things as yet unimagined, the inventions that still demand toil and risk – and lots of funding.

This highlights a limited opportunity for a different approach – unique, negotiated patent terms. If a drug had to be priced high to generate sufficient return over a limited period of exclusivity, extending that period could reduce the price to some degree. For instance, doubling the exclusive marketing period could allow the supplier to earn its return over a longer time, while still allowing a material price reduction. Of course, other factors come into play, such as the growing risk that a competing product will come onto the market, or that side effects would come to light. But this is at least a constructive basis on which to negotiate lower prices, rather than simply confiscating pricing power as many governments do now.

Myth 4: Pharmaceutical suppliers should price their products to be "affordable"

The claim that all drug inventions should be affordable to those who need them has a corollary: those in need have a right of access to a pharmaceutical

invention. As discussed above, neither the law nor economics supports such an entitlement. That the economics of making something bears no necessary relationship to the economic circumstances of someone who might need or want it seems not to occur to affordability advocates. We have already discussed the absurdity of assuming drug companies must bear the burdens of affordability for their own products.

While such coerciveness might have misguided compassion at its root, it is perhaps also emphasized by resentment of the strictness of property laws and devaluation of the effort and sacrifice that earning something entails – an implicit belief that society should provide for its consumers and not its providers. Such is the road to ruin. And it is beneficial to the consumer to produce and exchange value for the goods he consumes. Only a small minority of us, really, are deservedly charity cases.

To simply take a product – for example, to insist that the price of an orphan drug be reduced by 84 percent, as the New Regulations had prescribed (Rawson 2019) – can never be sustainable. Sustainability is a necessity if there is to be supply. "Society" cannot make anything. If it can build a consensus to pool its wealth to socialize the cost of expensive drugs, that is one answer. It is an answer on the only terms that will ever work; buy the drug at a price at which the seller is willing to sell. Nevertheless, drugs priced out of reach of those who need them are not in anyone's interests. Whatever its economic and philosophic necessities, the combination of possible remedy and the imminent death of a child or a young mother or a beloved grandparent is both a tragedy and bad optics.

Pricing at the high end of a market may be unfortunate, but prices are not set without reasons. This will bear out even more as the market shifts increasingly toward biologics. The generic versions of biologic drugs are known as "biosimilars." The biologic drug market is new so there are not yet many biosimilars on the market. To create a biosimilar is a project beset with uncertainties and costs that are orders of magnitude greater than for small-molecule generics. Biosimilars, made available after the exclusive marketing period for a biologic drug ends, are expected to be roughly 30 percent less expensive than the originals – not the dramatic price cuts seen for other generics.

Myth 5: The pharmaceutical industry is too profitable

Some observers allege that the pharmaceutical industry enjoys notoriously high-profit margins, particularly on patented drugs. For instance, the Stern School of Business has estimated gross profit margins for pharmaceutical drugs at 70.68 percent and biotechnology drugs at 64.20 percent (Damoda-

ran 2021a). Of course, if one supposes that there is a patent "monopoly," this seems surprisingly low.

However, such figures mean little. Gross profit margins are calculated as net sales less the cost of goods sold as a proportion of net sales (Carlson 2020). This margin is not useful in assessing enterprise profitability because it does not account for the volume of sales or the staggeringly large R&D expenses of patented drugs. Neither does it account for enterprise and overhead costs. This is because the cost of goods sold includes only the direct costs of producing these goods, including the cost of the materials and the labour used in its production (Fernando 2022).

Net profit margins are a somewhat more reliable indicator of sales profitability than gross profit margins (CFI Undated). Net profits are profits after all expenses, including interest and taxes. The estimated net profit margin for pharmaceutical drug manufacturing is 14.10 percent, much lower than the 70.68 percent figure of gross profit margins on sales (Damodaran 2021a).

> *Net profitability for the sale of a single successful drug is not meaningful where failure is the norm.*

Even then, sales profitability does not equate to enterprise profitability. While net profit margins account for operating expenses, interest, taxes, and other expenses, they do not account for the cost of drugs that never reach the market, as these are not included in the "costs of goods sold." Innovative industries are risky because many of their investments fail. As mentioned, only five out of 5000 drugs that begin pre-clinical trials ever reach human testing and only one of these five gets approved for human use (Winegarden 2014). Thus, net profitability for the sale of a single successful drug is not meaningful where failure is the norm.

Enterprise profitability is likely a better determination of industry-wide profitability. Return on equity (ROE) quantifies industry profitability (Maverick 2021). Stern has estimated the pharmaceutical drug industry's ROE at 18.98 percent (Damodaran 2021b). This figure accords with the US Government Accountability Office (GAO), which claims that among the 25 largest drug companies annual average profit margins were between 15 and 20 percent (USHR 2017). For all drug companies, this margin was 17.1 percent (USHR 2017). Stern data coincides with GAO data for the 25 largest drug companies, demonstrating that the largest drug companies do not monopolize industry profits.

When the ROE is adjusted for R&D costs, the pharmaceutical drug industry sees a decrease in its profitability to 11.98 percent. Unadjusted ROE assumes that R&D is expensed, which is required under the US Generally Accepted Accounting Principles (but not in Canada) (CFI Undated). Yet, as Professor Aswath Damodaran argues, R&D is better capitalized when accounting for profitability in the pharmaceutical industry. Simply put, R&D expenditure tends to be more long-term than investment into other forms of capital (Damodaran 2021b). This adjustment is likely the most accurate measure of pharmaceutical industry profitability due to the large up-front R&D costs to get a drug to market.

A comparison of pharmaceutical industry profitability (17.1 percent, without adjusting for R&D costs) to that of financial services (61.83 percent) or computers (29.56 percent), indicates that "Big Pharma" hardly merits its notoriety for profits – especially in its more important aspect, biologics.

Biologic Drugs

Biologics often have high prices (Canada, Standing Committee on Health 2018). Coupled with the claim that biologic treatments cost 22 times more than small molecule drugs at retail and have profit margins of up to 40 percent, it is no surprise that biologics have created controversy (Walker 2017). Yet, if we account for the greater production costs and the immense R&D costs associated with producing biologic drugs, the industry is not even profitable.

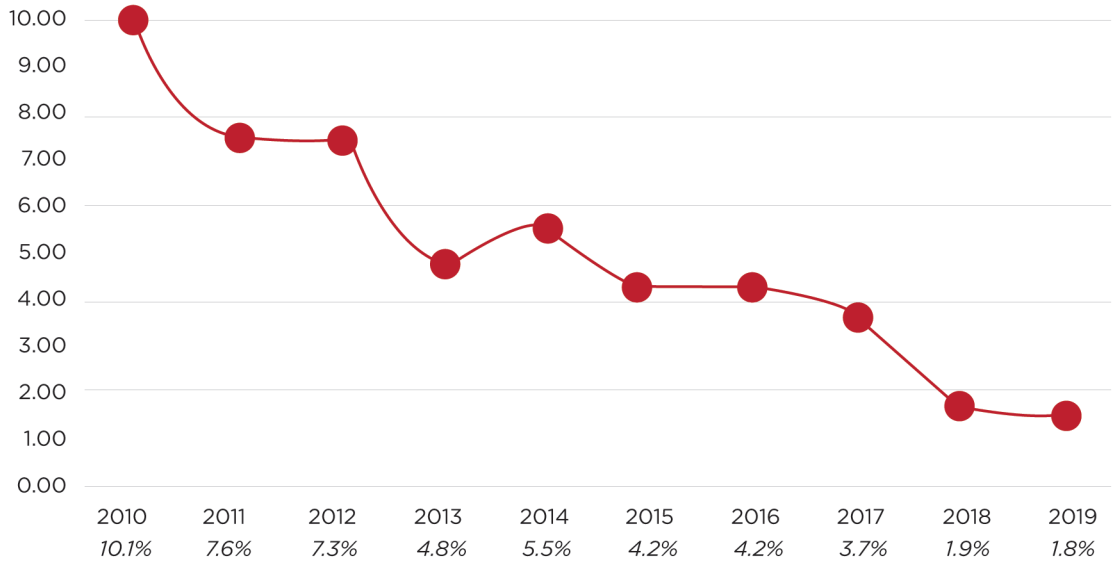
The net profit margin for biologic drugs is negative at -0.94 percent, while the ROE for biologic drug makers is -1.19 percent (Damodaran 2021b). When adjusted for R&D, the ROE for biologic drug makers is slightly higher at 1.30 percent. In reclassifying ROE to account for R&D, if the current R&D expense is significantly higher than in previous years, the ROE will increase upon adjustment. Alternatively, if the current R&D expense is similar to that of previous years, the ROE will decrease upon adjustment (Damodaran 2021b). The biologics industry revolution is recent.

Another key indicator of profitability, particularly important in the biologic industry, is the return on R&D investment. This has been developed and tracked since 2010 by the Deloitte Center for Health Solutions (Lesser and Terry 2019). In its 10-year report, Deloitte exposed the decline in returns on R&D in the biologic industry (see Figure 1).

From a high of 10.1 percent in 2010, the returns on R&D have declined nearly every year to a low of 1.8 percent in 2019. These declining rates of return deter investment and innovation. Biologic treatments still require high levels of investment before they are brought to market but, due to the inherently risky nature of the industry, investors need larger returns as an incentive (Lybecker

2016). Declining returns will drive away life-saving investment. The PMPRB will dramatically worsen this situation in Canada.

FIGURE 1: RETURNS ON R&D BASED ON 12 LARGE-CAP BIOPHARMA COMPANIES, 2010-2019



Source: Deloitte Centre for Health Solutions (Lesser and Terry 2019)

Industry Comparisons

Stern has estimated ROE by sector categorized into 95 industries including pharmaceutical and biologic drug manufacturing. The pharmaceutical industry is in the 74th percentile while the biologic industry is in the 28th percentile (Damodaran 2021b). These data are based on the R&D being expensed. If the ROE is adjusted for R&D being capitalized, these figures become 83rd and 22nd respectively.

Another study has combined the pharmaceutical and biologics industry and found an average ROE of 15.58 percent (CSI Market Undated). This is not much more than the total market average ROE of 12.03 percent. As of Q1 2021, the ROE of the pharmaceutical and biologics drug industry ranks 41st out of 105 sectors (CSI Market Undated). This puts the industry at the 61st percentile, which accords with the data from the Stern School of Business where the combination of pharmaceutical and biologics put the industry at the 59th percentile. Many other industries are far more profitable than life sciences.

Myth 6: The pharmaceutical industry gets even-handed treatment compared to other industries

Life science firms expend significant energy coping with hostile commercial and regulatory environments (Collier 2013). This hostility is worse in Canada; almost all companies here are foreign-based, which makes sense given the policy environment in Canada. Drug companies are often criticized for having many lobbyists. It would be irresponsible not to, given the complex and hostile political economy in which they operate. Simply put, these lobbyists are too busy playing defence against bad government policy to spend much time looking for special favours.

The life sciences industry may be no more virtuous than any other industry, but it is at the cutting-edge of impressive and fascinating science, and has an incredible impact on our species and its progress. However, like any industry, it should be left alone to be productive and serve society by profitably producing needed and innovative goods. Yet people are still quick to unjustly criticize the life sciences industry – in effect, justifying confiscatory policy by demonizing its victims – and this harms the body politic.

This may be borne out by the industry's defensive behaviour. During the COVID pandemic, drug companies made generous, conciliatory gestures towards the markets for their products. For instance, Gilead Sciences Inc. has one of the most promising treatments for COVID, Remdesivir. Gilead petitioned the US Food and Drug Administration (FDA) to retract the orphan drug designation benefiting Remdesivir and, in any event, relinquished the benefits of that designation (Lupkin 2020). It has also pledged to provide its entire 1.5 million dose supply at no cost to patients with the most severe symptoms (Owens 2020).

They are not alone in making such conciliatory gestures. Abbvie, in response to a compulsory licence for its product Kaletra in Israel to treat COVID-19, has pledged not to defend its patent rights to the product anywhere. Johnson & Johnson has pledged to make any vaccine it discovers available on a not-for-profit basis (Owens 2020). Medtronic has provided the plans for and the rights to make its ventilators to competitors (Owens 2020). Moderna has waived its patent rights to retrovirus vaccines (Garde, Branswell, Herper 2021).

Firms are supposed to maximize shareholder value. It is difficult to see how the recent decisions by these firms, at least in the short-term, do that. There

may be a problem at the root, and that may be with the intellectual property (IP) system we rely on for drug discovery and the politics of defending it in societies hostile to private enterprise.

Hostility is expressed also in the compulsory licensing measures many countries have implemented, often specifically in response to the pandemic. In Bill C-13, Canada implemented a very limited provision under the Act to allow the government to issue a compulsory licence to pharmaceutical patents and empower a third-party supplier to make the drug (Canada 2020). Many countries have done the same, with varying degrees of enthusiasm. Some commentators and politicians are seizing opportunistically on the pandemic to agitate for a return to the continual threat of compulsory licensing to control drug prices. However, because pharmaceutical companies are expressing willingness to share manufacturing capacity, there is little need to exercise the power to confiscate rights by compulsory licence.

Such generosity may have unintended, anti-competitive consequences. It is bad for the industry and us. To sell at cost would have the same impact as predatory pricing (Pharma Insider 2017). In other words, in a market that can be satisfied by extreme low-cost goods, what incentive remains for new entrants?

Hostility is expressed also in the compulsory licensing measures many countries have implemented.

It is precisely new entrants that we need. Most drug research is now done by small firms (Robinson 2020). These smaller companies attract capital and expertise on the anticipation of a payoff from the acquisition of the product, or the company, by a large company, which in turn manages the scaling, regulatory compliance, and commercialization challenges of a new drug. If larger companies pledge not to sell a product above cost, that incentive structure collapses. Larger companies will not have an incentive to acquire smaller companies, or at least, not at a high valuation. Investors will see the pay-off to be much less likely and will not invest. Highly qualified researchers will do something more profitable.

Further illustrative of the hostile climate for life sciences is the appalling and counter-productive proposal by India and South Africa for a World Trade Organization (WTO) waiver of all IP rights, including patents, to COVID-19 therapies, devices, and vaccines (Mathew 2021). That the US has chosen to support this proposal is profoundly disheartening. The *Wall Street Journal*

called it "bewildering" and "the single worst presidential economic decision since Nixon's wage-and-price controls" (2021).

The proposal is opportunistic and exploitative. IP has not been a material limit to access to vaccines or other therapies or devices – in no small part due to the many selflessly generous gestures outlined above. The issues that remain involve scaling and logistics. It is worth noting that there already are measured, emergency medical provisions to access IP in the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). A blanket waiver would, instead, create a free-for-all, achieving merely the wanton destruction of valuable IP.

A paper from Philip Stevens and Mark Schultz draws apt comparisons with other attempts to increase pharmaceutical availability in the developing world through compulsory licensing and points out their biggest flaw: they don't work, partially because the resulting products fall short of commercially available alternatives (Stevens and Schultz 2016). This is unsurprising. A narrow focus on IP protection – or the waiving of it – exclusive of all other factors, sets things up for failure. It presupposes ripe commercial pickings behind an imagined wall of IP monopoly. Of course, that is an illusion. The reality is that the assemblage of expertise and resources in a competitive commercial firm is never easily replicated.

What have pharmaceutical companies and the IP laws that support them done for the world lately? From no coronavirus vaccines at all to mass vaccination in less than a year is extraordinary, particularly given the typical timelines for vaccine development. As of May 2, 2022, 843 unique active compounds were under development for COVID-19, including 350 treatments, 257 antivirals, and 236 vaccines – over half of them from the United States (Biotechnology Innovation Organization 2022). Moreover, a waiver would benefit IP thieves like China, leading to enhanced credibility for counterfeit and impure or ineffective products in the supply chain (Wall Street Journal 2021). It also would likely ensure that companies will not respond to the next pandemic nearly as swiftly or effectively.

It is recklessly myopic to say, as many do, that a massive public health crisis is not the time for patents. That is completely wrong. Now is precisely the time to uphold the integrity of the system that serves us so well. If we undermine a system precisely when it is needed, it will not be there to serve us in the future.

Myth 7: Canada does not free-ride on the US consumer

Out of 56 countries ranked for their contributions to global pharmaceutical innovation, the US ranks first while Canada ranks 27th.[1] This puts Canada below all the PMPRB-7 (the basket of price-comparator countries) except France. By its "R&D composite score," which is a combined metric of government's health R&D funding and R&D investment as a share of GDP, Canada ranks even lower at 32nd (Wu and Ezell 2016).

The US "foots most of the bill for global life-sciences innovation" (Wu and Ezell 2016). This is because although the US produces 22 percent of global GDP (while accounting for only 4 percent of the global population), it accounts for 44 percent of global pharmaceutical R&D expenditure. The US is also the world's largest manufacturer of biologics (Wu and Ezell 2016).

Another study attempts to classify the country origins of newly discovered drugs to determine which countries contribute the most to pharmaceutical innovation (Kneller 2010). The study period ranged from 1998 to 2007 and covers 252 drugs. Fifty-eight percent of these drugs originated with pharmaceutical companies and 18 percent from biotechnology companies (Kneller 2010). The rest were attributed to miscellaneous universities, largely in the US.

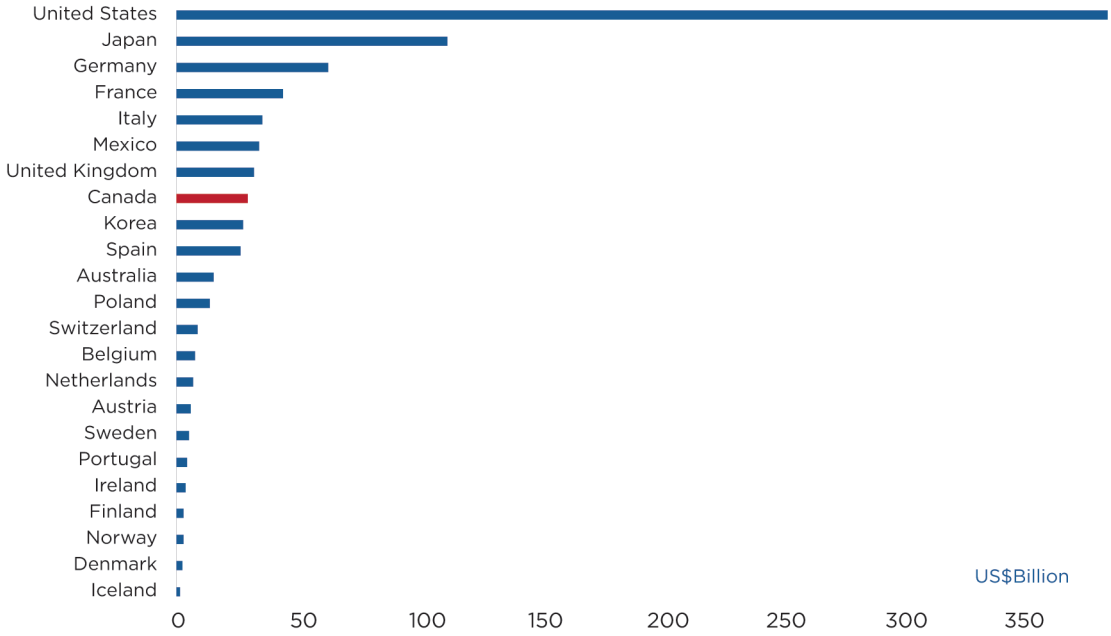
Out of the 252 drugs in the study, 118 originated in the United States (Kneller 2010). This means that nearly half of the drugs discovered within this study period can be attributed to a single country. Compared with this, Canada and Australia together (which were combined for the purpose of the report) only developed seven of the 252 drugs. The remainder originated in the EU and Japan, with no single country developing more than 25 drugs.

All countries freeload on US drug innovation (Pitts 2017). The global market is reaping the benefits of US R&D investment while American consumers bear the costs, as illustrated in Figure 2.

Figure 2 illustrates the disproportionate burden on American consumers of pharmaceutical spending. Pharmaceutical expenditure in the US is over triple what it is in Japan, the second country in the ranking, exposing the true magnitude of the disparity. The US is the largest purchaser of pharmaceuticals and it pays the highest prices for them (Pitts 2017).

The US pays around 3.5 times the price of its nearest competitor for both patented and generic drugs (see Figure 3), earns around 70 percent of total pharmaceutical profits, and develops a majority of new blockbuster drugs and biologics. All countries should promote and help pay for their fair share for pharmaceutical innovation.

FIGURE 2: TOTAL SPENDING ON PHARMACEUTICALS, 2015



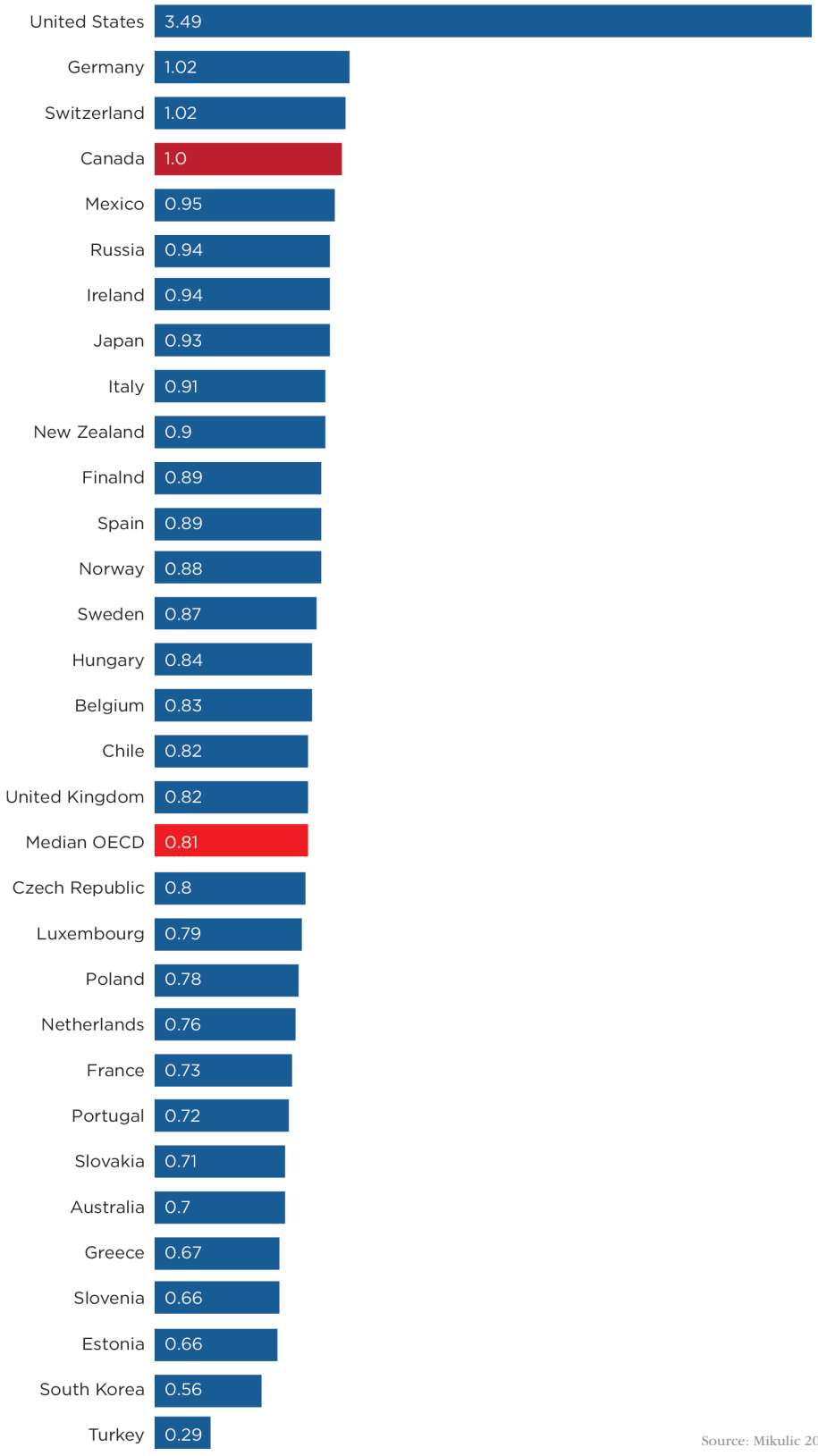
Source: Blomqvist and Wyonch 2019.

Precision Health Economics estimates that if OECD countries lifted their price controls, the number of new pharmaceuticals that would be developed would increase by 9 to 12 percent by 2030 (Owens and Ezell 2018). This could extend the life expectancy (of 15-year-olds) by up to 1.6 years (Goldman and Lakdawalla 2018). To increase prices in price-controlled countries in Europe by only 20 percent would lead to US$17.5 trillion in welfare gains for the US and Europe alike (Goldman and Lakdawalla 2018). If Canada also increased its prices, this number would be even greater. Patients would be the greatest beneficiaries of enhanced economic fairness.

Myth 8: Price controls do not affect drug discovery or supply

Two of the worst impacts of pharmaceutical price controls are the reduction of R&D investment and the innovation of fewer drugs – contrary to the PMRPB's bald denials. Golec and Vernon (2006) estimate that a significant reduction in R&D spending by EU drug manufacturers resulted in 46 fewer drugs being introduced to the market between 1985 and 2004. Others have estimated that if price-controlling OECD countries removed their price controls, R&D expenditure would rise by US$17 to US$22 billion, leading to the creation of up to 13 new drugs a year (Brouwers, Silverstein, and Wolff 2004). The US Congressional Budget Office predicts that if the US adopts price con-

FIGURE 3: RELATIVE DRUG PRICES INTERNATIONALLY, 2021



Source: Mikulic 2021.

trols on drugs covered by Medicare (which covers only 18 percent of the US population), it would result in reduced R&D spending, and yield eight to 15 fewer drugs by 2032 (CBO 2019). Ultimately, for every dollar not spent on R&D technology, the true loss is $7 (Hassett 2004). Price controls conceal this true cost in pursuit of short-term savings.

Price controls do not just limit drug discovery, they limit access to drugs that have been discovered. It was estimated that in the US where no national price controls exist, pharmacies had access to nearly 90 percent of all newly launched medicines. In other developed countries where price controls operate, access was reduced to 47 percent (Hassett 2004).

Effects on existing drugs, and the problem of parallel exports

Price regulation delays or prevents access to drugs. Kyle et al. (2003) report that drugs experience delays in their launch in price-controlled countries. Similarly, drugs manufactured in price-controlled countries experience delays in reaching foreign markets. One of the reasons for these delays is that many governments, including in Canada, use international reference prices to set the maximum allowable price of a new drug in the market. Hence, drug manufacturers are discouraged from launching new drugs in price-controlled markets as doing so pushes the global price for that drug down. If the PMPRB sets the maximum allowable price lower than the price the manufacturer wanted to sell the drug for in France, for example, the manufacturer could delay selling the drug in Canada in fear of France re-evaluating its price (Danzon, Wang, and Wang 2005).

Regulatory approvals also cause delays. Canada has large data and disclosure requirements, including confidential price information. Pharmaceuticals are banned from being used in Canada until Health Canada conducts its own duplicative review, one which has already been done in the US and Europe. This is a costly process, although a recent study suggests Canada is no longer much slower than other nations in completing it as it used to be (Rawson 2018). However, another study confirms substantial delays, including regulatory delays, in drugs reaching Canadians – delays that are unnecessary (Rovere and Skinner 2022).

The PMPRB adds further uncertainty, as price disputes and litigation can arise. The CEO of Life Sciences Ontario claims that the delays caused by price regulation and the approval process can be up to three years (Zoomer 2021). Speed of access must be a key criterion for the evaluation of our pharmaceutical policies. We should not duplicate reviews undertaken by other responsible regulatory authorities, or at least not delay the introduction of new drugs while we wait for such reviews, nor allow price controls or negotiations to delay or prevent access to pharmaceuticals for patients in need.

Danzon, Wang and Wang (2005) conclude that countries with strict price controls have both longer delays on average and fewer drugs launched in the market. This effect is magnified for countries that are parallel exporters (e.g., those that export drugs without the patent owner's permission). Canada is a parallel exporter of patented drugs to the US because of its geographical proximity and large price differentials (Houston and Attaran 2019). This has the dual effect of reducing the Canadian supply of an existing drug and causing drug launch delays. Shockingly, a 2010 study estimated that if only 10 percent of US prescriptions were filled from Canadian sources, Canada's drug supply would run out in 224 days (Houston and Attaran 2019). Subsequently, drug manufacturers would have no incentive to resupply these drugs to Canada, given their worry about further lost profits through parallel importation. Indeed, GlaxoSmithKline stopped supplying drugs to many Canadian pharmacies to prevent this exact phenomenon (Houston and Attaran 2019).

Canada's drug gap manifests primarily in the oncology and rare diseases classes.

The Canadian federal government enacted an interim order under the *Food and Drugs Act* prohibiting the export of drugs to individuals outside Canada if there is a reasonable apprehension of a drug shortage (Canada 2021). The need for this order is ironic: Canada has to protect itself from the very consumers off whom it freeloads.

From 2000-2019, Canada ranked 9th in the proportion of new medicines launched globally, at 66 percent. This figure was lower for biologics, at 62 percent (Canada 2021). Moreover, Canada has experienced a "significant drop" in drug launches since 2018. Only 43.2 percent of pharmaceutical drugs launched globally in 2018 reached the Canadian market (Voss 2020). Canada's drug gap manifests primarily in the oncology and rare diseases classes, which is arguably where new drug launches are most required.

All pharmaceutical executives surveyed predicted that the PMPRB price controls would have an adverse impact on their launch plans in Canada (Life Sciences Ontario 2020). Notably, 74 percent of executives forecast a significant negative impact on product launches and supply of current drugs to the Canadian market, whereas only 23 percent of executives estimated a significant negative impact on drug manufacturing. New drugs will still be manufactured, but outside Canada, with access to them in Canada being uncertain. With the PMPRB New Regulations aiming to reduce drug prices by a further 20 to 25

percent (Critchley and Owens 2018), this declining trend in access to new innovative drugs will only worsen.

Unsurprisingly, the countries without national price controls, the US and Germany, fared much better in getting access to new, innovative drugs, ranking 1st and 2nd, respectively (Life Sciences Ontario 2020). While 13 new medicines were launched in Canada in 2019, 35 were launched in the US, nearly triple the number. The PMPRB's lower drug prices are a bad deal for Canadian health care.

New medicines increase life expectancy as well as quality of life. While these gains are not easily quantified, monetary gains can be calculated by the amount of money that is saved because of access to new drugs. According to Innovative Medicines Canada, in 2018 Canada saved $2.1 billion in costs to the health care system because of treatment through drug clinical trials (IMC 2019). Such savings will be lost if access to new drugs is limited and delayed. New clinical trials alone fell by 60 percent in 2020 compared to the four preceding years, while there was no similar decrease in the US (Rawson and Adams 2020). Approval rates for new drugs in Canada also fell during this period – from 49 percent to 15.6 percent.

Societies such as Cystic Fibrosis Canada and the Canadian Cancer Society have advocated for greater drug access in Canada to treat patients with rare diseases who face drug shortages. Despite the high price tag for cystic fibrosis drugs, which reach up to US$300,000 per year, and the beneficial impact that price reductions would have on these expensive therapies, Cystic Fibrosis Canada has been critical of the New Regulations, claiming that the effect of price controls on new medicines would make Canada a "less desirable destination" for drug manufacturers. One case study is the drug Trikafta, which has been very slow to launch in Canada. Trikafta is a transformational drug that can increase the life expectancy of a child born with cystic fibrosis by 9.2 years (Cystic Fibrosis Canada Undated). Trikafta is significantly more effective than existing cystic fibrosis medications, and yet patients with this disease are dying before this drug becomes accessible in Canada (Cooke 2020).

Mortality costs

Pharmaceutical innovation saves lives, improves quality of life, and increases life expectancy. From 2000 to 2016, global life expectancy rose from 66.5 to 72.0 years (Lichtenberg 2019). How much of this increased longevity can be attributed to pharmaceutical innovation?

Lichtenberg (2019) analyses the effect of new drug launches on the years of life lost (YLL), a measure of premature death. The calculation works this way: if an individual is expected to live up to age 72, but dies at age 50 due to a rare disease, the YLL is 22 years. The study measures drug launches after 1981 and

their contribution to reducing the YLL. Between 1982 and 2015, the number of new chemical entities launched in the US was 719, but only 541 in Canada, putting Canada below all its PMPRB comparator countries – and below Argentina and Mexico (Lichtenberg 2019).

The study concludes that the YLL, assuming an individual should live to be 85, would be 2.16 times higher than it is had no new drugs been launched after 1981 (Lichtenberg 2019). To illustrate, this means that if a patient taking a drug to treat their disease would have a YLL of 10 years, living to the age of 75, the same patient without treatment would only live to the age of 63.4. Lichtenberg estimates that the number of life-years gained by drugs launched from 1981 to 2013 is a staggering 148.7 million years (Lichtenberg 2019). This means that the amount of pharmaceutical expenditure per life-year saved is only $2837, a small sum anyone would pay for the ability to live an extra year.

> *Canada's regulatory process causes undue delays in access to life-saving drugs.*

Delaying access to drugs in Canada has mortality costs. One study estimated the life-years lost due to delays in access to innovative cancer-treating drugs (Gotfrit et al. 2019). From the point of proof of drug efficacy at the clinical trial level until the first public reimbursement of 21 cancer-treating drugs, the total life-years lost was 39,076 for these 21 drugs (Gotfrit et al. 2019). Given that Canada had 541 new launches between 1982 to 2015, and that delays are only getting worse, the total life-years lost due to delays in drug access in Canada is immeasurably high.

If we assume that the total life-years lost for all drugs launched in Canada between 1982 to 2015 is comparable to the rate for cancer-treating drugs, this amounts to over one million life-years lost due to delays. Additional life-years are lost from 178 drugs that were never launched in Canada. Therefore, Canada's regulatory process causes undue delays in access to life-saving drugs, and this steadily increases mortality costs. Unfortunately, shorter life spans and unavailability of expensive drugs save public health care a lot of money, creating the appearance of a serious conflict of interest.

Indeed, many medicines that have appeared on the World Health Organization's list of essential medicines are not even sold in Canada. Many useful drugs have also been left "in regulatory limbo for decades" in Canada's health bureaucracy (Houston, Rea and Houston 2017). As a result, many Canadians are cut off from essential medicines. Canadians will increasingly be forced to seek treatment abroad – or simply do without.

The math is clear. Limiting and delaying drug access and research has huge and avoidable costs that make enlightened pharmaceutical pricing a great bargain. From a policy perspective and a humanitarian perspective, we should be doing everything reasonable to increase the massive benefits of the pharmaceutical industry to our country and mankind.

Myth 9: PMPRB is important for national pharmacare

The PMPRB's New Regulations were widely seen as potentially laying the groundwork for a national pharmacare program (Cision/Canada News Wire 2019), at least before much of the plan was finally scuttled. Indeed, perhaps that is why the government proved so unwilling to abandon the misconceived New Regulations until only recently, as doing so could signal abandonment of the pharmacare project.

Yet a pharmacare program might not even rely on PMPRB price controls. If a pharmacare program took up most or almost all of the existing retail pharmaceutical market and obtained its drugs wholesale under bulk acquisition agreements, then the PMPRB would become even more marginal and unnecessary. Alternatively, the PMPRB could be used as a façade for a completely monopsonistic purchasing system, putatively applying objective criteria to set prices at a level its government paymasters want to pay.

In any event, if the PMPRB is used one way or another to make pharmacare affordable, it will add dramatically to Canada's burden of illness and death.

Myth 10: US policy changes will not have an impact on Canada

Will the United States introduce price controls?

The United States has consistently been a powerhouse in drug research, drug development, and drug manufacturing, by fostering an environment that promotes innovation and protects it. The COVID-19 pandemic has highlighted the efficacy of the private sector in researching, developing, and producing vaccines, devices, and therapies to stop the pandemic.

Despite this, the US Democratic Party has introduced a bill to bring in drug price controls. The *Lower Drug Costs Now Act*, introduced in H.R. 3, purports to introduce a variety of price control measures, including international reference pricing, bulk negotiations, rebates, and direct price controls (CBO 2019). The bill requires the Department of Health and Human Services to negotiate maximum prices for:

- insulin;
- ≥25 brand-name drugs without generic competition from a pool of 125 drugs that account for the greatest national spending (or national Medicare spending) by 2023;
- ≥50 brand-name drugs from the same pool by 2024; and
- new drugs that exceed a specific price threshold. (CBO 2019)

According to the bill, the maximum price negotiated must not exceed 120 percent of the average price in a basket of comparator countries, including Australia, Canada, France, Germany, Japan, and the United Kingdom. If this information is not available (and it will likely not be for newly launched drugs, as the US is generally the first launch country of choice), then the maximum price will be 85 percent of the US average manufacture price (CBO 2019).

On top of this, the bill requires drug manufacturers to provide rebates to Medicare & Medicaid Centers for drugs that cost US$100 or more, and for which the average manufacturer price increases at a rate faster than inflation (CBO 2019). If the manufacturer fails to adhere to any of these price controls, they will be subject to civil penalties in the form of a 95 percent excise tax on sales revenues (CBO 2019).

H.R. 3 will impose price controls in the US based on reference prices in countries that have "decimated" the local pharmaceutical research industry (Turner 2021). While the Congressional Budget Office estimates that the bill will save US$345 billion for Medicare, it does so through antagonistic, confiscatory politics and at the cost of hindering drug development (Turner 2021). Savings for Medicare are lost revenues for manufacturers, which could have been re-invested in drug development. As a result, more than 100 drugs will no longer be produced over the next decade (Turner 2021). Canada and the whole world will lose access to all the new drug discoveries that will not be made.

The bill will also affect the biologics industry, reducing biopharma earnings by 58 percent (Guerra 2019). This will impede the most innovative drugs from being produced and will sacrifice over 80,000 jobs in the US (Turner 2021).

With the guiding star of US leadership in innovation and IP fading under the short-sighted Biden administration, the prospects for life sciences innovation are dim. The international system of price controls benefits from having a high price comparator against which everyone can boast savings. If the US lowers prices, how can the system that uses a basket of countries as comparators continue if everyone is reducing everyone else's prices? Once everyone discounts prices, what will happen? A race to the bottom? Or, since no true pricing signals exist anymore anywhere, do all prices become merely relativistic, without anyone being able to demonstrate whether they are higher or lower than some elusive, value-driven, free-market price? The result would be a fully socialized industry; we can line up for desultory supplies of the drugs, much as Soviet citizens did for toilet paper and shoes.

Re-importation

These worries also hold for drug re-importation, a crazy scheme episodically pursued with fluctuating enthusiasm in the United States, most extremely by the ideologue Senator Bernie Sanders. Yet, by executive order, the Trump administration authorized the states to make large-scale drug purchases from Canada for their Medicaid plans, which provide health care to poorer people. Florida and New Mexico have submitted plans for re-importation for FDA approval, a prerequisite to beginning drug purchases. Colorado is well on its way and others are expected to follow. Florida spends US$28 billion each year on drugs for Medicaid and reckons that purchasing them from Canada will save it between US$80 million and US$150 million in its first year – enough to make the effort worthwhile, but hardly a material portion of the state's overall budget. But the politics of exerting pressure to reform drug pricing may drive the process as much as short-term savings.

Re-importation is a wacky idea that will never work. As discussed above, any serious attempt to control US drug prices through re-importation from Canada would exhaust our drug supply quickly. It would look absurd for the US to effectively outsource drug price policy to Canada. And why would drug companies export to Canada at all if doing so would decimate their home market? We will be left without drugs. Sanders's bill on the subject would have forced drug companies to export, highlighting the Rube Goldberg lunacy of his economic illiteracy.

Myth 11: TRIPS ensures fairness in the international pharmaceutical trade

We are not aware of any nation that trades fairly in pharmaceuticals. Canada does not. In effect, a large consumer surplus is continuously imported with our drug supply, which is funded by the American consumer. Other nations pursue the same, selfish, extortionate behaviour, and American consumers bear the primary burden.

But what to do about it? If life sciences companies were to sell their goods in Canada too cheaply, Canada would be able to complain about "dumping" to the WTO. Dumping is a recognized infraction of trade rules (WTO Undated). But when nations gang up on the US to effectively force costs onto its economy, a tactic very similar to dumping, there is no recognized complaint. This reflects the terrible imbalance of trade negotiations in which productive, innovative economies negotiate to protect their producers – who benefit the whole world through trade – while other nations try to take what they can on the cheap. Trade treaties need to address this profound systemic flaw. Orderly trade can less easily function with such widespread expropriation of value from a single country than it can with some dumping. After all, dumping benefits the consumers of the importing country, if not its producers.

Canada relies on the US to innovate since we do not, then insists that the US consumer subsidize our access to those innovations. It is outrageous. We cannot make the cost of the drugs go away – no one can. We then shift the costs onto the backs of others. It may seem clever on Canada's part, but we shirk both our responsibility to help fund innovation and our opportunity to benefit from supporting an innovative economy of our own. We are not only penny-wise and pound foolish; we also miss being a moral society that treats people and businesses honourably and fairly.

But there might come a reckoning. Just because the United States has no recourse to the WTO for Canadian depredations, this does not mean it has no recourse at all. The US could make some sort of proportional price reduction for the US consumer a *quid pro quo* of allowing other nations to import its innovative pharmaceuticals. The US could, for instance, impose export fees equivalent to some or all of the lost wholesale pricing of the drug attributable to price controls (and, potentially, bulk purchase negotiations too) in the jurisdiction to which it was to be exported. It's likely the importing jurisdiction would allow prices to rise to the level required to meet the costs of the export fees. TRIPS would allow such a tactic. Importers would have to allow prices to rise to US levels or have no supply. To lower prices, the world would have to get together to figure out an equitable sharing of price increases through

the abolition of price controls. US levies could be rebated to the importers or made into a tax credit.

The US could also bring foreign drug producers to support price reform by implementing a rule requiring that no drug in the US is sold for more than it sells in its home jurisdiction. Thus, foreign drug companies that make up revenue confiscation in home jurisdictions by selling at a profit in the US, would face the same losses in the US as American companies do abroad. That is an irony of TRIPS; each member grants national treatment in access to its patent system, so foreign producers benefit from marketing in the US more than in their home countries – and more than US producers do in the exporters' countries.

It is time for a mixture of ingenuity and hardball if the harmful cabal of international drug price controls is to be broken.

Myth 12: Ending price controls will leave a dysfunctional market for patented pharmaceuticals

If all nations were to lift their price controls, huge economic gains would arise (see Myth 8 above). Pharmaceutical revenues would increase, R&D investment would increase, and new drugs would be discovered. The far wider sharing of the economic burdens and opportunities of R&D would even out inequalities and diminish local pressures for profits from higher-than-average price jurisdictions – of which Canada is one, making us a net winner from global liberalization. Canada would have more drugs, and better ones too. We would no longer face the risk of re-importation diverting our drug supply.

The US functions without price controls – despite the best efforts of the rest of the world to make sure it cannot. We have plain evidence that free markets work, even under difficult conditions. Imagine how much better it could be if we all stopped being parasites on the US innovation miracle.

Attempts to manipulate and cap pharmaceutical prices are a worldwide problem. It is an immoral strategy, creating in effect a trade externality in which nations shirk their proper share of drug development costs. Canada should take a principled stand and begin a process of education and negotiations to end drug price controls worldwide. This would be to universal benefit. We would save the costs of all the regulators, and worse, of all the delays and lack of access they engender. It is past time to let go of these obsolete and coercive tactics.

All this said, transitional issues may need to be addressed. If price controls were suddenly lifted, prices would presumably rise. How much would they rise by? With only free market price signals from the United States, it is very difficult to say. Would they rise to US levels? To a level proportionate to the US but reduced proportionally to match our lower GDP? Would they be restrained to encourage other nations to lift controls? We don't know and should study the matter further. If price increases created sudden difficulties and risked provoking too much opposition, then mechanisms could be used to manage the transition, such as gradually lessening caps on percentage increases from PMPRB prices for existing drugs.

Conclusions and recommendations

Canada has too long sustained the PMPRB, a policy mess that depresses our life sciences industry and the performance of our health care sector. Canada's drug price controls deprive us of access to many drugs on a timely basis – and, for many, at all. The PMPRB is outdated, concocted only to deal with older drug technologies and small molecule drugs. Indeed, it is maladapted for newer, and important, pharmaceutical technologies producing biologics, orphan drugs, and personalized medication. These new medications will save lives and money, if the PMPRB gets out of the way. Now that the attempt to revamp the PMPRB's mandate by regulatory change appears to have decisively failed, it should be ushered out.

Drug price controls are not in keeping with Canadian values. Price controls always depress supply and distort allocation. Price controls over any goods are all but unthinkable, and yet we apply them to the market for pharmaceuticals, where they perhaps do more harm than they could anywhere else in the economy. Pretending we don't understand simple economics; pretending Canadians overall are too poor to pay fair prices; pretending the pharmaceutical industry is an enemy instead of our most important health care ally – these pretenses dishonour us. It is past time to open our eyes and accept not only the great benefits of modern pharmaceutical science, but the responsibilities and opportunities that come with meaningful collaboration within the international life sciences industrial ecosystem.

The evidence is plain concerning the myths on which price controls rely:

- While it seems to be widespread to resent that patients, or someone on their behalf, must pay a price to access a prescribed drug, patients do not have any defined right of free access, or even affordable access, to a patented drug. For their own good, they are the market – not only they who must pay, but the only ones who will. Without their economic participation, there would simply be no drugs.

- Drug prices are not set arbitrarily high, and they cannot be. The value of a therapy in a given market, and competition, limit a drug's price. Profit margins on patented drugs are surprisingly small, given the enormous risk and cost of getting them to market. Their market prices cannot easily withstand the depredations of price controls, which is why Canada lacks many drugs and feels shortages in others.

- Monopsonic bulk purchases of drugs by government also cause harm although, since they are negotiated, seem not so punitive as price controls. Still, we must weigh the costs of under-paying both in terms of non-supply to patients in need, and on diminished research for new drugs.

- Drugs cannot be required to be priced affordably. The cost of producing and marketing a drug bear no necessary relation to affordability. Just because a drug is technically feasible doesn't mean it can be sold affordably for many, or even at a price that a free market would consider a reasonable value – the ultimate upward limit on pricing freedom.

- Far from being too profitable, as is widely supposed, the pharmaceutical industry isn't profitable enough. It would be in everybody's interest if the pharmaceutical industry were, in fact, more profitable, because it would generate more valuable research. Insufficient profitability stunts development of next-generation cures.

- Canada's drug price controls allow us to free ride flagrantly on the US consumer. Our refusal to pay sustainable prices in the market for pharmaceuticals forces the economic burden of drug research onto the one economy that willingly meets its obligations to do so – the US. We prefer to create for them a severe drug affordability problem, rather than pay our fair share.

- Drug price controls depress drug discovery and supply, leading directly to lost health and lost lives.

- Canada is almost certain not to have a pharmacare plan anytime soon, but if it did, the PMPRB would not help make it work. Any such plan would in any event lead to still more constrained drug availability in Canada.

- The US is seriously considering drug price controls, a result of high prices caused by the refusal by Canada and other nations to trade fairly in pharmaceuticals. US drug price controls would be a disaster for the industry, and it would be partly our fault.

- Trade agreements do not sufficiently protect producers, including the pharmaceutical industry. Forcing companies to underprice their products isn't actionable at the World Trade Organization, but it should be. The US

would be well advised to use tariffs and excise taxes and other means to equalize the economic burdens of pharmaceutical development.

- Pharmaceuticals can be sold in a market in which prices are not controlled. Such a system will work well.

We need to bring better learning – and more upright morality – to our policies governing drug importation, approval, and pricing. Improving Canadian policies begins with implementing the recommendations in our last paper (Owens, Rosenberg, and Sardar 2022), reprinted here in Appendix 3. Life sciences opportunities and better health care are ours for the taking, merely by maintaining a principled and consistent approach to a freer market for pharmaceuticals.

About the author

Richard C. Owens is a Munk Senior Fellow with the Macdonald-Laurier Institute and a lawyer who has specialized in business and commercial law, regulation of financial institutions, intellectual property and technology.

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Endnotes

1 Countries are ranked by levels of scientific research, drug pricing strategies, and IP policies.

Appendix I:
The PMPRB's economic impact

The production of biologics often scales slowly, creating high initial levels of scarcity that can best be resolved through high prices in the early stages of availability. The manufacturing processes are unique because while most drugs are chemicals, biologics are made by bacteria or cells (living organisms) (Sachgau 2015). This is why a non-biologic generic drug, like Advil, costs US$1 million to develop while a biologic drug can cost more than US$1 billion (Sachgau 2015).

Biologics must undergo intense preclinical tests and development to ensure their efficacy and safety before they are approved for marketing (Field and Boat 2010). Preclinical tests and small-scale manufacturing leads to higher costs and more time-consuming modes of production (Field and Boat 2010). Furthermore, the time between the end of a trial and the biologics substance manufacturing can range from one to five years (Lam 2016). Biologic companies therefore have to estimate patient populations, demand, and manufacturing capability years before they start production in order to reserve capacity where there is an industry-wide lack of it (Lam 2016).

Price plays an important role in responding to scarcity during production scaling. While a small-molecule facility can cost US$30 to US$100 million, a similar-scale biotech manufacturing facility can cost US$200 to US$500 million or more (Otto, Santagostino, and Schrader 2014). Additionally, while manufacturing small molecule drugs may require 40 to 50 critical tests, manufacturing a biologic might require over 250 (Morrow and Felcone 2004). The complexity of manufacturing biologics is exacerbated when scaling up biologics to meet commercial demand. Scaling up is the process of increasing the manufacturing yield of drug, usually by employing more machinery and personnel. The sensitivity of biologics complicates the scale-up process from the pre-clinical stage to market. Drug manufacturers must scale up without affecting the quality or performance of the active pharmaceutical ingredient (Högdin 2019).

At the pre-clinical stage, drug manufacturers may have to produce only a few hundred grams of the biologic to conduct safety studies. Yet, to proceed to clinical human trials, the manufacturers have to begin producing kilograms of it (Högdin 2019).

The first complication of the scale-up process is an issue with the biologic itself. Impurities that are negligible at the laboratory scale can become problematic at larger scales. A biologic's impurity profile may change completely at a larger scale of production, and the new profile may not meet approval requirements. This was the case with the development of a particular oligonucleotide, which had a purity percentage of 99.5 percent at the laboratory scale. After the drug was scaled up to commercial production, the purity percentage decreased to 94 percent, making it unsafe to administer to patients (Raval et al. 2018). This delayed the production process as the manufacturer had to address this impurity before production could resume, costing time and money.

The second complication is the specialized equipment that is required to produce a biologic drug. This includes single-use or stainless-steel bioreactors to prevent cross-contamination during production, and facilities that are specifically designed to control environmental conditions, such as unique refrigerators, like those used initially for the Pfizer COVID-19 vaccine (Smart 2021). Some biologics react to equipment surfaces, whether it be silicone or glass, and this has to be accounted for when scaling up production. Further, unique sterilization technology is required as some biologic drugs are not compatible with traditional terminal sterilization, which is the process of sterilizing a product in its final container (Smart 2021).

The biologic drug process also requires more experienced personnel able to handle these extremely sensitive biologics (AbbVie 2019). Finding the necessary expertise is a barrier to scaling up.

Dispensing biologic drugs into individual dosage containers is equally complex. Biologics are peculiarly sensitive to dispensing stresses, including thermal stress, shear forces, oxidation, and contamination. Large molecules are particularly liable to being heat-sensitive, and they can degrade if exposed to thermal stress. Biologic drugs often must be refrigerated at below room temperature, or even below freezing (Smart 2021). During the dispensing process, any prolonged exposure to the manufacturing environment can adversely affect the biologic as can any exposure to atmospheric oxygen and/or traditional sanitization agents used to disinfect equipment. This makes production and dispensation extremely difficult, particularly at a large scale. It also creates batch-to-batch variability, which can delay the approval process (Raval et al. 2018).

One type of biologic that is particularly not amenable to scaling up is autologous cell therapy. Autologous cell therapies use a patient's own cells for

the treatment, creating a personalized drug. Scaling up is difficult because cells must first be collected from the patient to create the treatment (Mirasol 2019). The cells must be transported to a manufacturing facility, processed individually, and transported back to the patient, all while retaining purity and sterility. Instead of scaling up, manufacturers generally have to "scale out" for autologous therapies (Mirasol 2019). This means incrementally increasing production without necessarily achieving economies of scale. It also requires hiring more personnel to complete the "manufacturing loop" for more autologous cell treatments (Mirasol 2019).

Managing the biopharmaceutical supply chain is very difficult, including increased use of single-use consumables (Sille Undated). Where a chain is reliant on a single-sourced supply, the chain can be easily interrupted, forcing costly solutions. For instance, a tsunami in Japan disrupted the supply of a single-sourced raw material for a chromatography resin called Sephacryl, which was used in biopharmaceutical manufacturing (Sille Undated).

The COVID-19 pandemic has made matters worse. Mike Piccareta, a partner with A.T. Kearney's Health Practice, claims there was already tight production capacity for biologics before the pandemic started. The health crisis, "coupled with the price increases and quality issues [they] saw coming into 2020, is compounding supply chain reliability issues for biopharmaceutical manufacturers" (Pillar 2020). COVID-19 has made it more difficult to secure the consumables for creating biologics as the supply chain is further strained by a rush to get materials for the COVID vaccine.

IP and biologics

Another explanation for the discrepancy in prices between biologics and small molecule drugs is intellectual property. Patenting biologics is more complex given their relative novelty, variability, and unpredictability. It remains uncertain exactly what biologics can be patented. IP protection of a biologic can be extremely costly (Brewster and Singh 2019). Moreover, continuing confusion about rules of patent interpretation to inventions describing large molecules and their variations, and deposits under the Budapest Treaty, continue to raise concerns that a variation in molecular structure sufficient to differentiate a product from the patent description but without therapeutic impact could substantially weaken the protection of an issued patent (Brewster and Singh 2019).

The biologics equivalent of a generic drug is known as a biosimilar. While it is relatively early days in the advent of biologics onto the market, biosimilar competition is growing and will become more of a factor in the market, eventually exerting more downward pressure on prices. It will be very important not to unduly inhibit the biologics market so that the benefit of such competition accrue faster. However, in contrast to generic drugs, biosimilars

cannot simply reverse engineer a chemical path to a given product (Price and Rai 2016). Instead, biosimilars must follow a complicated structure and manufacturing process (Brewster and Singh 2019). Often, biosimilars have to undergo preclinical trials due to the uncertain nature of these types of drugs, which bars the entry of many biosimilar products to the market (Price and Rai 2016). Due to the expensive task of developing biologic copies, the extreme cost savings often seen from small-molecule copies will likely not occur for biosimilars.

Appendix II:
Impacts of competition, insurance, and price controls on drug pricing

Economics dictates that competition increases supply and reduces price. Pharmaceuticals are not immune from economic rigour. Competition can occur between patented drugs; between brand-name, off-patent drugs; and even between generic suppliers.

Generics are often not perfect substitutes for brand-named drugs. Brand reputation for quality, and its advantage of having been specifically subject to clinical studies, means that it will usually obtain a premium in the market (Wagener 2021).

Some evidence indicates that brand-brand competition has a weak price impact, but that may be, ironically, because of the great impact that competition between patented medicines already have had on brand name, off-patent drugs. Patented drugs face two types of competition: "within-patent" and "between-patent." Within-patent competition is competition from generics after a brand-name drug's patent expires (Philipson and Dai 2003). Between-patent competition is competition from other patented drugs within the same therapeutic class, or for treating the same condition.

There is evidence that between-patent competition reduces drug sales for those in competition. Philipson and Dai (2003) conclude that between-patent competition affects the returns to innovators at least as much as within-patent competition. The study estimated that between-patent competition has at least twice the effect on reducing innovative returns than within-patent competition does.

The National Bureau of Economic Research provides a table that depicts the average number of drugs within a therapeutic class over the lifetime of a patented drug (see Table A1).

TABLE A1: THE AVERAGE NUMBER OF DRUGS WITHIN THE THERAPEUTIC CLASS OF THE PATENTED DRUG, OVER ITS PATENT LIFETIME

Drug Age	Number of Drugs
0	24.9
5	27.9
10	31.5
14	33.9

Source: National Bureau of Economic Research, from Lichtenberg and Philipson 2020.

The number of drugs within a therapeutic class increases with time. This accords with the finding that sales growth reduces by 3.6 percent within the first five years, and 5.9 percent at 10 years (Lichtenberg and Philipson 2020). As new drugs enter the market, market shares of existing drugs must reduce if the new drug is to be commercially viable.

While patented drugs do face competition that limits profits, some studies temper expectations for the effects of competition on prices. Sarpatwari et al. (2019) conducted a systematic literature review of drug price and competition data and found that the entry of new patented drugs into the pharmaceutical market did not lower prices of existing patented drugs within the same therapeutic class. Indeed, sometimes competition seemed to lead to increased prices, depending on the relative effectiveness and safety of the brands in competition, as new patented drugs with a relatively higher efficacy or safety boast pricing premiums.

For instance, new drugs that have modest or important therapeutic gains have prices up to 80 percent higher than existing alternatives. Conversely, "me-too" drugs – new patented drugs that are imitative enough to treat the same indication while being distinct enough to warrant a patent – are initially priced 51 percent lower to capture market share upon entry, but over the next eight years steadily increase in price in tandem with existing alternatives (Lu and Comanor 1998).

The *Wall Street Journal* used erectile-dysfunction drugs as a case study to illustrate the phenomenon. Despite their competition, both Viagra and Cialis experienced tandem price increases without any collusion (Rockoff 2016). Collusion is not necessary because list prices are public and drug manufacturers act independently when raising prices. In the US, one study concluded that drugs that have the same therapeutic gain are listed at around the same price as existing alternatives (Lu and Comanor 1998). Another study in Sweden found that these drugs were listed at about twice the price of existing

alternatives (Ekelund and Persson 2003). Additionally, the effect of moving from a pure monopoly to four firms with very similar products in the same therapeutic class is a price reduction of 6 percent (Hollis 2004). Hollis also found that prices for arthritic pain relievers increased when competitors entered the market (Hollis 2004).

The absence in some markets of material price declines as rivals proliferate is not evidence that competition has no impact. There may be intense pressure, for instance, not to raise prices. But, as with every other aspect of drug pricing, the market is so skewed by massive world-wide regulatory interventions that interpreting any particular set of pricing signals is exceedingly difficult.

Other factors affecting drug prices include non-price competition, public and private drug coverage, and, in Canada, the PMPRB's methodology itself.

Non-price competition

Price is rarely, if ever, the principal factor affecting drug choice. Drug manufacturers engage in non-price competition, including by advertising quality and efficacy to increase both awareness of the availability of the drug as well as sales and revenues. This has been described as "competition in creativity" (Comanor 1964). Drug companies advertise to patients, hospitals, and physicians to persuade them to use a manufacturer's drug because of better efficacy, tolerability, and/or quality, rather than price (Villar and Garcia 2017). The distinguishing qualities of the drug probably have a greater effect on drug sales than price does.

Insurance coverage

A very high percentage of drug purchases is insured. Subject to coverage rules, it is the clinician's determination, and not price competition, that causes the insurer to pay for a given drug. Drug coverage either through public or private health insurance mutes price signals to patients who do not pay the full price for a drug and so are more inelastic to drug prices (Papanastasiou 2016). This effect is compounded on the market scale of private health insurers, who are more likely than public health insurers to be inelastic to drug prices.

Private drug benefit plans are typically administered by insurance companies that are paid a percentage of plan costs (Lexchin 2015), diminishing insurer incentives to reduce them. Similarly, private plans are much more likely to list new (patented) drugs on their formularies as compared to public plans. Between 2004 and 2011, 81 percent of new drugs were insured by at least one private insurer, while only 47 percent were insured by at least one public insurer (Canadian Health Policy Institute 2013). Thus, patented drugs are more likely to be covered by private health insurers, who are also less likely to insist on lower drug prices. In Canada, at least 60 percent of the population has private health insurance (Elflein 2019).

Price controls

Patented drugs that come off patent sometimes continue with price increases at around the rate of inflation (Papanastasiou 2016). This is known as the generic competition paradox. In Canada, it seems at first glance misguided to attribute this paradox to the PMPRB, because the PMPRB does not have authority over off-patent drugs. However, the PMPRB's price review method might partly explain why drug manufacturers are punished for reducing prices with the entry of generics.

The PMPRB's price review method includes analysing a "basket of drugs" within the same therapeutic class of the incoming drug. If an incoming drug has only little or moderate therapeutic gain, its introductory price will be limited to the most expensive existing drug in its class (Swann 2009). The drug's price will then only be allowed to increase with inflation over its patent term. Thus, if a drug manufacturer reduces the price of its off-patent drug, it might have to set lower introductory prices for new drugs within the same therapeutic class (e.g., "new versions" of the older drug). Pharmaceutical drugs are not isolated inventions; they often build off each other. A drug company may create many drugs, each innovation making modest therapeutic gains. With PMPRB's price review scheme, the price of this newly innovated drug is a positive function of the older drug (Swann 2009).

Market power

Prices need to be high to profit in the short period of drug exclusivity, so firms resist price reductions. This is consistent with studies demonstrating that patent-to-patent competition lowers returns more than it lowers prices (i.e., price increases are constrained more than current prices dip, or loss of sales volume encourages maintaining profit margins).

The studies are few, and they conflict. It does seem clear, however, that patent-to-patent competition has a significant impact on drug profitability, and that competition is a material factor constraining drug prices. Of course, the market for pharmaceuticals is so regulated and artificial that it is very difficult to trust data on these issues. But it is extremely unlikely that pharmaceuticals are uniquely immune to laws of economics.

While prices are relatively inelastic, it is not clear that this provokes any need for price regulation. Inelasticity is explained in large part by consumer affluence (including access to insurance), and the need to maintain revenues during brief exclusive marketing periods. It is not evidence of abuse.

Appendix III:
Companion conclusions (from the first paper in this series)

Radical reform of drug pricing in Canada is needed.

Canada must immediately rescind the New Regulations. They will make a bad price control situation much worse. It is not fatal to the government to admit that the New Regulations go much too far and are a mistake. To rescind them will send an important signal to Canadians and internationally, and, hopefully, reverse the trend of declining registrations of new medicines, departing companies, and lack of investment in research in Canada.

Canada should phase out the PMPRB as soon as possible before its unconstitutionality is formally confirmed by the courts and any phased transition becomes more difficult or impossible. The legislation governing it should be rescinded. Canada's *Patent Act* (R.S.C., 1985, c. P-4) contains patent abuse provisions that are adequate to deal with excessive drug pricing and may be within federal government powers, unlike the PMPRB.

The PMPRB was a policy expedient intended to encourage the passage of patent reforms that have long since become a normal part of every nation's IP laws and to which Canada is in any event otherwise bound by trade and IP treaties. Those patent reforms are reasonable and sound policy. Most of the market the PMPRB was made to regulate has been taken over by negotiated bulk purchase agreements outside the scope of the PMPRB. These make the PMPRB less relevant and less able to reliably discharge its duties. Moreover, the patented pharmaceutical market will increasingly be dominated by biologics and personalized and orphan medications for which the PMPRB will not work as a regulatory tool.

To facilitate the phase-out of the PMPRB, we should analyse how markets would reach equilibrium, absent price controls. It is difficult to anticipate the effects on drug prices overall, or on patented drugs specifically, from the

abolition of price controls. Given the wide difference between Canadian and US prices, hikes in this country could be steep. Detailed economic analysis should be undertaken of the effects of removing price controls – objective studies, not by the PMPRB or its supporters – and studies based not on catastrophizing but as near as possible to market dynamics. If undue hardship were to result in a disadvantaged population, then procedures to mitigate or delay that hardship, including subsidies or a graduated relaxation of price controls, should be designed and applied. Canada is among the wealthiest countries, and a very large portion of its citizens have insurance plans to absorb the costs of drug prescriptions. We must pay our fair share and stop free-riding on US consumers.

Interestingly, since Canada is among the higher price jurisdictions worldwide (although not by much), if price controls dropped worldwide, it could certainly see its prices fall. As it is, one country alone, the United States, absorbs a wildly disproportionate share of the cost of new pharmaceuticals. If its share were widely divided amongst other nations, it may not lift prices in relatively more expensive countries by much even if, as we would hope, the industry would become more profitable overall.

On an international level, Canada should begin projects within the OECD and WTO to abolish drug price controls and develop guidelines for bulk pricing negotiations. Price controls place the world at risk of gravely depleted drug development funding, especially if the US joins the drug price control club, as it threatens now to do. Price controls cause massive distortions in international trade in goods based on life sciences IP and these distortions are not otherwise addressed by treaty. For Canada to take the lead on projects so important to world health would be to make the country more relevant on the world stage.

Canada should improve access to new drugs by adopting foreign drug registration reviews. Availability and quick approvals of pharmaceuticals must be key objectives of Canadian policy. To that end, Canada should rely on and not repeat foreign reviews of pharmaceuticals submitted for registration here. Delays in access, and non-access, occasioned by price controls and price negotiations should be avoided.

Government pharmaceutical negotiations must be transparent, particularly concerning delays in access and unavailability. All Canadians have an interest in a fast and comprehensive supply of pharmaceuticals. Government failure to acquire such a supply should be known. There cannot be a duty to register and acquire all products, but limits to health care available in Canada should be transparent.

Canada should unequivocally commit to building an innovation ecosystem. Coercion and horse-trading under industrial policy are wasteful, ineffective measures for economic growth and innovation. We must create favourable conditions for R&D investment in Canada – principally better IP protection, no price controls, lower taxes especially on capital gains, quicker market uptake of products, etc., if we are to have economic growth and innovation in life sciences in the 21st century. After all, no longer can the federal government exert substantial leverage through crippling IP protection, since it has pledged not to in TRIPS and many other trade agreements and IP treaties – pledges entirely in keeping with the modern knowledge of the value and importance of IP rights.

Finally, the United States should stand up for itself and take on the world's piratical price controls that exploit loopholes in international trade law to fleece the US consumer. Techniques such as tariffs, taxes, and penalties can be used to level the playing field and deprive countries like Canada of reliance on the US consumer and on freely confiscating the value of innovative drugs. To do so would only be fair redress.

> Canada shall be the star towards which all men who love progress and freedom shall come.
>
> – Sir Wilfrid Laurier

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TRUE NORTH
IN CANADIAN PUBLIC POLICY

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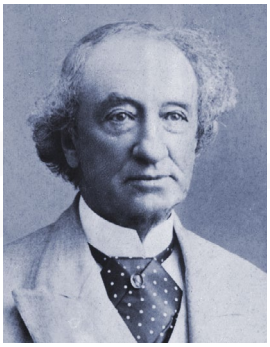

SIR JOHN A. MACDONALD

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WHAT IS IN A NAME?

The **Macdonald-Laurier Institute** exists to renew the splendid legacy of two towering figures in Canadian history:

Sir John A. Macdonald
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A Tory and a Grit, an English speaker and a French speaker, these two men represent the very best of Canada's fine political tradition. As prime minister, each championed the values that led to Canada assuming her place as one of the world's leading democracies. We will continue to vigorously uphold these values, the cornerstones of our nation.

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- Building Canada's energy advantage;
- Achieving reconciliation with Indigenous peoples;
- Making Canada's justice system more fair and efficient;
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- Regulating Canada's foreign investment; and
- Fixing Canadian health care.

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Paul Martin

I want to congratulate the **Macdonald-Laurier Institute** for 10 years of excellent service to Canada. The Institute's commitment to public policy innovation has put them on the cutting edge of many of the country's most pressing policy debates. The Institute works in a persistent and constructive way to present new and insightful ideas about how to best achieve Canada's potential and to produce a better and more just country. Canada is better for the forward-thinking, research-based perspectives that the **Macdonald-Laurier Institute** brings to our most critical issues.

The Honourable
Jody Wilson-Raybould

The **Macdonald-Laurier Institute** has been active in the field of Indigenous public policy, building a fine tradition of working with Indigenous organizations, promoting Indigenous thinkers and encouraging innovative, Indigenous-led solutions to the challenges of 21st century Canada. I congratulate **MLI** on its 10 productive and constructive years and look forward to continuing to learn more about the Institute's fine work in the field.

The Honourable
Irwin Cotler

May I congratulate **MLI** for a decade of exemplary leadership on national and international issues. Through high-quality research and analysis, **MLI** has made a significant contribution to Canadian public discourse and policy development. With the global resurgence of authoritarianism and illiberal populism, such work is as timely as it is important. I wish you continued success in the years to come.

The Honourable
Pierre Poilievre

The **Macdonald-Laurier Institute** has produced countless works of scholarship that solve today's problems with the wisdom of our political ancestors. If we listen to the **Institute**'s advice, we can fulfill Laurier's dream of a country where freedom is its nationality.

MACDONALD-LAURIER INSTITUTE

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