Ensuring early access to a COVID-19 vaccine in Canada: Regulatory Harmonization, Fair Market Prices, and Intellectual Property Rights.

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ABSTRACT

Given the huge demand for a COVID-19 vaccine, there is a serious potential for shortages and international queuing. The World Health Organization is concerned that there will not be equitable access across developed and developing countries. This paper argues that, even developed countries risk being deprioritized in the queue for access to a new COVID-19 vaccine if they have small markets, onerous regulatory and health technology assessment processes, restrictive pricing policies and funding mechanisms, or policies that jeopardize the intellectual property rights of vaccine makers. Canada is particularly vulnerable because it represents a small percentage of the global vaccines market and its processes and policies are a potential barrier to early access to a COVID-19 vaccine.

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Introduction

When the COVID-19 pandemic began, Canada and other countries experienced acute shortages of medicines, personal protective equipment, ventilators, and hospital beds. A zero-sum competition subsequently ensued between countries trying to secure scarce supplies. Recently, the World Health Organization (WHO) expressed concerns about a similar competition for access to a COVID-19 vaccine should one be developed. (WHO 2020a) If a vaccine is developed, significant increases to manufacturing capacity will be required to produce the billions of doses that will be needed to immunize the global population. Given that global demand for a COVID-19 vaccine will be universal, there is a serious potential for shortages and international queuing. The WHO is concerned that there will not be equitable access across developed and developing countries.

This paper argues that, even developed countries risk being deprioritized in the queue for access to a new COVID-19 vaccine if they have small markets, onerous regulatory and health technology assessment (HTA) processes, restrictive pricing policies and funding mechanisms, or policies that jeopardize the intellectual property rights of vaccine makers. Canada is particularly vulnerable because it represents a small percentage of the global vaccines market and its current processes and policies are a potential barrier to early access to a COVID-19 vaccine.

The potential cost of delaying access to a new COVID-19 vaccine is significant. A study conducted by researchers at the Imperial College of London concluded that if the virus was unchecked by mass quarantine it could result in a potential death rate of 0.9% of the case-positive population. (Ferguson et al 2020) If the entire national population were exposed to the virus this would translate into more than 338,000 Canadian fatalities.

To mitigate the spread of the virus, provincial and territorial governments declared public health emergencies. Mass quarantine (stay at home orders, and bans on public gatherings, travel, and normal business activities requiring physical interaction) was imposed in most jurisdictions across Canada. As of September 1, 2020, the actual COVID-19 death rate in Canada was 0.07% with 9176 fatalities, and 131,080 positive cases confirmed. (JHU 2020)

However, the country incurred significant economic costs as a result of the restrictions. As of June 12, 2020, the total cost of COVID-19 related spending by the Canadian federal government was $169 billion. Pandemic related spending by the provinces and territories will total an additional $67 billion by the end of 2020. On top of this, the associated GDP losses resulting from public health measures imposed by federal, provincial, and territorial governments could exceed $222 billion. (PBO 2020) These figures do not include the incremental health care costs attributable to COVID-19 cases.

Such costs are not sustainable. The successful early development of an effective vaccine is necessary to mitigate the need for economically costly public health measures to deal with the expected future waves of COVID-19 cases.

It is important that Canadian governments remove disincentives for vaccine makers to bring new therapies to Canadian patients. When a new vaccine is available, there is no guarantee supply will be sufficient to satisfy 100% of global demand. This could leave some countries waiting in line for access. Federal-provincial-territorial governments should be reviewing their policy environments to reduce barriers that could delay access to a new vaccine for COVID-19 in Canada.

Advanced Market Commitments

Canada's federal government has already been making advanced market commitments to vaccine makers in anticipation of a successful product being developed. There are several vaccine candidates in late stages of development. There is no guarantee that any of them will be successful in clinical trials, and the process is still many months from producing a definitive outcome. Nevertheless, as of October 5, 2020, advanced purchase and supply agreements have been signed with AstraZeneca, Sanofi, Novavax, Pfizer, Moderna and Johnson & Johnson to secure access to millions of doses of any new vaccines developed by these companies.

In principle, these agreements provide assurance that Canadians will get early access to a COVID-19 vaccine. At the same time, the federal government gets a predictable price and can estimate the budget impact in advance. Likewise, vaccine makers are able to negotiate an acceptable price and get predictable market demand, which allows them to make advanced decisions regarding investment in the capacity to supply the product.

Regulatory Harmonization

Expectations about the rapid development of a vaccine for COVID-19 should be tempered by the reality that typically, vaccine development is a long, complex process, often lasting 10-15 years from basic laboratory research to approval by the US Food and Drug Administration (FDA). (College of Physicians 2020) There is still no vaccine for SARS, a coronavirus which caused a regional pandemic in parts of Asia in 2002.

While the basic science and clinical testing cannot be accelerated beyond existing technological and financial resource constraints, governments can reduce part of the overall development time related to the regulatory process for approving new vaccines.

The most recent publicly available data for Canada were current to the fiscal year ending March 31, 2020. The data included 11 approved biologic drugs classified as New Active Substances (NAS). The time taken by the regulatory process is defined as the total number of calendar days between the date a submission is filed and the date it is approved, including processing, screening, review and any time taken by the company to respond to notices of deficiency or non-compliance. Regulatory processing time per approved NAS, ranged from 221 days to 1033 days in 2019-2020. The median regulatory processing time was 346 days, and the average was 389 days. (Health Canada 2020)

The most recent publicly available data for the regulatory approval process in the United States were current to the fiscal year ending September 30, 2019. The data included all filed new drug applications (NDA) and biologic license applications (BLA) together, with 13 new molecular entities (NME) separately indicated. Approval time includes time with the FDA, time with the sponsor, and the total time on the application. The data show the median regulatory approval process time for all NME approvals ranged from 156 days to 336 days in 2018-2019. The median time was 241 days, and the average was 232 days. (FDA 2019)

Because manufacturers typically seek HC's approval for new vaccines only subsequent to the FDA's approval (or the European Medicines Agency, EMA), any time spent in the Canadian regulatory process is additional to the time spent in the American process.

To facilitate rapid access to a new COVID-19 vaccine for Canadians, the federal government should harmonize the Canadian regulatory process with the American and European processes by directing Health Canada to adopt FDA/EMA approvals immediately as they occur. HC's scientific standard is the same as the FDA and the EMA, so presumably there should be no concerns about safety and effectiveness from harmonization. Harmonization would also save costs by eliminating redundant regulatory processes in Canada.

Health Technology Assessment

All drugs, including vaccines, are subject to health technology assessment (HTA) before they become eligible for public funding. New vaccines are subject to HTA evaluation by the National Advisory Committee on Immunization (NACI). All other new medicines are subject to HTA evaluation by the Canadian Agency for Drugs and Technology and Health (CADTH).[1]

The HTA process further extends the time to access new vaccines in Canada. Therefore, it is important to focus on eliminating unnecessary barriers to the speedy completion of these types of evaluations. Yet the NACI does not publish an annual report on its performance metrics as the CADTH does. The lack of transparency makes it difficult to know whether the process is running as efficiently as possible, whether it is adequately resourced, and whether it is sufficiently staffed. The NACI deserves closer scrutiny by policy makers looking for ways to smooth access to any COVID-19 vaccines that should be developed.

[1] INESSS for Quebec.

In addition, provinces and territories are responsible for procuring and funding vaccines. However, the provinces are not required to procure all the vaccines recommended by the NACI. In fact, many vaccines recommended by the NACI have not been covered under publicly funded immunization schedules in the provinces and territories. There is little doubt that the provinces and territories, perhaps with the assistance of the federal government, will find ways to procure and fund any new COVID-19 vaccine. But it is worth noting that the process of procuring new vaccines also extends the time to access, and deserves the attention of provincial and territorial policy makers who should be concerned with removing unnecessary barriers to accessing a new therapy.

Fair Market Prices

In addition to taking a long time, developing a new vaccine is expensive and there is a low probability of success. A 2018 study of 224 vaccine candidates for 11 priority epidemic infectious diseases, estimated that developing a vaccine from preclinical trials through to end of phase 2, including the cumulative cost of failed vaccine candidates, cost up to US$469 million on average, with lower and upper estimates ranging from US$137 million to US$1.1 billion. (Gouglas et al 2018) And a 2013 study found that the average vaccine has a market entry probability of only 6%. (Pronker et al 2013)

Vaccine makers require fair market prices to recover the risk adjusted capital cost of development, to reward innovation, and compensate for the value of the product reflected by the consumer's willingness-to-pay. In Canada, a COVID-19 vaccine will be publicly funded, which means the willingness-to-pay is a decision of public officials. Canadian governments have already signaled the societal economic value of a COVID-19 vaccine, which is implied by the cost of their policy responses to the pandemic.

A 2020 analysis estimated the politically acceptable cost per life-year implied by COVID-19 related spending by the federal government (excluding provincial-territorial government expenditures, and incremental health care costs) and GDP losses resulting from related public health policy responses, as of June 12, 2020. The analysis revealed the current government's willingness-to-pay to avoid mortality for one person, for one year. Cost (government expenditure plus GDP losses) per life-year ranged from C$138,000 under the worst-case scenario (death rate = 1% of the population, 338,303 deaths), and up to C$9.1 million under the best-case scenario (death rate < 0.035%, 8,124 deaths). (Skinner 2020)

In the absence of immunization, the economic costs associated with the COVID-19 pandemic will continue to mount. Governments will alternate from easing to re-imposing restrictions to deal with reemergence of positive cases. Effective vaccines can mitigate these costs and so, will have high economic value. New vaccines are expected to be priced far below the lowest cost per life-year implied by government policy responses to COVID-19, yielding a consumer surplus for Canadians, while saving potentially thousands of lives.

Policies that restrict fair market pricing could be a potential barrier to early access to a COVID-19 vaccine. Supply constraints and high global demand could create shortages, putting pressure on suppliers to deprioritize small market countries like Canada, Australia, United Kingdom, and New Zealand. Small wealthy markets can afford higher prices to offset lower volumes. But, if small markets have restrictive pricing policies, the risk of being placed at the back of the queue is increased.

The effect of restrictive pricing policies is particularly relevant to current developments in Canada. In January 2021, the Patented Medicine Prices Review Board (PMPRB) will implement revised regulatory guidelines governing price controls for patented prescription drugs. The guidelines introduce several rule changes, one of which is the addition of pharmacoeconomic value assessment to determine regulated prices.

The changes will have a significant impact on the prices of all patented drugs, including new vaccines. The PMPRB estimated that the combined changes would reduce the price ceilings for new medicines by more than half. Independent research has shown that the changes could reduce the maximum list prices allowed for innovative medicines by as much as 84 percent from current levels (Rawson and Lawrence 2020). Empirical research suggests that a severe reduction in prices will discourage pharmaceutical companies from launching new products in Canada (Skinner 2018). The PMPRB regulatory changes could discourage vaccine makers

from prioritizing Canada in the queue for a COVID-19 vaccine.

Further, the functional role of the PMPRB is redundant and obsolete as it pertains to vaccines generally. This view is echoed in a submission to the PMPRB Draft Guidelines Consultation, from the Public Health Agency of Canada's (PHAC) Centre for Immunization and Respiratory Infectious Diseases (CIRID 2020). CIRID expressed reservations regarding the proposed regulatory changes and their particular impact on vaccines, noting that:

- Approximately 85% of the vaccines used in publicly funded programs are purchased through a national Bulk Procurement Program managed by Public Services and Procurement Canada, which contracts directly with vaccine manufacturers using a competitive process.
- The addition of pharmacoeconomic evaluation in price regulations is redundant because PHAC is developing its own guidelines for the economic evaluation of vaccines.
- The pharmacoeconomic methods that the PMPRB intends to use are not entirely relevant to vaccines.
- Additional pharmacoeconomic factors should be considered for vaccines including costs and effects outside the health care system, population level benefits, herd effects, coverage levels, waning immunity and need for booster doses and disease carriage.
- The cost per quality adjusted life year (QALY) threshold for vaccines is too rigid.

The revised regulatory guidelines also impose significant further price reductions for drug products with larger patient populations. The PMPRB refers to the rule as the market size factor. Industry groups have raised concerns that the PMPRB's market size threshold conflicts with the Public Health Agency of Canada vaccination rate targets, because the rule penalizes manufacturers when revenues hit a certain threshold. This disincentives companies from providing higher volumes of vaccines, and conflicts with the public health mandate to achieve herd immunity, which requires large volumes of vaccine to protect the population. (VIC 2020)

The federal government should apply an exemption from PMPRB regulation to vaccines to remove one of the potential barriers to early access to a new COVID-19 vaccine for Canadians.

Intellectual Property Rights

Governments around the world might be tempted to violate the intellectual property rights of vaccine makers in order to get access to a new COVID-19 vaccine. However, using generic licensing to avoid patent obligations would be counterproductive and would do little to speed up access. Governments that signal they intend to leverage generic licensing instead of paying a fair market price for a new vaccine could be deprioritized in the queue.

Further, once a new vaccine is available, the process of developing, approving, and manufacturing a generic will extend the access delay. Manufacturing vaccines involves complex biological processes. Unlike chemical pharmaceuticals, there is no abbreviated regulatory approval for biologics. New vaccines must be tested for clinical safety and effectiveness before being approved for sale in Canada. It would be politically difficult for the federal government to justify delaying access to an available COVID-19 vaccine on the basis of cost avoidance regarding intellectual property rights.

International COVID-19 Strategies

Canada needs to act quickly to secure its place at the front of the queue for access to a new COVID-19 vaccine. Other wealthy countries have launched initiatives of their own, designed to protect the interests of their populations in gaining early access.

Australia

The Government of Australia's COVID-19 Vaccine and Treatment Strategy aims to secure access to new COVID-19 vaccines through advanced market commitments and industrial partnerships. The government has already signed an agreement with AstraZeneca to supply its COVID-19 vaccine candidate to Australia. It covers vaccine development, production, distribution, timing, and price. It commits to production of the vaccine in Australia, subject to safety and effectiveness.

Australia is investing $333 million in vaccines, therapeutics, and COVID-19 medicines. This includes $5 million for the University of Queensland's COVID-19 vaccine, which has commenced trials in Australia. The University has partnered with CSL to manufacture its vaccine in Australia. CSL has made a commitment that its dose allocation of the vaccine will prioritize the Australian market.

United Kingdom

The UK has made advanced market commitments to secure access to 6 different vaccine candidates, across 4 different vaccine types. Agreements have been reached with AstraZeneca, BioNTech/Pfizer alliance, Valneva, GSK/Sanofi Pasteur, Novavax and Janssen. (UK Government 2020)

Under two of the agreements, the government will co-fund a clinical trial of the Janssen vaccine, and will support a clinical trial of the Novavax vaccine through the National Institute for Health Research (NIHR). Together the companies will provide 90 million doses of any successful vaccine, and will locate some of the production of the new vaccines in Britain. If the vaccines are successful, both could be delivered to the UK in mid-2021.

New Zealand

In May 2020, New Zealand's government announced its COVID-19 Vaccine Strategy with the aim of ensuring early access to a safe and effective vaccine. The government has since entered an agreement with Auckland based biotechnology company Biocell to upgrade its local manufacturing capacity to help support vaccine production when a successful product is available. (NZ MOH 2020)

Recently, the government announced funding to secure access to promising vaccine candidates by investing early in the vaccine development process and using advanced market commitments to secure agreements with vaccine makers to guarantee early access for New Zealanders. However, to date, the government has made no announcements of any finalized agreements with vaccine makers.

The government's policy announcements regarding a COVID-19 vaccine are externally focused on financing, supporting, and participating in global access programs like the WHO's GAVI alliance, which is dedicated to ensuring equal access to a new vaccine across developed and developing countries.

United States

In May 2020, the US federal government launched a US$10 billion initiative called Operation Warp Speed (OWS). The program aims to deliver 300 million doses of a safe, effective COVID-19 vaccine for Americans by January 2021. (HHS 2020)

It involves the Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), National Institutes of Health (NIH), Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense (DoD).

The OWS is focusing on fast-tracking the 7 most promising vaccine candidates. To accelerate development, protocols steps will proceed simultaneously, instead of consecutively. For instance, the government will allow the start of manufacturing of the vaccine at industrial scale well before the demonstration of vaccine efficacy and safety. The US federal government is also making investments in the necessary manufacturing capacity at its own risk, giving firms confidence that they can invest aggressively in development and allowing faster distribution of an eventual vaccine. Manufacturing capacity developed will be used for whatever vaccine is eventually successful, regardless of which firms have developed the capacity.

The OWS is also securing advanced market commitments. For example, an agreement was reached with AstraZeneca to make available at least 300 million doses of its vaccine candidate for the United States, with the first doses delivered as early as October 2020 while Phase 3 clinical studies are underway.

Conclusion

Given the huge demand for a COVID-19 vaccine, there is a serious potential for shortages and international queuing. The World Health Organization is concerned that there will not be equitable access across developed and developing countries. This paper argues that, even developed countries risk being deprioritized in the queue for access to a new COVID-19 vaccine if they have small markets, onerous regulatory and health technology assessment processes, restrictive pricing policies and funding mechanisms, or policies that jeopardize the intellectual property rights of vaccine makers. Canada is particularly vulnerable because it represents a small percentage of the global vaccines market and its current processes and policies are a potential barrier to early access to a COVID-19 vaccine.

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