

Pharmaceutical security for Canada

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A secure drug supply is critical for high-quality health care and ensuring the health of all people in Canada. When supplies of medicines are compromised, clinicians might be forced to choose second-line therapies; pharmacists spend unnecessary time procuring supplies and, most critically, patients' health may be compromised.

Canada has experienced persistent pharmaceutical shortages for more than a decade,¹ with 1 study finding that nearly one-quarter of all marketed pharmaceuticals were in shortage at some point between March 2017 and September 2018.² This means that health care workers and patients or caregivers are often left scrambling to find alternatives. We argue that people in Canada should be able to access critical drugs at all times and suggest ways to achieve this goal.

What is hindering pharmaceutical security in Canada?

The Canadian pharmaceutical market is small, comprising just 2% (US\$18 billion) of global pharmaceutical revenue in 2019.³ The industry is dominated by large, foreign-owned firms that operate only small manufacturing facilities in Canada.³ With most firms being foreign owned, decision-making will not always reflect Canadian priorities, leaving Canada reliant on foreign decisions and susceptible to market forces and global conflicts.

During the last 10 years, imports as a percentage of total domestic drug expenditures increased from 74% to 93%.^{4,5} Canada's heavy reliance on pharmaceutical imports and global supply chains makes it vulnerable to disruptions in supply chains. Moreover, countries prohibit exports and prioritize the needs of their own citizens in times of emergency (e.g., the COVID-19 pandemic), leaving people in Canada with little recourse. Pharmaceutical shortages have negatively affected patients, health care professionals and the health care system for years. For example, shortages of epinephrine autoinjectors in Canada over the last 5 years have led many among the 2.6 million people who are at risk of anaphylaxis⁶ to experience stressful situations and possibly lead to severe, even life-threatening, consequences. Supplies of medications like hydroxychloroquine, used for years by patients with rheumatoid arthritis and inflammatory bowel disease, suddenly became scarce during the pandemic, as focus shifted to their use to treat COVID-19 infections.

In mid-June 2022, Health Canada listed 23 Tier 3 drug shortages on its website.⁷ Tier 3 drugs are those that have the greatest potential impact on Canada's drug supply and health care sys-

Key points

- Canada's pharmaceutical supply is highly dependent on foreign imports and vulnerable supply chains, a problem faced by many nations worldwide.
- Other high-income countries have taken action to build pharmaceutical security strategies to protect their citizens in the event of future emergencies.
- Pharmaceutical security — ensuring people in Canada have access to critical drugs at all times — should become a national priority.
- Establishing a critical drugs list, stockpiling essential medications and strengthening domestic manufacturing capacity for active pharmaceutical ingredients and drugs are actions that should be taken urgently.

tem, with low availability of alternative supplies, ingredients or therapies for these drugs. Included on the list are iodixanol, an iodine-containing nonionic radiocontrast agent; sustained-release morphine capsules; moxifloxacin solution for injection; and propylthiouracil.

Although the final forms of some pharmaceuticals are domestically produced, active pharmaceutical ingredients (APIs) — the raw materials that give any medicine its therapeutic effect — are almost exclusively imported. Over the last several decades, API manufacturing has shifted from Western countries to newer sites in India and China,⁸ which now account for 65% of the world's production by volume.⁹ Any disruption to these supply chains — for example, work interruptions, geopolitical upheavals or changes in export policies — can cause global shortages. Quality control can be another challenge with the offshoring of pharmaceuticals.¹⁰ If quality issues lead to production slowdowns, supply disruptions can occur.

Canada-based pharmaceutical companies are generally small and serve only niche segments of the market.¹¹ Moreover, after their success in the 1970s, Canadian-owned manufacturers of generic pharmaceuticals now comprise less than a third of the membership of the Canadian Generic Pharmaceutical Association. Consequently, increasing production within Canada to mitigate shortages is not a viable solution, at least at this time. Finally, shortages for generic drugs have also been attributed to their low price points, which have caused firms to exit the market. This becomes problematic when only 1 or 2 manufacturers of a generic drug exist, limiting redundancy in supply chains.²

What has been done to ensure pharmaceutical security in Canada and abroad?

A comparison between the approaches taken by Canada and some other high-income countries to bolster pharmaceutical security during the pandemic period is instructive.

Canada

Although efforts have been made in the last decade in Canada to monitor and report on drug shortages,¹² little has been done to ensure that people in Canada have access to critical drugs at all times. Recent investments to support the biomanufacturing and life sciences sector in Canada¹³ are aimed principally at pandemic preparedness and vaccines (e.g., Canada's partnership with Moderna to produce mRNA vaccines),¹⁴ but do not address all of the issues encompassing pharmaceutical security in this country.

Since March 2020, Health Canada has legislated 8 Interim Orders to prevent or alleviate pharmaceutical shortages during the pandemic. To date, these orders have provided only temporary solutions and do not address systemic issues in pharmaceutical supply. After mounting calls to develop an essential medicines list, Health Canada released a "critical drug reserve" list in April 2021; however, it contained only 12 drugs for supporting COVID-19 treatment.¹ The development of an essential medicines list has been recommended by the World Health Organization as a global measure, and nationally by Canada's federal Standing Committee on Health,¹² but remains unfulfilled.

The 2021 federal budget included funding to support growth in the domestic life sciences sector via venture capital catalyst initiatives, supporting company creation, a Stem Cell Network¹⁵ and \$250 million over 3 years to increase clinical research capacity.¹⁵ In January 2022, the federal government announced \$18.5 million in annual funding to the Centre for Research on Pandemic Preparedness and Health Emergencies.¹⁶ Although these investments are steps in the right direction, they do not address inadequacies in Canada's pharmaceutical supply beyond pandemics. Canada also maintains a national emergency strategic stockpile (NESS)¹⁷ to provide pharmaceuticals, medical equipment and supplies in the event of an emergency. However, the pandemic showed that the NESS was insufficiently stocked to meet even emergency demands¹⁷ and, more importantly, does not address the issue of chronic rotating drug shortages.

United States

In August 2020, the Executive Order on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs are Made in the United States¹⁸ directed the Food and Drug Administration (FDA) to identify a list of essential medications and produce reliable, long-term domestic supply chains for goods essential to public health. In October 2020, the FDA published a list of 227 essential medicines and medical countermeasures.¹⁹ Subsequent actions include limiting competition for essential medications produced in the US, dividing procurements among many US manufacturers and strengthening supply chains. In January 2021, the FDA began negotiating with the National Institute of

Standards and Technology to advance domestic manufacturing of drugs, medical devices and biologics via the adoption of innovative technologies. This use of new technologies would enable US-based pharmaceutical manufacturing to bolster its competitiveness with foreign countries.²⁰

Australia

In July 2021, the Australian government announced an investment of more than AUS\$36 million in manufacturing of medical products. Funding was given to 5 mostly Australian-owned pharmaceutical companies, to expand production capabilities and reduce reliance on international suppliers.²¹ In September 2021, a strategic agreement was struck between the government and industry to ensure an uninterrupted supply of medicines for Australians. The Medicines Supply Security Guarantee²² will require Australian medicine manufacturers to hold 4–6 months of stock of critical medicines — particularly those that have historically experienced shortages — within the country to provide a buffer in the event of global medicine shortages. Australia also intends to increase stockpiles of medicines within its National Medical Stockpile to higher levels than were held prepandemic.²³

European Union

In February 2021, the European Union (EU) initiated a structured dialogue to strengthen the resilience of pharmaceutical supply chains and ensure the security of medicinal supplies, without compromising affordability.²⁴ The first phase aims to close knowledge gaps in 4 key areas: robust supply chains (analyzing how to achieve a robust supply chain, while considering agility, flexibility and resilience), critical medicinal products (identifying critical medicines and tracing EU manufacturing capacity for those products), vulnerabilities (identifying vulnerabilities, including disruption challenges, and the financial impact of addressing these challenges) and innovation (identifying modernization needs, including priority areas for research and development and manufacturing processes, to ensure supply chains are adequate to meet EU public health needs). A second phase will propose measures to strengthen the resilience of pharmaceutical supply chains and ensure pharmaceutical security in Europe.

What steps are required to ensure pharmaceutical security in Canada?

A proposed measure with widespread support is that Canada should develop a critical drugs list, similar to that in the US.¹³ Proponents argue that priority should be given to those drugs deemed essential to avoid mortality or major morbidity, and those manufactured by only 1 to 2 companies, as markets with a single generic manufacturer are most likely to experience shortages.⁸ Drugs that require intervention to secure an uninterrupted supply should be identified in consultation among health professions, industry and government.

Essential drugs can be stockpiled in the NESS. Alternatively, drug manufacturers, wholesalers or importers can be mandated

to store a minimum supply of critical drugs, as in Australia. Alternatively, APIs needed to manufacture essential pharmaceuticals domestically can be stockpiled within the NESS. A central inventory management system, tracking the details of all pharmaceuticals in the NESS (including expiration dates, holding locations and quantities), should be implemented to provide inventory visibility and tracking in real time.

Calls to strengthen domestic drug-manufacturing capacity within Canada have been numerous. Targeted research and development in manufacturing technology will be needed to ensure Canada has the capability to manufacture critical medicines domestically, including APIs. Technology to make API production more efficient and cost-effective is currently being developed. For example, University of Montreal researchers are investigating continuous flow processing for API production.²⁵ This technique requires a substantially smaller plant footprint, is less hazardous and has faster turnaround time and better product quality than traditional API production techniques.²⁶ Continuous flow processing is also less expensive than traditional methods, allowing for 20%–76% lower capital expenditure and between 9% and 40% lower operating expenditures.²⁶ Investment in API and pharmaceutical manufacturing technologies should be integral to Canada's strategy to become pharmaceutically self-sufficient.

Expanding domestic drug manufacturing capacity may take several forms: establishing a Crown corporation to manufacture essential drugs; subsidizing domestically owned manufacturers that commit to essential drug production; or creating a nonprofit consortium that manufactures or sub-contracts for generic pharmaceuticals, similar to Civica in the US.²⁷ Because most drug shortages in Canada have involved generic drugs from single-source suppliers, establishing a public manufacturer of generic medicines in tandem with current manufacturers will help curb future shortages. The entity chosen for domestic manufacturing could function as a small but fully scalable operation, or it could provide a constant supply of essential drugs. To incentivize Canadian production, public procurement could include reserving partial tenders for companies conducting production activities in Canada. To support constant production, public group-purchasing organizations should be mandated to purchase entirely from the entity. To further promote pharmaceutical industry growth in Canada, incentives for venture capital should be provided. Essential medications that ultimately cannot be manufactured in Canada should be included in NESS's inventory and supply chains strengthened. This can be achieved by collaborating with reliable trading partners that are addressing similar challenges. For example, where manufacturing quality concerns may lead to shortages, Canada can enter into agreements with international partners to pool resources for conducting plant inspections. Another alternative is to proactively contract with existing commercial producers to produce pharmaceuticals, including vaccines, only in the event of shortages or other emergencies.²⁸ Higher pricing may result, but society could likely accept a trade-off between pricing and a secure supply.

Conclusion

Shortages of essential medications pose a substantial threat to health systems and place the health of people in Canada at risk. Canada's pharmaceutical supply has become highly dependent on foreign imports and vulnerable supply chains and recent Canadian investments for pandemic preparedness do not address the entirety of pharmaceutical shortcomings. A cohesive national policy is needed to address this problem.

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