

POLICY BRIEF No. 2

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Antimicrobial Resistance – One Health Consortium

Increasing Canada's support for the development of new antimicrobials

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Given the urgent need for new antibiotics, Canada should explore supporting novel antibiotics through market entry rewards, in line with new policies in the UK and Sweden, and as proposed in the US. This would also motivate patentees to seek timely approval of antibiotics in Canada.

THE ISSUE	BACKGROUND	CURRENT STATUS IN CANADA
<p>The world is facing a slowly developing crisis of pandemic proportions: the gradual loss of effective antimicrobial therapies due to antimicrobial resistance (AMR). The current stock of antimicrobials is, year by year, becoming less and less potent against common bacterial infections as a result of appropriate and inappropriate use of antimicrobials. There is an acute need to slow the increase in resistance by more appropriate use of antimicrobials and to develop new antimicrobials to replace the existing ones to decrease morbidity and mortality and unnecessary spending due to AMR. While it has never been more critical for countries to take leadership in this area, Canada is lagging behind in its support for antimicrobial research and development (R&D). Moreover, many new antibiotics are never submitted for approval in Canada.</p>	<p>A recent Council of Canadian Academies report indicates that more than a quarter of all human infections in Canada are resistant to first-line drugs.¹ The report also provides the likely scenario that if resistance against first-line antimicrobials increases to 40% (from the current 26%) by 2050, there would not only be substantial loss of life, but a decrease in Canada's cumulative GDP of about \$388B. This issue also impacts animals, as 78% of antimicrobials distributed for use in 2018 were for food production animals.²</p> <p>The Global AMR R&D Hub, a global partnership consisting of 17 countries, the European Commission and two philanthropic foundations, maintains a dashboard of antimicrobial research support that shows investment in AMR R&D, as well as incentives for antimicrobial R&D.^{3,4} The latter can be used to determine combinations of different policy incentives for supporting the development and commercialization of new antimicrobials.</p>	<p>Canada's overall support for antimicrobial R&D is currently limited. One way to support antimicrobial R&D is to create a commercially attractive market, i.e. through buying new antimicrobials when they are developed. An examination of data on sales of the most recent 10 novel antimicrobials over 2008-2018 shows that sales in Canada represent 0.3% of global expenditures, compared to Canada's 2.0% share of the global pharmaceutical market.⁵ The Global AMR R&D Hub assesses that in 2019, Canada invested about US\$21M of the world R&D investments of US\$1.49bn, about 1.4%. Despite substantial funding for basic and translational research in this area, Canada is not pulling its weight in creating incentives for developing new antimicrobials.⁶</p>

WHAT OTHER COUNTRIES ARE DOING: SOME EXAMPLES

United Kingdom. The UK has a new pilot market incentive program to stimulate the development of new antimicrobials, as part of its 5-year national action plan and 20-year vision for antimicrobial resistance. Launched in 2019, the program within Britain's National Health Service (NHS) will pay drug companies for antibiotics using a subscription-style model. This means that the NHS will pay pharmaceutical companies up-front for access to effective antimicrobials, rather than reimbursing them based on the quantity of antimicrobials sold. By delinking profit from the volume sold, the UK government only pays for antimicrobials based on their public health value, and encourages the development of new antimicrobials.⁷ The NHS will pay up to £100 million per new antimicrobial under this unique "subscription-based payment model".⁸

Sweden. The Swedish government has also recently introduced a pilot Market Entry Reward scheme, commissioning the Public Health Agency of Sweden (PHAS) to propose and pilot new models for reimbursing approved antimicrobials including a minimum annual revenue.⁹ As part of this program, the Ministry has entered into an agreement with four pharmaceutical companies to run a pilot study to test whether a new reimbursement model can ensure the availability of particularly medically important antimicrobials. In the agreements, the companies guarantee that Swedish healthcare has

sufficient access to selected antimicrobial products within specified time limits; in return, the company receives a minimal guaranteed annual income per product. The project is set to run until 2022.

United States. The PASTEUR Act would offer a market entry reward of up to US\$3bn for new antibiotics. Existing support from the Biomedical Advanced Research and Development Authority (BARDA) includes funding, technical assistance and a manufacturing network and has invested about \$1.5bn in supporting antibiotic research.¹⁰ The US also boasts CARB-X, a global non-profit partnership that provides non-dilutive funding to companies developing new antimicrobials, vaccines, rapid diagnostics and other products to prevent, diagnose and treat life-threatening bacterial infections. The initiative is funded by BARDA and National Institutes of Health, as well as a host of other stakeholder groups from around the world, including in the UK (Wellcome Trust), Germany's Federal Ministry of Education and Research, and the Bill & Melinda Gates Foundation.¹¹

IMPLICATIONS FOR POLICY IN CANADA

Canada could more effectively support antimicrobial R&D through a combination of incentive mechanisms including market entry rewards, participation in global non-profit partnerships, and direct funding of research grants.

While accepting **high prices for novel antimicrobials** will encourage companies to invest in antimicrobial R&D, the challenge with this is that hospitals, which are the chief purchasers, will normally balk at high prices and therefore encourage the use of lower-priced substitutes. Such a strategy reflects the opportunity cost of allocating more money to expensive antimicrobials within a limited budget. Provincial health ministries, facing their own constraints, are unlikely to encourage the use of high-priced antimicrobials. Given this situation, the federal government could offer **subsidies to hospitals when they purchase qualifying antimicrobials**. This is similar to the strategy in Germany and France; they allow hospitals to charge more for patients for whom novel antimicrobials are indicated.¹² There are, of course, some challenges that arise from such an approach. How large should the subsidy be? And is Canada a large enough market to have a meaningful impact? It is also unclear whether a subsidy can help to guide responsible use and stewardship.

Market Entry Rewards, like the subscription models being piloted in the UK and Sweden, can be operated within the existing system; they would require only that the Canadian government commit to pay a "prize" following successful registration of a new qualifying antimicrobial. The reward could be contingent upon the drug meeting certain conditions for availability, pricing, stewardship responsibilities, and continuing susceptibility of targeted pathogens.¹³ The advantage of a Market Entry Reward over subsidies is that the former is not necessarily dependent on the quantity used; this is good for stewardship, but means that the relationship between the usefulness of the antibiotic and the size of the reward is weak.

An interesting approach would be for Canada to fund a **global non-profit partnership directed at funding antimicrobial R&D**. For example, Canada may participate in funding CARB-X, which offers funding and technical assistance to companies that are developing new antimicrobials. This would be a way for Canada to collaborate internationally to support early stage research. One notable benefit of participating as a major funder in CARB-X is that almost all novel antimicrobials are presented to CARB-X, offering insight into the antibiotic pipeline. This information can be used to help shape domestic funding strategies. The Global Antibiotic Research & Development Partnership, founded by the World Health Organization and DNDi, represents another important opportunity for collaboration.

Finally, **increased direct funding for antimicrobial research in Canada** would help to support antimicrobial development while also supporting Canadian researchers and companies.

Thus, three key strategies can be recommended for Canada to its antimicrobial R&D policies, summarized below.



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