Cannabis clinical research in purgatory: Canadian researchers caught between an inflexible regulatory environment and a conflicted industry

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Informed cannabis health policy requires clinical evidence on the risks and benefits of commercial cannabis products. When Canada became the first G20 country to legalise cannabis, researchers envisioned a new era. Instead, Canadians can purchase products from cannabis stores, yet it is impossible to conduct high-quality research, independent from industry, on those very same products due to federal regulations.

It has long been understood that alcohol and tobacco research should be independent from cooperation with industry. The Framework Convention on Tobacco Control prohibits partnerships with industry as research funding creates a conflict of interest. The Framework Convention on Alcohol Control identified the detrimental effect of industry on policy.[1-4] Cannabis regulations obstruct similar protections

Unlike the longstanding alcohol and tobacco industries, the legal cannabis industry has only recently emerged, but the profit incentives to maximise product use and minimise research on risks remain the same. In 2018, the Government of Canada passed legislation to legalise cannabis for non-medical purposes.[5] Canadian consumers can purchase flowers, oils, edibles, concentrates, and topicals.[6] Product lines continue to diversify.

Researchers can study alcohol bought in liquor stores, but they cannot conduct clinical studies with products bought in cannabis stores because alcohol is considered a food while cannabis is considered a drug under the *Food and Drugs Act*.[7] Importantly, Health Canada—the Canadian regulator—requires drugs to be produced following Good Manufacturing Practices (GMP) to ensure pharmaceutical products are consistently manufactured and controlled according to quality standards.

In contrast, industry produces cannabis for both the recreational and medical markets under Good Production Practices (GPP), which are less stringent than GMP requirements. This incongruous regulatory environment results in the production of two general types of cannabis, one for *commercial* purposes under GPP standards and another for *research* purposes under GMP standards. Crucially, products sold in cannabis stores cannot be tested in human participants because commercial products do not meet the manufacturing requirements for research. As a result, obtaining cannabis for research depends on the willingness, ability, and good will of the cannabis industry to make research-grade products available, efforts that are unnecessary to sell product in the commercial market.

In fairness, some companies have produced research-grade products to assist researchers. This model of cooperation is analogous to those between academia and the pharmaceutical industry, but with a critical difference. The cannabis industry is not required to go through the standard drug approval process to seek approval for medical use. The cannabis industry has little incentive to support research to get their products approved for the medical market.

We are left with the paradox of having a regulatory system that allows access to cannabis for medical purposes since 2001, but makes it difficult to determine its safety and efficacy because it depends on industry to provide cannabis for research.[8] A recent letter signed by hundreds of researchers identified this challenge.[9]

Potentially of greatest importance to public health is that current regulations eliminate independent evaluation of commercial products. For instance, studies that evaluate the effects of vaping on respiratory function or edibles on cognition cannot be done without industry cooperation. Similarly, randomized trials comparing recreational products are not allowed without the direct participation of industry. Several peer-reviewed funded

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studies have been cancelled for lack of research-grade and placebo products. Moreover, Health Canada requires that researchers obtain research licences to store cannabis. Despite recent streamlining of this lengthy process, we argue that research sites should be allowed to store cannabis following manufacturers' storage requirements, without the need for licenses, as cannabis is no longer a controlled substance.

Canada's regulations effectively force academic-industry partnerships such that only research that industry finds acceptable can move forward. Cannabis companies are the final arbiters of what studies obtain products to be tested. It is understandable that industry has been reluctant to spend resources to manufacture research-grade products to study risks or medical indications for low-prevalence diseases. Researchers partnering with industry may be incentivized to minimize negative results to maintain access to study products.

What can be done to release research from this purgatory? Health Canada recently recognized that existing regulations are not ideal and "are exploring options for a more suitable regulatory framework".[10] Researchers have yet to see the outcome of these consultations or to learn how this amendment will lift the deadlock. Although Health Canada theoretically allows researchers to conduct observational studies using cannabis without requiring regulatory approval, findings from such studies are more prone to bias than those from controlled clinical trials.

Health Canada must allow commercial products to be investigated for therapeutic and non-therapeutic purposes by setting minimum regulatory conditions because the recreational and medical markets carry the same products. It is in the best interest of cannabis consumers and responsible cannabis companies to have their products tested by independent researchers. Otherwise, we all fail to protect public health.

Authors' contributions

All authors contributed to this commentary. SR and MC conceptualized this work and outlined the main arguments. EL wrote the first draft. All authors commented on and edited various versions of the commentary. All authors read and approved the final submission.

Declaration of interests

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