Canadian Covid Care Alliance
Alliance canadienne pour la prévention et prise-en-charge de la covid

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Dear Mr. Rodrigue, Minister of Health, and Committee Members,

RE: Canada Gazette, Part I, Volume 156, Number 51: Regulations Amending Certain Regulations Made Under the Food and Drugs Act (Agile Licensing)

The Canadian Covid Care Alliance is founded on principles of informed consent and medical autonomy. As an alliance of independent Canadian doctors, scientists and health care practitioners committed to providing top-quality and balanced, evidence-based information to the Canadian public, we wish to express our concerns regarding Health Canada's recently proposed "Targeted provisions and regulatory amendments to the Food and Drug Regulations and Medical Devices Regulations."

Canada's drug regulatory system historically has held to the highest standards; ensuring all medical products are proven both safe and effective and the benefits outweigh risks PRIOR to their authorization for use in Canada. Currently, to receive authorization to market a drug in Canada the manufacturer must meet the mandatory test demonstrating safety, efficacy and that benefits outweigh risk. The Canadian government recognizes that some therapeutic products and devices are both too complex and distinct for evaluation via our current regulatory pathways. Legislation was developed in 2019 in the *Food and Drugs Act* to create a framework that introduces a new pathway whereby the Minister may issue an *Advanced Therapeutic Products* (ATPs) licence if the applicant has provided evidence to support the

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conclusion that the benefits associated with the drug outweigh the risks and the risks associated with the product will be adequately managed and controlled. The holder of the licence may be subject to terms and conditions imposed by the licence. This new framework allows the Minister greater flexibility to grant rolling reviews and power to impose terms and conditions (T&Cs) thus increasing the ability to expedite authorization of novel therapeutic products classified as *ATPs.* ATPs may include but are not limited to high-risk products such as gene and cell therapies, gene editing, biologics, 3D bioprinting and artificial intelligence applications with the first of two products to be developed being adaptive machine learning-enabled devices. Health Canada is presently proposing further amendments to the Food and Drug Regulations and the Medical Devices Regulations to consolidate this framework and broaden the number of ATPs eligible for expedited authorization. According to Health Canada, these changes are intended to "advance [Canada's] modernization agenda and help to reduce regulatory irritants and roadblocks to innovation."[1]

While it is in the best interest of Canadians to encourage medical innovation and facilitate the entry of life-saving therapies, it is imperative that, in doing so, our high safety standards not be diluted or eliminated. In its efforts to enable rapid approval of therapeutic products, Health Canada is providing drug and medical device manufacturers a means of circumventing regulatory safety standards. The "Agile Licensing" framework[2] threatens to endanger Canadians, to erode basic tenets of personalized health care, and to lower the general standard of care to which Canadians are legally entitled and accustomed. As a result of these changes, Canadians will be denied robust regulatory protections in the name of regulatory flexibility. In no uncertain terms, this undermining of Canadian medical safety standards cannot be allowed to stand.

We have a number of specific concerns with the proposed amendments to the regulation:

1. Grants Products That Have Yet to Be Proven Safe Market Access

Currently, the approval of therapeutic products in Canada adheres to rigorous objective standards. To receive a notice of compliance products must be proven safe, effective and it

[1] https://www.canada.ca/en/health-canada/programs/consultation-proposed-agile-regulations-guidance-licensing-drugs-medical-devices.html

[2] https://www.canada.ca/en/health-canada/corporate/about-health-canada/activities-responsibilities/strategies-initiatives/health-products-food-regulatory-modernization/agile-licensing-drugs.html

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must be clearly shown that the benefits of the product outweigh the risks. This is usually established within the context of well-designed randomized controlled trials (RCTs). However, the ATP Pathway would allow manufacturers of novel products to effectively bypass this rigorous regulatory safety standard. Should the manufacturer provide "sufficient evidence to support the conclusion" that the benefits of product outweigh the risks and that the product risks can be managed" they may be granted early market access through an ATP licence potentially before the full complement of clinical trial data **proving safety and efficacy is available.**[3] This means that potentially harmful products could be placed on the market putting Canadians at risk of drug injury. This is especially concerning because what level of evidence is required and how risks are to be managed is ill-defined.

Further characterization of a product safety profile takes time especially for vulnerable populations such as pregnant women or children. Making drugs available before the information required to make personalized risk-benefit decisions is available limits Canadians' rights to informed consent–a universally recognized cornerstone of individualized healthcare and ethical medicine. It is essential to assess the benefit of therapeutic products within the framework of individualized health care. Centralized health care, when administering universal treatments to heterogeneous populations, can lead to unnecessary and unacceptable harms. The more novel the new therapeutic product, the higher the risks of unforeseen negative consequences and thus the need for extensive testing to prove safety before marking products available.

2. Industry Conflict of Interest and Profiting is Shaping Policy

Health Canada has a fiduciary duty to act in the best interest of Canadians and to protect them from abuse at the hands of drug and device manufacturers. It would seem that the economic advisory committees appointed by the federal government have played a central role in the creation of the ATP Pathway and the current amendments to the clinical trial framework. Industry mandates are focused on economic growth strategies and private sector concerns rather than on the safety of everyday Canadians. Their membership included strong representation from the private sector[4]. The influence of corporate interests in directing public health policy represents a considerable and potential conflict of interest which could lead to

[3] https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/regulating-advanced-therapeutic-products.html

[4] Vural, Herder and Graham (2021). From Sandbox to pandemic: Agile reform of Canadian drug regulation. Health Policy, 125:9, pp 1115-1120.

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an erosion of Canadian safety standards. Also concerning is the negligible input from citizen interest groups. **Witnessing the government partner with industry to undertake revisions to the *Food and Drug Regulatory Act* that serve to increase pharmaceutical industry profits by enabling rapid adoption of novel therapeutics, while expediting market access of under-tested products that have yet to be proven safe is an egregious breach of public trust**[3]. What is even more disconcerting is that these changes have been carried out outside the public eye with very few non-profit entities contributing to the development process. Although regulatory flexibility may spur on innovation as well as the Canadian economy, Health Canada's first priority should always be to ensure the safety of Canadians.

3. Lowering Standards for Evidence of Safety

Currently, a high standard of quality evidence must be met before a therapeutic product is approved for human use in Canada. "Agile Regulations" make it possible for The Minister of Health to authorize a product with suboptimal proof of safety under the condition that post-marketing surveillance or real-world testing continue. Post-market surveillance, or pharmacovigilance reporting, is a means of passively collecting product safety data in a broader population after a product has been proven safe and effective in a clinical trial. Pharmacovigilance reporting, however, has proven to be tedious and potentially unreliable. This type of surveillance dramatically under-reports adverse events and is not a replacement for the active rigorous safety monitoring of a well-conducted clinical trial. Passive surveillance is also unable to establish causal attribution of harm making it difficult to definitively assess when an ATP should be removed from the market. Collectively, these conditions constitute a significant lowering of safety standards used to approve medical products.

4. Putting Healthy Canadians and Animals at Risk

The proposed "Agile regulations" would create a new process that facilitates early market entry of new drugs and devices that address **emerging infectious diseases and prevention or diagnosis** of serious diseases/conditions in both human and veterinary medicine[5]. As infectious diseases are continually emerging and place at least some segment of the population at risk, current regulation might result in the conditional approval of a parade of ATPs. ATP regulations propose their use for prevention and diagnosis which would mean that they could be administered to **a healthy population** of humans and animals. As ATPs are by definition novel and as their safety profiles are often not fully characterized, this could place

[5] https://canadagazette.gc.ca/rp-pr/p1/2022/2022-12-17/html/reg1-eng.html

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healthy people at risk of injury that may have life-long consequences. Likewise use of these novel potentially under-tested products in livestock could have unintended consequences for human safety as it relates to consumption of livestock. While Canada has granted conditional approval to drugs used to treat rare diseases, cancers and severe genetic and neurological disorders their use has been notably limited[6]. Exposing healthy Canadians to novel potentially high-risk agents in order to improve innovation puts Canadians at unnecessary risk.

For these reasons, the CCCA calls for a halt to the adoption of any amendments to the *Food and Drugs Act* until the following criteria are met:

1. Before their use in healthy populations, all therapeutic products must first be PROVEN safe and effective through rigorously conducted randomized controlled trials. These trials must be published in peer-reviewed journals and their raw data must be made available for analysis by independent scientists with no conflicts of interest. **This is of particular importance for the authorization of potentially high-risk novel products or those marketed for prevention in healthy populations.**
2. We request the proposed amendments be studied by qualified independent health care providers and public representatives who are free from conflicts of interest, particularly those conflicts relating to financial, academic or career interests in the pharmaceutical industry.
3. Under no circumstance should passive post-marketing surveillance replace the rigorous active surveillance required to prove safety to market authorization. Should pharmacovigilance be used to complement existing randomized clinical trial data, predetermined thresholds for safety (safety signals), must be established, and products must be discontinued if these thresholds are reached so as to prevent further harm.
4. The public must be provided with objective evidence that these regulatory changes will benefit all Canadians. Members of the public must be included to better balance the range of interests that informed the development of the amendments and that currently favour industry and early innovation adoption initiatives over public safety. Novel safety tests must be added to address potential adverse effects introduced by the appearance of novel variables in products. For example, current mRNA injections have been contaminated by up to 48% RNA fragments, which have the potential to

[6] https://innovativemedicines.ca/wp-content/uploads/2023/04/6328_IMC_ME_IAA_Report_v6.pdf

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> unexpectedly inhibit or enhance information transfer. As more novel products are designed, additional risks for adverse effects must be addressed. With more biologics being introduced as therapeutics, the scope of novel adverse effects grows in proportion and they must be accounted for in the post-marketing surveillance

Safety standards for therapeutic products must be clearly defined and free from external influence before they can be properly used in the approval of new products for therapy or for use in the food supply. The health standards that safeguard Canadians should not be lowered in order to accelerate innovation on behalf of commercial interests. The success of a therapeutics program cannot be based on how quickly a product is brought to market. When the speed of scientific innovation is faster than the speed of safety, Canadians are put at risk.

Sincerely,

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