Notice of Intent for Interested Parties:

Tamper Resistance under the Controlled Drugs and Substances Act

Introduction:

This notice provides interested parties with the opportunity to input on a proposed new regulation under the *Controlled Drugs and Substances Act* that would require products containing specified controlled substances, or classes thereof, to have tamper-resistant properties in order to be sold in Canada. The Minister of Health intends to propose that controlled release oxycodone be subject to the proposed new tamper-resistance regulation.

Background: *Prescription Drug Abuse*

Prescription drug abuse has emerged as a significant public health concern in Canada. Prescription drugs are now the third most commonly abused substance among Canadian youth, after alcohol and marijuana. Prescription drug abuse can lead to addiction, overdose and death, and is damaging to Canadian families and communities by threatening public health and safety. Among the most commonly abused prescription drugs are opioid pain relievers, which contain controlled substances such as oxycodone, fentanyl and morphine. Canadian consumption of prescribed opioids has quadrupled since 2000. Opioid products come in several presentations, including immediate release tablets, controlled release tablets, solutions for injection, and patches. All forms can be abused. However, controlled release tablets and

patches typically include higher amounts of the active ingredient, making them more attractive for abuse. The development of drug formulations with tamper-resistant properties, i.e., properties that resist crushing, cutting, chewing, dissolution or other forms of tampering, is suggested to be one of several approaches that could help deter abuse.

Regulatory Proposal:

The *Controlled Drugs and Substances Act* , with its dual purpose of protecting public health and maintaining public safety, provides the Minister of Health with tools to restrict or prohibit activities with controlled substances and may be used to require that a drug containing a controlled substance have certain qualities, such as tamper-resistant properties.

The Minister of Health intends to propose a regulation that would require that products containing specified controlled substances, or classes thereof, listed on a schedule, have tamper-resistant properties in order for activities with these substances, such as sale, to be authorized in Canada. Under the proposed regulatory approach:

- The proposed regulation would set out criteria for tamper-resistant properties.

- Products containing a controlled substance (or class thereof) listed on a Schedule to the regulation would have to meet those criteria.
- For products that contain controlled substances that are included in the new Schedule, a manufacturer would have to submit scientific information to the Minister to demonstrate that the regulatory criteria for tamper-resistant properties have been met.
- The Minister would have decision-making authority to determine whether the criteria for tamper-resistant properties have been met and, in effect, allow the product to be sold in Canada. The Minister's approval of the tamper-resistant properties of a drug would be tied to the appropriate dealer's licensing scheme under the CDSA, which would remain separate from the Notice of Compliance process under the FDA from a regulatory decision-making perspective. However, Health Canada would strive to streamline the processes from an operational perspective.
- Health Canada would develop a guidance document for drug manufacturers to communicate the type of scientific studies and information that the Minister would expect to receive in order to determine compliance with the new regulatory criteria for tamper-resistant properties. A manufacturer would still be required to submit scientific evidence of any pharmaceutical product's safety, efficacy and quality as required by the *Food and Drugs Act* and its regulations.

The Minister also intends to propose that controlled release oxycodone be added to the Schedule to the proposed regulations.

Below are the concepts of what could be included as criteria for tamper-resistant properties in a proposed regulation.

> A tamper-resistant formulation is a product formulated with measures intended to reduce the likelihood of successfully tampering with the product for the purposes of abuse, as demonstrated by appropriate, controlled, in vitro and clinical studies.
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> A tamper-resistant formulation must satisfy the criteria set out in (1) **and** (2) below.
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> 1) A tamper-resistant formulation:
>
> > a) contains a medicinal ingredient that is a controlled substance which is inactive until it is processed inside the human body; or
> >
> > b) is formulated such that physical manipulation for the purposes of misuse will result in the release of a substance which counteracts the biologic activity of the medicinal ingredient; or
> >
> > c) is formulated such that physical manipulation for the purposes of misuse produces an unpleasant or aversive effect in the user; or
> >
> > d) when crushed or broken using manual or mechanical means, retains in vivo controlled-release properties of the intact tablet via one or more routes of administration and;

(i) when crushed or broken using manual or mechanical means, retains in vitro controlled-release properties of the intact tablet despite extractions in commonly available household solvents; or

(ii) when crushed or broken using manual or mechanical means and dissolved in water or any substance which could be injected intravenously in humans, forms a viscous substance which cannot be drawn into a syringe and so injected.

e) or, contains a mechanism other than (a), (b), (c) or (d) above intended to confer tamper-resistant properties.

2) When tampered and administered to humans via one or more routes of administration results in reduced drug liking relative to a non-tamper-resistant formulation of the same medicinal ingredient or of an alternative formulation or preparation of the same or different medicinal ingredient that meets established criteria that are considered to be acceptable as a surrogate for reduced drug liking.

Questions to Guide Input from Interested Parties:

Below are key questions for which Health Canada is particularly interested in receiving input. However, all input is welcome and should not be limited to responses to these questions.

1. Do you think that tamper-resistant products have a role to play within the Government of Canada's comprehensive strategy on addressing prescription drug abuse?

2. Should all controlled release oxycodone products be subject to a tamper-resistant regulation or only a subset of these products, for example those above a certain strength? Please provide a rationale or evidence to support your response.

3. Are there other controlled substances, or classes thereof, that you feel should be required to have tamper-resistant properties before they are allowed to be sold in Canada? If possible, please provide a rationale or evidence to support your response.

4. What criteria or evidence should be taken into consideration when determining which controlled substances should require tamper-resistant-properties in order to be sold in Canada?

5. Are the criteria outlined above for tamper-resistant properties appropriate?

6. How can tamper-resistant products be assessed in terms of their ability to effectively deter abuse?

7. What is the appropriate lead time required for the pharmaceutical supply chain to prepare for a requirement that a drug containing a controlled substance, or class thereof, have tamper-resistant properties in order to be sold in Canada, if that drug is already on the market?

8. Beyond their potential ability to curb abuse, what other impacts both positive and negative could potentially result from mandating tamper-resistant properties as a condition of sale on select pharmaceuticals that are at high risk for abuse and diversion?

9. Are there particular circumstances or scenarios under which exceptions to the proposed regulations should be authorized?

10. Are there any other comments you wish to offer to inform the Government's position on this issue?

The publication of this notice begins a 60-day comment period. Contributions can be sent by email, or mail at tamper.resistance@hc-sc.gc.ca (email), or 150 Tunney's Pasture Driveway, Main Stats Building Address Locator: 0302A Ottawa, ON K1A 0K9 (mail).

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