

Tamper Resistance under the Controlled
Drugs and Substances Act

Canadian Medical Association Response to
the Notice of Intent for Interested Parties

August 26, 2014



The Canadian Medical Association (CMA) is the national voice of Canadian physicians. Founded in 1867, CMA's vision is to be the leader in engaging and serving physicians, and the national voice for the highest standards for health and health care.

On behalf of its more than 82,000 members and the Canadian public, CMA performs a wide variety of functions. Key functions include advocating for health promotion and disease prevention policies and strategies, advocating for access to quality health care, facilitating change within the medical profession, and providing leadership and guidance to physicians to help them influence, manage and adapt to changes in health care delivery.

The CMA is a voluntary professional organization representing the majority of Canada's physicians and comprising 12 provincial and territorial divisions and 60 national medical organizations.



The Canadian Medical Association (CMA) is pleased to provide its response to the *Tamper resistance under the Controlled Drugs and Substances Act* consultation, published in the Canada Gazette on June 28, 2014. The CMA encourages Health Canada to accelerate the development of regulations to require products containing specified controlled substances, or classes thereof, to have tamper-resistant properties in order to be sold in Canada.

The CMA reiterates its overarching recommendation to the House of Commons Standing Committee on Health during its 2014 study on addressing prescription drug abuse¹; that the federal government work with provincial/territorial governments and other stakeholders to develop and implement a comprehensive national strategy to address the misuse and abuse of prescription medication in Canada. The CMA recommends that such a strategy must include prevention, treatment, surveillance and research, as well as consumer protection. One form of consumer protection is the requirement of modifications to the drugs themselves with the intent of minimizing their abuse potential.

The CMA also reiterates its recommendation made to Health Canada during the consultation on the *Controlled Drugs and Substances Act* (CDSA) and its regulations in 2014², that Health Canada establish higher levels of regulatory scrutiny for controlled prescription medication, with more stringent pre-approval requirements. In that brief, the CMA recommends that prescription opioid medication or other potentially addictive medications have tamper-resistant formulations³ to reduce the potential for misuse or abuse.

A similar position is taken by the National Advisory Council on Substance Misuse's strategy, *First Do No Harm: Responding to Canada's Prescription Drug Crisis*⁴, where one of the 58 recommendations made is that governments and other stakeholders "review existing evidence and/or conduct objective and independent research on the effectiveness of tamper-resistant and abuse-deterrent technology and packaging and make recommendations as needed to reduce the harms associated with prescription drugs and paediatric exposure."

Tamper-resistant technology aims to reduce abuse readiness and reduce dependence potential of psychoactive medications, by reducing or impeding the achievement of a rapid euphoric effect ("high") from tampering of the formulation. This can be accomplished by altering physical or chemical properties or absorption rate, prolonging half-life, developing

¹ Canadian Medical Association (2013) The need for a national strategy to address abuse and misuse of prescription drugs in Canada. CMA Submission to the House of Commons Standing Committee on Health. CMA. Retrieved from: https://www.cma.ca/Assets/assets-library/document/en/advocacy/Prescription-Drug-Abuse_en.pdf#search=The%20need%20for%20a%20national%20strategy%20to%20address%20abuse%20and%20misuse%20of%20prescription

² Canadian Medical Association (2014) Review of Controlled Drugs and Substances Act. Submission to Health Canada in response to the consultation on the Controlled Drugs and Substances Act and its regulations. CMA. Retrieved from: https://www.cma.ca/Assets/assets-library/document/en/advocacy/CMA_SubmissiontoHealthCanada-CDSA_Modernization.pdf#search=Submission%20to%20Health%20Canada%20in%20response%20to%20the%20consultation%20on%20the%20Controlled%20Drugs%20and%20Substances%20Act%20and%20its%20regulations%2E

³ There are different terms to characterize efforts to prevent the manipulation of psychoactive medications for abuse purposes: abuse or tamper resistant formulations, abuse or tamper deterrent formulations and others. In the literature, and for the purpose of this submission, terms are sometimes used interchangeably.

⁴ National Advisory Committee on Prescription Drug Misuse (2013) *First do no harm: Responding to Canada's prescription drug crisis*. Ottawa: Canadian Centre on Substance Abuse (p30). Retrieved from: <http://www.ccsa.ca/resource%20library/canada-strategy-prescription-drug-misuse-report-en.pdf>

prodrugs (inactive forms that are converted to active forms in the human body), or adding ingredients that are unattractive to users when the drug is altered.

The science around tamper resistance is relatively recent, and analytical, clinical and other methods for developing and evaluating such technologies is increasing. The regulations will have to account for this new and evolving area of expertise, in maintaining scientific rigour in the assessment and evaluation of new formulations both in the pre-approval stage as well as in the post-approval monitoring, while still ensuring efficacy for their target indication.⁵

Pre-marketing evaluations assess the potentially tamper-resistant properties of a product under controlled circumstances. They should include laboratory-based, pharmacokinetic and clinical abuse potential studies. Post-approval monitoring seeks to determine whether the marketing of the potentially tamper-resistant formulation results in changes in patterns of use, addiction, overdoses and deaths. It is important to understand whether there have been successful attempts to defeat or compromise such formulations. In the U.S., the Food and Drug Administration has not approved explicit label claims of abuse deterrence and will wait until there is sufficient post-marketing data.^{6,7} Generic manufacturers would have to be held to the same standards.

The availability of good quality, systematic surveillance data from Canadian populations is essential to demonstrate epidemiological trends, and would inform these regulations. Regulations must take into consideration the drugs that are most frequently diverted for abuse, the most frequent forms of abuse of each drug, those causing most overdoses and deaths and the populations that are most affected.

As stated previously, it is essential that such regulations be part of a comprehensive strategy to reduce abuse of prescription medications. Studies have shown that if no other measures are taken, people who are dealing with addiction and dependence will simply shift to another prescription drug that is not tamper-resistant, or even to illegal drugs. Deterrence is specific to the drug in question. Such has been the case with the introduction of oxycodone with the tamper-resistant formulation, OxyNEO®, with a significant reduction of oxycodone as a drug of choice. However, at the same time, there was a rise in the use of heroin and other opioids which did not have abuse deterrent technology^{8,9}.

Tamper-resistant technologies have not been proven to be 100% effective in preventing abuse. They are not successful in preventing the most common form of abuse, which is the ingestion of a large number of intact pills, although there have been some attempts at the addition of aversive agents. There is, however, the potential for a significant reduction in the

⁵ Center for Drug Evaluation and Research (2013) Guidance for Industry: abuse-deterrent opioids – evaluation and labeling. Draft Guidance. Food and Drug Administration. US Department of Health and Human Services. Retrieved from: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf>

⁶ Romach, MK, Schoedel, KA, & Sellers, EM (2013) Update on tamper-resistant drug formulations. *Drug and Alcohol Dependence* 130: 13-23.

⁷ Shaeffer, T (2012) Abuse-deterrent formulations, an evolving technology against the abuse and misuse of opioid analgesics. *J.Med.Toxicol.* 8:400-407.

⁸ Cicero, TJ, Ellis, MS, Surratt, HL (2012 Jul 12). Effect of abuse-deterrent formulation of OxyContin. *N Engl J Med.* 367(2): 187-9.

⁹ The Conference Board of Canada (2014) Innovations and policy solutions for addressing prescription drug abuse: summary report. Retrieved from: http://www.conferenceboard.ca/Libraries/CONF_PDFS_PUBLIC/14-0131_SummaryReport_June6.sflb

progression from oral to other forms of use, such as chewing, snorting, smoking and injecting. There is an additional challenge, which is the fact that information about procedures and recipes for drug tampering is available among people who use drugs, and sometimes is found on the Internet.

There is the possibility of negative unintended consequences in mandating tamper-resistant properties as a condition of sale for selected prescription drugs. There have been anecdotal reports that such forms might not be as effective in addressing the therapeutic needs of some patients. As well, some patients have had difficulties in swallowing tamper-resistant formulations of some drugs. It is essential that the regulations ensure that these medications have adequate clinical testing to ensure bioequivalence to the original formulations, without added adverse effects.

The regulations must also take into account the affordability of the new formulations – that the development costs of the tamper-resistant technology not result in an excessive increase in the cost to patients. This must be closely monitored so that there are adequate options for pain management.

Prescription drug abuse is a complex and very concerning health problem, and it will require more than a single policy solution. Safer drug formulations have the potential to be an important element of a comprehensive strategy, as medications are necessary tools for the treatment of pain. However, other components such as better surveillance and monitoring, clinical guidelines and tools, and enhanced access to withdrawal and addiction treatment services, as well as mental health and specialized pain services are also essential.

The CMA is pleased to provide the recommendations listed below on the development and establishment of new regulations and encourages Health Canada to accelerate the advancement of the draft regulations.

Recommendations

The CMA recommends that:

1. Health Canada accelerate the establishment requirements for tamper-resistant formulations with the intent of minimizing their abuse potential, as part of a comprehensive national strategy to address the misuse and abuse of prescription medication in Canada, in collaboration with provincial/territorial governments and other stakeholders.
2. both brand name and generic manufacturers be held to the same standards regarding tamper-resistant formulations.
3. the regulations account for the new and evolving area of expertise in tamper-resistance formulations, in maintaining scientific rigour in the assessment and evaluation of new formulations in the pre-approval and post-marketing stages.
4. the regulations ensure that tamper-resistant formulations maintain the same levels of efficacy for their target therapeutic indication as the original formulations, without added adverse effects.

5. the regulations include requirements for post-approval monitoring to determine whether the marketing of the potentially tamper-resistant formulation results in changes in patterns of use, addiction, overdoses and deaths.
6. Health Canada strengthen surveillance systems to collect necessary data from Canadian populations to inform these regulations regarding epidemiological trends, including the drugs that are most frequently diverted for abuse, the most frequent forms of abuse of each drug, those causing most overdoses and deaths and the populations that are affected.