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Public release of clinical information in drug submissions and medical device applications

Health Products and Food Branch

March 10, 2017

Canada 

Health Canada is the federal department responsible for helping Canadians maintain and improve their health. We assess the safety of drugs and many consumer products, help improve the safety of food, and provide information to Canadians to help them make healthy decisions. We provide health services to First Nations people and to Inuit communities. We work with the provinces to ensure our health care system serves the needs of Canadians.

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Preface

Health Canada's Health Product and Food Branch (HPFB) is the branch responsible for authorizing the sale and regulation of drugs and medical devices in Canada.

Clinical information, submitted by drug and medical device manufacturers, is used by Health Canada to assess the safety and efficacy of drug or safety and effectiveness of medical devices prior to permitting their sale in Canada. This detailed clinical information is far more comprehensive than that found in other sources including publications in scientific or medical journals, clinical trial registries or other information that HPFB published on its regulatory decisions.

Opening access to clinical information used to support the authorization has widespread health system benefits and can help Canadians make informed decisions about their health. It can also help Canadians to better understand the basis for HPFB's regulatory decisions.

This document introduces Health Canada's initiative to publicly release clinical information concerning the safety and efficacy of drugs and safety and effectiveness of medical devices.

It sets out the policy objectives, rationale and considerations for future regulations that would specify that certain clinical information contained in drug submissions or medical device applications would not be treated or cease to be confidential business information following a final regulatory decision and that would authorize the public release of that information.

Health Canada is committed to work openly and transparently with Canadians, stakeholders and international partners to develop and implement this initiative. Comments and opinions on this document are welcome by May 26, 2017.

1. Policy Statement

- Specified clinical information in drug submissions and medical device applications will be made available for non-commercial purposes¹ following completion of Health Canada's regulatory review process.
- Clinical information provided in drug submissions or medical device applications will continue to be treated as confidential during the regulatory review process. Specified clinical information will cease to be treated as confidential following a final regulatory decision.²
- Certain categories of commercial information that may be included with clinical information in drug submissions or medical device applications will be permitted to be exempted from public release. Drug and medical device manufacturers will be provided with an opportunity to comment on exemptions, for consideration by Health Canada prior to release of the clinical information.
- Information that may lead to identification of clinical trial participants will be removed in compliance with the *Privacy Act*.

2. Policy Rationale

Public access to clinical information on safety and efficacy of drugs or safety and effectiveness of medical devices for humans will support the Government of Canada's commitment to [Open Government](#) and increase public confidence in the regulatory decision making process by making available more information on which Health Canada's regulatory decisions are based.

Public access to clinical information will enable independent analyses of clinical data leading to a more comprehensive understanding of the drug or medical device. This will have distinct benefits for patients, health care providers, clinical trial participants and medical research.

Benefits for patients and health care providers:

- better inform health decisions; and
- promote appropriate use of drugs and medical devices.

Benefits for clinical trial participants:

- avoid duplication of research that unnecessarily exposes participants to harm; and

¹ Non-commercial means the information will not be used to support a marketing authorisation application anywhere in the world or sold, or traded to another person.

² Final regulatory decisions are: Notice of Compliance (NOC), Notice of noncompliance-withdrawn (NON-W), Notice of deficiency-withdrawn (NOD-W) that is not being re-examined under the reconsideration process, Medical Device Licence, or Refusal Letter of a medical device application that is not being re-examined under the appeals procedure.

- advance the altruistic aims of individuals who enroll in clinical trials by further advancing medical science.

Benefits for medical research:

- avoid duplicative studies that are an inefficient use of health resources; and
- enable secondary analysis of clinical information for purposes different from the original study.

3. Health Canada's Current Context

HPFB is the branch of Health Canada responsible for authorizing the sale and regulation of drugs and medical devices in Canada. Health Canada's authority to regulate the safety, efficacy and quality of drugs and safety, effectiveness and quality of medical devices is derived from the *Food and Drugs Act* and *Food and Drugs Regulations* and the *Medical Devices Regulations*, respectively.

Clinical information in drug submissions and medical device applications is currently treated as confidential business information (CBI). CBI can be disclosed to certain persons for the purpose of protection or promotion of human health or the safety of the public under section 21.1(3)(c) of the *Food and Drugs Act*. Health Canada has developed [guidance](#) to clarify the process to review requests for disclosure of CBI and the basis for decisions on whether or not to exercise this authority.

The *Food and Drugs Act* also permits the Governor in Council to make regulations that specify the business information obtained under the Act that is not CBI or the circumstances in which it ceases to be CBI. It also permits a regulation to be made authorizing the disclosure of this information. This is the basis for the development of regulations to support public release of clinical information in drug submissions and medical device applications.

4. International Context

Internationally, the European Medicines Agency (EMA) and the US Food and Drugs Administration (US FDA) have established or introduced initiatives to share clinical information while protecting privacy and commercial interests. Since 2010, the EMA has released clinical trial data for medicines on request under its [access to documents policy](#). In addition, the EMA is currently implementing its policy to [proactively publish clinical data](#) for human medicines in market authorization applications submitted since January 1, 2015. The [first publications of clinical study reports](#) occurred on October 20, 2016.

In September 2016, the US FDA issued the [final rule](#) to expand the previous clinical trial reporting for drugs, biologics, and medical devices that provided defined timelines for reporting of summary trial results including specified levels required for outcome measures, and submission of full protocols and statistical analysis plans. These new requirements will come into force in spring, 2017.

In addition to regulatory agency initiatives, pharmaceutical companies have also taken voluntary initiatives to provide qualified researchers with [access to clinical data](#) in order to advance medical science or improve patient care. Scholarly and academic

bodies have also called for more openness and transparency concerning clinical information. In spring 2016, the International Committee of Medical Journal Editors (ICMJE) [proposed](#) that as a condition for publication, authors are required to share with others the underlying clinical data to reproduce the findings. This proposal will go into effect 1 year after ICMJE adopts its data sharing requirements and supports some of the data-sharing elements outlined in the US Institute of Medicine's [report on sharing clinical trial data](#).

5. Proposed Approach

The regulations would specify the clinical information that will cease to be CBI and will provide an authority to disclose that information. Guidance would be developed to complement the new regulations. The regulations would apply to information in past submissions or applications as well as submissions or applications filed after the coming into force of the regulatory amendments.

Regulatory Approach

Health Canada intends to propose the following:

- a) Amendments to the *Food and Drug Regulations* would provide that following a final regulatory decision for the approval of the drug, clinical summaries, reports and supporting data of completed clinical trials submitted in support of a new or abbreviated drug submission or supplemental new or abbreviated drug submission for primary, secondary outcomes or exploratory endpoints that are not part of an ongoing clinical development program to support additional conditions of use or claims not identified in the submission will cease to be confidential business information. This includes methodological details that are not unique or used in an on-going development program, and insight into the stereochemistry of the product if already known, or not used for an ongoing clinical development program.
- b) Amendments to the *Medical Devices Regulations* would provide that summaries of all completed clinical studies or investigational testing in humans and detailed information of all completed clinical studies or investigational testing in humans submitted in support of a medical device application for primary, secondary outcomes or exploratory endpoints that are not part of an ongoing clinical development program to support additional conditions of use or claims not identified in the application will cease to be confidential business information following a final regulatory decision for the issuance of a medical licence. This includes methodological details that are not unique or used in an on-going development program.

Rationale: Clinical study reports, overviews, and summaries will cease to be CBI unless data contains information on secondary or exploratory end points which may constitute a component of an on-going development programme. The term "completed clinical trials" for drugs and "completed clinical studies" for medical devices is meant to exclude interim clinical study results. The disclosure of clinical results prior to the completion of the study may risk jeopardizing the completion of the study by un-blinding a blinded study.

Clinical study reports, overviews, and summaries for therapeutic products may include methodological details, specifications, and validation information. For drugs and medical devices, only portions of the methodological details (e.g. in-house modifications or procedures to analytical, immunogenicity, bioassay, or sample size calculations methods not commonly used by the industry) should be treated as confidential. For drugs, only clinical data that provides insight into the stereochemistry that is not already known and necessary for ongoing clinical development should be treated as confidential.

In support of the proposed regulations, Health Canada would develop guidance which would propose the process for identification of clinical information in drug submissions or medical device applications and redaction of CBI and personal information prior to public release. Drug or medical device manufacturers would be expected to provide specific justification for each proposed redaction based on regulations.

The proposed regulation would be aligned with leading practices of other regulators where feasible, to reduce the burden on industry and streamline access for researchers. Health Canada will aim to adapt existing work processes, enterprise systems, and applications to support public release of clinical information in a manner that complies with international and domestic laws.

Clinical Information for Public Release

Clinical information available for public release would be information used to assess the safety and efficacy of a drug or medical device in humans.

For drugs this would comprise clinical information contained in Common Technical Document (CTD) format and electronic Common Technical Document (eCTD) format in modules 2.5, 2.7 and module 5 and its appendices (with the exception of case report forms found in section 5.3.7). In non-CTD submissions, clinical study reports and related information are considered to be clinical information. (See Annex for details.)

For medical devices this would comprise the summary of all clinical studies for Class III and Class IV medical devices, and detailed information of all clinical studies for Class IV medical devices. Class I and II medical devices as defined in the *Medical Devices Regulations* are not required to submit summaries or detailed information of clinical studies and are therefore not included in the scope of this initiative. Public release of specified information would be aligned with Health Canada's future implementation of electronic filings in the International Medical Device Regulators Forum Table of Contents (ToC) format.

6. Next steps and anticipated outcomes

Health Canada intends to develop draft regulations based on the approach described in this paper, and will consult stakeholders on implementation of the proposed approach, including processes for review and redaction, mechanisms for public release of clinical information, and safeguards against commercial use. Options for phasing in implementation will also be considered.

Once in force, the regulations will establish a new channel for public access to clinical information in drug submissions and medical device applications following a final regulatory decision by Health Canada. The access to information process and Health Canada's authority to disclose CBI under s21.1(3)(c) of the *Food and Drugs Act* would continue to be available as other sources of information.

Annex A

Related sections of the Food and Drugs Act:

Confidential business information, in respect of a person to whose business or affairs the information relates, means — subject to the regulations — business information

- (a) that is not publicly available,
- (b) in respect of which the person has taken measures that are reasonable in the circumstances to ensure that it remains not publicly available, and
- (c) that has actual or potential economic value to the person or their competitors because it is not publicly available and its disclosure would result in a material financial loss to the person or a material financial gain to their competitors.

Disclosure: health or safety

21.1(3) The Minister may disclose confidential business information about a therapeutic product without notifying the person to whose business or affairs the information relates or obtaining their consent, if the purpose of the disclosure is related to the protection or promotion of human health or the safety of the public and the disclosure is to

- (a) a government;
- (b) a person from whom the Minister seeks advice; or
- (c) a person who carries out functions relating to the protection or promotion of human health or the safety of the public.

Regulations — therapeutic products

30(1.2) Without limiting the power conferred by any other subsection of this section, the Governor in Council may make regulations

(d.1) specifying the business information obtained under this Act in relation to an authorization under paragraph (a) that is not confidential business information, or the circumstances in which business information obtained under this Act in relation to such an authorization ceases to be confidential business information;

(d.2) authorizing the Minister to disclose, without notifying the person to whose business or affairs the information relates or obtaining their consent, business information that, under regulations made under paragraph (d.1),

- (i) is not confidential business information, or
- (ii) has ceased to be confidential business information.

Annex B

Drug clinical information that ceases to be CBI following a final regulatory decision in Common Technical Document (CTD) format:

Section	Description
5.1 Table of Contents of Module	
5.2 Tabular Listing of All Clinical Studies	
5.3 Clinical Study Reports	
5.3.1 Reports of Biopharmaceutical Studies	Studies that evaluate the rate and extent of release of the active substance from the medicinal product (PK and BA data)
5.3.2 Reports of Studies Pertinent to Pharmacokinetics (PK) using Human Biomaterials	In vitro studies to assess PK using biological systems.
5.3.3 Reports of human PK studies	In vivo PK studies
5.3.4 Reports of human pharmacodynamic (PD) studies	Receptor binding, receptor sensitivity, post-receptor effects, and chemical interactions
5.3.5 Reports of efficacy and safety studies	All available completed or on-going safety/efficacy-related studies on the drug in proposed and non-proposed indications.
5.3.6 Reports of post-marketing experience	Reports summarizing market experience (e.g., significant safety observations).
CSR Appendices (section 16)	
5.4 Literature References	Published articles, meeting minutes, regulatory advice.
2.5 Clinical Overview	
2.7 Clinical Summary	