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Regulations Amending the Food and Drug Regulations (Public Release of Clinical Information)

Statutory authority

Food and Drugs Act

Sponsoring department

Department of Health

REGULATORY IMPACT ANALYSIS STATEMENT

(*This statement is not part of the regulations.*)

Issues

Health Canada typically treats most clinical information provided by manufacturers in drug submissions and medical device applications as confidential business information (CBI). The Department does not have a formal policy or guidance on the identification of CBI in drug submissions and medical device applications. Consequently, the established practice is not to publicly release detailed clinical data in drug submissions and medical device applications, except where the information has entered the public domain or consent has been granted by the sponsor.

Without access to detailed clinical data, health professionals and researchers are unable to perform independent analyses of the evidence underlying published research findings and Health Canada's regulatory reviews. This approach limits transparency and misses opportunities to promote greater confidence in the oversight of drugs and medical devices. It is also out of step with Health Canada's key regulatory partners, including the European Medicines Agency (EMA) and the U.S. Food and Drug Administration, which have increased clinical data transparency over the past 10 years.

Background

Health Canada has the authority to regulate the safety, efficacy and quality of drugs and the safety, effectiveness and quality of medical devices. Health Canada's authority is derived from the *Food and Drugs Act* (FDA), the *Food and Drug Regulations* and the *Medical Devices Regulations*, respectively. In 2014, the *Protecting Canadians from Unsafe Drugs Act (Vanessa's Law)* amended the FDA to improve the safety of therapeutic products (see footnote 1) by introducing measures to, among other things,

> (a) strengthen safety oversight of therapeutic products throughout their life cycle;
>
> (b) improve reporting by certain health care institutions of serious adverse drug reactions and medical device incidents that involve therapeutic products; and
>
> (c) promote greater confidence in the oversight of therapeutic products by increasing transparency.

Most clinical information submitted to Health Canada in drug submissions and medical device applications is typically treated as CBI. This information is used to assess the safety and efficacy of a drug in humans and the safety and effectiveness of medical devices.

Vanessa's Law provided new transparency powers to the Minister of Health, including a new discretionary authority for the Minister to disclose CBI to eligible persons for the purpose of protecting or promoting human health or the safety of the public under the FDA. The Minister also has the authority under the FDA to disclose CBI for the purpose of identifying or responding to a serious risk of injury to the health of Canadians. A definition of CBI was also added to the FDA.

In addition, the FDA 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. These provisions are the basis for this regulatory proposal.

Objectives

The objective of this proposal is to provide public access to clinical information submitted to Health Canada in drug submissions for human use and medical device applications following a final regulatory decision.

Description

This proposal contains amendments to the *Food and Drug Regulations* and the *Medical Devices Regulations*.

Amendments to the *Food and Drug Regulations*

Proposed amendments to the *Food and Drug Regulations* would specify the kind of clinical information in drug submissions that would cease to be CBI following a final regulatory decision. Final regulatory decisions include the following: Notice of Compliance (NOC), Notice of Non-Compliance – withdrawn (NON-W) or Notice of deficiency – withdrawn (NOD-W).

Clinical information provided in drug submissions would continue to be treated as confidential during the regulatory review process.

The following clinical information would cease to be treated as confidential following a final regulatory decision and would be released to the public: clinical summaries, reports and supporting data of clinical trials submitted in support of a drug submission, except

> (a) information that the manufacturer did not use in the drug submission to support the proposed conditions of use or purpose for the drug; or
>
> (b) information that describes tests, methods or assays that are used exclusively by the manufacturer.

For the information that remains CBI [the information described in (a) and (b) above], Health Canada intends to establish in guidance a process that allows a manufacturer to propose redactions on any information within the submission that falls under the type of information described in (a) and (b). The manufacturer would also be asked to de-identify any personal information. Health Canada would then validate the proposed redactions and would publicly release the information that has ceased to be CBI, based on a phased-in implementation approach on disclosure.

Health Canada has established an external stakeholder group, which consists of industry and non-industry stakeholders, including clinical data transparency advocates, patient groups and health professionals, to seek input on the implementation aspects of this approach. More details on the work of this external stakeholder group are discussed in the “Implementation, enforcement and service standards” section of this document.

The following types of drug submissions would be within the scope of this regulatory proposal: New Drug Submissions (NDS), Extraordinary Use New Drug Submissions (EUNDS), Supplemental New Drug Submissions (SNDS), Supplemental Extraordinary Use New Drug Submissions (SEUNDS), Abbreviated New Drug Submissions (ANDS), Supplemental Abbreviated New Drug Submissions (SANDS), Abbreviated Extraordinary Use New Drug Submissions (AEUNDS), and Supplemental Abbreviated Extraordinary Use New Drug Submissions (SEUANDS).

As per the regulation-making authority under the *Food and Drugs Act*, the amendments would also authorize the Minister to release the information that has ceased to be CBI to the public without notifying the originator or receiving their consent.

The proposed amendments would apply to drugs for human use only, and would apply to clinical information in drug submissions filed with Health Canada before and after the coming into force of the Regulations.

Additional proposed amendments to Division 8 of the *Food and Drug Regulations* would specify that in a situation where the Minister issues a Notice of Non-Compliance (NON) or a Notice of Deficiency (NOD), the manufacturer may amend or supplement the submission by filing additional information or material within 90 days after the Minister issues the notice or by any later date, as specified in the notice.

Amendments to the *Medical Devices Regulations*

Proposed amendments to the *Medical Devices Regulations* would specify the kind of clinical information in applications for Class III and Class IV medical devices that would cease to be CBI following a final regulatory decision. Final regulatory decisions include the issuance of a Medical Device Licence or a Refusal Letter of a medical device application.

Clinical information provided in medical device applications would continue to be treated as confidential during the regulatory review process.

The following clinical information would cease to be treated as confidential following a final regulatory decision and would be released to the public: clinical summaries, reports and supporting data of clinical trials or investigational testing in humans submitted in support of any Class III or Class IV medical device application, except

> (a) information that the manufacturer did not use to support the conditions, purposes and uses for which the device is manufactured, sold or represented as submitted in the medical device application; or
>
> (b) information that describes tests, methods or assays that are used exclusively by the manufacturer.

For information that remains CBI [the information described in (a) and (b) above], Health Canada's intent is to establish in guidance a process that allows a manufacturer to propose redactions on any information within the submission that falls under the type of information described in (a) and (b). The manufacturer would also be asked to de-identify any personal information. Health Canada would then validate the proposed redactions and would publicly release the information that has ceased to be CBI, based on a phased-in implementation approach on disclosure.

Health Canada has established an external stakeholder group, which consists of a balanced representation from industry and non-industry stakeholders, including clinical data transparency advocates, patient groups and health professionals, to seek input on the implementation aspects of this approach. More details on the work of this external stakeholder group are discussed in the "Implementation, enforcement and service standards" section of this document.

As per the regulation-making authority under the *Food and Drugs Act* (FDA), the amendments would also authorize the Minister to release the information that has ceased to be CBI to the public without notifying the originator or receiving their consent.

The proposed amendments would apply to clinical information in applications for Class III and Class IV medical devices filed with Health Canada before and after the coming into force of the Regulations.

"One-for-One" Rule

The "One-for-One" Rule does not apply to this proposal, as the proposed amendments are not expected to increase the administrative burden on businesses.

Small business lens

The small business lens does not apply to this proposal, as there are no costs to small business (or costs are insignificant).

Consultation

On March 10, 2017, Health Canada published a white paper entitled *Public Release of Clinical Information in Drug Submissions and Medical Device Applications* for a 75-day consultation. On April 10, 2017, an article entitled "Health Canada to increase transparency" was published in the *Canadian Medical Association Journal* to promote awareness of the consultation document. In total, 45 submissions were received from a range of groups, including pharmaceutical and biotechnology industries (16), medical device industries (3), academia (13), health care professionals (5), and patients and the public (8).

Pharmaceutical and biotechnology industries: Several respondents asked that Health Canada's public release of clinical information be very closely aligned with the European Medicines Agency's clinical trial disclosure initiative (*European Medicines Agency Policy on Publication of Clinical Data for Medicinal Products for Human Use* — Policy 0070). In their view, international harmonization will allow for the transparency objectives to be achieved efficiently both from Health Canada's and industry's perspective. Several respondents asked that the proposal apply prospectively from the coming-into-force date only and that adequate time and consideration be given for the complexities associated with disclosing individual patient data. Several respondents also raised concerns about the burden on industry and Health Canada resources and recommended that non-prescription new drug submissions be excluded from this initiative.

Health Canada response: Health Canada intends to closely align this proposal with the European Medicines Agency's initiative on the publication of clinical data for medicinal products, in order to gain efficiencies for stakeholders and harmonize its policy with that of its

international counterparts. In order to achieve these objectives, Health Canada has established an external, multidisciplinary stakeholder group to seek input on the implementation details.

Medical device industry: Several respondents noted that the global approach in major jurisdictions (i.e. the United States and the European Union) to medical device clinical data transparency varies and is at different stages of development. Some industry stakeholders suggested that the implementation of medical device clinical data disclosure be delayed and aligned with recently published European Union medical device regulations (Regulation 2017/745 and in vitro device Regulation 2017/746). Several respondents noted that while drug companies can leverage their EMA policy 0070 transparency submissions, there is no similar opportunity for international alignment for medical devices.

Health Canada response: Health Canada is undertaking consultations with the external stakeholder group to seek input and recommendations to address issues that are unique to the medical device industry, which includes input on options to phase in the implementation for medical device applications.

Academia: Researchers reacted favourably to the proposal, noting that it will expand public access to information that will help Canadians and their health care providers make more informed health decisions. They agreed that the release should apply both prospectively and retrospectively and that all clinical data used to support market authorization should be released. Several respondents noted that the exceptions from the release of information should be removed or limited in order not to circumvent the policy objective. Concerns were also raised with respect to risks of delay in implementation and proper resourcing of this initiative.

Health Canada response: This proposal will apply to drug submissions and medical device applications filed with Health Canada before and after the coming into force of the regulations. Based on the feedback provided, the exceptions as outlined in the proposed regulations have been revised to (a) capture information that may be part of an ongoing clinical program; and (b) ensure that the exception for methods or assays that are used exclusively by a manufacturer (e.g. in-house procedure or modification of analytical assays) is limited to the description of the methods or assays and not the clinical information produced through their use.

Patient groups and health professionals: Reaction by patients and health professionals was favourable, with concerns focused on evidence that Health Canada is committed to early implementation and a process that avoids the delays experienced through the access to information process.

Health Canada response: This regulatory proposal has been developed in ways that would avoid the delays that are currently being experienced by users through the access to information process. Under this proposal, only a small amount of information contained in the

clinical information would have to be redacted prior to release. Health Canada is consulting the external stakeholder group on reasonable processing timelines for redactions.

Rationale

The proposed amendments to the *Food and Drug Regulations* and the *Medical Devices Regulations* are necessary to bring into force regulations that allow the Minister to specify what and when business information ceases to be CBI and to publicly disclose that information.

Providing public access to clinical information will enable independent or secondary analysis of the information by researchers, which would lead to a fuller understanding of the benefits, harms and uncertainties of drugs and medical devices. Health care providers can use this information to better inform health decisions and promote the appropriate use of drugs and medical devices for Canadian patients.

A small amount of information contained in the clinical information will continue to be CBI and will be redacted prior to release. The following two categories of information will continue to be CBI:

- Clinical data related to the efficacy of the drug or effectiveness of the device that the manufacturer did not use to support (1) the proposed conditions of use and purpose for the drug as submitted in the drug submission; or (2) the conditions, purposes and uses for which the device is manufactured, sold or represented as submitted in the medical device application. This data may be a component of an ongoing development program. For example, the drug manufacturer may be using the data to support future trials to gain approval for additional indications. This information could provide the competitors with clues on the drug's future uses and should therefore continue to be treated as CBI.
- Information that describes tests, methods or assays that are used exclusively by the manufacturer. Disclosure of the information pertaining to the exclusive features may prejudice the competitive position of the submission sponsor and should therefore continue to be treated as CBI.

The proposed amendments to Division 8 of the *Food and Drug Regulations* aim to align the Regulations with what Health Canada has been doing operationally, as per the *Management of Drug Submissions Guidance*, in issuing a Notice of Non-Compliance – Withdrawal (NON-W) or a Notice of Deficiency – Withdrawal (NOD-W) in situations where the manufacturer does not respond to an NON or an NOD within the prescribed time period, respectively. These amendments are necessary to clarify the policy intent that NON-W and NOD-W are considered final regulatory decisions in these scenarios and as a result, the clinical information would cease to be CBI.

Implementation, enforcement and service standards

Consultation with drug manufacturer on redactions of information that would continue to be treated as CBI

After Health Canada's issuance of a final regulatory decision, the manufacturer would be requested to provide a redacted version of the clinical information with supporting justification that would be based on the considerations outlined in this proposal. Health Canada would review the sponsor's proposed redactions on the basis of the exceptions outlined in the proposed regulations. It would provide the results of its review to the sponsor and provide an opportunity for the sponsor to respond to Health Canada's findings. Health Canada would retain the final decision on redactions in publicly released information. Clinical information would be made available on an Internet-based portal.

Consultation with external stakeholder group on proposed implementation plan

Health Canada is consulting with the external stakeholder group on aspects of the proposed implementation plan, including the processes for redacting CBI and options for phasing in the implementation approach for drug submissions and medical device applications. In addition, the external stakeholder group will be providing input on methods for the de-identification of patient data, terms of use conditions, considerations for the end user, and measurements for health system impacts.

The external stakeholder group's recommendations will contribute to the development of a draft guidance document that will be published on Health Canada's website for consultation within the 75-day *Canada Gazette*, Part I, consultation period. The final guidance document will be available at the same time as the coming into force of the proposed regulations.

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PROPOSED REGULATORY TEXT

Notice is given that the Governor in Council, pursuant to section 30 (see footnote a) of the Food and Drugs Act (see footnote b), proposes to make the annexed Regulations Amending the Food and Drug Regulations (Public Release of Clinical Information).

Interested persons may make representations concerning the proposed Regulations within 75 days after the date of publication of this notice. All such representations must cite the Canada Gazette, Part I, and the date of publication of this notice, and be addressed to Bruno Rodrigue, Office of Legislative and Regulatory Modernization, Policy, Planning and International Affairs Directorate, Health Products and Food Branch, Department of Health, Holland Cross, Tower A, Ground Floor, Suite 14, 11 Holland Avenue, Address Locator: 3000A, Ottawa, Ontario K1A 0K9 (email: LRM_MLR_consultations@hc-sc.gc.ca (mailto:LRM_MLR_consultations%40hc-sc.gc.ca)).

Ottawa, November 30, 2017

Jurica Čapkun
Assistant Clerk of the Privy Council

Regulations Amending the Food and Drug Regulations (Public Release of Clinical Information)

Amendments

1 (1) Paragraph C.08.004(1)(b) of the *Food and Drug Regulations* (see footnote 2) is replaced by the following:

> **(b)** if that submission or supplement does not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, issue a notice to the manufacturer to that effect.

(2) Subsection C.08.004(2) of the Regulations is replaced by the following:

(2) If a new drug submission or an abbreviated new drug submission or a supplement to either submission does not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, the manufacturer who filed the submission or supplement may amend the submission or supplement by filing additional information or material within 90 days after the day on which the Minister issues a notice to the manufacturer under paragraph C.08.004(1)(b) or within any longer period specified by the Minister.

(3) Paragraph C.08.004(3)(b) of the Regulations is replaced by the following:

> **(b)** if that submission or supplement does not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, issue a notice to the manufacturer to that effect.

2 (1) Paragraph C.08.004.01(1)(b) of the Regulations is replaced by the following:

> **(b)** if that submission or supplement does not comply with section C.08.002.01, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, issue a notice to the manufacturer to that effect.

(2) Subsection C.08.004.01(2) of the Regulations is replaced by the following:

(2) If an extraordinary use new drug submission or an abbreviated extraordinary use new drug submission or a supplement to either submission does not comply with section C.08.002.01, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, the manufacturer who filed the submission or supplement may amend the submission or supplement by filing additional information or material within 90 days after the day on which the Minister issues a notice to the manufacturer under paragraph C.08.004.01(1)(b) or within any longer period specified by the Minister.

(3) Paragraph C.08.004.01(3)(b) of the Regulations is replaced by the following:

> **(b)** if that submission or supplement does not comply with section C.08.002.01, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, issue a notice to the manufacturer to that effect.

3 The Regulations are amended by adding the following after section C.08.009:

Disclosure of Information in Respect of Clinical Trials

C.08.009.1 (1) In sections C.08.009.2 and C.08.009.3, information in respect of a clinical trial means information in respect of a clinical trial, within the meaning of section C.05.001, that is contained in a new drug submission, an extraordinary use new drug submission, an abbreviated new drug submission or an abbreviated extraordinary use new drug submission for a new drug for human use filed under section C.08.002, C.08.002.01 or C.08.002.1 or in a supplement to any of those submissions filed under section C.08.003.

(2) For greater certainty, the definition information in respect of a clinical trial includes information that is contained in a submission or supplement referred to in that definition and that is in respect of clinical testing involving human subjects in regards to which an application was filed under this Division before September 1, 2001.

C.08.009.2 (1) Information in respect of a clinical trial that is confidential business information ceases to be confidential business information when one of the following circumstances occurs with respect to the submission or supplement:

> **(a)** the Minister issues a notice of compliance under section C.08.004 or C.08.004.01;
>
> **(b)** in the case where the Minister issues a notice to the manufacturer under paragraph C.08.004(1)(b) or C.08.004.01(1)(b) and the manufacturer does not amend the submission or supplement under subsection C.08.004(2) or

C.08.004.01(2), the applicable period referred to in the relevant subsection expires;

(c) the Minister issues a notice to the manufacturer under paragraph C.08.004(3)(b) or C.08.004.01(3)(b).

(2) Subsection (1) does not apply to information in respect of a clinical trial that

(a) was not used by the manufacturer in the submission or supplement to support the proposed conditions of use for the new drug or the purpose for which the new drug is recommended; or

(b) describes tests, methods or assays that are used exclusively by the manufacturer.

C.08.009.3 The Minister may disclose, without notifying the person to whose business or affairs the information relates or obtaining their consent, any information in respect of a clinical trial that has ceased to be confidential business information.

Transitional Provisions

4 In sections 5 and 6, *information in respect of a clinical trial* has the same meaning as in section C.08.009.1 of the *Food and Drug Regulations*.

5 Despite subsection C.08.009.2(1) of the *Food and Drug Regulations*, information in respect of a clinical trial that is confidential business information and that is contained in a submission or supplement with respect to which one of the following circumstances occurred before the day on which these Regulations come into force ceases to be confidential business information on the day on which these Regulations come into force:

(a) the Minister issued a notice of compliance under section C.08.004 or C.08.004.01 of the *Food and Drug Regulations*;

(b) the Minister, after having notified the manufacturer under paragraph C.08.004(1)(b) or C.08.004.01(1)(b) of the *Food and Drug Regulations* that the submission or supplement did not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1 of those Regulations, issued a notice to the manufacturer, in view of the omission by the manufacturer to amend the submission or supplement, that indicated that the submission or supplement was considered to have been withdrawn;

(c) the Minister notified the manufacturer under paragraph C.08.004(3)(b) or C.08.004.01(3)(b) of the *Food and Drug Regulations* that the submission or supplement did not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1 of those Regulations.

6 (1) This section applies to information in respect of a clinical trial that is confidential business information and that is contained in a submission or supplement

(a) that was filed within 90 days before the day on which these Regulations

come into force; and

(b) with respect to which the Minister notified the manufacturer under paragraph C.08.004(1)(b) or C.08.004.01(b) of the *Food and Drug Regulations* before the day on which these Regulations come into force that the submission or supplement did not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1 of the *Food and Drug Regulations*.

(2) Despite subsection C.08.009.2(1) of the *Food and Drug Regulations*, information in respect of a clinical trial that is contained in a submission or supplement ceases to be confidential business information upon the expiry of whichever of the following periods applies if the manufacturer does not amend the submission or supplement within that period:

(a) 90 days after the day on which these Regulations come into force; or

(b) any longer period specified by the Minister.

7 Sections 5 and 6 do not apply to information referred to in subsection C.08.009.2(2) of the *Food and Drug Regulations*.

Coming into Force

8 These Regulations come into force on the day on which they are registered.

[49-1-o]

Footnote 1
Under *Vanessa's Law*, therapeutic products include prescription and over-the-counter drugs, vaccines, gene therapies, cells, tissues and organs, and medical devices. They do not include natural health products.

Footnote 2
C.R.C., c. 870

Footnote a
S.C. 2016, c. 9, s. 8

Footnote b
R.S., c. F-27

Government of Canada activities and initiatives

Apology to LGBTQ2 Canadians

(https://pm.gc.ca/eng/video/2017/11/28/prime-minister-delivers-apology-lgbtq2-canadians?utm_source=pm_eng&utm_medium=priority&utm_campaign=LGBTQ2apology)
Prime Minister Justin Trudeau delivers a formal apology in the House of Commons to LGBTQ2 Canadians

2018 is the Canada-China Year of Tourism—join the celebration!

(https://www.ic.gc.ca/eic/site/100.nsf/eng/home?open&WT.mc_id=CCYT2018_canada.ca-home_activities-initiatives_en)
Celebrate the people-to-people ties that connect our countries, and take in the wonders of our two great nations. Find out how you can be part of the experience. #2018CCYT

Canada Learning Bond - Call for Concepts

(https://www.canada.ca/en/employment-social-development/services/funding/learning-bond-concept.html)
Funding: Call for Concepts to Increase awareness and take-up of the Canada Learning Bond.