February 21, 2018

Mr. Bruno Rodrigue
Director, Office of Legislative and Regulatory Modernization
Policy, Planning and International Affairs Directorate
Health Products and Food Branch
Department of Health
Holland Cross, Suite 14
11 Holland Avenue
Ottawa, Ontario K1A 0K9

By electronic mail: LRM_MLR_consultations@hc-sc.gc.ca

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

Dear Mr. Rodrigue:

On behalf of Innovative Medicines Canada (IMC), I am writing in response to the proposed amendments to the *Food and Drug Regulations* (the "Proposed Regulations"), as published in the *Canada Gazette*, *Part I* on December 9, 2017, with respect to the public release of clinical information. Our comments on the Proposed Regulations build on our record of engagement with Health Canada on this subject in recent years, including our comments on the March 2017 White Paper on Public Release of Clinical Information in Drug Submissions and Medical Device Applications.

IMC is the national voice of Canada's innovative pharmaceutical industry. We advocate for policies that enable the discovery, development and commercialization of innovative medicines and vaccines that improve the lives of all Canadians. We support our members' commitment to being valued partners in the Canadian health and regulatory systems.

Our members are the stakeholders that would be most impacted by the Proposed Regulations. We have identified several significant concerns with the proposed amendments related to the disclosure of Confidential Business Information (CBI), particularly Health Canada's overly broad approach to disclosure of CBI. Further, our members wish to impart their great concern with the apparent lack of alignment with evolving international approaches to CBI disclosure – and in particular the European Medicines Agency (EMA) Policy 0070.

Our members' ability to comprehensively review and fully appreciate the potential impacts of the Proposed Regulations has been compromised given that Health Canada has not released implementation guidelines during the regulatory consultation process, despite having committed to doing so in the Regulatory Impact Analysis Statement (RIAS) accompanying the proposals. It is our understanding that publication of a draft Guidance Document has been delayed until after the conclusion of the consultation period. This is an unfortunate development, which has negatively impacted our ability to provide meaningful feedback regarding the policy and practical issues underlying the implementation of the Proposed Regulations.

Below, we outline various concerns respecting the scope of application and implementation of the Proposed Regulations as well as the policy rationale advanced in support of the changes.

- *Compliance with International Trade Obligations and the Protection of "Trade Secrets"*

Consistent with our previous submissions to Health Canada regarding CBI, IMC wishes to convey our concerns regarding the impact of the Proposed Regulations, as currently drafted, on Canada's compliance with its international trade obligations under North American Free Trade Agreement and the Agreement on Trade-Related Aspects of Intellectual Property Rights. In particular, we would emphasize the treaty-enshrined mandate that confidential information is to be protected against disclosure except where its disclosure is necessary to protect the public[1].

The 2014 *Protecting Canadians from Unsafe Drugs Act (Vanessa's Law)* and the regulations enabled by that legislation failed to utilize the well-defined legal concept of "trade secrets". Under the current proposal, Health Canada similarly does not define such language nor does it provide any clear direction relating thereto. As a result, the Proposed Regulations create an opportunity for potential disclosure of CBI, even if inadvertent, in a manner that runs contrary to Canada's international trade obligations. In contrast, the United States has enacted Section 301(j) of the *Federal Trade Secrets Act*, which prohibits US Food and Drug Administration (FDA) employees from revealing any information acquired under the authority of section 505 of the *Federal Food, Drug and Cosmetic Act* concerning any method or process that – as a trade secret – is entitled to protection. The FDA has recognized this information to include safety and effectiveness data for new drugs derived from studies. Violation of this section is a criminal offence, regardless of knowledge or intent[2].

The absence of a clear definition of "trade secrets" is particularly problematic in view of the potential for retroactive application of the Proposed Regulations to prior submissions, which may inadvertently contain trade secrets that are embedded in clinical trial documentation in differing formats (formula, chemistry and manufacturing information, etc.). As a result, under the Proposed Regulations, industry would lack the ability to review and appropriately protect this information simply due to its format and location within historical submissions.

[1] North American Free Trade Agreement, 32 I.L.M. 289 and 605 (1993) (NAFTA), at Article 1711(5); Agreement on Trade-Related Aspects of Intellectual Property Rights, 1869 UNTS 299; 33 ILM 1197 (1994), at Article 39.3.
[2] Federal Food, Drug, and Cosmetic Act at Section 303(a); see also United States v. Park, 421 U.S. 658 (1975).

- *Harmonization and Alignment of Approaches with the United States (US) and European Union (EU)*

Health Canada has identified alignment with international regulators as a key rationale underlying the Proposed Regulations. However, IMC contends that the Proposed Regulations do not in fact align – in either concept or practice – with transparency regimes in the US or EU in a number of key respects:

- In the EU, the definition of "commercial confidential information" (CCI) was recently reviewed by the General Court, which ultimately recognized that there was a *prima facie* case that a general presumption of confidentiality applies to all documents submitted for the purpose of a marketing authorization application[3]. The EMA's Proactive Disclosure Policy defines CCI as: "any information contained in the clinical reports submitted to the Agency by the applicant [marketing authorization holder (MAH)] that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the applicant/MAH."[4] Moreover, EMA Policy 0070 does not apply to medical devices, and therefore the Canadian proposals are not aligned with the EU in this additional respect.
- In the US, CCI is defined as "valuable data or information which is used in one's business and is of a type customarily held in strict confidence or regarded as privileged and not disclosed to any member of the public by the person to whom it belongs."[5] Courts have held that CCI includes preclinical and clinical safety and efficacy data submitted to the FDA in new drug applications.[6]

The perceived risk of policy misalignment with Canada's major trading partners is exacerbated by the absence of a corresponding Health Canada Guidance Document that might provide greater clarity on implementation issues, including:

1. External guidance on the procedural aspects related to the submission of clinical reports for the purpose of publication in accordance with the Proposed Regulations;

2. External guidance on the anonymization of clinical reports for the purpose of publication in accordance with the Proposed Regulations; and

3. External guidance on the identification and redaction of CBI in clinical reports submitted to Health Canada for the purpose of publication in accordance with the Proposed Regulations.

Practically speaking, material differences in the approach proposed by Health Canada will likely result in partial or full duplication of efforts for local Canadian market authorization holders and a consequent inability to leverage clinical documentation already processed in other jurisdictions. The resulting additional and substantial burden on manufacturers should be reconsidered since it may ultimately lead to delays in bringing innovative products to Canadian patients.

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[3] Case T-44/13 R *AbbVie Inc and AbbVie, Ltd v EMA*, 25 April 2013, para 66.
[4] European Medicines Agency policy on publication of clinical data for medicinal products for human use, Policy 70, 2 October 2014. See http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/10/WC500174796.pdf
[5] *21 C.F.R.* at Section 20.61(b).
[6] See, e.g. *Jerome Stevens Pharms., Inc. v. FDA*, 402 F.3d 1249, 1251, 1256, 1258 (D.C. Cir. 2005).

Efforts to align with other jurisdictions must also take into consideration the current degree of flux in other transparency regimes, some of which are not yet fully operational, such as the EU regime. Health Canada is encouraged to focus instead on the more established approaches of other jurisdictions, and to ensure that its proposed regulatory framework is not misaligned or significantly broader in scope in comparison.

- *Scope of Authority and Information Subject to Release CBI*

IMC has several concerns with regard to the scope of application of the Proposed Regulations. First and foremost, the Proposed Regulations authorize the Minister to release information that has ceased to be CBI to the public without first notifying the originator or receiving their consent. IMC cannot support this proposed lack of advance notice, which will inevitably create regulatory uncertainty and disincentivize the marketing of innovative medicines in Canada.

In addition, IMC has serious concerns with that the regulatory proposal would use the regulation-making authority under the *Food and Drugs Act* to allow the Minister to specify when clinical information ceases to be CBI. This authorization is intended to apply to all submissions without limitation, retrospective or otherwise, including information contained in past submissions or applications. We note that historical submissions were made under a regulatory regime that consistently and predictably treated this information as CBI. As such, this information was provided to Health Canada under the reasonable expectation that the information was – and would continue to be treated as – CBI.

This proposed retroactive applicability is clearly contrary to the EMA's application of Policy 0070, which explicitly is <u>not</u> retrospective in nature. Also, while it continues to evolve in other respects, Policy 0070 applies only to marketing authorization applications, line extensions and extensions of indications made after one of two prospective dates.

In addition, and similar to the EMA, Health Canada has confirmed the importance of adhering to the *Privacy Act* in the implementation of regulations that allow for the public release of clinical information – so as to ensure, in particular, that individual participants of clinical trials are not identifiable. This protective measure is needed to ensure the continued integrity of the clinical trial process in Canada and protect Canadian citizens' private information. However, Health Canada has not identified who will be the "Data Controller", an important decision in the context of this proposed regulatory regime. It is the Data Controller that would have the responsibility of ensuring adequate anonymization of clinical information and be liable should individuals be wrongly identified.

- *Administrative Burden*

Health Canada has adopted the position that the broad scope of the regulatory proposal is justified by EMA Policy 0043 relating to access to documents and that this position applies to submissions retrospectively. This extension of one policy rationale to a different issue is inappropriate. Policy 0043 is broadly comparable to Canada's federal *Access to Information Act* and administrative processes, and therefore does not justify the unlimited, retrospective scope of the proposals relating to CBI that is contained in the clinical information accompanying applications made to Health Canada.

IMC also disagrees with the statement in the RIAS that the Proposed Regulations the "are not expected to increase the administrative burden on businesses". The Proposed Regulations would unquestionably increase administrative burden on both the innovative pharmaceutical industry and Health Canada in terms of both costs and resources. Much of the additional burden would come from the administrative, technical and scientific evaluation of past regulatory records. In particular, the retrospective application of the Proposed Regulations would create a substantial regulatory and administrative burden for both industry and Health Canada to implement the process for public release of data from past submissions. Particularly where data is not in an electronic format, substantial effort and resources will be required to digitize the information as well as to review and redact confidential information. In many cases, this historical information would not have been filed in the Common Technical Document structure, nor would it meet current regulatory standards that have evolved in light of advancements in scientific technologies and best practices for benefit/risk assessment now mandated by Health Canada.

- *Comment on Policy Rationale Regarding the Public's Use of Information*

In the Rationale section of the RIAS, Health Canada states the following about the end use of clinical 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."

IMC is concerned that independent analyses of clinical data may result in inaccurate or incomplete conclusions regarding the safety or efficacy of a product, or potentially lead to increased off-label use. This potential for misinterpretation calls for a reconciliation of any independent analysis with that performed by the drug sponsor so as to account for any subsequent Health Canada safety reviews or other analyses which reaffirm the benefit/risk of the product. There is a real risk of differing messages and information emerging in respect of a given product, particularly in the public domain, which may not align with Health Canada's view of the product and its level of benefit/risk. It is unclear how and under what circumstances these differing views may be reconciled.

We are also concerned with any development that may be perceived as undermining or questioning the ultimate regulatory authority of Health Canada. It is not appropriate to have industry being placed in a position of defending the data submitted and approved by Health Canada to the media or to the general public.

- *RIAS Comment on Response to Pharmaceutical Industry Concerns*

The RIAS provides a summary of the Spring 2017 consultation on the White Paper on Public Release of Clinical Information in Drug Submissions and Medical Device Applications. Health Canada, in its RIAS response to the submissions from the pharmaceutical and biotechnology industries, communicates its intention to "loosely align" the Proposed Regulations with the EMA's initiative, while noting that an external stakeholder group has been established to gather input on implementation details. IMC appreciates the

opportunity to participate in this process as an external stakeholder, but would like to see greater incorporation of its feedback in the Proposed Regulations and/or the rationale for diverging from industry recommendations and concerns.

- *Implementation Issues and Redaction*

In the regulatory proposal, Health Canada states that it would seek to consult with drug manufacturers so that they may redact information that should continue to be treated as CBI. The burden of redaction and de-identification of personal information contained in clinical information would be the responsibility of the sponsor, who would then provide Health Canada with a redacted version and supporting justification. Health Canada would then review the proposed redactions and provide the results to the sponsor while allowing the opportunity for the sponsor to respond.

While it is encouraging that the Proposed Regulations provide some opportunity for the sponsor to respond after Health Canada reviews any proposed redactions, Health Canada would ultimately make the final decision as to what would and would not continue to be CBI. This would greatly limit any procedural options for sponsors to protect CBI or to appeal decisions made in this regard. In contrast, the EMA provides an opportunity for judicial review in cases where agreement is not reached between the regulator and industry sponsor. This important aspect of procedural fairness is lacking in the Proposed Regulations and we urge Health Canada to consider incorporating similar measures in future drafts.

With the view of clarifying what information may be redacted, IMC recommends that the proposed new C.08.009.2(2) be given broader treatment. In particular, an additional exclusion should be added to this provision that would permit sponsors to redact confidential information regarding the chemistry, manufacturing and control (CMC) of the product. IMC cautions that there may be circumstances in which CMC information may be contained within certain clinical documents. As a default, this CMC information is maintained by the sponsor as being commercially confidential, rather than being material to the clinical safety and efficacy information that is contained within such a clinical document. Manufacturers must have confidence and explicit assurances that redactions of any commercial confidential CMC information located within clinical documents will be accepted by Health Canada as a valid regulatory exemption to disclosure.

Sponsors also require reasonable and predictable assurances that any clinical information to be released will not be used for commercial purposes. Health Canada has indicated its intent to create a Terms of Use requirement, but no details have been made available as to the proposed mechanisms or processes that will be enacted to ensure protection of clinical information by end users. Clarity around enforcement is critical for all stakeholders, including any potential actions that could be contemplated in circumstances where the information has been used for personal/commercial gain. IMC therefore requests that additional clarification be included within the final regulations to (a) clearly indicate that any information released following the implementation of the regulations cannot be used for personal and/or commercial gain, and (b) affirm and outline the expected nature of any enforcement of that prohibition.

The regulatory proposal also states that clinical information would be made available on an internet-based portal. No further details have been provided by Health Canada regarding how this portal would function, to

what extent it would make content available or downloadable, nor how it would protect company information by way of terms of use, or otherwise.

IMC recommends that any initiative to make clinical information accessible by way of a web-based platform should be modeled after the approach currently employed by the EMA, which is based on a mature operational system designed around stringent terms of use. This would enable Health Canada to develop a workable and evidence-based approach that balances the interest of providing public access to information with ensuring appropriate safeguards for sponsors against harmful commercial use. As in the EU, these safeguards should include requirements that users agree to clear terms of use and have a valid Canadian passport. Users seeking access to information should also be asked to certify that the information will not be used for commercial use nor be licensed to any third party. To be effective, such terms of use should be accompanied by appropriate penalties/consequences for individuals that use the data for commercial gain. We refer in particular to the following sections of Annex 1 of EMA Policy 0070: Section 2 (restricting users' access to online content), Section 3 (terms of use regarding online content), and Section 4 (limiting the liability of regulator and sponsor for errors or misuse of content) and Section 7 (assigning jurisdiction over disputes).

- *Scope of Information Subject to the Proposed Regulations*

In addition to our recommendation that limitations be placed on the scope of the Minister's authority to release CBI without prior notice, IMC urges Health Canada to clearly delineate the specific content that is subject to release. Such limitations are critical to ensuring that sponsors have confidence that their CBI and intellectual property will continue to be protected. Accordingly, IMC recommends that Health Canada align its scope of application and related definitions with EMA Policy 0070.

We provide several examples of how the Proposed Regulations, as currently drafted, present risks that CBI could be inadvertently captured in the information subject to release:

- In rare cases, an interim Clinical Study Report can be used to support an initial filing of an indication, making it crucial that assurances be put in place to ensure that CBI in this form would be protected from release.
- Advice received from a recognized regulatory agency not already in the public domain should be considered out of scope for release, including reviewer reports and meeting minutes.
- Clinical trial study documents may be submitted to Health Canada months or years after the issuance of a Notice of Compliance as part of an ongoing commitment made by the sponsor under existing regulations. It is important to clarify whether or not these documents would be subject to release under the Proposed Regulations, and if so whether such release would be proactive or upon request.
- In certain circumstances, exploratory endpoints may be submitted to Health Canada that are not in support of a current, ongoing clinical development program or a risk/benefit evaluation of a submission. Without appropriate limitations being placed on the scope of application of the Proposed Regulations, there is a risk that this type of information would not be protected as CBI but rather released and made available to the advantage of a competitor not specifically related to the compound/drug in question.

In light of the above concerns, IMC recommends that the scope of information subject to release be appropriately and clearly limited so as to avoid unwarranted, anti-competitive disclosure. We suggest alignment with EMA definitions that have been clarified in this regard [see Section 2 ("Definitions") of EMA Policy 0070].

Conclusion

Innovative Medicines Canada requests that Health Canada address the principle-based and practical concerns outlined above. Our recommendations are made with the view of advancing the Federal Government's stated objective of providing public access to clinical information submitted to Health Canada, so that it may be implemented in a manner that is predictable and workable for both the industry and for Health Canada.

IMC's members continue to invest in the research and development of innovative medicines, and in so doing require confidence that Health Canada will continue to protect the trade secrets and intellectual property contained within interim developmental or clinical data. Regulatory proposals that do not provide proper protection, particularly if they are also misaligned with the regimes of Canada's major trading partners, risk undermining the attractiveness of investing in the Canadian market.

IMC also recommends greater use of the external stakeholder advisory group, established by Health Canada within the context of the present consultation, in order to ensure that future drafts of the regulations contain the appropriate limitations on the release of CBI. Stakeholders must likewise play a key role in consultations on any associated draft guidance documents to ensure that implementation is practicable. Meaningful consideration of and response to industry concerns around both regulatory and guidance aspects of the Proposed Regulations is critical to ensuring that the resulting changes provide public access to clinical information submitted to Health Canada in drug submissions while ensuring that personal/private information, CBI, trade secrets and intellectual property are considered and protected appropriately.

We would be pleased to discuss the content of our submission with you further upon request.

Sincerely,

Declan Hamill
Vice President, Legal, Regulatory and Compliance