Health Canada Consultation:

Public Release of Clinical Information in Drug Submissions and Medical Device Applications

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Bad Science Watch

Bad Science Watch is an independent Canadian consumer protection organization dedicated to promoting good science in public policy.

The following was prepared by volunteers and represents what we believe to be an honest, fair, and science-based evaluation. We are an independent body that is funded by private donations and we do not represent any corporate interests.

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General Statement

Bad Science Watch is supportive of the effort to make clinical trial information used to make regulatory decisions available to the public and we would like to thank Health Canada for the opportunity to comment on the most recent white paper concerning the release of clinical trial information.

As a signatory to the global "AllTrials" campaign (AllTrials), Bad Science Watch supports the ideal of all trials registered and all trials reported. Put simply, any publicly funded clinical trial involving humans would have a legal obligation to be registered with Health Canada, and the results of that trial would have to be published within a specific timeline after it was complete.

The minimum standards of registering and reporting on interventional clinical trials has been recognized by the WHO Statement on Public Disclosure of Clinical Trials Results (Moorthy et al., 2015). We hope that Canada will follow the progress made in the European Union and the United States with the European Clinical Trials Register and ClinicalTrials.gov respectfully and update our registration and reporting regime to be in line with international standards.

The justification for these standards is quite simple. The 2008 update to the Helsinki protocol focused on honoring the service of human participants in clinical trials and added the ethical responsibility of allowing the information from these trials to be used for the public good, necessitating registration and reporting of all trials (World Medical Association, 2013). The results from the efforts of millions of volunteers needs to be accessible to researchers and physicians so they can make the best evidence-based treatment decisions and to avoid duplication of work that puts new volunteers at needless risk. Finally, the extensive public investment in research should result in the accessibility of the results of that research to the public, rather than letting it to languish hidden in private databases.

While we understand the importance of return on investment and the risks that drug and device manufacturers take to bring their product to market, most research starts with publicly funded basic research and the public needs these results to make good evidence based decisions about their health. Commercial interests can be protected with patents and other regulations while their research remains open to scrutiny. In fact, many pharmaceutical manufacturers have already signed onto the "AllTrials" campaign and have committed to release this information. Companies that have made public commitments include GSK, Pfizer, Bayer, and many others.

Support of Dr. Lexchin Letter

Dr. Joel Lexchin, emeritus professor in the faculty of health at York University, has drafted a letter in response to this public consultation. We support his group's analysis of the current white paper and are a signatory to it [see *Appendix A*]. In brief, the following criticisms are important and need to be addressed in the policy:

1. Some language allows the company to withhold information under the presumption that they are using it in ongoing clinical investigations and therefore represents a commercial risk if disclosed. All clinical trial information that was used to gain license approval for a drug or device license should be released within a specific time period after approval.
2. The white paper allows some methodological details to be withheld to protect proprietary research methods. Complete methodological details should be included in release of clinical trial information and burden of proof should remain on the company to justify any redaction of these details
3. Health Canada must have a clear list of what documents are released along with the content of these documents.
4. Release of clinical trial results should be proactive and complete, and not subject to application for release.
5. Protracted exchanges between the company and Health Canada can interfere with information release, so there must be a legally binding release of clinical trial results within 60 days of the notice of compliance.
6. Health Canada must provide clear policies that would explain when they would not align their practices with other regulators.
7. Upon notice of compliance, reviewer's reports must be released within a strict time period.
8. Names of external all external reviewers used should be published, along with any conflict of interest information.

These criticisms are important and should be heeded. Bad Science Watch has additional issues with this white paper, described below.

Additional Issues

Trials Registry

This white paper only concerns clinical trial reports that are connected to a successful notice of compliance and licensure. While this is important, it is not sufficient to ensure that Health Canada meets its duty to study participants and the public at large. It is important that Canadian researchers and researchers conducting trials in Canada first be obliged to register their trial before any trial participants are enrolled.

This should be a legal requirement for any release of funds by the granting agency and for acceptance as evidence to support licensure. Once a trial has been registered, results from the trial, regardless of whether it is used to support licensure, should be released within one year of completion of the trial.

The current white paper only speaks to clinical trial reports that are connected with a successful notice of compliance, but it is important that all trials that are conducted are both registered and results

released. This will go furthest in prevention of duplication of efforts and fulfill the obligation the researchers have of releasing information paid for by the public to the public.

This registry should, at minimum, comply with the WHO International Clinical Trials Registry Platform and be aligned with ClinicalTrials.gov and the European Clinical Trials register to allow comparison and integration of results.

Timelines for Release

The timelines as stated in the HC white paper are related to the receipt of notice of compliance. This is unacceptable and not a requirement in either the ECTR or ClinicalTrials.gov. Rather, all clinical trial reports should be released within 12 months of their completion.

Retroactivity

Including the preceding recommendations, the White Paper provides a strong basis for transparency in medicines going forward; however, clinical trials on the treatments being used today were conducted decades ago. Health Canada's regime must therefore make allowances to release these archival results. We recommend that Health Canada work to release all clinical study reports it currently holds.

Where Health Canada lacks the legal authority to release such reports, the proactive publication rate of past results should be a consideration in future drug and medical device licensing requests.

Any new registry should also ensure that past clinical trial reports that are held by Health Canada be released. Drugs and devices that are currently on the market deserve as much scrutiny as newly licenced products.

NHP inclusion

This white paper deals with pharmaceuticals and medical devices. The latter are often left out of such reporting and we support their equal inclusion in this process. However, we were concerned that non-prescription and natural health products were left out of this disclosure process. NHP makers have used the label of Confidential Business Information to prevent release of their own trial information for these products. We bear no less a responsibility to the participants of the trials for NHPs than we bear to those who participate in pharmaceutical trials.

This process should include this information to allow public scrutiny of not only the process of licensure but the evidence used to justify the sale of these products.

Conclusion

It is clear that the international effort to advocate for the release of clinical trial information through the AllTrials campaign is having an effect. Pharmaceutical, medical device manufacturers, and governments

alike see the benefit of releasing this information and we hope that Health Canada follows their example and works with the public and industry to create a structure for access and tracking of clinical trials.

References

"All Trials Registered. All Results Reported". AllTrials. N.p., 2017. Web. 14 May 2017. www.altrials.net

Moorthy, V.S., Karam, G., Vannice, K.S., and Kieny, M.-P. (2015). Rationale for WHO's New Position Calling for Prompt Reporting and Public Disclosure of Interventional Clinical Trial Results. PLOS Med. *12*, e1001819.

World Medical Association (2013). World medical association declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA *310*, 2191–2194.

Appendix A

Full Text of Dr. Joel Lexichin's Letter:

Thank you for the opportunity to comment on the Health Canada white paper entitled "Public release of clinical information in drug submissions and medical device applications". Health Canada's proposed policy change could be a major step towards transparency. We support the public release of clinical information because Canadians and their clinicians require this information to be publicly accessible in order to make informed decisions. Greater transparency will also help Health Canada make better decisions by allowing independent scrutiny of clinical information. This ability to review the evidence will further enhance the trust that Canadians should have in the safety and efficacy of health care products. We urge Health Canada to introduce regulations under the Food and Drugs Act in a timely manner that gives legal force and effect to the policy proposed in the white paper, as modified by the changes we outline below.

We recommend the following changes, which must be subsequently translated into legally binding regulations enacted pursuant to the Food and Drugs Act, to ensure that this proposed policy will achieve its objective of greater transparency. These changes will help avoid sponsor practices that can severely restrict the release of information and subvert any attempt at transparency. Our general suggestion is that Health Canada must significantly limit the exemptions and restrictions in the proposed policy and remove barriers to accessing clinical information. Finally, there is additional information that was not mentioned in the document that must be released.

Exemptions and redactions

1. The following exemptions to the release of information must be removed from the policy because they are open to abuse: "secondary or exploratory end points which may constitute a component of an on-going development programme", "interim clinical study results" and "methodological details (e.g. in-house modifications or procedures to analytical, immunogenicity, bioassay, or sample size calculations methods not commonly used by the industry)". If Health Canada obtained this information in order to make regulatory decisions then Health Canada has an obligation to release it. These exemptions invite sponsors who wish to suppress information – as they currently do by inappropriately labelling it "confidential" – to use these labels to subvert transparency. All aspects of the scientific methodology are key components of credible science and should be made public. Specifically, withholding methodological details may mean that information such as assays used to access the efficacy of vaccines remain undisclosed thereby preventing independent assessment of their efficacy. Similarly, withholding information about non-conventional sample size calculations may mean that the ability to test and replicate analyses of efficacy may not be possible.

2. Health Canada's policy must clearly state that the burden of proof is on industry sponsors to justify why certain information falls under the narrowly defined exceptions to public disclosure. In this regard, any redactions to the material that is released must be kept to a minimum and there should be written reasons given for the redactions. Experience has shown that the greater the

number of redactions the more difficult it is to interpret the information and the less use the documents are in helping to understand the benefits and harms of medicines.

3. Health Canada must produce a list of the types of documents that it will release based on its transparency policy along with a clear definition of the content of each of these documents.

Restrictions

4. Health Canada must proactively release clinical information without requiring people to apply for its release. We do not support Health Canada applying any restrictions on who can receive clinical information or how that data can be used. Health Canada may preclude information obtained under other provisions of the Food and Drugs Act, for example, information that remains "confidential business information" from commercial use upon disclosure. However, information that is deemed clinical information following a regulatory decision should be available without restriction upon publication.

Barriers

5. Health Canada must have the legal authority and be obliged to publish clinical information after a single exchange with companies pertaining to redactions and, in any event, no later than 60 days after a product receives a Notice of Compliance. Protracted exchanges between Health Canada and sponsors can be used as a delaying tactic to the release of information and are a major barrier to transparency. Health Canada should have the authority to release information after a single exchange with companies except under exceptional circumstances.

6. Health Canada must be specific about what circumstances would prevent it from aligning its practices with those of other regulators where those regulators have more liberal policies about the release of information than those proposed by Health Canada.

Additional information

7. Health Canada must release all its reviewers' reports once a product has received a Notice of Compliance. Similar to the release of information that the companies submit, there must be strict time windows for the release of these reports and strict criteria about what information can be redacted.

8. If external reviewers are used at any time during the drug approval process the names of these reviewers along with their conflicts of interest must be publicly released.

Health Canada's discussion paper begins with the statement that "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." We believe that to fulfill this promise the information used in the drug approval process must be freely available in a timely manner to anyone who wants to examine it with only minimal restrictions.

We would be pleased to discuss our recommendations with Health Canada.

Sincerely

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