Health Canada Santé Canada

Canada

Updates on Health Canada's discretionary authority to disclose CBI under paragraph 21.1(3)(c) of the *Food and Drugs Act* and regulatory proposal to permit public release of clinical information

March 20, 2018
Presentation to CAPRA
Montreal

YOUR HEALTH AND SAFETY... OUR PRIORITY.

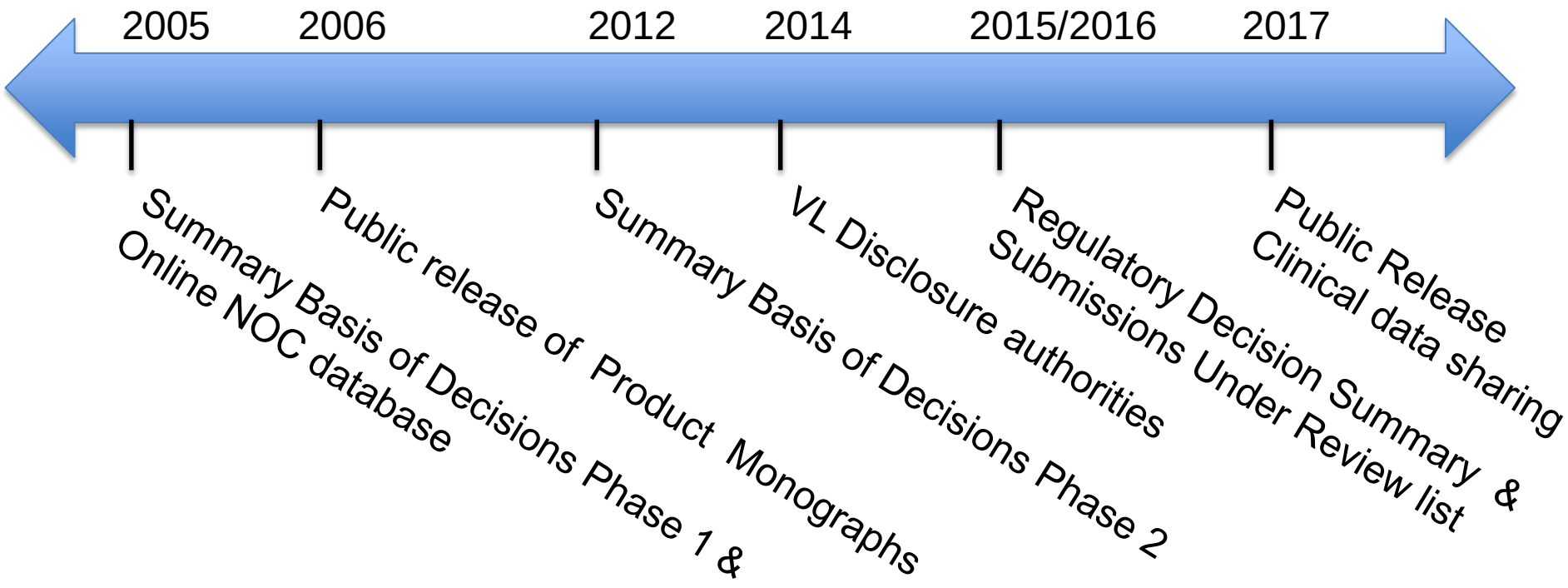
Objective

To provide an update on Health Canada's two recent information-sharing initiatives:

1. New authority under the *Food and Drugs Act* that gives the Minister of Health discretionary authority to disclose CBI to eligible persons for the purpose of protecting or promoting human health or the safety of the public (paragraph 21.1(3)(c)).

2. Health Canada's regulatory proposal to permit public release of clinical information in drug submissions and medical device applications.

Transparency at Health Canada: Proactive Disclosure Initiatives related to Drugs and Medical Devices



Recent amendment to the *Food and Drugs Act*

- Vanessa's Law amended the *Food and Drugs Act* to improve safety of therapeutic products by
  a) strengthening safety oversight of therapeutic products throughout their lifecycle;
  b) improving reporting of serious adverse drug reactions and medical device safety incidents; and
  c) promoting greater confidence in the oversight of therapeutic products by increasing transparency.

Vanessa's Law entered into force November 6, 2014

New CBI disclosure authorities in the *Food and Drugs Act*

Amendments to the *FDA* defined confidential business information (CBI) to be information in respect of a person to whose business or affairs the information relates, means — subject to the regulations — business information

- that is not publicly available;
- in respect of which the person to whom the information relates has taken steps to keep it confidential; and
- that has economic value to that person because it is confidential and its disclosure would result in material loss.

New CBI disclosure authorities in the *Food and Drugs Act*

- 21.1(2) Authority to disclose CBI, without notifying the originator, if the Minister believes that the product may present a **serious risk of injury to human health.**

- 21.1(3) Minister's authority to disclose CBI, without notifying the originator, if the **purpose is related to the protection or promotion of human health or safety of the public**, and the disclosure is to:

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

Guidance on Disclosure of CBI under s21.1(3)(c) of the FDA

Finalized Guidance was published on March 10, 2017:

https://www.canada.ca/en/health-canada/programs/public-release-clinical-information-drug-submissions-medical-device-applications.htm

Purpose:

- Formalizes the review process and clarifies Health Canada's requirements
- Sets out principles and considerations for deciding
  a) whether or not a request meets the requirements of the Act, and
  b) whether or not the request warrants the exercise of HC's discretion to disclose CBI
- Provides standard request form, conflict of interest declaration, and sample confidentiality agreement

Revisions have not fully addressed concerns regarding HC's disclosure of submission information:

- Industry and academics views are polarized on key issues, hard to reconcile
- Both groups seek greater certainty, predictability regarding HC's approach to disclosure of submission information
- Propose addressing these concerns with policy and regulations on public release of clinical information

CBI Disclosure Requests - Current Status

Health Canada has received 13 requests for CBI disclosure under section 21.1(3)(c) of the Act:

- 12 requests were for unpublished clinical study reports
- 2 requests resulted in disclosure (totalling approximately 36,000 pages)

- Case-by-case review process and confidentiality agreements are burdensome to administer.

- Health Canada's broad discretion to disclose CBI without notifying the originator is unique internationally for therapeutic products.

Reporting:

- Information on each request under FDA s21.1(3)(c) is provided online.

https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/request-disclosure-confidential-business-information/completed-requests.html

Regulation making authorities within the *Food and Drugs Act*

30 (1.2) (d.1) a regulation making authority to specify when information regarding a therapeutic product authorization is not or ceases to be confidential business information (CBI)

and,

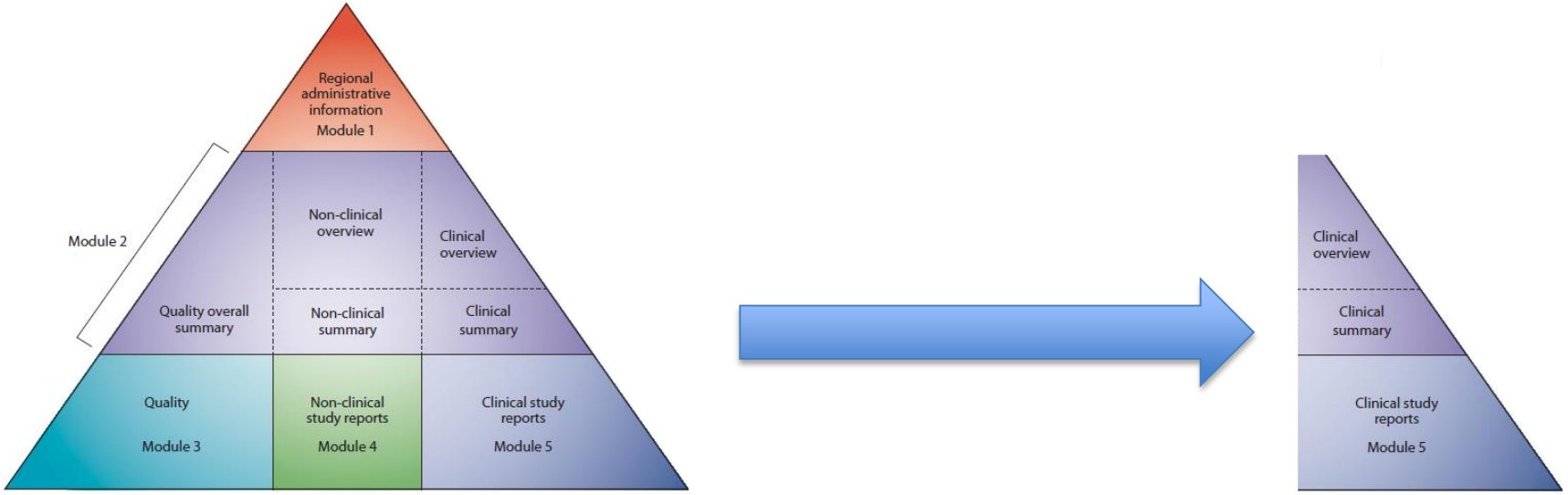
(d.2) to authorize disclosure of such information.

Current:

The *FDA* CBI definition is applied to Drug submissions and Medical Device applications

Proposed:

Clinical information would cease to be CBI following a final regulatory decision (positive or negative)



s.21.1 (3)(c) CBI disclosure authority	Regulatory proposal:
ALL CBI is in scope	Only safety and efficacy data is in scope
• Not tailored to medical research interests	• Tailored to medical research interests
• No redaction of commercially sensitive information	• Redaction of all commercially sensitive information
• No notification to sponsor	• Consultation with sponsor
• Not internationally aligned with other regulators	• Internationally aligned with other regulators
• Recipient agrees to maintain confidentiality of CBI, is permitted to publish analysis	• Data is publicly released, users agree to non-commercial purposes

Clinical information that ceases to be CBI

In Scope:

Safety and efficacy/effectiveness information related to clinical trials, clinical studies, investigational tests used to support the proposed conditions of use or purpose (e.g. claims) in the drug submission or medical device application.

Specific categories of clinical information that may qualify for redaction:

1. **Proprietary methodological details**

   e.g. Innovative test methods developed in-house and used for additional drug development.

2. **Future clinical study plans and secondary outcomes/exploratory endpoints not used to support application for use**

   e.g. Study outcomes that reveal a new clinical indication.

Other information that is out of scope and will qualify for redaction:

3. **Information on the structure and chemistry of the therapeutic product**

   e.g. Undisclosed stereochemistry of a molecule.

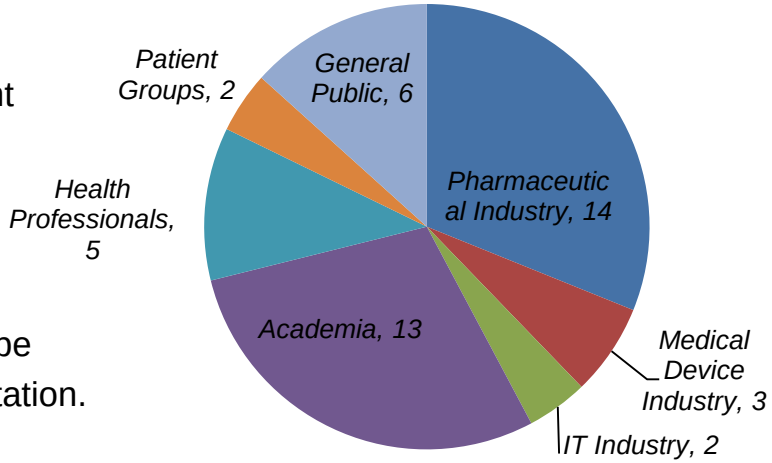
4. **Other commercial information**

   e.g. Contract information, names of suppliers.

What we heard - white paper consultation

45 submissions received from wide range of stakeholders

Industry: Generally cautious. Drug industry focussed on aligning information released with current EMA model. Some want non-Rx NDS excluded. Some medical device stakeholders question question coverage of devices and seek a delay to align with implementation of recent EMA directives.



Academic Researchers: Generally favourable. Cautious about scope of information eligible for redaction, seek more details on implementation.

Patient Groups and Health Professionals: Generally favourable. Focus on commitment to early implementation and avoiding delays experienced in ATI process.

'What We Heard Report' has been posted on Health Canada's website:
https://www.canada.ca/en/health-canada/programs/consultation-public-release-clinical-information-drug-submissions-medical-device-applications/what-we-heard.html

Many comments were technical and provide helpful starting point for stakeholder engagement on implementation.

Expert Reference Group

- Health Canada issued a call for experts to participate in targeted stakeholder engagement sessions

- Health Canada selected experts from four areas of expertise:
  - Criteria and processes for redacting commercially-sensitive information
  - De-identification of patient information
  - Terms of use and end user experience; and
  - Indicators of health system impact

- An Expert Reference Group has met via WebEx and Teleconference to provide feedback on Health Canada issue analyses and implementation recommendations.

https://www.canada.ca/en/health-canada/programs/consultation-public-release-clinical-information-drug-submissions-medical-device-applications/meeting-table.html

Regulatory proposal – considerations

On December 9, 2017 proposed regulations were published in *Canada Gazette I*.

In addition to information specified in regulatory proposal:

- For drugs, information eligible for release would be closely aligned with the EMA, permitting manufacturers to submit the same redactions to both regulators.
- Users would be required to agree to use the information only for non-commercial purposes.
- Manufacturers will have an opportunity to propose redaction of specified categories of clinical data, with a time-limited consultation process to be set out in guidance. Manufacturers will be required to provide specific justification, and HC will make final decision on redactions.
- A phased-in proactive publication of clinical information is being proposed and on request for past submission that would be subject to a fixed number of disclosures per year.

75-day public comment period closed on February 22, 2018. Approximately 20 submissions were received and undergoing an analysis.

Reference:
Regulatory Proposal drugs: http://gazette.gc.ca/rp-pr/p1/2017/2017-12-09/html/reg3-eng.html
Regulatory Proposal medical devices: http://gazette.gc.ca/rp-pr/p1/2017/2017-12-09/html/reg4-eng.html

Implementation

Proposed amendments to the *FDR* and *MDR* would specify the kind of clinical information in drug submissions that would cease to be CBI following a final regulatory decision.

Certain information in a submission would continue to be treated as Confidential Business Information (CBI). If present in a clinical study report, overview, or summary this CBI would be eligible for redaction:

Regulatory proposal: information in clinical information that would continue to be treated as CBI	**Description in draft guidance (to be published in March/April 2018).**
Information that was not used by the manufacturer to support the proposed conditions of use for the drug or the purpose for which the drug is recommended OR information not used by the manufacturer in medical device application referred to in paragraphs 32(3)(b) or (4)(b).	Clinical data not used to support the proposed use or indication could be used commercially, e.g. exploratory endpoints that generate new hypotheses used by a competitor for potential product development for other uses and indications.
Information that describes tests, methods or assays that are used exclusively by the manufacturer.	Descriptions and specification of proprietary/innovative assays, bioassays and immunogenicity assays. Description of proprietary/innovative analytical methods (e.g., methods used for PK/PD determination)

Interim Analyses

- Interim analyses of clinical studies are used to compare treatment arms with respect to efficacy or safety at a time prior to formal completion of a trial.

- While interim studies would not be considered CBI, there may be situations where their disclosure could introduce bias in the study results and not be ethical.

- Draft guidance will specify that sponsors would be required to demonstrate that the clinical trial is ongoing in order to not release the interim analysis as part of the public release package.

Interim Analysis Type	Disclosed
An interim analysis that established clear superiority of the treatment for the condition(s) of use and is used to stop the trial early.	Yes
Interim analysis of an ongoing trial which, if disclosed, would impact the integrity of the study results and possibly weaken confidence in the conclusions drawn.	No
Any interim analysis of a clinical study that has been either completed or discontinued.	Yes

Individual participant records

- Clinical case report forms (CRFs) and individual patient listings (appendix 16.2 of CSR in the ICH format) are documents that record information on each trial subject required by the clinical study protocol.

- These records would not be considered to be CBI. However, they include large volumes of structured and unstructured personal information that would require redaction or de-identification prior to public release. Anonymization of these records presents a significant operational challenge and risks substantially reducing the utility of the information they contain.

Safeguards against commercial use

Data protection. Clinical information subject to data protection would continue to be protected following public release, preventing a competitor from receiving an NOC for a submission that relies on the protected information until the term of protection has expired.

Terms of Use. End users will be required to agree to:

- Use the information for non-commercial purposes only (e.g., research)
- Not use the information to support an application for marketing authorisation anywhere in the world.
- Will not seek to re-identify the trial subjects or other individuals in the disclosed information and will alert HC in circumstances where inadvertent re-identification has taken place.

Watermarking. Clinical information published by Health Canada on the PRCI web portal will contain a watermark indicating that it was released by Health Canada for non-commercial use.

Disclosure of personal information under the *Privacy Act*

- The federal *Privacy Act* defines ‘personal information’ as ‘information about an identifiable individual’.

- Clinical information contains information that falls under the definition of personal information in the *Privacy Act* and must be adequately de-identified prior to public disclosure.

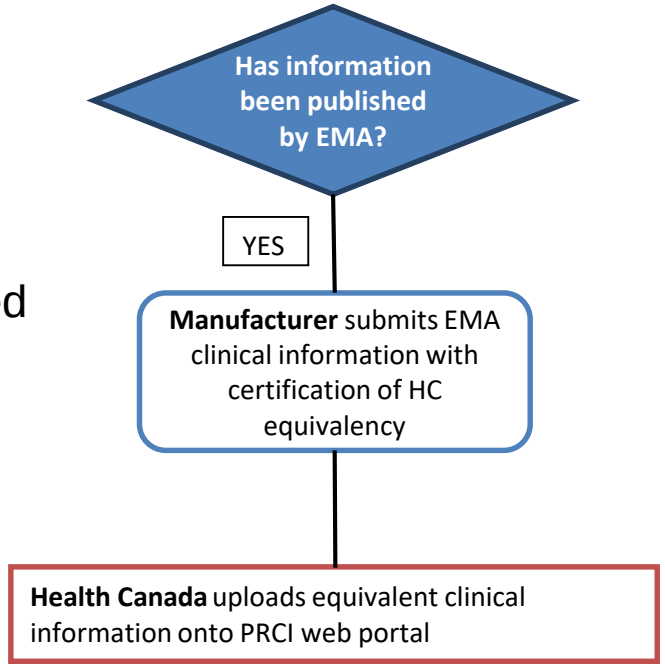
- In order to maximize the release of analytically-valuable information and retain the most utility of the published clinical information, anonymisation techniques of clinical information will be set out in the draft guidance.

Implementation of regulations

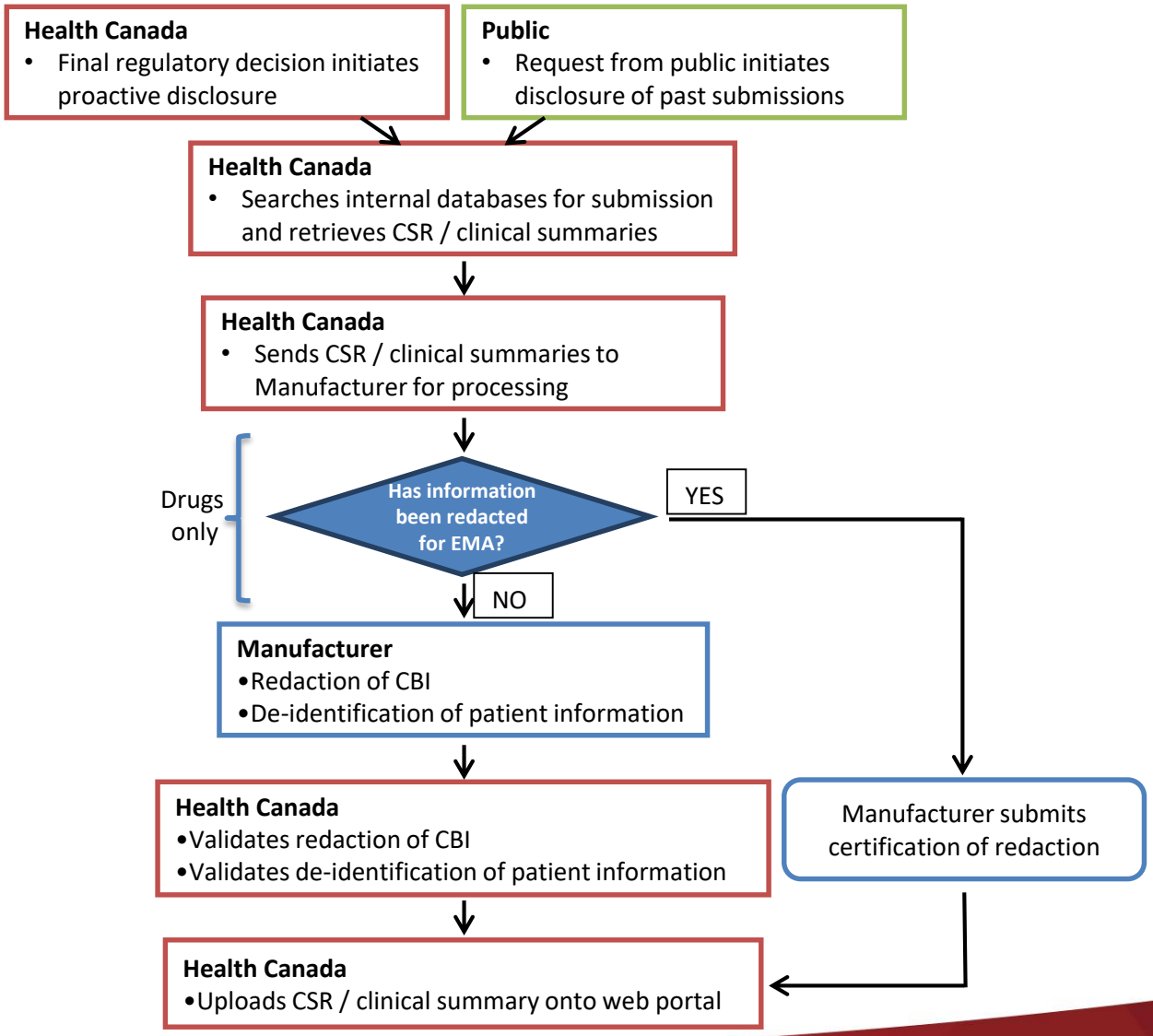
- Regulations would apply to past and future submissions/applications
- Health Canada receives 100+ New Drug Submissions per year and has received 1000s of submissions prior to 2017.
  - Health Canada is proposing a proactive publication of clinical information in submissions filed after the regulations come into force.
    - Subject to a phased-in schedule
  - Health Canada is proposing to disclose clinical information in past submission on request.
    - Subject to a fixed number of disclosures per year

Proposed approach for an expedited process for equivalent information published by the EMA

In order to expedite the publication of clinical information the draft guidance will include a streamlined process to make use of existing redactions or annonymizaton previously submitted under policy 070 to the European Medicines Agency.



Proposed process map for drugs and medical devices



Next Steps

- Comments received in response to the regulatory proposal published in Canada Gazette I are being analyzed.

- Draft guidance document on the implementation of public release of clinical information will be published for a 75-day comment period in April 2018.