

FINAL REPORT

Applying an SGBA+ lens to medical device regulation

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Public Summary

What is the problem?

Medical devices can prevent, diagnose, cure or treat medical conditions. Sometimes devices malfunction, which can cause harm to patients. Women have been particularly affected because devices used in both women and men such as pacemakers and knee implants were not tested for safety in women when developed, and other devices specific to women such as breast implants and pelvic mesh resulted in harm to many women before removal from the market. As a result, Health Canada developed an Action Plan on Medical Devices to improve the process of licensing and monitoring devices and ensure they are safe for diverse patients who vary by: (1) Sex – biological female or male, (2) Gender – social roles of women, men and gender-diverse persons, and (3) Intersectional factors – attributes such as age, culture, ethnicity, education and employment. All of these characteristics can influence device safety and performance, so it is important to test devices among diverse patients prior to wide-spread sale and use, monitor the attributes of patients who experience device-related harm, and communicate with healthcare professionals and patients about who is at risk of potential harms.

What did we do?

As part of that Action Plan, we analyzed Health Canada documents used to license, monitor and communicate about devices for the presence or absence of instructions about sex, gender or intersectional factors. We examined: (1) 56 general documents used by device companies to prepare licensing application or reports of device problems, and by Health Canada staff to review applications or reports, and (2) 50 documents publicly-shared by Health Canada with healthcare professionals and patients for devices known to have caused harm to women (breast implants, pelvic mesh, intrauterine birth control devices) and to women and men (pacemakers, knee implants).

What did we find?

Few general documents included instructions about sex, gender or intersectional factors. Most of those pertained to device testing, and not monitoring or communication about device-related problems. Also, instructions aimed at device companies and Health Canada staff for the same tasks did not match. No device-specific documents used to communicate with healthcare professionals or patients about device-related problems included instructions about sex, gender or intersectional factors. For example, a 111-page document on the safety of pelvic mesh reviewed 50 research studies and 473 complaints involving 467 serious injuries, but did not provide details about the attributes of study participants or persons who were injured.

What does this mean?

This work identified more than 340 ways that Health Canada can improve the 106 documents analyzed (and documents specific to other types of devices) so that device companies and Health Canada staff have more guidance on when and how to describe sex, gender and intersectional details of persons included in studies that test device safety and in reports of device-related problems. The 105-page full report of this work also includes 20 recommendations on how Health Canada can plan to update the documents, and related policies and processes, and inform and education all involved, including device companies, Health Canada staff, healthcare professionals and patients about the importance of reporting about sex, and intersectional details. In future, greater reporting of these details may result in the development and use of devices that are safe for everyone.

Executive Summary

Background

While devices can prevent, diagnose, cure or treat medical conditions, some have caused harm, particularly among women. International regulatory agencies have advocated that clinical trials include both women and men when therapies relevant to both are tested. However, research shows that few studies of device safety and efficacy reported participant sex, age or ethnicity. By order of the Minister of Health, Health Canada developed an Action Plan on Medical Devices. The Action Plan included analysis of how Health Canada could strengthen sex-gender-plus-based analyses (SGBA+) in regulatory policies and processes across the device lifecycle, which spans the review of evidence on safety and efficacy, licensing and post-market surveillance and communication of device-related adverse events.

SGBA+

Sex refers to biological sexes (female, male). Gender refers to socially-construed roles, behaviours, expressions and identities of girls, boys, women, men and gender-diverse persons. Sex/gender analysis refers to an analytical process used to assess how diverse groups of women, men and non-binary people may experience and respond to clinical care, policies, programs and initiatives. Intersectionality refers to factors that interact with sex and/or gender to influence identity, experiences and inequities, including age, race, ethnicity, culture, immigration status, education, income, employment, marital/partnership status, ability (versus dis-ability), sexual orientation, urbanity/rurality, region of residence.

Purpose

The overall AIM of this project was to explore how SGBA+ is considered in Health Canada regulatory policies and processes across the medical device lifecycle. OBJECTIVES were to:

1. Analyze internal and external documents used by Health Canada for regulatory decision-making across the medical device lifecycle for the presence and absence of SGBA+ details
2. Identify opportunities to improve SGBA+ reporting in general and device-specific documents for industry, Health Canada staff, healthcare professionals and patients, and strategies needed to promote and support SGBA+ considerations by all.

Methods

We employed deductive and summative content analysis to quantitatively and qualitatively describe SGBA+ considerations in documents that Health Canada recommended as those most commonly used by industry or HC staff including general guidance, standard operating procedures and forms. We also examined publicly-available device-specific documents by which Health Canada communicates about regulatory decisions including device licence approval, reports of evidence of device safety and efficacy, and notifications of device-related adverse events. We sampled device-specific documents that are typically used in women only (breast implants, transvaginal mesh, birth control devices) and in both women and men (implantable pacemakers, knee implants) that had been associated with device-related adverse events. For each general guidance document, we extracted: title, publication date, number of pages, purpose and explicit SGBA+ content (sex, gender, intersectionality). For each device-specific document, we extracted: source, device type, device name, device class, date of approval or AMDE report, safety issues, hazard severity, action taken, and information reported to healthcare professionals or patients. We noted gaps in SGBA+, referring to opportunities to explicitly recommend or report SGBA+ considerations. We used summary statistics to report document characteristics and content, and reported findings in tables and text with exemplar quotes to illustrate how SGBA+ was addressed.

Findings

A total of 56 general documents (1,461 pages, mean 25.6, median 17.0, range 1 to 231) and 50 device-specific documents (most half to one page) were reviewed. A small proportion of general documents (6.7% sex, 11.1% gender, 15.6% intersectionality) addressed SGBA+. For example, *Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences* encourages the inclusion of females in research but addresses only one stage of the device lifecycle, and does not refer to gender or intersectional factors. No publicly-available device-specific documents addressed SGBA+. This was true of devices specific to biological females (breast implants, intrauterine devices, pelvic mesh) and those relevant to both females and males (pacemakers, knee implants). For example, documents retrieved from Medical Device Incidents and Recall and Safety Alerts databases provided no details about the number and characteristics of affected persons, or review of data from either published research or post-market surveillance. Similarly, a one-page Safety Review of drug-releasing intrauterine devices thought to potentially suppress lactation noted review of 24 studies and 19 Canadian reports of decreased milk production, and a 111-page Clinical Evaluation Report of transvaginal mesh included high-level results of 50 studies and 473 complaints involving 467 serious injuries, but neither provided details about the characteristics of study participants/affected persons or sub-analyses.

Recommendations

Overall, SGBA+ should be fully and consistently addressed in general and device-specific documents targeted to industry, HC staff, healthcare professionals and patients across the device lifecycle. A total of 341 instances were identified where SGBA+ could be strengthened among 45 general documents developed by Health Canada. Given that no device-specific documents fully addressed SGBA+, numerous opportunities are possible to strengthen SGBA+. A further 20 recommendations, many including additional sub-recommendations, offer guidance on how to update documents and related processes, and knowledge translation needed to inform and educate all stakeholders.

Limitations

Security clearance to access internal device-specific documents was not granted by Health Canada so we did not analyze the content of documents submitted by industry containing evidence on device safety and efficacy from published research, manufacturer studies or post-market surveillance reports. However, given that general guidance does not compel industry to report SGBA+ and the single Clinical Evaluation Report specific to pelvic mesh included no SGBA+ details, we could fairly safely assume that documents describing evidence/data to which we lacked access did not include SGBA+ details. This document identifies SGBA+ gaps in sources, documents and related processes, and offers high-level recommendations on how to address those gaps, but does not provide detailed SGBA+ content as updating documents, underlying information systems and related processes requires nuanced decision-making by those who oversee and are involved in the work, which was beyond the scope of this project.

Conclusions

Current regulatory policies and processes do not appear to be promoting the reporting, review and communication of SGBA+ considerations for devices (women-specific, relevant to both women and men) across the device lifecycle. This report includes numerous recommendations, which may not be easy to digest and even more challenging to address given the complexity of medical device regulation and Canada's role in the international device market. Health Canada can review, prioritize and reflect on how to adopt recommendations that emerged from this work. Strengthening consideration of SGBA+ in the device regulatory lifecycle could ensure that devices are safe and effective for diverse users.

Background

Medical devices are instruments essential to the prevention, diagnosis, cure or treatment of a disease or abnormal physical condition [1]. Devices include those with lower (e.g. wheel chair, endoscopes) and higher (e.g. orthopedic or cardiovascular implants) risk for adverse medical device events (AMDEs). AMDEs are not uncommon: among 30,002 devices approved by the United States Food and Drug Administration (FDA) between 2005 and 2012, 249 were recalled, half during the first two years on the market [2]. A Canadian population-based study found that, among 24,849 new devices licensed from 2005 to 2015, there were 7,226 recalls of which 5% had the potential for serious harm or death, and 60% for temporary adverse health consequences [3]. AMDEs can have serious negative implications for patients; for example, population-based analysis of American device-related injury surveillance data showed that 454,383 AMDEs occurred in a one-year period in a broad range of devices from 15 medical specialty groups [4]. The most common associated injuries were contusions/abrasions, punctures and lacerations, and 13% resulted in patient hospitalization [4]. Device design and function is among the top three contributions of patient safety incidents in hospitals [5]. Another study found that 37% to 47% of AMDEs in the United States and United Kingdom were attributed to device design, manufacturing, quality control, labeling or packaging [6].

Research shows that device design could be improved through greater rigour in testing of safety and effectiveness. For example, registry data from Sweden and Australia showed that the 10-year risk of revision after primary total knee arthroplasty was 4% to 6% [7]. Our systematic review of 265 knee implant studies (1986-2014, 59,217 patients) found that most devices were evaluated in only one study, largely uncontrolled single cohorts, enrolled fewer than 100 patients, and followed patients for less than 2 years [8]. Our research showed that devices prone to AMDEs could be detected earlier, and information about potential risks or precautions shared with healthcare professionals and the public to avoid further AMDEs. Our interviews with physicians that implant orthopedic and cardiovascular devices found that multiple physician (e.g. view about what constitutes an AMDE), organization (purchase agreements requiring use of particular device) and health system (e.g. no reporting mechanism) factors limited the identification and reporting of AMDEs [9]. Physicians said these constraints could compromise use of the best device for a given patient. Our consultation with representatives of industry, regulatory agencies, professional societies, and quality improvement agencies; and lawyers, ethicists, policy-makers, researchers, clinicians, and consumers via interviews (n=37) and an in-person meeting (n=47) confirmed that enhancements are needed across the medical device lifecycle to improve device design and evaluation, and monitor and report AMDEs [10].

Attention has recently focused on ensuring that devices are safe and effective for all users. The International Consortium of Investigative Journalists, including 250 reporters from 36 countries, were exploring devices and coordinated the simultaneous release of news items about AMDEs, a project labelled The Implant Files (<https://www.icij.org/investigations/implant-files/>). Notably, the initiative also found that, among 340,000 cases of injury or death, 67% were women. Devices specific to women such as breast implants, transvaginal mesh and a female sterilization device have been linked to high rates of AMDEs with serious health implications, but were approved for market with no clinical trial evidence or evidence based on a short follow-up time, with little subsequent completion of post-approval studies [11-13]. Growing awareness of these problems has prompted national initiatives to issue recommendations for improving the regulation of, and communication about health products for women [14,15]. Organizations like the United States Food and Drug Administration have mandated that clinical trials of medical therapies relevant to both women and men include patients with diverse

characteristics, as have the European Medicines Agency and Japanese Medicines Regulatory Agency). However, analysis of 82 pre-market approval studies of 42 devices in 2015 found that participant age, race and sex were reported in 65%, 51% and 66% of studies, respectively, and sub-analyses by age, race and sex were reported by 9%, 4% and 17% of studies, respectively [16]. Another analysis of publicly-available approval documents for 22 high risk or novel devices approved by the FDA between 2014 and 2017 similarly found that only 3 (14%) of the devices provided subgroup analyses for both effectiveness and safety by sex, race and age [17].

One way to enhance the safety and effectiveness of devices is to ensure that regulator policies and processes acknowledge and support diversity across the device lifecycle, which spans device testing, review and approval of new device licence applications, monitoring for AMDEs among marketed devices, and public reporting of AMDEs as they arise. Diversity refers to sex-and-gender-plus-based analyses (SGBA+), where plus refers to demographic characteristics (e.g. age, race, culture, socioeconomic status) that may interact with sex or gender to influence the use and clinical outcomes of devices. Analysis of regulator policies and processes may identify exemplar cases that could be broadly shared and emulated, or gaps that represent opportunities to strengthen SGBA+ considerations.

Purpose

The overall AIM of this project was to explore how SGBA+ is considered in Health Canada policies and processes across the medical device lifecycle including the review of evidence on safety and efficacy, licensing and post-market surveillance and communication of device-related adverse events. Health Canada can review and adopt recommendations that emerged from this work, and identify additional recommendations triggered by these findings. The OBJECTIVES were to:

1. Analyze internal and external documents used by Health Canada for regulatory decision-making across the medical device lifecycle for the presence and absence of SGBA+ details
2. Identify opportunities to improve SGBA+ reporting in general and device-specific documents for industry, Health Canada staff, healthcare professionals and patients, and strategies needed to promote and support SGBA+ considerations by all.

Approach

Context

In response to mounting evidence on AMDEs and lack of consideration of sex/gender in scientific research, by order of the Minister of Health, Health Canada developed an Action Plan on Medical Devices with three aims:

- Post-market – All hospitals across Canada must report AMDEs to Health Canada
- Pre-market – By order of the Minister of Health, Health Canada developed an Action Plan on Medical Devices with three aims: (1) Improve how medical devices get on the market: assess how Health Canada considers sex/gender in licensing of new drugs and devices and in post-market activities such as surveillance; established the Scientific Advisory Committee on Health Products for Women, who will advise on strengthening regulation of drugs and devices; (2) Strengthen surveillance of devices already in use; and (3) Provide Canadians with more information about medical devices.

Operational plan

To address the above-mentioned three aims, the Canadian Institutes of Health Research funded this project to focus on the medical device lifecycle. To plan and guide the project, the Investigator (ARG)

prepared a project charter (**Appendix 1**), which was reviewed and approved by Health Canada on November 25, 2020. Briefly, the following points define agreed-upon scope for the project:

In scope:

- Documents and processes across the regulatory device lifecycle including pre- and post-market
- Select Class II, III and IV devices for which AMDEs have been reported that are used in both men and women, and used in women-only
- Internal and external documents recommended by an HC working group as those that HC staff or industry most commonly employ
- Identify gaps in consideration of SGBA+ in both documents and processes, and provide high-level recommendations for how HC could address those gaps

Out of scope:

- Class I devices
- Review of documents for all Class II, III and IV devices beyond select sampled devices
- Internal HC documents not provided by HC
- Preparation of content or development of processes to address identified gaps

Sex-gender based analysis

As a guide, we used an established SGBA+ framework developed by the Canadian Institutes of Health Research for incorporating sex and gender in health research [<https://cihr-irsc.gc.ca/e/50835.html>] that we elaborated with considerations for intersectional factors [18] (**Appendix 2**). Sex refers to biological sexes (female, male). Gender refers to socially-construed roles, behaviours, expressions and identities of girls, boys, women, men and gender-diverse persons. Sex/gender analysis refers to an analytical process used to assess how diverse groups of women, men and non-binary people may experience and respond to clinical care, policies, programs and initiatives. Intersectionality refers to factors that interact with sex and/or gender to influence identity, experiences and inequities, including age, race, ethnicity, culture, immigration status, education, income, employment, marital/partnership status, ability (versus disability), sexual orientation, urbanity/rurality, region of residence.

Methods

Project design

To assess how SGBA+ is considered in regulatory decision-making and reflected in information for industry, healthcare professionals and patients, we employed content analysis of documents [19]. More specifically, we employed manifest content analysis, which refers to quantitative and qualitative description of explicit content as reported in written communication without analyzing its underlying meaning or generating theory [20]. We employed both deductive and summative content analysis procedures to first organize and describe content in categories (deductive), and then count and compare categories included in documents by device lifecycle stage, type of document and SGBA+ considerations (summative) [19,20]. With no reporting criteria specific to content analysis, we complied with the Standards for Reporting Qualitative Research [21].

Eligibility and acquisition

We included documents across the device lifecycle (device testing, review and approval of new device licence applications, monitoring for AMDEs among marketed devices, and public reporting of AMDEs) recommended to us by Health Canada. Such documents were used by or aimed at industry, healthcare professionals, patients or Health Canada regulatory staff. AMDEs referred to alerts, warnings or recalls

of problems associated with device design, function, packaging, labelling or instructions that could result in sub-optimal use and clinical outcomes. Documents included general guidance to industry for designing and conducting device testing, applying for a new medical device licence or amendment, or providing details about AMDEs or action plans in response to AMDEs plus related forms/templates; and general guidance for Health Canada staff to support the review of new medical device license applications or amendments, analysis of reports of AMDEs, or preparation of communication related to new or amended devices, or alerts or recalls pertaining to AMDEs including standard operating procedures and forms/templates. Documents also included publicly-available device-specific information related to licencing, amendments, and recalls or safety alerts. We sampled devices that are typically used in women only (breast implants, transvaginal mesh, birth control devices) and in both women and men (implantable pacemakers, knee implants) that had been associated with AMDEs [2-4,7,11-13]. We retrieved the aforementioned documents by copying information available only on web pages and downloading documents available on the web sites of Health Canada or other agencies. Health Canada provided us with standard operating procedures. The complete list of sources of data (documents, databases, web sites) is available in **Appendix 3**.

Table 1. Sampling and source of documents

Methods	Element	Examples
Sampling	Device lifecycle	Device testing Review and approval of new device license applications Monitoring/communicating medical incidents
	General documents	Guidance documents for industry Standard operating procedures used by Health Canada staff Forms/templates used by industry and Health Canada staff
	Device-specific documents	Commonly-used devices associated with AMDEs Women: breast implants, transvaginal mesh, birth control devices Women and men: implantable pacemakers, knee implants
Sources	General documents	Web sites of Health Canada and other agencies (copied information on web pages, downloaded files) Provided by Health Canada (standard operating procedures, internal forms/templates)
	Device-specific documents	Copied information or downloaded files identified in: Clinical Information on Drugs & Health Medical Device Active License Listing Drug & Health Product Register Medical Device Incidents Recalls & Safety Alerts Database Canada Vigilance Adverse Reaction Database Canadian Adverse Reaction Newsletter (Health Infowatch)

Data collection

For each general guidance document, we extracted: title, publication date, number of pages, purpose and SGBA+ content (sex, gender, intersectionality). Concurrent with data extraction for each document, we noted gaps in SGBA+ content, referring to opportunities to explicitly recommend or report SGBA+ considerations as per the SGBA+ framework (**Appendix 2**). For each device-specific document, we extracted: source or database, device type, device name, device class, date of approval or AMDE report,

evidence underlying studies of safety and efficacy or post-market surveillance data, safety issues, hazard severity, action taken, and information reported to healthcare professionals or patients. For each type of source or database, which employed a similar format for information specific to a range of devices, we noted the presence of or gaps in SGBA+ content as described.

Data analysis

We used summary statistics to describe the number and type of documents overall and by device lifecycle stage; and the number of documents that addressed each of sex, gender and intersectionality overall, and by type of document and device lifecycle stage. We reported findings in tables and text, which included exemplar quotes to illustrate how sex, gender and intersectionality were addressed. Approaches, methods and data were discussed with and reviewed by the same two Health Canada representatives throughout the project via 9 meetings (one in-person) and 30 email communications (**Appendix 4**) from February 2020 to October 2021. One of those meetings also involved three HC staff who provided an overview of medical device regulation in Canada, and application/review processes and related documents for pre-market review, investigational testing and post-market risk detection, assessment and management.

Results

Findings are organized in three broad sections: (1) SGBA+ in general documents plus recommendations for approaches to enhance SGBA+ in those documents and related processes; (2) SGBA+ in device-specific records or documents plus recommendations to enhance SGBA+ in those records or documents and related processes; and (3) Integrated recommendations and summary of key high-level findings.

SGBA+ in general documents

Documents included

A total of 56 documents were reviewed (Table 2) including 1,461 pages in total and a mean of 25.6 pages per document (17.0, range 1 to 231). Documents included publicly-available guidance documents largely aimed at industry, internal standard operating procedures, and forms or templates used by industry, HC staff or both. We also reviewed several external documents that HC staff and industry refer to.

Table 2. General documents included

Lifecycle stage	Document type				Sub-total
	Public guidance	Standard operating procedures	Forms or templates	External documents	
Clinical trial review	3	3	3	3	12
Submission review	10	2	5	3	20
Authorization and monitoring	9	7	3	---	19
General relevance	---	---	---	5	5
Sub-total	22	12	11	11	56

SGBA+ in general documents

Overall, a small proportion of internal and external documents used by Health Canada for regulatory decision-making across the device lifecycle addressed SGBA+ considerations (Table 3). Document-specific gaps representing opportunities to strengthen SGBA+ are summarized in **Appendix 5, 6, 7 and 8**.

Table 3. SGBA+ considerations in general documents

SGBA+	HC documents addressing SGBA+ n (%)			Total HC documents addressing SGBA+ n (% of 45)	External documents addressing SGBA+ n (% 11)
	Public guidance (n=22)	Standard operating procedures (n=12)	Forms or templates (n=11)		
Sex	2 (9.1)	1 (8.3)	0 (0.0)	3 (6.7)	3 (27.3)
Gender	2 (9.1)	3 (25.0)	0 (0.0)	5 (11.1)	3 (27.3)
Intersectionality	2 (9.1)	5 (41.7)	0 (0.0)	7 (15.6)	8 (72.7)

SGBA+ by device lifecycle stage

CLINICAL TRIAL REVIEW (**Appendix 5**)

A total of 12 documents pertained to clinical trial review. A small proportion of public guidance documents referred to sex, gender or intersectionality. No standard operating procedures or forms/templates did so. A higher proportion of external documents to which industry, the public and HC staff are referred to addressed sex, gender or intersectionality.

Table 4. Clinical trial review documents addressing SGBA+

SGBA+	HC documents addressing SGBA+ n (%)			Total HC documents addressing SGBA+ n (% of 9)	External documents addressing SGBA+ n (% of 3)
	Public guidance	Standard operating procedures	Forms or templates		
Sex	2 (66.7)	0 (0.0)	0 (0.0)	2 (22.2)	2 (66.7)
Gender	2 (66.7)	0 (0.0)	0 (0.0)	2 (22.2)	2 (66.7)
Intersectionality	2 (66.7)	0 (0.0)	0 (0.0)	2 (22.2)	3 (100.0)

While some documents referred to SGBA+ concepts, statements were brief, simply stating a word or phrase, or vague, providing little guidance on the rationale for, or approaches or processes for considering sex, gender or intersectionality. For example:

HC documents:

Referring to research participants “...inclusion and exclusion criteria, including the participants’ ages, sex and diagnosis...”

“Subjects should be selected to be representative of the population intended to be treated with the device, with appropriate inclusion of children, women, and ethnic groups.”

External documents:

Referring to research participants: “...demographic, geographic and cultural considerations (e.g. age, ethnicity, gender)...”

Two exceptions that provided greater detail were noted. The two documents could provide some guidance to HC on how to update other documents. However, some limitations were noted in both.

HC documents:

Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences

SEE **Appendix 5** for details

- 30-page document offers guidance on the study and analysis of sex differences in clinical trials of therapeutic products (e.g. considerations for women of child-bearing potential, or women who are pregnant or breast-feeding)
- It largely focuses on drug trials, with a small section pertaining to medical devices
- The document focuses solely on sex-related differences, and does not address gender or intersectionality: “While this guidance recognizes the importance of the elements of a diversity framework, such as ethnicity, socioeconomic status, disability, sexual orientation, migration status, age and physical status (early menopause etc.), it focuses on sex-related differences in clinical trials.”
- Thus, HC might consider updating this document to include guidance related to considerations of gender and intersectionality in trial design and analysis, or create a separate document that does so (and at the same time, clearly distinguishes sex from gender and explains the relevance of intersectional factors)

External documents:

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2

- 231-page document offers guidance on the ethical conduct of research involving humans
- It addresses fairness/equity in research participation, noting “culture, language, gender, race, ethnicity, age and disability”, and research involving the First Nations, Inuit and Métis peoples of Canada, and also includes approaches for informed consent for vulnerable populations
- However, several opportunities were identified to elaborate and strengthen discussion of gender and intersectionality throughout including sampling, recruitment, consent, participation and follow-up; hence, the need for HC to enhance its own documents.

SUBMISSION REVIEW (**Appendix 6**)

A total of 20 documents pertained to submission review. Among HC documents, only 1 standard operating procedure referred to intersectionality; no public guidance documents or templates/forms did so. Two of three external documents to which industry, the public and HC staff are referred to addressed intersectionality. Submission review documents for specific recommendations for each documents by section and content.

Table 5. Submission review documents addressing SGBA+

SGBA+	HC documents addressing SGBA+ n (%)			Total HC documents addressing SGBA+ n (% of 17)	External documents addressing SGBA+ n (% of 3)
	Public guidance	Standard operating procedures	Forms or templates		
Sex	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gender	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Intersectionality	0 (0.0)	1 (50.0)	0 (0.0)	1 (5.9)	2 (66.7)

Mention of devices specific to women were not counted as instances of sex, gender or intersectionality; for example, warning of risks on labelling for menstrual tampons, or definition of device inclusive of those preventing conception.

In the few documents that referred to SGBA+ concepts, statements were brief, simply stating a word or phrase, or vague, providing little guidance on the rationale for, or approaches or processes for considering sex, gender or intersectionality. For example:

HC document:

Referring to research participants, “Have the clinical studies been performed in special populations?”

External documents:

“If applicable, information about patient selection criteria”

Referring to a definition for contraindications, “Labelling elements that describe situations, such as patient populations... in which the device should not be used...”

AUTHORIZATION/POST-MARKET (*Appendix 7*)

A total of 19 documents pertained to submission review. A small proportion of HC standard operating procedures referred to sex, gender or intersectionality; no public guidance documents or templates/forms did so. Authorization and post-market monitoring/communication documents for specific recommendations for each documents by section and content.

Table 6. Authorization and post-market documents addressing SGBA+

SGBA+	HC documents addressing SGBA+			Total HC documents addressing SGBA+ n (% of 19)
	Public guidance	Standard operating procedures	Forms or templates	
Sex	0 (0.0)	1 (14.3)	0 (0.0)	1 (5.3)
Gender	0 (0.0)	3 (42.9)	0 (0.0)	3 (15.8)
Intersectionality	0 (0.0)	4 (57.1)	0 (0.0)	4 (21.1)

In the few HC documents that referred to SGBA+ concepts, statements were brief, simply stating a word or phrase, or vague, providing little guidance on the rationale for, or approaches or processes for considering sex, gender or intersectionality. For example:

Referring to reporting of benefits by, “...age, gender, dose, etc.”

Referring to differing adverse events, “...in patient groups, for example, pediatrics, geriatrics, pregnant/lactating women...”

In a checklist of causality assessment, “age, gender, ethnic origin...”

OTHER DOCUMENTS (*Appendix 8*)

A total of 5 external documents offered general information of relevance across the medical device lifecycle. A small proportion referred to sex, gender or intersectionality. Documents relevant across the medical device lifecycle for specific recommendations for each documents by section and content.

Table 7. Additional external documents addressing SGBA+

SGBA+	Total HC documents addressing SGBA+ n (% of 5)
Sex	1 (20.0)
Gender	1 (20.0)
Intersectionality	3 (60.0)

In the few external documents that referred to SGBA+ concepts, statements were brief, simply stating a word or phrase, or vague, providing little guidance on the rationale for, or approaches or processes for considering sex, gender or intersectionality. For example:

Referring to research participants, “Populations evaluated should represent, where appropriate, ethnically and genetically diverse populations so as to be representative of the population(s) where the device is intended to be marketed.”

Referring to differing indications of use in different countries, “...different intended use populations (e.g., disease, race, sex/gender)...”

Recommendations

GENERAL DOCUMENTS

A total of 341 recommendations to incorporate or strengthen SGBA+ arose from review of 45 Health Canada documents (mean 37.8, median 24, range 18 to 76) by document category (Table 8). This is a conservative figure because counts largely reflect sections of documents and not multiple possible improvements within sections. For recommendations specific to documents, see *Appendix 5* (clinical trial review), *Appendix 6* (submission review) and *Appendix 7* (authorization, monitoring and communication). For recommendations on how to prioritize and address SGBA+ gaps in documents, related regulatory processes, and adjunct communication and education strategies, see ensuing sections: Updating Documents and Processes, and Knowledge Translation.

With respect to SGBA+, in brief:

- Few HC documents of any type address SGBA+, those that do provide scant information, and advice is not consistent across documents for industry and HC staff. For example, *Causality Assessment*, Appendix 1 briefly advises HC staff to consider gender, age or ethnic origin in identifying the cause of adverse events, but corresponding forms to be completed by HC staff for causality/signal assessment do not at all prompt for SGBA+ details, nor do corresponding guidance documents or reporting forms to be used by industry for reporting problems or incidents.
- External documents that HC staff or industry may refer to for guidance (e.g. ISO, IMDRF) similarly did not address SGBA+.
- *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS2) mentions inappropriate exclusion from research of women or other individuals due to culture, race, ethnicity,

language, age, or disability, but it’s not clear to what extent industry or HC staff refer to this document.

- *Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences* mentions a “diversity framework” but acknowledges that the document focuses entirely on encouraging the inclusion of females (including considerations for pregnant or breast-feeding females) in clinical trials to identify and analyze sex-related differences.
- *Considerations* therefore does not address the need to consider gender or intersectional factors in study design, inclusion/exclusion criteria, or data collection, analysis and interpretation.
- Given that *Considerations* focuses on clinical trials, it does not address the full device lifecycle. For example, the need to collect data on sex, gender and intersectional factors for post-market surveillance of device incidents
- *Considerations* should be updated to reflect the full range of what constitutes SGBA+ across the device lifecycle
- Both TCPS2 and *Considerations* are “guidelines”, which means they are not mandatory
- Guidance documents used by industry to prepare applications or reports, and forms, templates or checklists used by HC staff to review applications or reports largely contain no requirements for SGBA+ information
- Prominently featuring SGBA+ in all documents would emphasize to industry the need to address SGBA+, and trigger HC staff to fully consider SGBA+ in regulatory decision-making
- Moreover, SGBA+ should be fully and consistently addressed in documents and forms across the regulatory device lifecycle, and across documents and forms used for corresponding purposes by industry and HC staff.

Table 8. Recommendations to strengthen SGBA+ by document type and device lifecycle stage

Lifecycle stage	Number of SGBA+ recommendations			Sub-total	Mean	Median Range
	Public guidance (n=22)	Standard operating procedures (n=12)	Forms or templates (n=11)			
Clinical trial review	22	15	23	60	20	22 15-23
Submission review	43	18	76	137	45.7	43 18-76
Authorization and monitoring	64	55	24	144	47.7	55 24-64
Sub-total/Overall	129	88	124	341	37.8	24 18-76

UPDATING DOCUMENTS and PROCESSES

Few HC documents address SGBA+ and those that do provide scant information. The same was true of external documents referred to as sources of supplemental information. In addition to numerous specific recommendations for enhancing SGBA+ in all documents reviewed (SEE **Appendix 5, 6 and 7**), additional options for ameliorating strategies include the following:

1. Enhance SGBA+ considerations in publicly-available guidance documents, internal standard operating procedures, and templates/forms. This could be done using one or more of the following approaches, which Health Canada can consider by weighing the noted pros and cons of each, and in so doing, potentially identifying additional implications or alternative approaches.

Table 9. Approaches to enhance SGBA+ in documents and processes

Approach	Pros	Cons
Enhance content throughout each of the documents by adding additional details in text, tables, figures or boxes.	<p>SGBA+ advice may be more relevant if tailored to document context (document topic, section topic, content details, etc.)</p> <p>Formatting techniques could be employed (e.g. tables, boxes, figures, spacing, bolded or highlighted text) to call attention to SGBA+ considerations</p> <p>Integrating advice throughout all document types functions as education, training and reminders to industry/public and HC staff</p>	May require considerable time and effort to review and edit all documents including decisions on what to revise and how, creation of content, and review and approval of updated documents
Add appendices to each document that include SGBA+ guidance, and throughout documents, refer to those appendices	<p>SGBA+ advice would be tailored to document topic</p> <p>May require less time and effort compared with integrating SGBA+ content throughout documents</p>	<p>Readers may not refer to appendices</p> <p>Readers may not easily link advice in appendices to guidance in documents</p>
Develop new documents specific to SGBA+ including a publicly-available guidance document and internal standard operating procedure	<p>Dedicated document may emphasize the importance of SGBA+</p> <p>May require less time and effort compared with revising documents, either throughout or via appendices</p>	<p>Stakeholders may not refer to a separate document</p> <p>Readers may not easily link advice in a separate document to guidance in other documents</p>

2. To promote awareness and consideration of SGBA+, include SGBA+ considerations in application forms/templates and HC review protocols and forms/templates as a mandatory field in which stakeholders note how SGBA+ is/was considered, and if not, justify exclusions by explaining why sex, gender or intersectionality were not relevant or not feasible to assess. To ensure this is thorough and consistent, consider developing a structured framework or checklist of SGBA+ considerations to insert in all relevant documents.
3. When updating documents, consider the following:
 - Ensure consistency across corresponding public guidance documents, application forms, an HC standard operating procedures and templates/forms
 - At least one document refers to Therapeutic Products Programme; considering updating documents with the new name of the medical devices department/division
 - Replace research “subjects” or “cases” with “participants” or “persons”, which is now standard and acknowledges the role of individuals as actively engaged in research
 - Replace “disability” with “ability”

- Be consistent with language for adverse event, adverse incident, medical device incident, risk, concern, etc.
 - Cross-check documents and version dates; for example:
 - a. This report reviewed *Guidance Document for Mandatory Problem Reporting for Medical Devices* (2011). Check that content aligns with *Mandatory reporting of serious adverse drug reactions and medical device incidents by hospitals* (2019), and if there is a need for both documents
 - b. Check for consistency or overlap between *Standardized Health Product Risk Communication Template* (no date) and *Mandatory medical device problem reporting form for industry* (2018)
 - c. HC refers to *ISO 14155:2011 Clinical investigation of medical devices for human subjects — Good clinical practice* (2011) when there is a 2020 update.
4. With respect to post-market activities, documents largely pertain to signal assessment, causality assessment and reporting/communicating about problems by HC staff. Guidance is lacking on how HC staff are to communicate with healthcare professionals, patients or the public about recalls or warnings. Guidance is also lacking on how industry, hospitals or healthcare professionals are to consider SGBA+ when collecting, analyzing or reporting data for post-market surveillance.
5. The scope of this report includes identifying SGBA+ limitations in relevant documents, which represent opportunities for enhancing SGBA+ in those documents, and ultimately in the medical device lifecycle. Next steps for Health Canada may include the following:
- Assess the time and resources required to do the following to inform decisions about human resource needs and timeline:
 - Review the numerous specific recommendations for each document to decide which documents warrant updates, what should be update and how. While that was done as part of this report, final decisions should be made by those who oversee use of the documents because they possess critical medical device and contextual/organizational knowledge
 - Reflect on optional approaches to update documents [SEE Recommendation #1 Table]
 - Develop a communication strategy for HC staff and industry
 - Develop an education strategy for HC staff and industry
 - Develop a communication strategy to inform healthcare professionals who use devices, patients, the public and other relevant groups (e.g. professional societies, advocacy groups, CADTH) about impending improvements, and prospectively about improvements as they occur
 - Prepare a strategic and operational plan that includes timeline, benchmarks and human resource requirements for updating documents, communicating with all stakeholders and implementing changes.

KNOWLEDGE TRANSLATION

6. When enhancing SGBA+ considerations in all document types, use the opportunity to provide education, and in so doing: distinguish sex and gender, distinguish gender elements (e.g. gender identity versus sexual orientation), and elaborate on intersectionality including Indigenous, visible minority, ability (11 elements), culture, etc. To do so, **SEE standardized terms and categories used by Statistics Canada, Canada’s Employment Equity Act and the Ontario Human Rights Commission**
7. The large number of related documents may be confusing to users. Consider:
- a. Merging related documents; for example, include templates/forms in corresponding guidance document

- b. Creating packages that include related documents and templates/forms
 - c. Developing an over-arching one-page “quick guide” or infographic that displays the process in algorithm form, and specifies documents and templates/forms relevant to each stage. **NOTE: this may also be an opportunity to highlight where and how SGBA+ is relevant**
8. Given shortcomings in external documents to which industry, the public and HC staff are currently referred, identify more detailed or current sources of information about SGBA+ to create a reference list. This could be used as a stand-alone document, but also as a standard addition to all documents, or to update references or links to resources in current documents. A good starting place is the Canadian Institutes of Health Research web site on how to integrate sex and gender into research, which includes definitions, videos, training modules, links to webinars and webcasts, and links to other resources. SEE <https://cihr-irsc.gc.ca/e/50836.html>.
9. Train and coach HC staff in SGBA+ using one or more of the following options:
- Hold meetings or workshops to raise awareness about enhanced documents as they are updated with SGBA+ content
 - Implement mandatory reading or completion of CIHR SGBA+ modules for all staff
 - Ensure that staff with higher-level review/authorization responsibilities undertake more rigorous training compared with staff that perform intake reviews
 - Provide additional training to select individuals who are deployed as internal champions or knowledge brokers who can share information, serve as coaches, and lead initiatives
 - Engage staff in developing in-house SGBA+ guidance, which functions as an experiential learning opportunity, and may generate guidance that is tailored to their roles/functions
 - Organize a series of in-service workshops featuring invited speakers including SGBA+ research experts and members of the public who represent diverse groups
 - Embed flags or reminders in information systems used to review and process applications
10. SGBA+ concepts may be new to industry and HC staff so lead-time may be required before instituting changes to pre-alert stakeholders about impending changes and the rationale for enhancements; provide education about SGBA+ and how to address SGBA+ in applications or reviews; and address questions and concerns. Hence, a communication strategy, messaging and related materials such as infographics must be planned to share information and expectations. Applicants and staff may be more likely to accept and comply with impending changes if they are part of the planning process.

SGBA+ in device-specific documents

Sources and documents included

NOTE: HC did not authorize security clearance to review internal pre- or post-market device-specific documents such as industry license applications for new devices or reports related to problems arising in association with devices use, or HC reviews of those applications or reports; thus the following section is based only on publicly-available documents.

A total of eight publicly-available databases were searched or browsed for documents (reports or records) published from 2015 to 2020 specific to pacemakers, total knee implants, breast implants, transvaginal mesh and birth control devices. A total of 50 documents were reviewed. All pertained to authorization and post-market stages of the device lifecycle. Table 10 summarizes the number of available reports by device lifecycle stage, source and type of device. Data extracted from those reports is available in **Appendix 9**.

Table 10. Device-specific documents included

Lifecycle stage and source	Documents by device type (n)					Sub-total
	Implantable pacemakers	Total knee implants	Breast implants	Transvaginal surgical mesh	Birth control devices	
SUBMISSION						
---	---	---	---	---	---	---
AUTHORIZATION						
Medical Device Active License Listing	---	---	---	---	---	---
Drug & Health Product Register – Regulatory Decision	2	3	1	---	1	7
Drug & Health Product Register – Summary Decision	---	---	2	---	---	2
POST-MARKET						
Clinical Information on Drugs & Health Products	---	---	---	1	1	2
Drug & Health Product Register – Safety Review	---	---	1	1	---	2
Medical Device Incidents	5	7	4	2	2	20
Recalls and Safety Alerts	2	2	4	2	1	11
Health Product InfoWatch	---	---	3	2	1	6
Sub-total	9	12	15	8	6	50

SGBA+ in device-specific sources/documents

Overall, no publicly-available device-specific documents addressed SGBA+. This was true of devices specific to biological females (breast implants, intrauterine devices, pelvic mesh) and those relevant to both females and males (pacemakers, knee implants). Document-specific gaps representing opportunities to strengthen SGBA+ are included in **Appendix 10**.

Table 11 summarizes standard content available in the range of publicly-available documents by device lifecycle stage and source with select examples specific to biological females. For instance, at the authorization stage, documents provided no details about research underlying device licence approvals. Similarly, in the post-market domain, documents describing the investigation of device-related problems retrieved from Medical Device Incidents and Recall and Safety Alerts databases provided no details about the number and characteristics of affected persons, or review of data from either published research or post-market surveillance. While documents retrieved from the Drug & Health Product Register – Safety Review mentioned the number of research studies or post-market incidents reviewed, reports did not describe the studies or data, characteristics of participants/those affected or sub-analyses. For example, a one-page Safety Review of birth-control releasing intrauterine devices thought to potentially suppress lactation mentioned review of 24 studies and 19 Canadian reports of decreased milk production, but provided no further details. The most extensive document of 111 pages, a Clinical Evaluation Report produced by Ethicon (manufacturer) retrieved from Clinical Information on Drugs &

Health Products, reviewed evidence on the safety of transvaginal mesh (Gynecare Gynemesh). While it included published research (50 studies) and post-market surveillance data (473 complaints involving 467 serious injuries), no details were provided about the characteristics of study participants/affected persons or sub-analyses by those characteristics.

Table 11. Standardized content in sources and device-specific documents

Source	Content	Example	SGBA+ content
AUTHORIZATION			
Medical Device Active License Listing	Specifies only date of approval and device identifier	---	---
Drug & Health Product Register – Summary Decision	Purpose of application, information reviewed by Health Canada, decision issued, date of decision	Natrelle 410 Truform Microcell Silicone-Filled Breast Implants Class IV (new licence) Approved 2018-06-19 Half-page report	No details about SGBA+ “What information did Health Canada review? Safety and effectiveness was supported by conformity to applicable standards, physical and mechanical bench testing such as gel bleed testing, similarities to previously approved 410 Biocell implants, and worldwide marketing history data with comparison between the subject device and the predicate.”
POST-MARKET			
Clinical Information on Drugs & Health Products Contains only 29 records so not comprehensive	Literature review, clinical data on safety and efficacy, post-market surveillance data, and benefits versus risk analysis (some details redacted)	Gynecare Gynemesh (Ethicon) Class III Approved 2009-11-20 Public release 2019-08-29 Clinical Evaluation Report (111 pages) produced by Ethicon	Little detail about SGBA+ Sex Relevant to sex only because used to treat pelvic issues among biological females (e.g. should not be used in pregnant women or women planning future pregnancies because the mesh will not stretch) Gender None Intersectional factors Notes patient age one of two risk factors for vaginal graft exposure No details about the characteristics of women or SGBA+ analyses in published research (50 studies) or post-market surveillance data (473 complaints involving 467 serious injuries) reviewed in the report
Drug & Health Product Register – Safety Review	Key messages, overview, safety review findings, conclusions and action, and references	Birth control hormone (levonorgestrel, LNG)-releasing IUDs: Mirena, Jaydess and Kyleena Issued 2017-09-21 One page report	No SGBA+ details Problem: Decreased breast milk production (suppressed lactation) Review of 24 studies (concluded highly effective birth control and that these products do not affect breastfeeding) and 19 Canadian reports of decreased milk production (16 reports suggested that the IUDs may have played a role; 3 reports did not include sufficient information).

			<p>“Health Canada’s review concluded that there is currently limited evidence to suggest a link between LNG-IUS products and the risk of decreased breast milk production.”</p> <p>The report did not describe the studies/data, participants or their characteristics</p>
Medical Device Incidents	Date of approval, hazard severity and description of incident	Memory Gel Cohesive III (Mentor Medical Systems) Class IV (annual update with conditions) Issued 2017-10-10 68 incidents Brief record as shown here	<p>No details about SGBA+</p> <p>Hazard Severity: I (potential for death/injury) 2019-06-26 E2303 - Capsular Contracture A0101 - Patient-Device Incompatibility A0406 - Material Deformation A0412 - Material Rupture Capsular contracture associated with breast</p>
Recalls and Safety Alerts	Starting date, posting date, communication type, hazard classification, reason for alert, affected products	Capio Vaginal Support System Medical Device Recall (5 affected products and multiple lots or serial numbers for each) 2018-02-15 1 page report	<p>No SGBA+ details</p> <p>Hazard severity: II (may cause temporary adverse health consequences)</p> <p>“Increasing trend in reports regarding the Capio suture breakage and/or detachment of the Capio suture darts from both the Capio suture and the pelvic floor kit mesh assembly”</p> <p>No details about number and characteristics of affected persons, or review of data (either published or post-market)</p>
Health Product InfoWatch Monthly newsletter on select topics. Not searchable, must browse tables of contents for each issue	Possible complications, indications	Biocell breast implants June 2019 Issue Brief record as shown here, with links to record in Recalls and Safety Alerts and to Summary Safety Review	<p>No SGBA+ details</p> <p>“Health Canada’s safety review evaluated the risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). This safety review found that there was an increased risk of BIA-ALCL with the use of highly textured (macro-textured) implants, in comparison with those having less textured or smooth implants. Biocell breast implants made by Allergan are the only macro-textured implants currently available in Canada. Health Canada has suspended the licences held by Allergan for their Biocell textured breast implants. Health Canada will work with all breast implant manufacturers to strengthen the Instructions for Use of all breast implants regarding the risk of BIA-ALCL. Health Canada has also communicated this information to Canadians.”</p>

Recommendations

DEVICE-SPECIFIC SOURCES and DOCUMENTS

Table 12 highlights key SGBA+ deficits of each source and corresponding documents, along with recommendations for enhancing SGBA+ content, related processes for doing so, and other logistical considerations to enhance the information publicly-shared by HC.

Table 12. Recommendations to strengthen SGBA+ in device-specific documents across sources

Source	Current content	Recommended content or enhancement
AUTHORIZATION		
Medical Device Active License Listing	Specifies only date of approval and device identifier	HC offers multiple data sources that are not linked. Recommendations: <ul style="list-style-type: none"> Using device identifier, link to related device-specific documents in other sources so that a searcher is able to retrieve complete data on a given product across the device lifecycle. Ideally, searchers could access any type of document across the device lifecycle for a given product through a single interface
Drug & Health Product Register – Summary Decision	Purpose of application, information reviewed by Health Canada, decision issued, date of decision	These documents do not report information reviewed by HC. Recommendations: <ul style="list-style-type: none"> Report the number and type of studies including characteristics of study participants and sub-analyses by those characteristics Explicitly report whether a given device was assessed for safety and efficacy among diverse potential users To do so requires that industry must report these details to HC when applying to medical device licenses
POST-MARKET		
Clinical Information on Drugs & Health Products Contains only 29 records so not comprehensive	Literature review, clinical data on safety and efficacy, post-market surveillance data, and benefits versus risk analysis (some details redacted)	Reports are lengthy, and do mention the number of published research studies reviewed and post-market incidents reported, but no details are provided about the characteristics of participants or affected persons, or whether those characteristics influenced or were associated with safety or efficacy outcomes. The number of these reports is few (n=29). Moreover, the reports are produced by the manufacturer. Recommendations: <ul style="list-style-type: none"> Require manufacturers to include characteristics of participants/persons when reporting studies and incidents, and sub-analyses, and based on those findings, explicitly comment on the relevance of SGBA+ or the absence of sufficient evidence on safety and efficacy among diverse persons HC should conduct an arms-length critical review of the data and conclusions and include such a report with those supplied by industry HC should describe the criteria or rationale for inclusion of reports in this source, and whether the intent is to ultimately include such reports for all devices or certain types of devices, or whether this source will continue to offer reports for only select devices
Drug & Health Product Register – Safety Review	Key messages, overview, safety review findings, conclusions and action, and references	These reports are brief (one page). They mention number of studies or incidents reviewed, but do not detail the characteristics of participants or affected persons, or the influence of association of characteristics with safety outcomes. Recommendations: <ul style="list-style-type: none"> Report the number and type of studies including characteristics of study participants and sub-analyses by those characteristics Explicitly report whether a given device was assessed for safety and efficacy among diverse potential user To do so requires that industry must report these details to HC when applying to medical device licenses
Medical Device Incidents	Date of approval,	These reports of individual incidents provide scant details in the form of standardized categories (e.g. patient-device incompatibility, material deformation) such they are

	hazard severity and description of incident	<p>likely of little use to either healthcare professionals, patients or the public because the meaning of standardized category labels is not clear. Furthermore, no details are provided about the characteristics of affected persons to enable the identification of potential associations between characteristics and the number and type of all incidents reported for a given device. Furthermore, healthcare professionals, patients or the public are not informed of recommended actions (for example, if the patient has the affected device, should they be concerned).</p> <p>Recommendations:</p> <ul style="list-style-type: none"> • More clearly explain what the incident descriptor categories mean • Include the characteristics of affected persons in records of individual incidents • Specify recommended action (or explicitly note that no concern or action is warranted) • As incidents accumulate (for example, 68 incidents were noted for Memory Gel Cohesive III, Mentor Medical Systems), provide regularly-updated synthesized reports of the number and type of incidents, and the characteristics of affected persons • Using device identifier, link to other documents across the device lifecycle for that given product
Recalls and Safety Alerts	Starting date, posting date, communication type, hazard classification, reason for alert, affected products	<p>These brief reports (1 page) identify problems affecting multiple products (devices, lots or serial numbers), but apart from briefly naming the problem (e.g. suture breakage, detachment), provide no review of data (either published or post-market) or details about number and characteristics of affected persons, nor whether concern or action is warranted</p> <p>Recommendations:</p> <ul style="list-style-type: none"> • More clearly explain the problem • Include the characteristics of affected persons • Specify recommended action (or explicitly note that no concern or action is warranted) • Prospectively synthesize data on the number and type of incidents, and the characteristics of affected persons • Using device identifier, link to other documents across the device lifecycle for that given product • Assess overlap between multiple sources/types of documents that all offer limited information, need for multiple sources, and resource implications of consolidating and elaborating these sources • As part of that investigation, assess who is using the range of sources, and frequency and purpose of use
Health Product InfoWatch Monthly newsletter on select topics. Not searchable, must browse tables of contents for each issue	Possible complications, indications	<p>Records are brief and provide no data about the number and characteristics of affected persons from either research studies or post-market surveillance data, nor what healthcare professionals or patients should do. While the record does link to Recalls and Safety Alerts and Summary Safety Review, as noted above, those sources and documents are not informative. The monthly newsletter is not comprehensive of all devices associated with incidents, and content is not searchable.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> • More clearly explain the problem • Include the characteristics of affected persons • Specify recommended action (or explicitly note that no concern or action is warranted) • Using device identifier, link to other documents across the device lifecycle for that given product • Assess overlap between multiple sources/types of documents that all offer limited information, need for multiple sources, and resource implications of consolidating and elaborating these sources • As part of that investigation, assess who is using the range of sources, and frequency and purpose of use

UPDATING SOURCES, DOCUMENTS and PROCESSES

SGBA+ considerations must be enhanced in publicly-available documents aimed at healthcare professionals, patients and the public that describe the implications for persons with diverse characteristics of: (1) evidence of safety and efficacy upon which devices are authorized for use, and (2) incidents associated with devices in the post-market domain. This could be done using one or more of the following approaches in Table 13, which consolidates information presented in Table 12. Health Canada can consider these recommendations by weighing the noted pros and cons of each, and in so doing, potentially identify additional implications or alternative approaches.

Table 13. Approaches to enhance SGBA+ in device-specific sources and documents

Approach	Pros	Cons
11. For documents on the safety and efficacy upon which devices are approved, report the number and type of studies including characteristics of study participants and sub-analyses by those characteristics	Explicitly reporting whether a given device was assessed for safety and efficacy among diverse potential users, thereby emphasizing SGBA+ implications, ensures that the public, including healthcare professionals and patients, understand that devices are safe and effective for diverse users, instilling confidence among users about HC regulatory processes and about devices	To do so requires that industry must report these details to HC when applying to medical device licenses To support this, guidance documents and forms for industry, and standard operating procedures, forms and templates for HC staff must be updated May require considerable time and effort to review and edit all documents including decisions on what to revise and how, creation of content, and review and approval of updated documents
12. For documents on device safety and efficacy prepared by industry, HC should conduct an arms-length critical review of SGBA+ data and conclusions and publicly share that report along with the corresponding industry report	This may further bolster public confidence in HC regulatory processes, and in the safety and efficacy of approved device for diverse users	To do so requires that industry must report these details to HC when providing evidence from published research and/or post-market data
13. For documents that report device incidents, more clearly explain the problem, include the characteristics of affected persons, prospectively synthesize accumulated incidents pertaining to the same device, and specify recommended action (or explicitly note that no concern or action is warranted)	Healthcare professionals and patients will understand if and how the alerts or warnings pertain to them and what they should do about it, if anything	To report the characteristics of affected persons requires that industry must report these details to HC. Elaborating the details in incident reports and prospectively synthesizing incidents for the same device will require updating of HC databases, standard operating procedures, forms and templates along with relevant training

<p>14. Using device identifier, link to related device-specific documents across sources so that a searcher is able to retrieve complete data on a given product across the device lifecycle. Ideally, searchers could access all documents pertaining to a given device through a single interface</p>	<p>The public (healthcare professionals, patients) will be better informed about device safety and efficacy for diverse users if information is clear, comprehensive and easy to access</p>	<p>To eliminate the current multiple incomplete and overlapping sources of data will require a complete overhaul of information systems</p>
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15. To promote awareness of SGBA+ and its implications for device safety and efficacy, require that SGBA+ be fully defined in all publicly-available device-specific documents (e.g. summary decision, clinical evaluation, safety review, medical device incidents, recalls and safety alerts), explicitly noting which SGBA+ aspects were considered, and which are relevant or not relevant to the device, its use, or potential benefits or harms. As noted in Recommendation 2, to ensure this is thorough and consistent, develop an SGBA+ checklist or framework to insert in all documents.
16. To prepare industry and HC staff for impending changes, and in the interim, to encourage awareness of, reporting and assessment of SGBA+, prepare worked examples for each type of document to illustrate how to consider and report SGBA+, and its implications for device safety and efficacy.
17. In the course of searching for and then extracting data from publicly-available device-specific documents, it became apparent that information sources are incomplete with respect to SGBA+, overlapping and not linked. Therefore, ongoing discussions about updating SGBA+ in device-specific documents must simultaneously consider the need for multiple sources, and the resource implications of consolidating sources, as doing so could ultimately reduce the need to update multiple information systems. Preliminary investigation might assess who is using the range of sources, for what purpose and frequency of use as a means of determining which sources should be kept and which are either unnecessary or could be more readily integrated with other sources.
18. The scope of this report includes identifying SGBA+ limitations in relevant documents, which represent opportunities for enhancing SGBA+ in those documents, and ultimately in the medical device lifecycle. To prioritize action, next steps for Health Canada may include the following:
- a. Review the numerous recommendations for both general (previous section) and device-specific documents to decide on what to update in the short- and long-term and how to go about doing so. While this report offered pros and cons of various recommendations, final decisions should be made by those who oversee use of the documents because they possess critical medical device and contextual/organizational knowledge.
 - b. Develop a communication strategy for HC staff and industry
 - c. Develop an education strategy for HC staff and industry
 - d. Develop a communication strategy to inform healthcare professionals who use devices, patients, the public and other relevant groups (e.g. professional societies, advocacy groups, CADTH) about impending improvements, and prospectively about improvements as they occur
 - e. Prepare a strategic and operational plan that includes timeline, benchmarks and human resource requirements for updating documents, communicating with stakeholders and implementing changes.

KNOWLEDGE TRANSLATION

19. Prior recommendations considered knowledge translation to industry and HC staff. Additional knowledge translation must be targeted to users of publicly-available device-specific documents including healthcare professionals and patients who use(d) devices. Until device-specific sources and documents are updated to reflect SGBA+ considerations, Health Canada might:
- Develop an SGBA+ vision and mission statement along with goals and a timeline, and share that on the Medical Devices Directorate web page, and also on the web pages by which users access the various sources of device-specific documents.
 - Form an advisory committee including healthcare professionals who use a range of devices and patients of diverse characteristics with personal experience of a range of devices to partner with Health Canada in visioning, prioritizing, planning and implementing the recommendation included in this report.

Integrated recommendations

Overall, SGBA+ should be fully and consistently addressed in documents and forms across the regulatory device lifecycle. Recommendations to achieve this are summarized here by document users. The recommendations pertain to: updating sources and documents, related processes, and knowledge translation.

Table 14. Recommendations to enhance SGBA+ in the regulatory device lifecycle by document users

Industry and HC staff	Healthcare professionals and patients
<ol style="list-style-type: none"> <i>Considerations</i>, currently referred to as the key source of guidance for SGBA+, should be updated to reflect the full range of what constitutes SGBA+ (currently only addresses sex) across the device lifecycle (currently focused only on clinical trials) Enhance SGBA+ considerations in publicly-available guidance documents, internal standard operating procedures, and templates/forms. <ol style="list-style-type: none"> Enhance content throughout each of the documents by adding additional details in text, tables, figures or boxes. Add appendices to each document that include SGBA+ guidance, and throughout documents, refer to those appendices Develop new documents specific to SGBA+ including a publicly-available guidance document and internal standard operating procedure To promote awareness and consideration of SGBA+, include SGBA+ considerations in application forms/templates and HC review protocols and forms/templates as a mandatory field in which stakeholders note how SGBA+ is/was considered, and if not, justify exclusions by explaining why sex, gender or intersectionality were not relevant or not feasible to assess. To ensure this is thorough and consistent, consider developing a structured framework or checklist of SGBA+ considerations to insert in all relevant documents. When updating documents, consider the following: <ul style="list-style-type: none"> Ensure consistency across corresponding public guidance documents, application forms, an HC standard operating procedures and templates/forms 	<ol style="list-style-type: none"> For documents on the safety and efficacy upon which devices are approved, report the number and type of studies including characteristics of study participants and sub-analyses by those characteristics For documents on device safety and efficacy prepared by industry, HC should conduct an arms-length critical review of SGBA+ data and conclusions and publicly share that report along with the corresponding industry report For documents that report device incidents, more clearly explain the problem, include the characteristics of affected persons, prospectively synthesize accumulated incidents pertaining to the same device, and specify recommended action (or explicitly note that no concern or action is warranted) Using device identifier, link to related device-specific documents across sources so that a searcher is able to retrieve complete data on a given product across the device lifecycle. Ideally, searchers could access all documents pertaining to a given device through a single interface

<ul style="list-style-type: none"> • At least one document refers to Therapeutic Products Programme; considering updating documents with the new name of the medical devices department/division • Replace research “subjects” or “cases” with “participants” or “persons”, which is now standard and acknowledges the role of individuals as actively engaged in research • Replace “disability” with “ability” • Be consistent with language for adverse event, adverse incident, medical device incident, risk, concern, etc. • Cross-check documents and version dates; for example: <ul style="list-style-type: none"> ○ This report reviewed Guidance Document for Mandatory Problem Reporting for Medical Devices (2011). Check that content aligns with Mandatory reporting of serious adverse drug reactions and medical device incidents by hospitals (2019), and if there is a need for both documents ○ Check for consistency or overlap between Standardized Health Product Risk Communication Template (no date) and Mandatory medical device problem reporting form for industry (2018) ○ HC refers to ISO 14155:2011 Clinical investigation of medical devices for human subjects — Good clinical practice (2011) when there is a 2020 update. <p>5. With respect to post-market activities, documents largely pertain to signal/causality assessment and reporting by HC staff. Guidance is lacking on how HC staff are to communicate with healthcare professionals, patients or the public about recalls or warnings. Guidance is also lacking on how industry, hospitals or healthcare professionals are to consider SGBA+ when collecting, analyzing or reporting data for post-market surveillance.</p> <p>6. The scope of this report includes identifying SGBA+ limitations in relevant documents, which represent opportunities for enhancing SGBA+ in those documents, and ultimately in the medical device lifecycle. To prioritize action, next steps for Health Canada may include the following:</p> <ul style="list-style-type: none"> • Assess the time and resources required to do the following to inform decisions about human resource needs and timeline: • Review the numerous specific recommendations for each document to decide which documents warrant updates, what should be updated and how. While that was done as part of this report, final decisions should be made by those who oversee use of the documents because they possess critical medical device and contextual/organizational knowledge • Reflect on optional approaches to update documents [SEE Recommendation #1 Table] • Develop a communication strategy for HC staff and industry • Develop an education strategy for HC staff and industry • Develop a communication strategy to inform healthcare professionals who use devices, patients, the public and other relevant groups (e.g. professional societies, advocacy groups, CADTH) about impending improvements, and prospectively about improvements as they occur • Prepare a strategic and operational plan that includes timeline, benchmarks and human resource requirements for updating 	<p>16. To promote awareness of SGBA+ and its implications for device safety and efficacy, require that SGBA+ be fully defined in all publicly-available device-specific documents (e.g. summary decision, clinical evaluation, safety review, medical device incidents, recalls and safety alerts), explicitly noting which SGBA+ aspects were considered, and which are relevant or not relevant to the device, its use, or potential benefits or harms. As noted in Recommendation 2, to ensure this is thorough and consistent, develop an SGBA+ checklist or framework to insert in all documents.</p> <p>17. To prepare industry and HC staff for impending changes, and in the interim, to encourage awareness of, reporting and assessment of SGBA+, prepare worked examples for each type of document to illustrate how to consider and report SGBA+, and its implications for device safety and efficacy.</p> <p>18. In the course of searching for and then extracting data from publicly-available device-specific documents, it became apparent that information sources are incomplete with respect to SGBA+, overlapping and not linked. Therefore, ongoing discussions about updating SGBA+ in device-specific documents must simultaneously consider the need for multiple sources, and the resource implications of consolidating sources, as doing so could ultimately reduce the need to update multiple information systems. Preliminary investigation might assess who is using the range of sources, for what purpose and frequency of use as a means of determining which sources should be kept and which are either unnecessary or could be more readily integrated with other sources.</p> <p>19. The scope of this report includes identifying SGBA+ limitations in relevant documents, which represent opportunities for enhancing SGBA+ in those documents, and ultimately in the medical device lifecycle. To prioritize action, next steps for Health Canada may include the following:</p>
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documents, communicating with all stakeholders and implementing changes.

7. When enhancing SGBA+ considerations in all document types, use the opportunity to provide education, and in so doing: distinguish sex and gender, distinguish gender elements (e.g. gender identity versus sexual orientation), and elaborate on intersectionality including Indigenous, visible minority, ability (11 elements), culture, etc. To do so, SEE standardized terms and categories used by Statistics Canada, Canada's Employment Equity Act and the Ontario Human Rights Commission
8. The large number of related documents may be confusing to users. Consider:
 - a. Merging related documents; for example, include templates/forms in corresponding guidance document
 - b. Creating packages that include related documents and templates/forms
 - c. Developing an over-arching one-page "quick guide" or infographic that displays the process in algorithm form, and specifies documents and templates/forms relevant to each stage. NOTE: this may also be an opportunity to highlight where and how SGBA+ is relevant
9. Given shortcomings in external documents to which industry, the public and HC staff are currently referred, identify more detailed or current sources of information about SGBA+ to create a reference list. This could be used as a stand-alone document, but also as a standard addition to all documents, or to update references or links to resources in current documents. A good starting place is the Canadian Institutes of Health Research web site on how to integrate sex and gender into research, which includes definitions, videos, training modules, links to webinars and webcasts, and links to other resources. SEE <https://cihr-irsc.gc.ca/e/50836.html>.
10. Train and coach HC staff in SGBA+ using one or more of the following options:
 - Hold meetings or workshops to raise awareness about enhanced documents as they are updated with SGBA+ content
 - Implement mandatory reading or completion of CIHR SGBA+ modules for all staff
 - Ensure that staff with higher-level review/authorization responsibilities undertake more rigorous training compared with staff that perform intake reviews
 - Provide additional training to select individuals who are deployed as internal champions or knowledge brokers who can share information, serve as coaches, and lead initiatives
 - Engage staff in developing in-house SGBA+ guidance, which functions as an experiential learning opportunity, and may generate guidance that is tailored to their roles/functions
 - Organize a series of in-service workshops featuring invited speakers including SGBA+ research experts and members of the public who represent diverse groups
 - Embed flags or reminders in information systems used to review and process applications

- a. Review the numerous recommendations for both general (previous section) and device-specific documents to decide on what to update in the short- and long-term and how to go about doing so. While this report offered pros and cons of various recommendations, final decisions should be made by those who oversee use of the documents because they possess critical medical device and contextual/organizational knowledge.
 - b. Develop a communication strategy for HC staff and industry
 - c. Develop an education strategy for HC staff and industry
 - d. Develop a communication strategy to inform healthcare professionals who use devices, patients, the public and other relevant groups (e.g. professional societies, advocacy groups, CADTH) about impending improvements, and prospectively about improvements as they occur
 - e. Prepare a strategic and operational plan that includes timeline, benchmarks and human resource requirements for updating documents, communicating with stakeholders and implementing changes.
20. Prior recommendations considered knowledge translation to industry and HC staff. Additional knowledge translation must be targeted to users of publicly-available device-specific documents including healthcare professionals and patients who use(d) devices. Until device-specific sources and documents are updated to reflect SGBA+ considerations, Health Canada might:
- a. Develop an SGBA+ vision and mission statement along with goals and a timeline, and share that on the Medical Devices Directorate web page, and also on the web pages by which users access the various sources of device-specific documents.
 - b. Form an advisory committee including healthcare professionals who use a range of devices and patients of diverse characteristics with personal experience of a range

<p>11. SGBA+ concepts may be new to industry and HC staff so lead-time may be required before instituting changes to pre-alert stakeholders about impending changes and the rationale for enhancements; provide education about SGBA+ and how to address SGBA+ in applications or reviews; and address questions and concerns. Hence, a communication strategy, messaging and related materials such as infographics must be planned to share information and expectations. Applicants and staff may be more likely to accept and comply with impending changes if they are part of the planning process.</p>	<p>of devices to partner with Health Canada in visioning, prioritizing, planning and implementing the recommendation included in this report.</p>
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Discussion

Brief summary

This report is based on content analysis of: 56 general documents resulting in 341 recommendations specific to the 45 documents developed by Health Canada and 11 broad recommendations; and 50 device-specific documents identified in 8 publicly-available sources resulting in 1 overall specific recommendation and 9 broad recommendations. While a total of 20 recommendations emerged, many included additional sub-recommendations.

The overall key finding is that SGBA+ is not fully and consistently addressed in general or device-specific documents, standard operating procedures, forms or templates targeted to industry, HC staff, healthcare professionals or patients across the device lifecycle. The vast majority of documents included no mention of SGBA+ considerations. A small number of documents referred to sex (e.g. need to recruit biological females in clinical trials, certain devices are used largely by biological females). There was little to no mention of gender (sometimes used interchangeably with sex) or intersectional factors. Therefore, current regulatory processes may not be ensuring the safety and efficacy of devices for patients with diverse characteristics, and healthcare professional and patient users of devices are not informed of this fact. The overall recommendation is that Health Canada must promote and enable the reporting, review and communication of SGBA+ considerations for all devices (women-specific, relevant to both women and men) across the device lifecycle.

Strengths and limitations

Strengths of this work include the use of rigorous content analysis methods [19,20], fully documenting analysis processes and data, use of an established SGBA+ framework based on that of the Canadian Institutes of Health Research further tailored to include intersectional factors [18], and compliance with standards for conducting and reporting content analyses [21]. Furthermore, the author, a Senior Scientist and Professor, has considerable experience in content analysis and knowledge translation, and knowledge of the medical device lifecycle, having led a pan-Canadian research team in a multi-part research study on the identification and reporting of AMDEs [3,8-10]. While one investigator extracted and summarized data, that is work was conducted in partnership with two staff from Health Canada, who provided input and guidance throughout the process, and independently reviewed the findings at two time points. We anticipate that the report and its findings will undergo further independent scrutiny by others at Health Canada to ensure that it is free from errors and inaccuracies.

Several factors may limit the interpretation and application of the findings. We did not analyze the content of all relevant files. However, based on advice from Health Canada, we reviewed the documents most commonly referred to by industry and HC staff. More importantly, security clearance to access

internal device-specific documents was not granted by Health Canada so we did not analyze the content of documents submitted by industry containing evidence on device safety and efficacy from published research, manufacturer studies or post-market surveillance reports (apart from one Clinical Evaluation Report that did not include SGBA+ information). However, given that general guidance (other than *Considerations*, which is limited to sex) does not compel industry to report SGBA+ and the aforementioned Clinical Evaluation Report included no SGBA+ details, we could fairly safely assume that documents describing evidence/data to which we lacked access did not include SGBA+ details. We also did not analyze documents pertaining to all Class II, III and IV devices. However, we sampled documents for devices that have been associated with AMDEs [2-4,7,11-13], including devices specific to women (breast implants, pelvic mesh, intrauterine devices) and those used in both women and men (pacemakers, knee implants). Finally, this document identified SGBA+ gaps in sources, documents and related processes, and offers high-level recommendations on how to address those gaps, but does not provide detailed SGBA+ content for documents, as updating documents, underlying information systems and related processes requires nuanced decision-making by those who oversee and are involved in the work, which was beyond the scope of this project.

Implications

This report includes numerous recommendations, which may not be easy to digest, and even more challenging to address given the complexity of medical device regulation. A number of interacting multi-level factors may influence the feasibility of responding to these recommendations. At the system level, as described by Health Canada staff, requiring additional information places a burden on industry, which conflicts with encouraging medical device trials in Canada. Moreover, Canada is a small medical device market comparatively-speaking, so trials taking place here are subject to the criteria and processes established elsewhere. Therefore, it may be unlikely that industry would tailor international trials to Canadian requirements for SGBA+. At the organizational level, initial and ongoing updating of documents with SGBA+ considerations might be facilitated by consolidating overlapping and incomplete sources of data, which will likely require an overhaul of information systems. Updating of documents and underlying information systems may not be immediate, and instead, as components are updated, they could be gradually integrated into Health Canada's regulatory system. Furthermore, other organizational initiatives, related or unrelated to SGBA+, may require resources and time, and be prioritized over these recommendations. At the individual level, change is difficult and may be met with reluctance and resistance by both industry representatives in Canada and HC staff. Considerable knowledge translation targeting all stakeholders will be required including communication, education and engagement. Knowledge translation principles and research evidence show that engaging stakeholders from the outset in pre-identifying potential barriers, and planning and undertaking change leads to outputs that are more likely to be relevant and adopted [22,23].

Conclusions

Current regulatory policies and processes do not appear to be promoting the reporting, review and communication of SGBA+ considerations for devices (women-specific, relevant to both women and men) across the device lifecycle. This report includes numerous recommendations, which may not be easy to digest and even more challenging to address given the complexity of medical device regulation and Canada's role in the international device market. Health Canada can review, prioritize and reflect on how to adopt recommendations that emerged from this work. Strengthening consideration of SGBA+ in the device regulatory lifecycle could ensure that devices are safe and effective for diverse users.

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APPENDIX 1. Project Charter approved November 25, 2020

OVERVIEW

Medical devices are essential innovations that sustain life and enhance health-related quality of life. However, device design and function is a top-three determinant of patient safety incidents in hospitals [1]. Studies in the United Kingdom and United States attributed 37% to 47% of adverse medical device events (AMDEs) to device design, manufacturing, quality control, labeling or packaging [2]. The impact of AMDEs is profound. Analysis of Food and Drug Administration reports of pacemaker and implantable cardioverter-defibrillator (ICD) malfunctions issued from 1990 to 2002 found that the mean annual replacement rate was 20.7 per 1,000 for ICDs and 4.6 per 1,000 for pacemakers, and 61 deaths (31 ICD, 30 pacemaker) were attributable to device malfunction [3]. Analysis of registry data from Sweden and Australia showed that the ten-year risk of revision after primary total knee arthroplasty was 4% to 6%, and up to 20% of patients experienced problems after arthroplasty [4]. Thus, patient safety hinges on strengthening pre-market evaluation and licensing of devices and post-market surveillance of AMDEs.

With a CIHR Planning Grant, we interviewed and then met with Canadian and American multi-sector stakeholders to identify optimal post-market surveillance strategies. They recommended a multicomponent system including reporting by facilities, clinicians and patients, supported with some external surveillance for validation and real-time trials for high-risk devices, but first advocated for more research to understand AMDE reporting [5]. Our systematic review revealed little research on AMDE reporting [6], and interviews with 16 clinicians identified no policies or infrastructure to support AMDE reporting [7]. Then, with a CIHR Operating Grant, we showed that:

- Many devices in use are not supported by evidence of safety and effectiveness
 - Systematic review of 265 knee implant studies (1986-2014, 59,217 patients) – most devices were evaluated in only one study, largely uncontrolled single cohorts, enrolled fewer than 100 patients, and followed patients for less than 2 years [8].
- Many devices are prone to cause temporary or serious harm
 - Analysis of data from Health Canada on device recalls – among 24,849 new devices licensed from 2005-2015, there were 7,226 recalls of which 5% had the potential for serious harm or death, and 60% for temporary adverse health consequences [9].
- Physicians said several interacting factors could compromise use of the best device for a given patient, but given those constraints, they did not typically report AMDEs
 - Interviews with 22 physicians across Canada who implant cardiovascular and orthopedic devices – device purchase and use is largely based on physician preference, or advice from trusted colleagues and less-trusted industry representatives; and often limited to devices specified in hospital-supplier purchasing agreements; furthermore, hospitals did not have policies, processes or infrastructure in place to support AMDE reporting [10-13].

We shared findings at a one-day meeting November 3, 2016 with 49 patients with medical devices, researchers, clinicians, and representatives of Health Canada, professional associations, a law firm, a medical-legal insurance agency, health technology assessment agencies, research and development hubs, supply chain management services and medical device sponsors. They identified pre-and post-market action and research essential to enhancing medical device safety in Canada. Concurrent to our research, the International Consortium of Investigative Journalists, including 250 reporters from 36 countries, were exploring devices and coordinated the simultaneous release of news items about AMDEs, a project labelled The Implant Files (<https://www.icij.org/investigations/implant-files/>). Notably, the initiative also found that, **among 340,000 cases of injury or death, 67% were women**. There is significant evidence to demonstrate that biological and social differences between women and men

contribute to differences in their health. Sex (biological attributes) and gender (socio-cultural factors) influence our risk of developing certain diseases, how well we respond to medical treatments, and how often we seek health care. Gender and gender-related intersectional factors also influence access to and quality of care. Accounting for sex and gender in health research can make health research more rigorous, reproducible, applicable, effective and safe for everyone. In response to mounting evidence on AMDEs and lack of consideration of sex/gender in scientific research, by order of the Minister of Health, Health Canada developed an Action Plan on Medical Devices with three aims:

- Post-market – All hospitals across Canada must report AMDEs to Health Canada
- Pre-market – By order of the Minister of Health, Health Canada developed an Action Plan on Medical Devices with three aims:
 1. Improve how medical devices get on the market
 - Assess how Health Canada considers sex/gender in licensing of new drugs and devices and in post-market activities such as surveillance
 - Established the Scientific Advisory Committee on Health Products for Women, who will advise on strengthening regulation of drugs and devices
 2. Strengthen surveillance of devices already in use
 3. Provide Canadians with more information about medical devices

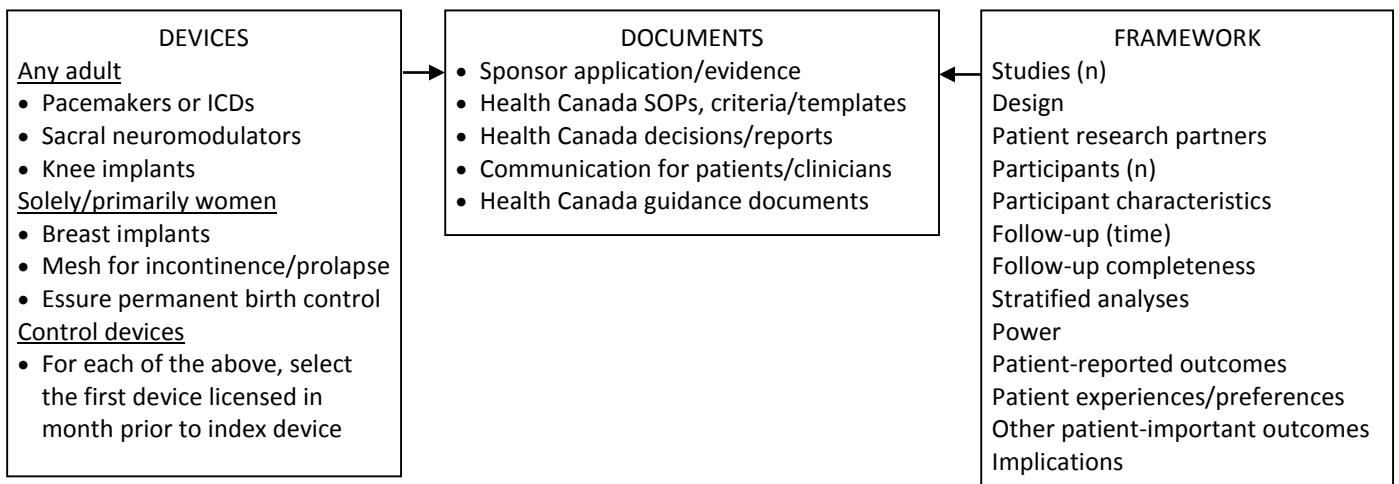
Goals

The overall aim of this project is to co-design and jointly undertake an analysis with Health Canada of sex/gender considerations across the medical device lifecycle including the review, licensing and post-market surveillance of new medical devices. The objectives are to:

3. Analyze internal and external documents used by Health Canada for SGBA+ details
4. Identify opportunities to improve SGBA+ considerations, and strategies needed to promote and support those changes.

Approach

For each type of device, we will assess the presence/absence of details on sex, gender, or intersectionality as applicable in each type of document. Documents include general guidance, standard operating procedures and forms, and device-specific applications, forms, reports and communications. The criteria were derived from CIHR’s considerations for the appropriate integration of sex/gender in research. Lack of documents/data sources or lack of SGBA+ information in documents/data sources will be flagged so that HC can consider if and how to update or modify those documents/sources.



Definitions

Term	Acronym	Definition
Medical device	Device	Non-drug technologies or instruments vital to the prevention, diagnosis, cure or treatment of a disease or abnormal physical condition
Adverse medical device event	AMDE	Unexpected performance of a device requiring corrective action or replacement or leading to associated harm caused by device design, manufacturing, quality control, labeling, packaging or accompanying instructions
Sex/gender-based analyses	SGBA	An analytical process used to assess how diverse groups of women, men and non-binary people may experience policies, programs and initiatives
Intersectionality	SGBA+	Sex/gender analyses go beyond biological (sex) and socio-cultural (gender) differences. Other factors referred to as “intersectional” also influence identity and experiences. Intersectional factors include socioeconomic and other characteristics that interact with gender and contribute to inequities; for example, age, education, culture/ethnicity, and urban versus rural/remote dwelling

Scope

Domain	In scope	Out of scope
Regulatory lifecycle function	<p><u>Pre-market</u>: Health Canada guidance documents, sponsor applications for, Health Canada reviews of, and Health Canada communication about new device licenses; and sponsor or Health Canada communication for patients or clinicians about those devices</p> <p><u>Post-market</u>: monitoring (i.e. recalls), incidents (i.e. reports) or decisions (i.e. removal from market)</p>	---
Devices	Class II, III and IV index devices – for which AMDEs have been reported that are used in both men and women, and used in women-only	Class I devices; See Risks and Mitigation regarding device-specific records
Documents	Health Canada to supply: <ul style="list-style-type: none"> • Process map along with a list of relevant documents for each step • List of internal and external documents used in the medical device lifecycle • Records specific to each type of device 	See Risks and Mitigation regarding device-specific records
Time frame	Documents should reflect sponsor application processes and documents, and Health Canada criteria and review templates in current use	Documents updated following project launch

Team

Member	Acronym	Role	Responsibility
Alysha Croker	AC	HC Manager	HC project lead, communicate with AG, coordinate HC activities, review plans and findings with HC working group
Mathew Stock	MS	HC Policy Analyst	HC project support, assists AC
Health Canada	HC	Refers to AC, MS and/or HC project working group	Co-design and jointly undertake project with AG
Anna Gagliardi	AG	Senior Scientist, Professor funded by CIHR to work with HC on this project	Co-design and jointly undertake project with HC

Milestones [CIHR extension to Jan 31, 2022 due to broad-based research delays imposed by COVID-19]

Milestone	Responsibility	Timing	Tentative Date
Share “placemat” and general documents (public/internal)	HC	Launch	Nov 2020
Pilot test data extraction from general documents (+HC review)	AG, HC	Month 1	Dec 2020
Data extraction from general documents	AG	Month 2	Jan 2021
Data extraction from general documents	AG	Month 3	Feb 2021
Summary of results, gaps and corresponding recommendations	AG	Month 4	Mar 2021
Pilot test data extraction from device documents (+HC review)	AG, HC	Month 5	Apr 2021
Data extraction from public device documents	AG	Month 6	May 2021
Data extraction from public device documents	AG	Month 7	June 2021
Data extraction from internal device documents	AG	Month 8	July 2021
Data extraction from internal device documents	AG	Month 9	Aug 2021
Summary results, gaps, corresponding recommendations	AG	Month 10	Sept 2021
Review of compiled results including gaps/recommendations	HC	Month 11	Oct 2021
Edit recommendations and reports	AG	Month 12	Nov 2021
Final meeting to discuss findings and conclude project	AG, HC	Month 13	Dec 2021
Dissemination (e.g. power point/Final report to CIHR)	AG	Month 14	Jan 2022

Beyond the responsibilities listed in the table above, HC will remain available to support AG throughout the project (e.g. answering questions or providing resources) and will arrange a consultation session with HC staff to describe their roles and how they use documents/templates.

Deliverables

- Report of gaps/recommendations to address SGBA+ in general documents (guidance, SOPs, forms)
- Report of gaps/recommendations to address SGBA+ in device documents (based on example devices)
- Overall high-level recommendations for related processes (e.g. training, knowledge translation)
- Final meeting to discuss findings and conclude project (month 13)
- Tools for dissemination (power point presentation, one-page infographic/policy brief)

Risks/Mitigation

Risk	Probability	Impact	Mitigation
Delayed start	High	Time frame and deliverables	Adjust objectives, methods, scope, and deliverables
AG unable to interpret records	High	Time frame	HC to advise
HC wants to broaden scope of regulatory lifecycle to include post-market	Medium	Time frame and deliverables	Reduce the number and type of devices examined (i.e. analyze 1 or 2, rather than 3 devices in each category; eliminate control devices)
Analyses take longer than expected	Medium	Time frame and deliverables	Reduce the number and type of devices examined
Delay in or unable to access internal device documents	High	Time frame and deliverables	Restrict device-specific analyses to publicly-available device records only
Turnover of HC staff	Low	Sharing of data and time frame	AG and AC to maintain detailed records of correspondence and decisions
HC interest in project wanes	Low	Project	CIHR and Scientific Advisory Committee to advise

Assumptions

These assumptions will be validated during the planning process and early stages of the project. If they impact proposed activities or milestones, they will result in project risks:

- HC will assemble and send AG required documents and records, or AG will have remote access
- If documents or records are incomplete or unavailable, alternate devices will be chosen
- Given the current pandemic, HC is focused on essential services
- Given the need for security clearance, all work must be done solely by AG
- Analysis of documents or records by AG may take longer than expected given need to balance this project with other professional responsibilities (i.e. other studies, prepare/submit research funding applications, supervise staff/students, teach, committee chair/memberships, etc.)
- The pilot test and HC review of pilot test will identify and resolve potential complications
- AG will generate a final report identifying gaps and recommendations to strengthen consideration of SGBA+, then HC must decide whether and how to adopt modified processes or templates
- If the Scientific Advisory Committee on Health Products for Women recommends additional approaches or deliverables out of scope as per this Charter (e.g. engage patient research partners in this work), HC can decide if they wish to independently pursue those recommendations outside of the context of this Charter

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APPENDIX 2. Integrating sex, gender and intersectional factors in research

Domain	Strength	Weakness
Sex	<ul style="list-style-type: none"> • Clear articulation that the phenomenon, condition or disease under study has, or does not have, a different incidence or prevalence based on sex • Inclusion or recruitment of male and female cells, tissues, animals or humans when studying models of disease that affect males and females • Documentation and analysis of the sex of the cells, tissues, animals or humans used in the protocol • Proposed experimental design that disaggregates results by sex • Builds on what is already known about sex differences and sex-related mechanisms in the field of study 	<ul style="list-style-type: none"> • Does not provide a compelling justification for a single-sex study • Ignores observed sex differences already reported in the literature, or fails to build on published data in the design of the proposed studies • Does not report the sex of the cells, tissues, animals or humans being studied • Does not describe how sex will be accounted for and considered in the analysis plan • Does not demonstrate a commitment to disaggregate the data by sex • Conflates and/or confuses the terms sex and gender
Gender	<ul style="list-style-type: none"> • Literature review: reports what is known about gender, gender-theories, and/or intersectionality in the field of study, where relevant • Methods: describes how gender will be measured or investigated in the population under study • Recruitment method: addresses and mitigates bias • Analysis: describes how gendered sub-groups will be compared and that the findings will be reported separately in the results section • Implementation and knowledge translation plan: considers aspects affected by gender 	<ul style="list-style-type: none"> • Reports that gender is irrelevant without adequate justification • Does not measure gender within the population under study when it is possible and relevant to do so • Does not describe how gender will be accounted for and considered in the analysis plan • Does not demonstrate a commitment to disaggregate the data by gender and/or present suitable subgroup analyses • Conflates and/or confuses the terms sex and gender
Intersectionality	<ul style="list-style-type: none"> • Background: Describes how intersectional factors (e.g. age, race, ethnicity, culture, immigration status, education, income, employment, marital/partnership status, ability (versus disability), sexual orientation, urbanity/rurality, region of residence) are relevant to the context • Methods: Describes how the study will measure or assess intersectionality • Recruitment: Describes how sampling and recruitment techniques will ensure that participants will vary by relevant intersectional factors • Analysis: Reports sub-analyses by relevant intersectional factors • Implementation: Describes how application of the findings should consider relevant intersectional factors 	<ul style="list-style-type: none"> • Reports that intersectionality is not relevant without justification • Does not assess intersectionality when it is possible and relevant to do so • Does not describe how the analysis plan considers intersectionality • Does not report sub-analyses by intersectionality factors • Does not discuss implications per intersectionality factors

Adapted from CIHR: <https://cihr-irsc.gc.ca/e/50835.html> and [18]

APPENDIX 3. Sources of data

Clinical trial review [Pre-submission meeting, Clinical trial application, Clinical trial completion]

General Documents		Device-specific Documents	
Public	Provided	Public	Provided
<p>2.2 Clinical trial application</p> <ul style="list-style-type: none"> • Applications for Medical Device Investigational Testing Authorizations Guidance Document • Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences • Preparation of an Application for Investigational Testing - In Vitro Diagnostics Devices <p>2.3 Clinical trial completion</p> <ul style="list-style-type: none"> • ISO 14155:2011 Clinical Investigation of medical devices for human subjects — Good clinical practice • International Medical Device Regulators Forum (IMDRF): Clinical Investigation • Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 	<p>2.1 Pre-submission meeting</p> <ul style="list-style-type: none"> • SOP for meeting framework <p>2.2. Clinical trial application</p> <ul style="list-style-type: none"> • SOP to screen new investigational testing authorization • Form Investigational testing screening • SOP Preparation of the Scientific Review Report for Investigational Testing Authorization • Form New Investigational Testing Authorization Evaluation Report • Form Revised Investigational Testing Authorization Evaluation Report 	---	---

Submission review [Pre-submission meeting, Product submission]

General Documents		Device-specific Documents	
Public	Provided	Public	Provided
<p>3.1 Pre-submission meeting</p> <ul style="list-style-type: none"> • Guidance on supporting evidence to be provided for new and amended applications <p>3.2 Product submission</p> <ul style="list-style-type: none"> • Management of applications for medical device licenses • How to complete the application for a new medical device license • Draft Health Canada IMDRF table of contents for medical device applications guidance • IMDRF Non-In Vitro Diagnostic Device Market Authorization Table of Contents 	<p>3.2 Product submission</p> <ul style="list-style-type: none"> • SOP Technical Screening of Class III and IV Device Licence Applications • Form Consolidated Screening Medical Devices • SOP Preparation of the Scientific Review Report for Medical Device Licence Applications • Form Class IV Medical Device License Evaluation Report • Form Executive Summary Non-In Vitro Diagnostic Devices • Form Class IV In Vitro Device License Evaluation Report 	<p>3.2 Product submission</p> <ul style="list-style-type: none"> • Clinical Information Drugs & Health Products (n=15 records): licensed devices, date, clinical evidence summary 	---

<ul style="list-style-type: none"> • IMDRF In Vitro Diagnostic Medical Device Market Authorization • Guidance for the labelling of medical devices • Labelling of In Vitro Diagnostic Devices • IMDRF Principles of Labelling for Medical Devices and IVD Medical Devices • Fees for the Review of Medical Device License Applications • Guidance for the Interpretation of Significant Change of a Medical Device • Guidance for the Risk-based Classification System for In Vitro Diagnostic Devices • Guidance on the Risk-based Classification System for Non-In Vitro Diagnostic Devices <p>SEE application forms: https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/forms.html</p>	<ul style="list-style-type: none"> • Form Executive Summary In Vitro Diagnostic Device License Evaluation Report 		
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4. Authorization and Post-Market [Authorization, Ongoing monitoring, Evolution of product and knowledge]

General Documents		Device-specific Documents	
Public	Provided	Public	Provided
<p>4.2 Ongoing monitoring</p> <ul style="list-style-type: none"> • Mandatory reporting of serious adverse drug reactions and medical device incidents by hospitals • Guidance on Medical Device Compliance and Enforcement • Guidance Document for Mandatory Problem Reporting for Medical Devices • Mandatory medical device problem reporting form for industry • Medical Devices Recall Guide <p>4.3 Evolution of product/knowledge</p> <ul style="list-style-type: none"> • Guidance Document for Industry - Issuance of Health Professional Communications and Public Communications by Market Authorization Holders • Form Standardized Health Product Risk Communication Template 	<p>4.1 Authorization</p> <ul style="list-style-type: none"> • SOP Preparing the DED Licence Recommendation Memorandum <p>4.2 Ongoing monitoring</p> <ul style="list-style-type: none"> • SOP Prioritization and Management of Potential Signal Files in the Marketed Health Products Directorate • Form Screening/Triage/Prioritization of Incoming Signals • SOP Signal Assessment • Form Signal Assessment • Form Signal Assessment Review Report • SOP Causality Assessment • SOP Causality Assessment Background Information • SOP Periodic Safety Update Report Review Level II 	<p>4.1 Authorization</p> <ul style="list-style-type: none"> • Medical Device Active License Listing (MDALL): licensed devices, date, Identifier • Drug & Health Product Register: <ul style="list-style-type: none"> ○ Regulatory Decision Summary (data reviewed, reason approved/not approved) ○ Summary Basis of Decision (scientific rationale for approval) <p>4.2 Ongoing monitoring</p> <ul style="list-style-type: none"> • Drug & Health Product Register: <ul style="list-style-type: none"> ○ Summary Safety Review (safety issues, HC decisions, actions) • Recalls & Safety Alerts Database: hazard severity, affected products, reason, action (recall or warning) 	<p>---</p>

<ul style="list-style-type: none"> • Guide for using the Standardized Health Product Risk Communication Template • Risk Communication - Protecting Canadians Through Information 	<ul style="list-style-type: none"> • SOP Benefit Risk Assessment Review 4.3 Evolution of product/knowledge • SOP Health Product InfoWatch Production 	<p>4.3 Evolution of product/knowledge</p> <ul style="list-style-type: none"> • Adverse Reaction Database: type of reaction, serious/not serious • Canadian Adverse Reaction Newsletter: quarterly summary consumer advisories, one detailed summary of HC review/outcome • Health Product InfoWatch: monthly publication for healthcare professionals on product advisories, summary safety reviews and other safety information 	
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Relevant across medical device lifecycle

IMDRF Essential principles of safety and performance of medical devices and IVD medical devices

IMDRF Methodological principles in the use of international medical device registry data

Food & Drugs Act: <https://laws-lois.justice.gc.ca/eng/acts/f-27/>

Medical Devices Regulations: <https://laws-lois.justice.gc.ca/eng/regulations/sor-98-282/>

APPENDIX 4. List of meetings and email communication

MEETINGS

Feb 11, 2020 (early meeting with A Croker in Ottawa)
Apr 1, 2020 launch meeting (I must do work due to confidentiality, delay in access to data)
June 18, 2020 (given delay in access to HC data, discuss public sources of data)
Oct 29, 2020 (meeting with Scientific Advisory Committee on Health Products for Women)
Nov 27, 2020 (review of preliminary data extraction)
Feb 19, 2021 (revised draft report including their feedback + device sampling)
Mar 25, 2021 (review progress and next steps)
April 6, 2021 (review progress and next steps)
May 13, 2021 (meeting with HC staff)

EMAIL

Mar 18, 2020 (launch)
Mar 23, 2020 (progress check-in)
May 1, 2020 (delay in HC security clearance to access data)
June 29, 2020 (received access key for lap top but await security clearance to access data)
Oct 7, 2020 (shared powerpoint presentations for SAC meeting)
Oct 15, 2020 (shared project charter)
Oct 18, 2020 (summary of documents they recommend for review)
Nov 6, 2020 (progress check-in)
Nov 23, 2020 (HC feedback on project charter)
Dec 4, 2020 (draft data extraction from general documents)
Dec 8, 2020 (HC feedback on project charter)
Dec 20, 2020 (shared additional data extraction)
Feb 9, 2021 (early draft report of data extracted from general documents)
Feb 12, 2021 (schedule meeting)
Feb 15, 2021 (device sampling options)
Feb 19, 2021 (request for missing documents)
Mar 3, 2021 (scheduling meeting, progress update)
Apr 6, 2021 (summary of Mar 25 meeting and feedback on data extraction)
Apr 9, 2021 (scheduling meeting with HC staff)
Apr 19, 2021 (scheduling meeting with HC staff)
Apr 23, 2021 (planning agenda for meeting with HC staff)
Apr 30, 2021 (confirming date for meeting with HC staff)
May 7, 2021 (finalizing agenda for meeting with HC staff)
May 17, 2021 (shared powerpoint slides from May 13 meeting with HC staff)
May 24, 2021 (additional follow-up from May 13 meeting with HC staff)
June 7, 2021 (progress update)
Jun 8, 2021 (provided redacted evaluation report for Accu-Chek Inform II submission given lack of internal permission to share other internal documents)
July 2, 2021 (progress check-in)
July 20, 2021 (progress check-in)

APPENDIX 5. Clinical trial review documents (n=12)

Document	Purpose	SGBA+ Content			SGBA+ Flags
		Sex	Gender	Intersectionality	
<p>PUBLIC GUIDANCE</p> <p>Applications for Medical Device Investigational Testing Authorizations</p> <p>October 2018 (46 pages)</p> <p>PLUS Application forms: Device intended use Patients by SGBA+ Study objectives Submission checklist (add SGBA+ considerations)</p> <p>Investigational testing https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/forms/new-ita-form_fillablePDF_EN-Nov07.pdf</p> <p>Revised investigational testing In addition to above. Checklist of modifications https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/forms/Revision-to-ITA-form_fillable-eng-Nov07.pdf</p>	<p>To assist manufacturers and importers in preparing the documentation necessary to obtain an authorization for the sale or importation of a medical device under an Investigational Testing Authorization (ITA), while assuring the protection of research subjects, and promoting excellence in research and development in Canada.</p>	<p>Protocol Methods Provide a full description of the subject selection, including:</p> <ul style="list-style-type: none"> inclusion and exclusion criteria, including the participants' ages, sex and diagnosis of primary and secondary (if applicable) conditions (p 27) 	<p>Protocol Methods Subjects should be selected to be representative of the population intended to be treated with the device, with appropriate inclusion of children, women, and ethnic groups (p 27)</p> <p>Additional Considerations Inclusion of women, children, and vulnerable populations: Efforts should be made to maximize compliance with the International Council for Harmonisation (ICH) Document E11 entitled Clinical Investigation of Medicinal Products in the Paediatric Population and the Health Canada Guidance Document: Considerations for Inclusion of Women in Clinical Trials</p>	<p>Protocol Methods ...appropriate inclusion of...ethnic groups (p 27)</p>	<p>Introduction Device identification, description, design philosophy, indications and marketing history</p> <p>Risk Assessment and Risk Reduction Measures Risk assessment, previous studies, precautions</p> <p>Institutional information (characteristics of study team, steering or safety committee, patient or public research partners)</p> <p>Protocol Background, Methods, Investigators Brochure</p> <p>Additional Considerations: Clinical Trial Design and Statistical Considerations</p> <p>Responsibilities of Manufacturers and Importers: Record Keeping, Mandatory Problem Reporting</p> <p>Requests for Revisions to an ITA</p> <p>Appendix 2 – Useful Documents (refer to CIHR Sex/Gender training document and videos</p> <p>Appendix 3 – Determining When an ITA Application is Required (include SGBA+ in algorithm)</p>

<p>Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences</p> <p>May 2013 (30 pages)</p> <p>SEE NOTE BELOW TABLE</p>	<p>To guide the study and analysis of sex differences in clinical trials of therapeutic products in order to generate evidence on optimal use of products in both women and men</p>	<p>INTRODUCTION</p> <p>Objectives this guidance addresses considerations pertaining to the appropriate inclusion of women in all stages of clinical trials and research with the aim of identifying and analyzing sex-related differences that may affect the safety and efficacy of a therapeutic product (p 3)</p> <p>Principles This guidance is consistent with... the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2010) where it states that "Women shall not be inappropriately excluded from research solely on the basis of gender or sex" (p 4)</p>	<p>and Analysis of Sex Differences (refer to Appendix 2). (p 29)</p> <p>INTRODUCTION</p> <p>Objectives Mentions "sexual orientation" (p 3)</p>	<p>INTRODUCTION</p> <p>Objectives While this guidance recognizes the importance of the elements of a diversity framework, such as ethnicity, socioeconomic status, disability, sexual orientation, migration status, age and physical status (early menopause etc.), it focuses on sex-related differences in clinical trials (p 3)</p>	<p>Appendix 5 – Frequently Asked Questions (add: how do I know when to address SGBA+?)</p> <p>Either expand this document to include intersectionality or create a separate similar document pertaining to intersectionality, and distinguish gender from sexual orientation</p> <p>Consider replacing "subjects" with participants; TCPS II: prefers the term "participant" because it better reflects the spirit behind the core principles: that individuals who choose to participate in research play a more active role than the term "subject" conveys.</p>
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		<p>Policy Statements Clinical trials should enrol subjects representative of the population(s) expected to use the therapeutic product:</p> <p>It is recommended that a representative number of womenFootnote4 be included in clinical trials for therapeutic products that are intended to be used specifically by women or by heterogeneous populations that include women</p> <p>It is recommended that women, including those of child-bearing potential and postmenopausal women, be included at the earliest possible stages of clinical trial</p> <p>researchFootnote5 so that potential sex-related</p>			
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		differences are identified and taken into consideration when planning Phase III pivotal trials (p 4)	SEE Additional Details		
<p>Preparation of an Application for Investigational Testing - In Vitro Diagnostics Devices</p> <p>February 1999 (29 pages)</p>	<p>To assist device manufacturers or sponsors in preparing documentation required to obtain authorization for the sale of an in vitro diagnostic device for investigational testing according to the <i>Medical Devices Regulations</i>. This document will also assist investigators and institutions involved in the investigational testing of IVDDs in Canada to understand their roles and responsibilities in this process.</p>	---	---	---	<p>Refers to Therapeutic Products Programme; should this be replaced with name for new medical devices unit?</p> <p>Rejection or Refusal of an Application</p> <p>Add: investigational testing is not planned in target users with a range of characteristics including sex, gender and intersectional factors</p> <p>Additional Guidance</p> <p>Refer to: Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences</p> <p>Indications for obtaining authorization</p> <p>Add to (d): ...with target populations representing the range of target user characteristics including sex, gender and intersectional factors</p> <p>Device identification (81b)</p> <p>Specify if device is used in both women and men, or women only</p>

				<p>Design philosophy (81d) Identify any features that have been or can be tailored for women and men</p> <p>Marketing history (81e) Add: Report problems according to user characteristics that include sex, gender and intersectional factors</p> <p>Risk assessment and reduction Add: Identify if potential risks pertain to target user characteristics including sex (pregnancy, breastfeeding), gender or intersectional factors, and refer to: Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences</p> <p>Manufacturer or Sponsor Responsibilities Specify that both record-keeping and problem reporting include the characteristics of participants including sex, gender and intersectional factors</p> <p>Clinical Protocol Include a separate section in which all sex, gender and intersectional considerations are identified including the study rationale, goal, objectives, research team, research design, sampling, recruitment, data collection, data analysis, dissemination and implementation; and a rationale if not (this is now standard for CIHR research funding applications)</p>
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<p>HC SOPs</p>	<p>Guidance for HC staff to ensure that pre-submission or pre-clinical meeting requests are properly completed, assess if meeting is warranted, schedule and organize both the meeting and a HC advance preparatory meeting, and log the meeting and associated documents before and after the meeting</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>Specify if patient or family research partners are collaborating with the manufacturer, sponsor or participating investigational sites, not as study participants, but as members of the research team to ensure that the study addresses diverse needs, concerns and preferences (distinct from “lay users”, which are noted under Additional Requirements). Justify if this is not the case. Provide characteristics of patient/family research partners including sex, gender and intersectional factors to illustrate diversity</p>
<p>[pre-submission] Meeting framework</p> <p>No date (3 pages)</p>	<p>Guidance for HC staff to ensure that pre-submission or pre-clinical meeting requests are properly completed, assess if meeting is warranted, schedule and organize both the meeting and a HC advance preparatory meeting, and log the meeting and associated documents before and after the meeting</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>Logistical details for scheduling meetings – however, any standard operating procedures or templates/forms could include flags or reminders about SGBA+ for HC staff; for example, this meeting framework could remind staff to check if SGBA+ is addressed, and if not, then a meeting may be needed</p>
<p>Screen new investigational testing authorization applications</p>	<p>Guidance for HC staff to use the internal system</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>Technical details for logging in and navigating the internal information system; however, the system could</p>

No date (42 pages)	when reviewing new Investigational testing authorization applications for Class II, III and IV devices against Medical Devices Regulations				include embedded flags and reminder Also, if ITA guidance and application forms are updated to address SGBA+, the information system must also be updated along with these screening instructions.
Preparation of the Scientific Review Report for Investigational Testing Authorization August 2010 (16 pages)	Guidance for HC staff in drafting an evaluation report for Investigational Testing Authorization applications. Includes section titles and suggested content.	---	---	---	If ITA guidance and application forms are updated to address SGBA+, this report template must be updated accordingly. SEE aforementioned recommendations, which should be addressed in: Background Information Rationale for Investigation Device Description Design Philosophy Marketing History Risk Assessment Pre-Clinical Studies Clinical Studies Investigational Testing Protocol Recommendations (include explicit sub-section for SGBA+) Reference Documents (refer to Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences)
HC FORMS					
Investigational testing screening No date (2 pages) **Corresponds to SOP Screen new investigational testing authorization applications	Template/checklist for HC staff to summarize if section-specific details were present/absent in the Investigational Testing Application along with	---	---	---	If ITA guidance and application forms are updated to address SGBA+, this report template must be updated accordingly. SEE aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed

	comments and an overall decision for authorization				
New Investigational Testing Authorization Evaluation Report No date (6 pages) ** Corresponds to SOP Preparation of the Scientific Review Report for Investigational Testing Authorization	Template for HC staff to assist in drafting an evaluation report for Investigational Testing Authorization applications. Includes section titles.	---	---	---	If ITA guidance and application forms are updated to address SGBA+, this report template must be updated accordingly. SEE aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed
Revised Investigational Testing Authorization Evaluation Report No date (4 pages)	Template for HC staff to assist in drafting an evaluation report in response to an application for revisions to an original Investigational Testing Authorization application	---	---	---	If ITA guidance and application forms are updated to address SGBA+, update this template to query whether and how any revisions impact SGBA+ considerations, possible impact on study conduct and outcomes, and mitigation strategies.
NON-HC					
ISO 14155:2011 Clinical investigation of medical devices for human subjects — Good clinical practice February 2011 (66 pages) **Note: there is a 2020 update to this document, which I did not assess given that HC employs this 2011 version	Guidance for the design, conduct, recording and reporting of research in human subjects to assess the safety or performance of medical devices for regulatory purposes [does not apply to in vitro diagnostic medical devices]	NOTE: pertains largely to informed consent process Information to be provided to the subject [for informed consent] Risks and inconveniences for the subject and, when applicable, for an embryo,	---	NOTE: pertains largely to informed consent process Definition: vulnerable subject individual whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation, whether justified or not, of benefits associated	HC may or may not have influence over ISO Standards However, HC might develop guidance on SGBA+ to supplement this Standard. Such guidance might be addressed as noted above in existing documents, elaborated in Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences and/or included in a newly-developed document dedicated to SGBA+

		foetus, or nursing infant (p 12)	
		with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate	EXAMPLE Individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable subjects include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor, members of the armed forces, and persons kept in detention (p 7)
		Areas to strengthen SGBA+ in this Standard: Terms and Definitions Add SGBA+	Ethical considerations Expand definition of vulnerable populations and how to handle informed consent Clinical investigation planning Risk analysis, justification for research design, case report forms describing enrolled subjects, monitoring plan, labelling and instructions **does not refer to sampling and recruitment Clinical investigation conduct Adverse events documentation, clinical investigation amendment and subject identification log, accounting for subjects **does not refer to sampling and recruitment Suspension or termination Clinical investigation report Responsibilities of sponsor Safety evaluation and reporting, selection of personnel (add SGBA+ training) Responsibilities of PI Qualification of principal investigator (add SGBA+ training), safety reporting

			<p>only when they cannot be carried out in non-vulnerable populations and shall follow the additional EC procedures where applicable. These clinical investigations shall be designed specifically to address health problems that occur in the vulnerable population, and offer the possibility of direct health-related benefit to the vulnerable population. (p 9)</p>	<p>Annex A Clinical Investigation Plan template Description of device, research design, risks, subjects, statistical considerations, deviations, adverse events, vulnerable population, suspension or premature termination; in addition, include specific SGBA+ section to summarize information included throughout</p> <p>Annex B Investigator Brochure Description of device, pre-clinical testing, existing clinical data, risk management,</p> <p>Annex C Case Report Form Elaborate “demographics” to specify SGBA+ details</p> <p>Annex D Clinical Investigation Report Add SGBA+ to structured summary template. In report, address SGBA+ in device description, clinical investigation plan, results, discussion and overall conclusions</p> <p>Annex F Adverse event categorization include requirement to report by SGBA+ details</p>	
<p>International Medical Device Regulators Forum (IMDRF): Clinical Investigation October 2019 (11 pages)</p>	<p>Guidance on when and how to conduct a clinical investigation of the safety and performance of a medical device [does not apply to</p>	<p>---</p>	<p>General Principles of Clinical Investigation Design demographic, geographic and cultural considerations (e.g.</p>	<p>General Principles of Clinical Investigation Design demographic, geographic and cultural considerations (e.g. <u>age, ethnicity, gender</u>) (p 9)</p>	<p>HC may or may not have influence over IMDRF guidance</p> <p>However, HC might develop guidance on SGBA+ to supplement this guidance. Such guidance might be addressed as noted above in existing documents, elaborated in</p>

	in vitro diagnostic medical devices]		age, ethnicity, <u>gender</u> (p 9)		<p>Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences and/or Included in a newly-developed document dedicated to SGBA+</p> <p>Areas to strengthen SGBA+:</p> <p>Definitions (add SGBA+)</p> <p>General Principles</p> <p>When to undertake an investigation, key considerations</p> <p>Clinical Investigation Design</p> <p>Add: follow SGBA+ principles, type of device, clinical applications, risks, performance, elaborate “demographics”, protocol details, statistical considerations, final study report</p>
<p>Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2</p> <p>December 2018 (231 pages)</p>	<p>Guidance to promote the ethical conduct of research involving humans aimed at ethics review boards, research organizations and researchers</p>	<p>Inappropriate Exclusion Research Involving Women</p> <p>Women have historically been inappropriately excluded from participating in some research. This exclusion of women, where unwarranted, has delayed the advancement of knowledge, denied potential benefits to women, and exposed women</p>	<p>Fairness and Equity in Research Participation</p> <p>This chapter addresses inclusion in research of individuals and groups that might be inappropriately excluded on the basis of attributes such as culture, language, <u>gender</u>, race, ethnicity, age and disability. (p 49)</p>	<p>How to Apply This Policy</p> <p>In designing and conducting research or reviewing the ethics of research, researchers and REBs must be mindful of the perspective of the participant. It may be necessary to consider the various contexts (e.g., social, economic, cultural) that shape the participant’s life, to properly evaluate the implications of the research in terms of</p>	<p>HC may or may not have influence over future versions of TCPS</p> <p>However, SGBA+ content in TCPS II may be used to justify need to update SGBA+ in HC guidance, SOPs and forms</p> <p>HC might develop guidance on SGBA+ to supplement this guidance. Such guidance might be addressed as noted above in existing documents, elaborated in Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences and/or included in a newly-developed document dedicated to SGBA+</p>

		<p>to harm when research findings from male-only research projects were generalized inappropriately to women, as has often been the case in clinical drug trials. The inclusion of women in research advances the commitment to justice, improves the generalizability of research findings to women where that is a goal of the research, and is essential to ensure that women and men benefit equally from research.</p> <p>Article 4.2 Women shall not be inappropriately excluded from research solely on the basis of <u>gender</u> or sex. (p 50)</p> <p>Article 4.3 Women shall not be inappropriately excluded from research solely on</p>	<p>the core principles. (p 10)</p> <p>Fairness and Equity in Research Participation This chapter addresses inclusion in research of individuals and groups that might be inappropriately excluded on the basis of attributes such as <u>culture, language, gender, race, ethnicity, age and disability</u>. (p 49)</p> <p>Research Involving the Elderly As the population ages, the proportion of elderly people is increasing, and so is their life expectancy. Research designed to improve our understanding of a wide range of aspects of aging and the lives of elderly people is important for ensuring that they stay fully integrated into society and maintain a continuing high quality of life. Medically, elderly patients are the highest consumers of drugs, yet</p>	<p>Areas to strengthen SGBA+ in TCPS II:</p> <p>Core Principles Respect for persons (factors that influence informed consent, participation); Welfare (during and after study participation); Justice (equity, vulnerability; process of recruitment);</p> <p>How to Apply This Policy Perspective of the participant (elaborate)</p> <p>Scope Risks Consent Acknowledge need for consent processes to accommodate SGBA+ characteristics, vulnerability, decision-making capacity</p> <p>Participants Vulnerability Equitable distribution of research benefits</p> <p>Clinical Trials No mention of sampling and recruitment; SGBA+ not mentioned under Medical Device Trials, safety monitoring,</p>
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		<p>the basis of their reproductive capacity, or because they are pregnant or breastfeeding. (p 51)</p>	<p>many of these treatments have not been tested adequately on elderly patients. Research that takes into account the differential effects on the elderly and how best to accommodate their needs provides scientific evidence that can inform changes to policies and standards of care for the elderly.</p> <p>Article 4.5 Elderly people shall not be inappropriately excluded from research solely on the basis of their age. (p 52)</p> <p>Decision-Making Capacity The core principles of Justice and Concern for Welfare entail special ethical obligations toward individuals who lack capacity to decide whether to participate in research. This section sets out conditions that apply to research involving those who cannot consent for themselves due to a lack of decision-making capacity.</p>	
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			<p>Article 4.6 Subject to applicable legal requirements, individuals who lack capacity to decide whether to participate in research shall not be inappropriately excluded from research. Where a researcher seeks to involve individuals in research who do not have decision-making capacity, the researcher shall, in addition to fulfilling the conditions in Articles 3.9 and 3.10, satisfy the REB that:</p> <ul style="list-style-type: none"> a. the research question can be addressed only with participants within the identified group; and b. the research does not expose the participants to more than minimal risk without the prospect of direct benefits for them; or c. where the research entails only minimal risk, it should at least have the prospect of providing benefits to participants or to a group that is the focus of the research 	
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				<p>and to which the participants belong.</p> <p>Participants Vulnerability In general, researchers should be familiar with the cultural, social and economic circumstances of prospective participants, groups or communities. Researchers should anticipate, to the best of their ability, needs of participants, groups and their communities that might arise in any given research project. Especially when groups, and their communities, have a wide range of pressing needs due to their low socioeconomic circumstances, these needs can present significant ethical challenges for researchers. An equitable distribution of research benefits (discussed below) can help ensure that individuals, groups and communities whose circumstances may make them vulnerable in the context of</p>

				<p>research are not inappropriately included in research based on these circumstances. (p 54)</p> <p>Research Involving the First Nations, Inuit and Métis Peoples of Canada</p> <p>Notes that CIHR, SSHRC and NSERC have developed program guidelines for research involving Indigenous peoples and issues.</p> <p>SEE entire chapter and Article 9.1 to 9.22 on how to interpret TCPS II in this context (p 107-132)</p>	
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NOTE: Additional SGBA+ data extracted from Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences

INTRODUCTION (continued)

Scope and application

This guidance addresses considerations regarding women of all ages, including women of child-bearing potential and women who are not of child-bearing potential (see definitions, Appendix A), as subjects in clinical trial research. Some of the issues addressed in this guidance may also be pertinent to adolescent girls (12 up to 18 years of age) who are subjects in clinical trial research

Addresses considerations pertaining to pregnant or breastfeeding women and to sexual partners of clinical trial subjects

It is structured to provide separate recommendations for clinical trials that include non-pregnant women (informed consent; pregnancy prevention/contraception; inadvertent pregnancy) as well as clinical trials that include pregnant and breastfeeding women (p 5-6)

Background

there is evidence of sex-related differences in the use of, and in response to, some medical devices. For example, response to cardiovascular devices may be influenced by the later age at which women tend to develop heart disease, women's smaller heart structure or physiological differences. Responses to musculoskeletal implants reflect anatomical differences by sex, and some in vitro diagnostic devices are sex specific but most may be used for both males and females. Also, there are selected analytes (e.g. certain cardiac markers) where ranges for normal and disease states are sex dependent

Women constitute a large portion of the consumers of therapeutic products, including prescription drugs, medical devices and natural health products. Some of these products are used for conditions unique to women's physiology (e.g. menstruation, menopause, and pregnancy), others for conditions that have greater prevalence in women (e.g. autoimmune diseases; osteoporosis) and others for conditions that tend to affect both women and men equally (p 7)

Accordingly, Health Canada encourages sponsors to collect and document information concerning differences between sexes in response to therapeutic products and regarding therapeutic products used in pregnancy and while breastfeeding. Increased information on the safety and efficacy of products used in pregnancy, or while breastfeeding, can inform health care decisions.

Analysis of clinical trial data by sex may identify clinically relevant sex differences in therapeutic response and, as a result, minimize the risks, maximize benefits and promote the optimal use of therapeutic products in both women and men (p 8)

GUIDANCE FOR IMPLEMENTATION

Where sponsors intend a therapeutic product to be used by both women and men, it is recommended that sponsors include both sexes in: (a) nonclinical studies; and: (b) in clinical trials to allow detection of potential sex-related differences in efficacy and in safety.

In some instances, further confirmatory studies in a single sex may be appropriate, in particular when a product is intended for use in one sex exclusively. Evaluation of the effects of phases of the menstrual cycle on therapeutic product response in females should also be considered (p 9)

Non-clinical studies

Nonclinical studies conducted in both male and female animals to determine pharmacokinetics, pharmacodynamics, pharmacology and toxicology can suggest potential sex-related differences in concentration response, safety and/or efficacy. The results of such studies may provide signals for potential sex-related differences in humans to be further explored in human studies. Nonclinical studies may provide early signals of the teratogenic potential of products under development. Such information is an important consideration for the informed consent process for human studies, particularly where women of childbearing potential or pregnant women may be exposed to the product. (See also Section 2.3). (p 9)

The timing of nonclinical studies, in relation to the inclusion of women of childbearing potential or pregnant women in clinical trials, should be carefully considered because of the potential for teratogenic effects of therapeutic products.

Assessment of embryo–fetal development can be deferred until before Phase III for women of childbearing potential using precautions to prevent pregnancy in clinical trials.

Where abnormalities of reproductive organs or their function (spermatogenesis or oogenesis) have been observed in experimental animals following the administration of a substance, the decision to include subjects in a clinical trial should be based on a careful risk-benefit evaluation. (p 10)

Design considerations in the conduct of clinical trials

Where therapeutic products are to be used by both women and men, the potential for sex-related differences in response to these products should be identified and assessed, since such differences may affect the safety and/or efficacy of the product.

Signals of potential clinically relevant differences by sex should be identified and analyzed throughout the entire clinical development program. Signals can be identified from a variety of sources: knowledge about differences between men and women in the manifestation and prevalence of a condition; data from nonclinical studies to indicate there may be sex differences; known sex differences in pharmacokinetics (PK) and pharmacodynamics (PD)Footnote6 and/or in efficacy or safety of a therapeutic

product of a similar class to the therapeutic product under investigation. In addition to the above, signals from early phase clinical studies/trials should guide the design and data analysis for subsequent clinical studies/trials to assess whether there are clinically relevant differences between women and men in response to therapeutic products. Such differences should ultimately be reflected in the product information.

Sponsors are encouraged to consider the following elements in the conduct and design of clinical trials

- Both women and men should be included in all phases of clinical trials, including early phases. Inclusion of both women and men in early phase trials would enable identification of potential sex-related differences in drug metabolism, which may have implications for differences in drug response. Early phase trials may suggest potential differences by sex, or uncertainty regarding whether or not differences exist, for follow-up in subsequent studies. This may not be possible or feasible for each product. In such instances, there should be a plan to develop the information needed.
- Inclusion of women of child bearing potential in these early phase trials involves a consideration of the risk/benefit ratio for a healthy female volunteer exposed to a potentially embryotoxic therapeutic product, relative to a female with a serious or life-threatening condition. The Informed Consent document should include sufficient information regarding the potential risks to inform women so that they may make informed decisions about the potential risks and benefits of the therapy and the trial.
- The timing for inclusion of women in clinical trials, (including the timing for inclusion of women of childbearing potential) and the use of pregnancy prevention measures should be considered when designing clinical trials.
- If data from early phase trials do not indicate potential sex-related differences, it cannot be assumed that clinically relevant differences do not exist. It is therefore recommended that the statistical section of the study protocol for Phase III trials include pre-specified plans for assessing sex related differences on efficacy and safety. The pre-specified plans for assessing such differences should be carried out once the overall treatment effect has been shown to be significant. Post hoc analysis to assess sex related differences should only be carried out in trials that are already completed or ongoing, and the analysis should be labeled as post hoc. In addition, if there are scientific reasons to suggest the potential existence of sex related differences, stratification by sex at the study design stage should also be considered. Where possible differences by sex are identified based on this analysis, this would be hypothesis generating and signal a need for further study prior to marketingFootnote10. In cases where it is determined that additional data is required to assess sex related differences, and when such data is to be provided post-approval, Health Canada encourages that post-market studies be implemented and conducted in a timely manner, and that the studies be designed appropriately, so as to provide as definitive an answer as possible, to the question of sex related differences.
- Where sex-related differences in therapeutic product response are identified, it is important to confirm the reasons for these differences (e.g. whether they are related to organ size/weight, physiological differences), including but not limited to pre- or post-menopausal state, or potential route of administration, dose, dosing regimen, dosage form or product formulation), in order to determine how to mitigate the effect of sex-related differences in the clinical setting, as appropriate.
- Relevant findings as outlined above, with respect to sex differences in response to therapeutic products, should be reflected in the product monograph in each appropriate section and/or subsection.

ENROLLMENT OF WOMEN

Informed consent

Sponsors must ensure that subjects provide their free and informed consent to enroll in a clinical trial, consistent with provisions outlined in the Medical Devices Regulations [81.(k)(ii)] and ISO 14155 standard, Clinical Investigation of Medical Devices for Human Subjects

As part of the regulatory requirement for the ethical conduct of a clinical trial, fully informed consent is needed. Sponsors have an obligation to fully inform clinical trial subjects, both female and male, in addition to all other risks, about (a) the potential risks of reproductive and foetal toxicity, including teratogenicity; and about (b) pregnancy prevention, so that prospective subjects understand how and when to take precautions to prevent pregnancy in the context of a trial.

The Informed Consent Form and the Investigator's Brochure should include all available information regarding the potential risk of foetal and reproductive toxicity. However, if the study excludes pregnant or breastfeeding women, and requires the use of birth control during the entire trial and a period after the trial is over, the

emphasis on the potential foetal and reproductive toxicity may be reduced. While animal models cannot always predict all possible human toxicities, if animal reproductive toxicity studies are complete, the results should be presented with an appropriate explanation of their significance in humans.

If foetal and reproductive toxicity studies have not been completed other pertinent information should be provided, such as a general assessment of foetal toxicity in therapeutic products with related structures or pharmacologic effects. If relevant information is not available from reproductive toxicity studies, the Informed Consent Form as well as the Investigator's Brochure should explicitly note that the potential for reproduction and embryo-foetal risk cannot be excluded.

It is also expected that adequate counseling will be provided to subjects concerning what is known or not known about foetal and reproductive toxicity, and about the importance of using a reliable method of contraception. Clinical trial subjects should also be apprised of procedures in place, should inadvertent pregnancy occur in the context of a trial.

If further information about reproductive and foetal toxicity about a product under investigation (including teratogenic effects) becomes available during the course of a clinical trial, this additional information should be provided to clinical trial subjects (via updated informed consent). Equally, the clinical trial investigator and the regulator should be notified.

Pregnancy Prevention/Contraception

In accordance with good clinical practice, clinical protocols should include measures to minimize the possibility of foetal exposure to the investigational product when the investigational product has been estimated to pose a risk to the health of the foetus and/or the pregnant woman. Precautions include:

1. Use of reliable method(s) of contraception (See also Appendix A), and/or abstinence, for the duration of therapeutic product exposure.
When the product under investigation (e.g. drug or natural health product) may lessen the effectiveness of a hormonal contraceptive agent, clinical trial subjects should be advised to use an additional non-hormonal method of contraception (e.g. double barrier methods) for the duration of the exposure. Information on the duration of contraception beyond the study period should be provided to subjects
2. Initial pregnancy testing prior to participation in the clinical trial and, where necessary and appropriate, study entry only after a confirmed menstrual period. If pregnancy is confirmed prior to the start of the trial in general, the subject should not be enrolled in the trial. Exceptions may be considered on a case by case basis (e.g. cancer patients fully informed about the foetal risks).
3. Additional pregnancy testing, as necessary and appropriate, at predetermined intervals, based on risks and benefits. Considerations may include the length of the trial, the subject population and the specific product.

Where required, contraception should be extended beyond the last dose of the investigational product. The duration will differ by product (e.g. length of half-life) and will depend on what is known and not known about the product with respect to reproductive toxicity. The duration required will also depend on the pharmacokinetics/pharmacodynamics of the product and will usually be longer for biologics than for pharmaceuticals.

Inadvertent pregnancy in clinical trials

The following recommendations are offered for the management and follow-up of an inadvertent pregnancy, should it occur in the context of a clinical trial and when it is estimated that the investigational product poses a risk to the health of the foetus and/or the pregnant woman:

- Subjects (female and male) should be advised to report, immediately, to the Investigator a suspected or confirmed pregnancy that occurs in the course of a clinical trial
- Sponsors should have documented procedures for investigators to follow in case an inadvertent pregnancy occurs in the course of a clinical trial
- Treatment should generally be discontinued if this can be done safely and the pregnant subject withdrawn from the trial.
- Follow-up procedures regarding the course of the pregnancy should be discussed with the subject, as appropriate.

- The outcome of each pregnancy should be recorded and followed-up. For live births, longer term follow-up of a child is recommended, when possible and appropriate. Outcome data of foetal exposure comprise both structural malformations (typical birth defects) that are often, but not always, detected in the neonatal period, and non-structural or longer-term functional effects that are not easily detected in the immediate neonatal period. Some cardiac, renal and intestinal malformations are not always diagnosed immediately postpartum, and data regarding the incidence of these malformations is significantly influenced by duration of follow-up and availability of diagnostic tests.
- Where congenital anomaly/birth defect occurs in the context of a clinical trial, sponsors are required to report this to the regulator within 15 days of becoming aware of the event.

Inclusion pregnant/breastfeeding women

Pregnant and breastfeeding women are generally excluded from clinical trials because of real or perceived harm to the woman, the developing foetus and/or the infant. Many women use therapeutic products during pregnancy and when breastfeeding for treatment of chronic conditions, or for conditions that arise during pregnancy, despite lack of evidence for safety or efficacy. In addition, some women may become pregnant while on medication.

The inclusion of pregnant and/or breastfeeding women in pre-market trials is encouraged when it is considered safe for the women, developing fetus and/or infant based on the guidance below. Post-market surveillance or clinical trials may be alternative or additional ways of gathering data.

Considerations for including pregnancy women

A decision to enrol pregnant women in a specific trial should be individualized and based on a careful risk/benefit assessment taking into consideration: the nature and severity of the disease; the availability and results of previous nonclinical data on pregnant and non-pregnant animals, and results from clinical data; the availability of alternative therapy/therapies and knowledge about their associated risks; the stage of pregnancy in relation to overall development of the foetus, especially regarding foetal brain development; and the potential for harm to the woman, the foetus or child. A key consideration in the study of therapeutic products used by pregnant women will be follow-up of the pregnancy, foetus and child. Longer term follow-up of a child is recommended when possible. The inclusion of pregnant women in clinical trials should be considered when:

- The specific use of the therapeutic product is for pregnant or breastfeeding women (e.g. for obstetrical or pregnancy related problems).
- The studies are of agents that can be expected to address an unmet, or inadequately met, health need for pregnant women and/or foetuses (e.g. pregnant women with HIV; other life threatening conditions).
- The studies are of agents which can be expected to improve pregnant women and/or foetal outcomes as compared to existing therapy.
- Animal studies have been conducted, including studies on pregnant animals, and there is data on non-pregnant women on which to base an estimate of risk to the woman and/or foetus.
- For a new drug or new indication there is anticipated or actual use of the drug in pregnant women and women of childbearing potential.
- Research involving pregnant women should be research of potential health benefit to pregnant women or the foetus. Any potential benefit to foetuses should be weighed against possible risks to the pregnant women.
- The risk to the foetus is not greater than that from established procedures routinely used in an uncomplicated pregnancy, or in a pregnancy with complications comparable to those being studied, and the purpose of the research is the development of biomedical knowledge which cannot be obtained by any other means.

Consideration for including breastfeeding women

Should be considered when:

- A new indication is being sought for an approved therapeutic product and there is evidence of use or anticipated use of the therapeutic product by breastfeeding women;
- After market authorization, use of a therapeutic product in breastfeeding women becomes evident (e.g. via reports in the medical literature, general media, anecdotal information or adverse event reports);

- There is concern that the consequences of uninformed dosages for use while breastfeeding are potentially serious and/or severe. This includes the following circumstances:
 - product is under review for market authorization and is expected to be used by women of reproductive age;
 - Marketed medications that are commonly used by women of reproductive age (e.g. antidepressants, anti-hypertensives, anti-infectives, anti-diabetics and analgesics);
- The risk to the infant or mother is not greater than that from established procedures routinely used during breastfeeding, is comparable to those being studied, and the purpose of the research is the development of biomedical knowledge which cannot be obtained by any other means.

Post-market studies

As with pediatrics and other populations, it is anticipated that most studies regarding the safety and efficacy of therapeutic products in pregnant or breastfeeding women will be carried out following initial marketing for use in the general population. Health Canada strongly encourages the gathering of data on pregnant and breastfeeding women. This would include monitoring the outcome of a pregnancy with regard to the health of the woman and child, in the short and longer term.

There are circumstances in which consideration should be given to include pregnant or breastfeeding women in clinical studies, including clinical trials. In the vast majority of cases, studies will be conducted in pregnant or breastfeeding women already prescribed and taking the medication.

Consultation with Health Canada

Health Canada's Health Products and Food Branch should be consulted prior to undertaking these studies to seek information on what is acceptable in the Canadian context.

Considerations specific to medical devices

While some medical devices are sex specific (e.g. condoms, prostate cancer treatment for men; pregnancy test kits and intra-uterine contraceptive devices for women), the vast majority of medical devices are intended for use by both men and women. These include orthopaedic implants, interventional cardiology devices, diagnostic imaging instruments, various implants such as those for use in ophthalmology and in-vitro diagnostic devices.

Where medical devices are to be used by both women and men, clinical investigations should be designed to identify whether there are differences by sex that affect the safety and efficacy of the device, including the nature and extent of those differences.

Because of the invasive nature of many medical devices, testing in healthy volunteers does not usually occur. This necessitates the use of nonclinical, including animal, model testing to help assess the preliminary safety and performance of these medical devices.

Protocols should address any known or foreseeable factors that may affect outcomes or interpretation of results. These may include subject related factors such as age, sex or lifestyle. The methods for addressing these factors in the investigation, including for example, subject selection, investigation design (e.g. stratified or randomized), or statistical analysis should be described.

Initial human clinical investigations with devices involve small pilot studies with patients as subjects. Where the pilot studies indicate the concept is feasible, these would be followed by larger studies with well-designed protocols. Ideally, these studies should be powered for subgroup analysis, where appropriate, to be able to draw valid conclusions about sex differences in response to medical devices.

Where study size does not support meaningful subgroup analysis, post-market follow-up should be considered.

APPENDIX 6. Submission review documents (n=21)

Document	Purpose	SGBA+ Content			SGBA+ Flags
		Sex	Gender	Intersectionality	
<p>PUBLIC GUIDANCE</p> <p>Guidance on supporting evidence to be provided for new and amended applications for Class III and Class IV devices [not IVDDs]</p> <p>July 2012 (42 pages)</p> <p>PLUS applications forms: Device intended use Review document checklist SGBA+ considerations</p> <p>New class II licence New class III licence New class IV licence New private label Class II amendment Class III amendment Class IV amendment Private label amendment</p> <p>SEE https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/forms.html</p>	<p>Guidance to assist manufacturers in preparing scientific information that supports new and amended device applications</p>	---	---	---	<p>Definitions Add: SGBA+</p> <p>Table of Contents Add: SGBA+ (in addition to relevant details appearing in specific sections, include a section dedicated to highlighting how SGBA+ addressed throughout, and rather than N/A, rationale for SGBA+ details not addressed)</p> <p>Executive Summary Brief statement on type of device (e.g. women-only) and relevant SGBA+ considerations pertinent to safety/performance</p> <p>Device Description Categorize device by target users (e.g. women-only), implications of device modifications on SGBA+</p> <p>Design Philosophy Indications/Contraindications Labels/Documentation Explicitly note if and how SGBA+ relevant</p> <p>Marketing History Report incidents/recalls by SGBA+ details</p> <p>Safety and Effectiveness Describe study participants and impact/outcomes by SGBA+ details in published research, in primary clinical studies, and in risk assessment analyses Also note other key details such as power, statistical analyses, etc. used to include and report on SGBA+ differences in safety and effectiveness</p>

Management of applications for medical device licenses April 2020 (22 pages)	Provides applicants with information on how HC manages applications for new and amended device licenses (screening and review process, timing, fees, etc.)	---	---	---	---	<p>Pertains to logistical details of processes but could explicitly acknowledge SGBA+</p> <p>Tools/Guidance Add: Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences, and any other documents specific to, or amended with SGBA+ details that emerge as a result of this study</p>
How to complete the application for a new medical device licence March 2018 (21 pages)	To assist new medical device license applicants in completing an application form	---	---	---	---	<p>Definitions Add: SGBA+</p> <p>Device Classification Add: category of device based on target user (e.g. women-only)</p> <p>Attestations Explicit confirmation that devices proven safe and effective for range of target users by SGBA+ details</p> <p>Purpose Intended use, patient population, anatomical/physiological details</p> <p>Device History Incidents, recalls or other problems and number of individuals affected by SGBA+ details</p> <p>Standards In addition to formal ISO standards (e.g. Clinical Investigation of medical devices for human subjects — Good clinical practice), refer to other “standards” such as TCPS II, IMDRF Clinical Investigation, Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences, etc.</p>
Draft Health Canada IMDRF table of contents for medical device applications guidance	To assist in preparing information packages for	---	---	---	---	<p>System requirements (e.g. file format, file name, path length, submission media, table of contents template)</p>

No date (15 pages)	various pre- and post-market regulatory activities in a manner that complies with international standards				<p>Definitions Add: SGBA+</p> <p>Summary Add: numbered item specific to SGBA+ considerations</p> <p>Full Report Add: SGBA+ considerations should be explicitly described in relevant sections, and also in a section dedicated to summarizing how SGBA+ was addressed throughout</p> <p>Recall Add: (d) may not prove safe or effective in individuals or groups who vary by SGBA+ details</p> <p>Table of Contents/Folder Structure Under Context, add SGBA+; here, describe how SGBA+ considered throughout (Required – if not deemed relevant, provide rationale, for each SGBA+ detail)</p>
Guidance for the labelling of medical devices July 2015 (19 pages)	To assist manufacturers in complying with Medical Device Regulations labelling requirements [excludes IVDD]	Appendix 2 – Labelling for Menstrual Tampons Absorbency, Toxic Shock Syndrome warnings and risks, duration of use, proper hygiene during use, when to seek medical attention, tampon composition,	---	---	<p>Definitions Add: SGBA+</p> <p>SGBA+ could be addressed in a separate section and/or addressed in any of the following: Purpose/Indications Adverse effects Contraindications Directions for use Warnings and cautions</p>
Labelling of In Vitro Diagnostic Devices April 2016 (25 pages)	To assist manufacturers in complying with Medical Device Regulations labelling requirements for IVDDs	---	---	---	<p>Definitions Add: SGBA+</p> <p>SGBA+ could be addressed in a separate section and/or addressed in any of the following: Purpose/Indications (elaborate on “description of the patient population the IVDD is to be used in” Adverse effects</p>

						Contraindications Directions for use Warnings and cautions Performance characteristics
Fees for the Review of Medical Device License Applications April 2020 (15 pages)	Guidance on fees for the review of Class II, III and IV medical device license applications or amendments	---	---	---	---	Pertains to logistical details (applicable fees, invoicing, fee payment, mitigation measures, etc.)
Guidance for the Risk-based Classification System for In Vitro Diagnostic Devices No date (17 pages) **Based on Medical Device Regulations	To assist manufacturers in applying for IVDD licenses by clarifying the application of risk classification rules	---	---	---	---	Summary of Classification of IVDDs Add: application of device or interpretation of results given SGBA+
Guidance on the Risk-based Classification System for Non-In Vitro Diagnostic Devices June 2015 (28 pages) **Based on European Union's Council Directive 93/42/EEC and Medical Device Regulations	To assist manufacturers in applying for non-IVDD licenses by clarifying the application of risk classification rules	Definitions Device - means an instrument, apparatus, contrivance or other similar article, or an in vitro reagent, including a component, part or accessory of any of them, that is manufactured, sold or represented for use in	---	---	---	Add: Section specific to SGBA+ where, in addition to classification, additional details are provided on SGBA+ details relevant to the disease or condition, purpose of device, how it is used, possible impact on results, implications of risk/uncertainty in interpreting results by SGBA+ details
		(a) diagnosing, treating, mitigating or preventing a disease, disorder or abnormal physical state, or any of their symptoms, in human beings or animals, (b) restoring, modifying or	---	---	---	Definitions Add: SGBA+ Add: Supplement categorization of devices based on invasiveness or active/non-active, or special rules by adding a section specific to SGBA+ where additional information is provided on SGBA+ details relevant to the disease or condition, purpose of device, how it is used, possible impact on physiologic function or clinical outcomes, and implications of risk/uncertainty in safety and effectiveness based on SGBA+

	<p>correcting the body structure of human beings or animals or the functioning of any part of the bodies of human beings or animals, (c) <u>diagnosing pregnancy in human beings or animals, (d) caring for human beings or animals during pregnancy or at or after the birth of the offspring, including caring for the offspring, or (e) preventing conception in human beings or animals (p 3)</u></p> <p>Invasiveness “...device that is intended to diagnose, monitor, control or correct a defect of...a fetus in utero...” (p 5)</p> <p>“devices that penetrate the body through a body orifice...single use vaginal dilator...Intrauterine contraceptive device (IUD) and introducer...female condom or non-latex condom” (p 7)</p> <p>Active</p>		
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		<p>"...intended to be used for mammographies..." (p 13)</p> <p>Special Device Rules Breast Implants (p 19)</p>			<p>Definitions Add: SGBA+</p> <p>Recall Add: (d) may not prove safe or effective in individuals or groups who vary by SGBA+ details</p> <p>Significant change Add: (e) design, intended use, safety or effectiveness may differ by SGBA+ details</p> <p>Tools to Assess Changes Mention SGBA+ in General Principles, Flowchart C, List of Examples of Significant Changes</p> <p>Process/Procedures Recall by SGBA+ details</p> <p>Also, consider adding a section specific to SGBA+ summarizing all possible implications that may arise due to changes</p>
<p>Guidance for the Interpretation of Significant Change of a Medical Device April 2011 (38 pages)</p>	<p>To assist manufacturers in deciding if proposed changes to a Class III or Class IV medical device are significant, requiring application for an amended license</p>	<p>----</p>	<p>----</p>	<p>----</p>	<p>Logistical details to assess application completeness and resources/time needed for in-depth review of the application, and log details in the internal information system, but could acknowledge and promote SGBA+</p> <p>Definitions Add: SGBA+</p> <p>If SGBA+ is incorporated in guidance documents, update this SOP (and corresponding internal information system) with check boxes and comment boxes for a specific section dedicated to</p>
<p>HC SOPs Technical Screening of Class III and IV Device Licence Applications September 2019 (28 pages)</p>	<p>To assist HC staff in screening Class III and Class IV license applications [not assess scientific data]</p>	<p>----</p>	<p>----</p>	<p>----</p>	<p>Logistical details to assess application completeness and resources/time needed for in-depth review of the application, and log details in the internal information system, but could acknowledge and promote SGBA+</p> <p>Definitions Add: SGBA+</p> <p>If SGBA+ is incorporated in guidance documents, update this SOP (and corresponding internal information system) with check boxes and comment boxes for a specific section dedicated to</p>

				<p>Safety and Effectiveness Studies - Clinical Studies Have the clinical studies been performed in special populations? Are these populations representative of Canada? (p 26)</p>	<p>SGBA+ details, or mention of SGBA+ details within specific sections (e.g. device description, summary of recalls, review complexity, clinical studies), and include guidance on how to noted SGBA+ issues in a deficiency letter</p> <p>Logistical details and instructions on how to employ the internal information system, writing style, etc. Also includes criteria by which to evaluate supporting data</p> <p>Definitions Add: SGBA+</p> <p>Report Instructions Add: bullet point specific to assessment of type of device and SGBA+ in scientific evidence</p> <p>Include criteria/checklist points throughout the following sections and in a section dedicated to summarizing SGBA+ implications included throughout: type of device and who uses it; reason for modification and SGBA+ implications, design philosophy, indications, contraindications, labelling details, warnings and precautions, incident reports (even if not explicit in primary studies, report an analysis and/or risk assessment by SGBA+), safety and effectiveness studies (elaborate on SGBA+ in sampling, power, statistical analyses, and the number, design and quality of studies that comprise supporting evidence), explanation of recommendation, Appendix 2 (rate of morbid events)</p> <p>Guidance Documents Refer to TCPS II, Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences</p>
<p>Preparation of the Scientific Review Report for Medical Device Licence Applications August 2018 (39 pages)</p>	<p>To assist HC staff in preparing a medical device license application evaluation report including scientific data</p>	<p>---</p>	<p>---</p>		
<p>HC FORMS</p>					
<p>Consolidated Screening Medical Devices</p>	<p>Template/checklist for HC staff to summarize if</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>If manufacturer guidance and application forms are updated to address SGBA+, this report template must be updated accordingly. SEE</p>

No date (3 pages) **Corresponds to SOP Technical Screening of Class III and IV Device Licence Applications	section-specific details were present/absent in new or amended license applications along with comments, notes to the reviewer, a list of deficiencies, and a recommendation					aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed
Class IV Medical Device License Evaluation Report No date (8 pages) **Corresponds to SOP Preparation of the Scientific Review Report for Medical Device Licence Application	Template for HC staff to assist in drafting an evaluation report for new or amended license applications.	---	---	---	---	If manufacturer guidance and application forms are updated to address SGBA+, this report template must be updated accordingly. SEE aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed
Executive Summary Non-In Vitro Diagnostic Devices No date (2 pages) **Corresponds to SOP Preparation of the Scientific Review Report for Medical Device Licence Application	Template for HC staff to assist in drafting a summary of a review of a new or amended license application.	---	---	---	---	This form includes standard wording for high- level/overall observations. However, if manufacturer guidance and application forms are updated to address SGBA+, the corresponding SOP must be updated accordingly, as it would inform the preparation of this executive summary. SEE aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed
Class IV In Vitro Device License Evaluation Report No date (8 pages)	Template for HC staff to assist in drafting an evaluation report for new or amended license applications.	---	---	---	---	If manufacturer guidance and application forms are updated to address SGBA+, this report template must be updated accordingly. SEE aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed
Executive Summary In Vitro Diagnostic Device License Evaluation Report	Template for HC staff to assist in drafting a	---	---	---	---	Includes standard wording for high-level/overall observations but could acknowledge and promote SGBA+.

<p>No date (1 page)</p> <p>**Corresponds to SOP Preparation of the Scientific Review Report for Medical Device Licence Application</p>	<p>summary of a review of a new or amended license application.</p>			<p>However, if manufacturer guidance and application forms are updated to address SGBA+, the **corresponding SOP must be updated accordingly, as it would inform the preparation of this executive summary. SEE aforementioned recommendations for details needed in sections and inclusion of an overall section to comment on how thoroughly SGBA+ was addressed</p>
NON-HC				
<p>IMDRF Non-In Vitro Diagnostic Device Market Authorization Table of Contents</p> <p>March 2019 (53 pages)</p>	<p>To provide applicants and reviewers with guidance on the format of market authorization submissions</p>	---	---	<p>HC may or may not have influence over IMDRF guidance</p> <p>Rudimentary outline of sections/sub-sections to include in applications with little guidance on the desired or optimal content</p> <p>However, HC might develop guidance on SGBA+ to supplement this guidance. Such guidance might be addressed as noted above in existing documents, elaborated in Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences and/or included in a newly-developed document dedicated to SGBA+</p> <p>Areas to strengthen SGBA+:</p> <p>Definitions/Acronyms</p> <p>Add: SGBA+</p> <p>Acceptance for Review Checklist</p> <p>Certifications/Declarations of Conformity</p> <p>General Summary</p> <p>Device Description/History</p> <p>Indications/Contraindications</p> <p>Incidents/Recalls</p> <p>Clinical Evidence (overall summary, clinical evaluation report, clinical trials, literature review, other clinical evidence) **refers to “human factors testing”, <u>which seems to mean testing in patients</u></p> <p>Labelling</p>

IMDRF In Vitro Diagnostic Medical Device Market Authorization March 2019 (54 pages)	To provide applicants and reviewers with guidance on the format of market authorization submissions	---	---	---	"If applicable, information about patient selection criteria" (p 23)	Quality Management (monitoring) Areas to strengthen SGBA+: Definitions Hierarchy Presentation Terms/Acronyms Device Description Indications Global Market History Risk Management and in relevant studies (e.g. assay validation) Clinical Evidence Labeling and Promotional Material Quality Management
IMDRF Principles of Labelling for Medical Devices and IVD Medical Devices March 2019 (28 pages)	Guidance on labelling content, instructions for use and information intended for patients (not advertising or promotional material)	---	---	---	Definitions Contraindication: Labelling elements that describe situations, such as <u>patient populations</u>in which the device should not be used because the risk of use clearly outweighs any possible benefit. (p 7)	Definitions: Add: SGBA+ Labeling Elaborate "special needs of the persons for whom the device is intended" Precautions Instructions for Use (warnings, precautions, measures to be taken, limitations) Information for patients (adverse events, warnings, risks, warning signs)

APPENDIX 7. Authorization and post-market monitoring and communication documents (n=20)

Document	Purpose	SGBA+ Content			SGBA+ Flags
		Sex	Gender	Intersectionality	
<p>PUBLIC GUIDANCE</p> <p>Mandatory reporting of serious adverse drug reactions and medical device incidents by hospitals</p> <p>June 2019 (46 pages)</p> <p>PLUS Medical device problem report form for healthcare professionals:</p> <p>Affected person details and consequences</p> <p>Contributing factors</p> <p>Impact</p> <p>Device information (evidence of safety and effectiveness among diverse users)</p> <p>Potential device/use contributing factors</p> <p>Actions taken</p> <p>Additional details</p> <p>Instructions for completing the report</p> <p>https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting/mandatory-reporting-hospital-device-eng.pdf</p>	<p>To provide hospitals with information that enables compliance with regulatory requirement for hospitals to report serious medical device incidents to Health Canada</p>	---	---	---	<p>Definition of a medical device incident: suggest you add a few examples of MDIs as you did for ADRs</p> <p>Roles/Responsibilities</p> <p>Suggest you add sub-category for Patients, and recommend that hospitals develop mechanisms by which patients can also play an important role in recognizing and reporting MDIs to hospitals</p> <p>Reporting criteria for MDIs</p> <p>SGBA+ details of affected persons</p> <p>Information Required</p> <p>Device category (suggested in earlier comments to categorize devices according to recipient group, e.g. women-specific)</p> <p>SGBA+ details of the affected person (explicitly elaborate on “information about the affected person” or co-morbid conditions or treatments), and note previous issues with same device group plus SGBA+ details for those persons</p> <p>Who identified/reported the MDI (e.g. hospital staff or physician, community physician or allied health, patient or family)</p> <p>Identification of duplicate reports</p>

					<p>Inclusion of SGBA+ details would assist in identifying duplicate reports of same MDI</p> <p>Appendix 1 Definitions Add: SGBA+</p> <p>Appendix 4 Quick Reference Guide Add SGBA+ to What to report and Why to report</p>
<p>Guidance on Medical Device Compliance and Enforcement June 2015 (13 pages)</p>	<p>Provides industry with information about compliance and enforcement actions (licensing, inspection and investigation)</p>	---	---	---	<p>Describes how HC responds if companies do not investigate complaints or file recall reports, etc. but could acknowledge and promote SGBA+ considerations</p> <p>Non-compliance (5.4.1) Licensed devices that have been subject to change that may influence safety or effectiveness by SGBA+ details</p> <p>Requirement to notify users Specify risk by SGBA+ details</p> <p>Appendix A SGBA+ may be relevant to the following requirement descriptions: Safety and Effectiveness Labelling Contraceptive Device Advertising Device Licensing Establishment Licensing Complaint Records Complaint Handling Procedure Recall Procedure Mandatory Problem Reporting Recall Notification</p>
<p>Guidance Document for Mandatory Problem Reporting for Medical Devices</p>	<p>To assist industry in understanding how to interpret and comply with</p>	---	---	---	<p>Definitions Add: SGBA+ Criteria</p>

October 2011 (21 pages)	mandated problem reporting	---	---	---	<p>Details about person(s) affected including SGBA+</p> <p>Content</p> <p>Device category (suggested in earlier comments to categorize devices according to recipient group, e.g. women-specific)</p> <p>SGBA+ details of the affected person and note previous issues with same device group plus SGBA+ details for those persons</p> <p>Who identified/reported the MDI (e.g. hospital staff or physician, community physician or allied health, patient or family)</p> <p>Criteria HC will use to assess adequacy</p> <p>Risk assessment, implications or actions relevant to users by SGBA+ details</p> <p>Final report</p> <p>SGBA+ details as outlined above including enhanced post-market surveillance and preventive action that considers SGBA+ details</p>
Mandatory medical device problem reporting form for industry April 2018 (5 pages)	Template for industry to report medical device incidents to Health Canada	---	---	---	<p>Instructions</p> <p>Medical device information (device category)</p> <p>Incident information (affected persons by SGBA+</p> <p>Complainant (who identified/reported)</p> <p>Investigation (root cause and corrective action by SGBA+ details)</p> <p>Include explicit field in form to reflect the above-named recommendations rather than generic text box</p>

<p>Medical Devices Recall Guide November 2016 (58 pages)</p>	<p>To assist industry in understanding how to recall medical devices, report medical device recalls, and maintain related documentation</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>Keep distribution records Develop procedures for recalls Notifying affected clients (about device safety and effectiveness by SGBA+) Customer and device details Report recalls to Health Canada Nature/degree of hazard Nature/size of population at risk Users ability to detect problem In either Type I, II and/or III, include a clause potential for adverse health consequences to affect some groups more than others given SGBA+ details Implications of significant change Recall communications Notification of users Tracking responses to recalls Recall process overview Definition (alerting customers, on-site correction, modifying labelling) Initiating a recall Establish reasons for problem Notify users Conducting a recall Risk assessment Changes to medical device Recall communications/notifying users Evaluation of effectiveness of actions Appendix A Definitions Add: SGBA+ Appendix B Recall process flowchart Appendix D Distribution Records Checklist Appendix E Checklist for recalls</p>
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					<p>Checklist for self-assessment of procedures</p> <p>Appendix F Guidelines for writing procedures</p> <p>Appendix G How to write recall reports</p> <p>Appendix H References (add SGBA+ links to internal and external guidance)</p>
<p>Guidance Document for Industry - Issuance of Health Professional Communications and Public Communications by Market Authorization Holders</p> <p>May 2010 (29 pages)</p>	<p>To assist industry in preparing communications about health and safety concerns for professionals (individuals, hospitals) and patients or the general public</p>	---	---	---	<p>Definitions</p> <p>Add: SGBA+</p> <p>Correspondence with Health Canada</p> <p>See standard format/content</p> <p>Medical literature references</p> <p>Standard format and content</p> <p>Adverse event, seriousness, cause, persons affected, number of events by SGBA+ details, risk management plans</p> <p>Appendix B Communication Checklist</p> <p>Appendix D Tips for writing public communications (nature of hazard, risk, elaborate "sensitive populations", uncertainties, probabilities, actions recommended)</p>
<p>Form: Standardized Health Product Risk Communication Template</p> <p>No date (2 pages)</p>	<p>Template for industry to report risks to patients or the general public, or individual or organizational healthcare providers</p>	---	---	---	<p>Key messages</p> <p>Issue/health risk</p> <p>Background information (device category, affected persons)</p> <p>Information for consumers/health professionals</p> <p>Consider adding explicit section specific to SGBA+</p>
<p>Guide for using the Standardized Health Product Risk Communication Template</p> <p>November 2015 (3 pages)</p>	<p>To assist in using the standardized template for communicating about health and safety concerns</p>	---	---	---	<p>Audience (persons who may be affected)</p> <p>Key messages (risks, actions recommended)</p> <p>Background information (device category, risk, cause, number and type of events, affected persons)</p>

						Information for consumers and health professionals
Risk Communication - Protecting Canadians Through Information No date/possibly 2011 (2 pages)	Information for the general public on how Health Canada informs users about recalls and how to interpret urgency	---	---	---	---	General/high-level, brief document summarizing the various communication tools that HC uses to inform stakeholders about risks If these SGBA+ recommendations are adopted, could specify here that communications describe risk by SGBA+ details
HC SOPs						
Preparing the DED Licence Recommendation Memorandum November 2011 (4 pages)	Guidance to help section heads prepare evaluation memos for senior managers that highlight reviews that result in issuing or refusing a licence	---	---	---	---	Content Add SGBA+ details and elaborate on device category, key evidence on safety and effectiveness, clinical evidence
Prioritization and management of potential signal files in the marketed health products directorate March 2017 (6 pages)	To help HC staff apply criteria that inform decisions about which suspected safety problems to prioritize for signal evaluation	---	---	---	---	Responsibilities Designate someone with the responsibility of assessing SGBA+ considerations Definitions Add: SGBA+ Signal evaluation (elaborate on “special populations”) No signal evaluation (note if SGBA+ considerations are to be monitored) Process Map Add: SGBA+
Causality Assessment July 2012 (13 pages)	To provide HC with a causality assessment standardized format	---	---	Appendix 1: Causality assessments • Gender; • Age; (p 6)	Appendix 1: Causality assessments • Gender; • Age; (p 6)	Definitions Add: SGBA+ Device category Issue

					Case definition Findings (number and SGBA+ details of cases) Appendix 1 Causality assessment (elaborate on gender, age) Appendix 1 Causality assessment methods
Causality Assessment Background Information March 2014 (17 pages) To be used with SOP Signal Assessment Causality Assessment	To help HC staff in assessing and preparing documentation of association between product and incidents or adverse events	---	Causality assessment template Age, gender, ethnic origin (p 10)	Causality assessment template Age, gender, ethnic origin (p 10)	Definitions Add: SGBA+ Causality assessment process (criteria and rationale should consider number, type and quality of case reports by SGBA+ details) Process Map Diagram Causality Assessment Document Template (background, labelling, definitions, affected persons and SGBA+ considerations) Causality assessment template (elaborate on SGBA+ details in event, exposure, concomitant conditions, rationale and comments, summary, references)
Periodic Safety Update Report Review Level II March 2014 (16 pages)	To provide HC staff with help in reviewing and preparing reports for safety updates prepared by industry	5.4.6.5 Identified or possible safety issues in specific patient populations Are the frequencies of specific adverse events different in any patient groups, for example, pediatrics, geriatrics, pregnant/lactating women, patients with compromised organ function, than	---	5.4.6.5 Identified or possible safety issues in specific patient populations Are the frequencies of specific adverse events different in any patient groups, for example, pediatrics, geriatrics, pregnant/lactating	Definitions Add: SGBA+ Identification data (device category) Review (product overview, current and previous concerns, comments, Canadian exposures, actions, changes to Core Data Sheet, corresponding labelling, discussion/comparison table, summary of adverse events, assessment of adverse events, elaborate on “specific patient populations”, previous cases in Canadian adverse event database, safety concerns, supporting literature, risk factors, assessment of industry actions, overall

		in the overall population? (p 10)	women, patients with compromised organ function, than in the overall population? (p 10)	assessment, recommendations, risk management	
Benefit Risk Assessment Review May 2011 (17 pages)	To provide HC staff with a structured format to be used for a benefit-risk assessment (medical devices not specifically included in scope but could be applied to devices)	Evaluation of Risk Trends, patterns and/or correlations of ARs within relevant subgroups, (in consideration of identifiable subgroups, predisposing risk factors, AR predictability). This may include the following variables: <u>age</u> , <u>sex</u> , <u>dose</u> , <u>latency</u> , <u>duration of therapy</u> , <u>demographics</u> , <u>concomitant drugs</u> , <u>pre-existing medical conditions</u> , <u>overdose and/or food or drug interactions</u>) (p 12)	5.2.1.4 The discussion of the benefits could include the following areas for the above mentioned data categories: • Trends, patterns and/or correlations of benefits under study (This may include among others: <u>age</u> , <u>gender</u> , <u>dose</u> , <u>etc.</u>); (p 9)	5.2.1.4 The discussion of the benefits could include the following areas for the above mentioned data categories: • Trends, patterns and/or correlations of benefits under study (This may include among others: <u>age</u> , <u>gender</u> , <u>dose</u> , <u>etc.</u>); (p 9)	Definitions Add: SGBA+ Identification Data (device category, reason for assessment, patient exposed, regulatory actions, information provided by industry, factors affecting rates of adverse events) Benefit (device category, stratification of evidence, elaborate on "age, gender", study design, statistics, high level summary) Risk (special population of concern, characterization of safety issue, summary of case reports, causality, study designs, statistics, interpretation, summary Benefit-Risk Assessment Evaluation (summary, analysis, conclusions, limitations, uncertainties) Recommendations Conclusions, considerations, recommendations

					duration of therapy, <u>demographics</u> , concomitant drugs, pre-existing medical conditions, overdose and/or food or drug interactions) (p 12)	
Health Product InfoWatch Production February 2019 (15 pages)	Overview of publications process (content, format, editorial review, etc.)	---	---	---	High level overview of logistics Responsibilities Specify who should assess and/or review SGBA+ content (speaks to levels of expertise and need for training) Add SGBA+ considerations in Definitions, supporting evidence/cited literature, device category and indications, number of adverse events, SGBA+ details of affected persons, etc.	
HC FORMS						
Screening/Triage/Prioritization of Incoming Signals No date (4 pages)	Template for HC staff to document details and decisions regarding need for signal assessment review	---	---	---	Device category Details of signal/adverse event (add number and characteristics of affected persons) Intended use/risks Recommendation (include checkbox for SGBA+ considerations, specify in Risk Communication) Instructions to Prioritization Committee Summary (issue, adverse event data, Canadian cases, international cases, labelling, regulatory actions, recommendations)	
Signal Assessment No date (5 pages)	To provide HC with a causality assessment standardized format	---	---	---	Add SGBA+ to Definitions and in: Issue Purpose	

					<p>Background Issue Analysis Analysis of adverse events in Canada and internationally Causality assessment (including literature) Summary Considerations Option analysis Recommendations</p>
Signal Assessment Review Report No date (4 pages)	Template for HC staff to document signal assessment reviews	---	---	---	<p>Add SGBA+ to: Issue Purpose Background and Issue Analysis Considerations Recommendations References (dedicate sub-section) Executive Summary</p>

APPENDIX 8. Additional external documents relevant across the device lifecycle (n=5)

Document	Purpose	SGBA+ Content			SGBA+ Flags
		Sex	Gender	Intersectionality	
Food and Drugs Act (Canada) October 2020 (71 pages)	Federal regulation to permit the manufacture, import or sale of medical devices and conditions that apply	---	---	---	HC may or may not have influence over IMDRF documents, but may wish to develop or annotate HC Internal or external documents as follows: Recognize SGBA+ in: Definitions Devices (sections 19 to 21)
Amendments to the Food and Drugs Act: Guide to New Authorities (Canada) June 2021 (23 pages)	Clarifies <i>Medical Device Regulations</i> specific to power to: require and disclose information, order a label change, order a recall, require assessments, or require tests/studies	---	---	Annex A – Key elements for consideration about serious risk: The vulnerability of the patient population and/or sub-population that are exposed to the particular therapeutic product. Vulnerable populations may include, but are not limited to: <u>children, the elderly, pregnant and lactating women, and immunocompromised patients (p 23)</u>	HC may or may not have influence over Acts, but SGBA+ could be recognized in the following sections: Scope Principles In each section (disclose information, label change, recall, assessments, tests and/or Key Elements for Consideration about Serious Risks
Medical Devices Regulations December 2019 (68 pages)	Federal regulations for the import, sale and advertising of medical devices	Contraceptive Devices – Advertising 24 (1) For the purposes of subsections 3(1) and (2) of the Act and subject to section 27, a condom may be advertised and sold to the general	---	---	HC may or may not have influence over IMDRF documents, but may wish to develop or annotate HC Internal or external documents as follows: Recognize SGBA+ in: • Definitions Manufacturers Obligations • Safety and Effectiveness

		<p>public for the purpose of preventing the transmission of sexually transmitted diseases if the advertisement and the label of the condom claim only that the condom reduces the risk of transmitting sexually transmitted diseases.</p> <p>(2) For the purpose of subsection 3(3) of the Act and subject to section 27, contraceptive devices, other than intrauterine devices, may be advertised to the general public by any means other than by the distribution of samples of the devices door-to-door or through the mail. (p 12)</p>	---	<p>7.1.4 The performance characteristics of the IVD medical device should be evaluated according to the intended use statement which may include the following:</p>	<ul style="list-style-type: none"> • Labelling (intended use, precautions) • Applications for a Medical Device License (intended use, reported problems, studies, elaborate on “subjects representative of the intended users”, risk assessment) • Application for a Medical Device License Amendment (change that would affect SGBA+ • Additional Information – Issuance (ongoing testing) • Obligation to Inform • Disclosure of Information in Respect of Clinical Studies • Suspension (risk to health or safety of patients/persons) • Mandatory Problem Reporting • Provision of Information • Recall • Implant Registration <p>Custom-Made Devices and Special Access</p> <p>Medical Devices for Investigational Testing Involving Human Subjects</p>
<p>IMDRF Essential principles of safety and performance of medical devices and IVD medical devices</p> <p>January 2018 (34 pages)</p>	<p>To harmonize documentation and procedures used to assess device safety and performance across jurisdictions</p>	<p>7.1.4 The performance characteristics of the IVD medical device should be evaluated according to the intended use statement which may include the following:</p>	---	<p>7.1.4 The performance characteristics of the IVD medical device should be evaluated according to the intended use statement which may include the following:</p> <p>(c) Populations evaluated should represent, where</p>	<p>HC may or may not have influence over IMDRF documents, but may wish to develop or annotate HC internal or external documents as follows:</p> <p>Include SGBA+ considerations in:</p> <p>Definitions</p> <p>Essential Principles – General</p> <ul style="list-style-type: none"> • Risk management plan • Packaging • Clinical evaluations

		<p>(c) relevant populations, for example, pediatric c.f. adult, <u>pregnant women</u>... (p 27)</p>		<p>appropriate, <u>ethnically</u> and <u>genetically diverse</u> populations so as to be representative of the population(s) where the device is intended to be marketed. (p 27)</p>	<ul style="list-style-type: none"> • Conditions of use • Labeling/instructions for use • Use by lay persons <p>Essential Principles – IVD</p> <ul style="list-style-type: none"> • Performance characteristics in intended users <p>Use of Standards</p>
<p>IMDRF Methodological principles in the use of international medical device registry data</p> <p>August 2016 (26 pages)</p>	<p>To support harmonization of medical device registries (focus on implants)</p>	<p>Widening Indications However, approvals in different countries may have different indications for use (e.g. different intended use populations (e.g., disease, race, <u>sex/gender</u>)... (p 13-14)</p>	<p>Widening Indications However, approvals in different countries may have different indications for use (e.g. different intended use populations (e.g., disease, race, <u>sex/gender</u>)... (p 13-14)</p>	<p>Intrinsic and extrinsic ethnic factors Specific characteristics of the populations differ across countries, even for the same indication. Intrinsic factors include genetic information, body mass index, body composition, and other ethnic features; extrinsic factors involve aspects shaped by the cultural and behavior climate such as medical practice patterns, diet, and other environmental conditions. (p 10)</p>	<p>HC may or may not have influence over IMDRF documents, but may wish to develop or annotate HC internal or external documents as follows:</p> <p>Definitions Add: SGBA+</p> <p>Clinical Evaluation of Performance and Safety Using International Registry Data Elaborate on need to specify SGBA+ characteristics to enhance “poolability”</p> <p>Methodological Opportunities Identification of sub-group effects Nest randomized trials in registries Comparative effectiveness</p> <p>Signal Detection SGBA+ considerations are relevant to analyses across sub-categories of methodological opportunities</p> <p>General Recommendations Harmonize collection of SGBA+ data</p>

APPENDIX 9. Device-specific documents included by source

Database	Devices			
	Implantable pacemakers	Total knee implants	Breast implants	Transvaginal surgical mesh OR birth control device
SUBMISSION				
Clinical Information on Drugs & Health Products (licensed devices, approval date, clinical evidence summary from tests/trials)	none	none	none	Gynecare Gynemesh (Ethicon) Class III Approved 2009-11-20 Public release 2019-08-29 *** Cut 380A QL Intrauterine Device (Mona Lisa) Class III Approved 2011-11-22 Public release 2019-08-23
AUTHORIZATION				
Medical Device Active License Listing (MDALL): Provides no details other than date and device identifier #	---	---	---	---
Drug & Health Product Register: 1) Regulatory Decision Summary (reason approved/not approved) 2) Summary Basis of Decision (scientific rationale for approval)	<u>Regulatory Decision Summary</u> 1/ Mitra Transcatheter Pacemaker System (Medtronic) Class IV (new) Approved 2016-10-05 2/ Acuity X4 (Cardiac Pacemakers Incorporated) Class IV (new) Approved 2016-02-03 <u>Summary Basis of Decision</u> none	<u>Regulatory Decision Summary</u> 1/ Persona the Personalized Knee System (Zimmer) Class III (amendment) Approved 2020-07-30 2/ Triathlon Total Knee System (Howmedica Osteonics) Class III (amendment) Approved 2020-01-29 #305236 3/ Legion Knee System (Smith & Nephew) Class III (amendment) Approved 2019-12-27 <u>Summary Basis of Decision</u> none	<u>Regulatory Decision Summary</u> 1/ Natrelle 410 Truform Microcell Silicone-Filled Breast Implants (Allergan) Class IV (new) Approved 2018-06-19 <u>Summary Basis of Decision</u> 1/ Memory Gel Cohesive III (Mentor Medical Systems) Class IV (annual update with conditions) Issued 2017-10-10 2/ Saline Filled Breast Implant (Ideal Implant) Class IV (new)	<u>Regulatory Decision Summary</u> None (all for hernia or abdominal wall support) Flexi-T Intrauterine Device (Prosan International) Class III (amendment) Approved 2020-05-19 <u>Summary Basis of Decision</u> Mesh none Intrauterine none

MONITORING			
Drug & Health Product Register: Summary Safety Review (limited detail on safety issues, HC decisions, actions)	None	None	Issued 2015-02-18
Medical Device Incidents (limited detail on number and type of incidents)	Micra Transcatheter Pacemaker System (Medtronic) Class IV (new) Approved 2016-10-05 No incidents	Persona the Personalized Knee System (Zimmer) Class III (amendment) Approved 2020-07-30 64 incidents; for example: 2019-12-20 (unassigned) F26 - No Health Consequences or Impact E2403 - No Clinical Signs Symptoms or Conditions A0401 - Break B01 - Testing of Actual/Suspected Device C21 - Results Pending Completion of Investigation D16 - Conclusion Not Yet Available	<p>Potential Risk of Cancer (Breast implant associated anaplastic large cell lymphoma) Issued: 2019-05-30</p> <p>Natrelle 410 Truform Microcell Silicone-Filled Breast Implants (Allergan) Class IV (new) Approved 2018-06-19 No incidents</p> <p>Memory Gel Cohesive III (Mentor Medical Systems) Class IV (annual update with conditions) Issued 2017-10-10 68 incidents; for example: 2020-07-28 CPG 323 (unassigned) E0708 - Bronchitis E0107 - Cognitive Changes E0804 - Conjunctivitis E0717 - Dyspnea E2312 - Fatigue E2318 - Hair Loss E2320 - High Blood Pressure/Hypertension E1902 - Fungal Infection E0120 - Memory Loss/Impairment E0733 - Pneumonia E1714 - Rash E0839 - Visual Impairment E0135 - Taste Disorder E0712 - Cough</p>
	Acuity X4 (Cardiac Pacemakers Incorporated) Class IV (new) Approved 2016-02-03 2 incidents (unassigned) 2020-03-27 F1903 - Device Explanation F19 - Surgical Intervention E2403 - No Clinical Signs Symptoms or Conditions F1905 - Device Revision or Replacement A051201 - Device Dislodged or Dislocated B12 - Trend Analysis B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established 2020-03-18 E1906 - Unspecified Infection F1903 - Device Explanation F19 - Surgical Intervention A26 - Insufficient Information B12 - Trend Analysis B18 - Device Discarded	<p>Surgical mesh products made from non-absorbable synthetic (polypropylene) material that are used for the transvaginal repair of pelvic organ prolapse (POP) Issued: 2019-07-26</p> <p>Gynecare Gynemesh (Ethicon) Class III Approved 2009-11-20 Public release 2019-08-29 50 incidents; for example: 2020-06-04 (unassigned) E2333 - Prolapse F1903 - Device Explanation F19 - Surgical Intervention F12 - Serious Injury Illness Impairment A26 - Insufficient Information B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p> <p>2019-07-10 (injury) Blood loss (Retired - use 234) E2324 - Incontinence E2326 - Inflammation Injury (Retired - use 636) Revision surgery (Retired - use 1257) A040503 - Material Erosion B12 - Trend Analysis B14 - Analysis of Production Records B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p>	

<p>C20 - No Findings Available D15 - Cause Not Established</p> <p>Other examples/assigned: Altrua 60 (Boston Scientific) 2020-02-12 / Injury F1903 - Device Explantation E2403 - No Clinical Signs Symptoms or Conditions F1905 - Device Revision or Replacement A160601 - Premature Elective Replacement Indicator B01 - Testing of Actual/Suspected Device B12 - Trend Analysis C19 - No Device Problem Found D14 - No Problem Detected</p> <p>Endotak Reliance SG (Boston Scientific) 2020-02-05 / Death F02 - Death E2403 - No Clinical Signs Symptoms or Conditions A0721 - Circuit Failure B01 - Testing of Actual/Suspected Device C20 - No Findings Available D15 - Cause Not Established</p>	<p>Triathlon Total Knee System (Howmedica Osteonics) Class III (amendment) Approved 2020-01-29 #305236 32 incidents; for example: 2020-07-31 (unassigned) E0402 - Hypersensitivity/Allergic reaction E1906 - Unspecified Infection E1602 - Arthritis E2330 - Pain F23 - Unexpected Medical Intervention E1618 - Metal Related Pathology E1628 - Osteomyelitis E1720 - Skin Inflammation Irritation F28 - Appropriate TermCode Not Available A26 - Insufficient Information B11 - Historical Data Analysis B14 - Analysis of Production Records B15 - Analysis of Data Provided by User/Third Party B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p> <p>2017-07-27 (injury) Revision surgery (Retired - use 1257) A0401 - Break A040503 - Material Erosion A040507 - Naturally Worn Device damage (Retired)</p>	<p>E1402 - Breast Discomfort/Pain E2338 - Swelling Edema A26 - Insufficient Information B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p> <p>2019-06-26 CPG 333 (potential for death/injury) E2303 - Capsular Contracture A0101 - Patient-Device Incompatibility A0406 - Material Deformation A0412 - Material Rupture Capsular contracture associated with breast implant (Retired - use 67) B01 - Testing of Actual/Suspected Device B12 - Trend Analysis B14 - Analysis of Production Records C070601 - Deformation Problem D12 - Known Inherent Risk of Device</p> <p>Saline Filled Breast Implant (Ideal Implant) Class IV (new) Issued 2015-02-18 40 incidents; for example: 2019-08-12 (potential for death/injury) F1903 - Device Explantation F19 - Surgical Intervention A0412 - Material Rupture B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p>	<p>IUD</p> <p>Cut 380A QL Intrauterine Device (Mona Lisa) Class III Approved 2011-11-22 5 incidents; for example: 2020-01-15 (unassigned) E160501 - Abdominal Cramps E1011 - Flatus E1415 - Uterine Perforation E1002 - Abdominal Pain F1903 - Device Explantation F19 - Surgical Intervention A23 - Use of Device Problem A150208 - Entrapment of Device A150202 - Malposition of device B11 - Historical Data Analysis B14 - Analysis of Production Records B17 - Device Not Returned C20 - No Findings Available D12 - Known Inherent Risk of Device D15 - Cause Not Established</p> <p>2019-06-18 (potential for death/injury) Details not specified</p> <p>Flexi-T Intrauterine Device (Prosan International) Class III (amendment) Approved 2020-05-19 No incidents</p>
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		<p>Legion Knee System (Smith & Nephew) Class III (amendment) Approved 2019-12-27 13 incidents; for example: 2020-03-20 (unassigned) E0505 - Hematoma E0506 - Hemorrhage/Bleeding E1906 - Unspecified Infection E2330 - Pain E1615 - Joint Laxity F1905 - Device Revision or Replacement A040101 - Fracture A051207 - Unstable A26 - Insufficient Information B01 - Testing of Actual/Suspected Device B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p> <p>2019-05-01 (injury) Revision surgery (Retired - use 1257) A0401 - Break B01 - Testing of Actual/Suspected Device B11 - Historical Data Analysis B12 - Trend Analysis C070601 - Deformation Problem C070603 - Fracture Problem D15 - Cause Not Established</p> <p>Persona the Personalized Knee System (Zimmer) Class III (amendment) Approved 2020-07-30</p>	<p>2017-07-05 (potential for death/injury) F1903 - Device Explantation Revision surgery (Retired - use 1257) A0412 - Material Rupture B01 - Testing of Actual/Suspected Device C0706 - Stress Problem Identified D03 - Cause Traced to Manufacturing</p>	<p>Gyneccare Gynemesh (Ethicon) Class III Approved 2009-11-20 Public release 2019-08-29 NONE</p>
<p>Recalls & Safety Alerts Database (hazard severity, affected products, reason,</p>	<p>2 examples above: none Other pacemakers 45 records from 1995 to 2020; for example:</p>		<p>Natrelle 410 Truform Microcell Silicone-Filled Breast Implants (Allergan) Class IV (new) Approved 2018-06-19</p>	

<p>action - recall or warning)</p> <p>Limited detail</p>	<p>Recall ACCOLADE Pacemaker 2017-12-19 Type II Hazard Intermittent oversensing of the Minute Ventilation (MV) sensor signal with certain Boston Scientific pacemaker and cardiac resynchronization therapy pacemaker systems (pacemakers). MV sensor signal oversensing may cause pre-syncope or syncope due to periods of pacing inhibition.</p> <p>Recall 2017-11-17 Nanostim Leadless Cardiac Pacemaker Type II Hazard As part of Abbott's post market surveillance and clinical trial monitoring processes, we have been made aware of docking button detachments that have occurred following implant or during attempted retrieval of Nanostim Leadless Cardiac Pacemaker (LCP) devices, model number SIDLCP. In all three cases that have occurred, there has been no impact to the electrical function (e.g., pacing, sensing, communication) and no clinical impact or symptoms resulting from the docking button detachment or exposed cables.</p>	<p>Recall (lots/serial #s) 2017-08-15 Type III Hazard Potential for intermittent cracks in the raw material batch used to produce the affected products. The cleanliness of the affected products could be compromised if cracks penetrate the surface of the instrument as a result of the raw material issue.</p> <p>Triathlon Total Knee System (Howmedica Osteonics) Class III (amendment) Approved 2020-01-29</p> <p>Recall (lots/serial #s) 2018-02-02 Type III Hazard Stryker has discovered that the product/lot combination may contain the incorrect size implant from what is labeled on the box.</p>	<p>Recall (lots/serial #s) 2019-05-30 Type II Hazard Health Canada has suspended the licenses for Allergan's Biocell textured breast implants (the only macro-textured implants available in Canada), based upon the rare but serious risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), Allergan is voluntarily recalling BioCell breast implants as a precautionary measure.</p> <p>Advisory 2019-05-28 Health Canada suspends Allergan's licences for its Biocell breast implants after safety review concludes an increased risk of cancer (SEE separate file for text of this record)</p> <p>Saline Filled Breast Implant (Ideal Implant) Class IV (new) Issued 2015-02-18</p> <p>Recall (lots/serial #s) 2019-05-30 Type II Hazard Health Canada has suspended the licenses for Allergan's BioCell textured breast implants (the only macro-textured implants available in</p>	<p>Other mesh: Recall Capiro Vaginal Support System 2018-02-15 (lots/serials) Type II Hazard Increasing trend in reports regarding the Capiro suture regarding the Capiro suture breakage and/or detachment of the Capiro suture darts from both the Capiro suture and the pelvic floor kit mesh assembly</p> <p>Advisory 2019-07-26 Before considering surgery to repair POP: Ask your surgeon or physician about all treatment options and understand the risks and benefits of each treatment option. There are options that do not involve surgery, and surgical options that do not involve mesh (SEE separate file for text of this record)</p> <p>IUDs Cut 380A QL Intrauterine Device (Mona Lisa) Class III Approved 2011-11-22 NONE</p> <p>Flexi-T Intrauterine Device (Prosan International) Class III (amendment) Approved 2020-05-19 NONE</p>
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			<p>Canada), based upon the rare but serious risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), Allergan is voluntarily recalling Biocell breast implants as a precautionary measure.</p> <p>Advisory 2017-11-24 A safety review on the risk of BIA-ALCL was initiated by Health Canada to determine a Canadian-specific rate of BIA-ALCL cases relative to the number of implants sold over the past 10 years. The safety review determined that the rate of BIA-ALCL reported to Health Canada is low and cases are mainly associated with breast implants with textured surfaces.</p> <p>Advisory 2019-05-28 Included in above advisory with Biocell silicone implants and Allergan removed from market</p>	<p>Other intrauterine devices Recall (lots/serials) 2015-12-22 Type II Hazard Bayer observed an increase in reports of device breakage for Nova-T In 2015. The reported breakage was noticed during insertion, or shortly after insertion, in connection with expulsion of the T-body loop with attached threads.</p>
<p>COMMUNICATION Canada Vigilance Adverse Reaction Database: Reports are submitted by consumers, health professionals and industry. Includes type of reaction, serious/not serious. Data from 1965 to 2020-09-30</p>	<p>Searches: pacemaker, Micra, Acuity, Altrua, Endotak, ACCOLDADE, Nanostim Results: none</p>	<p>Searches: knee, Persona, Triathlon, Legion Results: none</p>	<p>Searches: breast, Natrelle, Memory Gel, Saline Results: none</p>	<p>Searches: mesh, Gynemesh, Capio Results: none IUD 41 adverse reaction reports SEE pdf export file</p>

<p>Canadian Adverse Reaction Newsletter: monthly predecessor of Health Product Infowatch; includes a few detailed summaries of HC review/outcome for specific items and quarterly summary of health professional and consumer advisories NOT searchable 1991-2014</p> <p>Scan of topics in each issues shows focus is on drugs other than Lyme disease test kit and wound closure products</p>	<p>November 2016 Issue <i>St. Jude Medical implantable defibrillators</i></p> <p>Health Canada informed Canadians that some batteries in implantable cardioverter defibrillators and cardiac resynchronization therapy devices manufactured by St. Jude Medical may deplete earlier than expected. Early battery depletion may occur suddenly, anywhere between hours and days, and without warning. Link to Recalls and Safety Alerts 2016-10-15 SEE online https://healthcanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/60592a-eng.php</p>		<p>June 2019 Issue <i>Biocell breast implants</i></p> <p>Health Canada's safety review evaluated the risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). This safety review found that there was an increased risk of BIA-ALCL with the use of highly textured (macro-textured) implants, in comparison with those having less textured or smooth implants. Biocell breast implants made by Allergan are the only macro-textured implants currently available in Canada. Health Canada has suspended the licences held by Allergan for their Biocell textured breast implants. Health Canada will work with all breast implant</p>	<p>Single incision mini-sling made from non-absorbable synthetic material (polypropylene)</p> <p>October 2020 Issue <i>Single incision mini-sling made from non-absorbable synthetic material (polypropylene)</i></p> <p>This safety review evaluated the long-term (beyond 3 years) safety and effectiveness of single incision mini-slings (SIMS) used to treat stress urinary incontinence. Health Canada's review could not make conclusions due to lack of high quality post-market information. Health Canada has asked for additional long-term post-market safety and effectiveness information, including clinical data from the literature and ongoing clinical</p>
<p>Health Product InfoWatch</p> <p>Monthly newsletter on product advisories and other safety information aimed primarily at healthcare professionals. Each publication includes a monthly recap of health product advisories and summary safety reviews, as well as a growing selection of new health product safety information. Selection of items; not meant to be comprehensive. Published since 2015. Issues available online. NOT searchable.</p>	<p>August 2016 Issue <i>Trifecta Heart Valve</i></p> <p>This safety review evaluated the risk of structural valve deterioration associated with the use of Trifecta</p>			

<p>Browsed all issues; not all issues include mention of devices; emphasis on drugs; devices mentioned: barbed sutures, EpiPen, percutaneous radiofrequency ablation catheters, Ophthalmic viscosurgical devices, SurgiWrap adhesion barrier film, fentanyl-detection test strips, Paradigm insulin infusion pump, thermography devices, intraocular lenses, NovOpen insulin cartridge holders, infrared thermometers, hospital beds, colorectal stents, intranasal mucosal atomization device, kidney dialysis machines, surgical heater-cooler devices, Cook Catheters with Beacon Tip Technology, digital temperature thermometers, System 83 Plus device to reprocess complex endoscopes, Becton-Dickinson disposable syringes, negative pressure wound therapy device</p>	<p>heart valve. Health Canada's review concluded that there was not enough long-term evidence available to make changes to the instructions for use at this time. Health Canada will continue to monitor safety information including the manufacturer's 10-year long patient studies and other patient safety reports regarding the Trifecta heart valve. Link to Summary Safety Review 2016-08-15 SEE online <u>https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-trifecta-heart-valve-assessing-potential-risk.html</u></p>		<p>manufacturers to strengthen the instructions for Use of all breast implants regarding the risk of BIA-ALCL. Health Canada has also communicated this information to Canadians. Link to Summary Safety Review 2019-05-30 SEE file</p> <p>March 2019 Issue <i>Breast implants</i></p> <p>Health Canada is in the process of updating its safety review of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) following an increase in reports of Canadian cases. As of January 1, 2019, Health Canada has received reports of 22 confirmed and 22 suspected Canadian cases of BIA-ALCL. In its initial safety review in 2017, Health Canada found that the rate of BIA-ALCL cases was low, with 5 confirmed Canadian cases of BIA-ALCL reported by Canadian manufacturers in the last 10 years. Increased awareness by healthcare professionals and the public about BIA-ALCL is believed to be contributing to the increased reporting of cases of BIA-ALCL to Health Canada. Link to Recall and Safety Alerts 2019-02-12. SEE file</p> <p>December 2017 Issue</p>	<p>studies, from the manufacturers of SIMS. Health Canada plans to review SIMS within one year, taking into account the new and additional information provided by the manufacturers. Link to Summary Safety Review 2020-09-18 SEE file</p> <p>August 2019 Issue <i>Surgical mesh products</i></p> <p>This safety review evaluated the risk of complications associated with non-absorbable synthetic surgical mesh for the transvaginal repair of pelvic organ prolapse (POP). Health Canada's safety review found that, compared to other treatment options, the transvaginal implantation of non-absorbable synthetic surgical mesh to treat posterior compartment prolapse poses a greater risk of complications. Health Canada's review also found that the use of non-absorbable synthetic mesh for the transvaginal surgical repair of anterior and/or apical prolapse should only be used for patients who have significant risk factors for recurrence of POP, patients that have recurrent POP, or for whom alternative surgical treatments are not appropriate. Health Canada is working with the manufacturer to remove synthetic surgical</p>
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			<p><i>Breast implants</i></p> <p>This safety review evaluated the risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). Health Canada's safety review determined that the rate of BIA-ALCL in Canada is low. Nearly all the cases were associated with implants that have a textured surface. Health Canada is working with manufacturers who will update the safety information on the product labelling for breast implants. In addition, Health Canada will actively monitor all reported Canadian cases of BIA-ALCL through a yearly follow-up with the manufacturers of breast implants. Health Canada has also communicated this information to healthcare professionals and the public. Link to Summary Safety Review 2017-11-24 and Recall and Safety Alerts 2017-11-24 SEE online</p>	<p>mesh devices indicated for the transvaginal repair of posterior compartment POP from the Canadian market. Health Canada has also communicated this safety information to Canadians. Link to Summary Safety Review 2019-07-29 SEE file</p> <p>October 2017 Issue <i>Levonorgestrel-releasing intrauterine systems</i></p> <p>This safety review evaluated the risk of suppressed lactation associated with levonorgestrel-releasing intrauterine systems (Mirena, Jaydess and Kyleena). Health Canada's review concluded that there is currently limited evidence to suggest a link. Health Canada is considering updating the Canadian product monographs for these products to mention that cases of decreased breast milk production have been reported. Link to Summary Safety Review 2017-09-21 SEE file</p>
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June 2016 Issue

Essure Permanent Birth Control System

This safety review evaluated the potential risk of complications such as changes in menstrual bleeding, unintended pregnancy, chronic pain, perforation and migration of device, allergy and sensitivity or immune-type reactions with the use of Essure. Health Canada's review concluded that there are risks associated with the use of Essure that need to be better communicated and further monitored. Health Canada will work with the manufacturer to strengthen the product labelling regarding these safety concerns and to develop a Patient Information Sheet and Checklist intended to be reviewed and signed prior to the use of the device. Health Canada has also communicated this information to healthcare professionals. [Link to Summary Safety Review 2016-05-25 and Recalls and Safety Alerts 2016-05-30](#)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-essure-permanent-birth-control-system-assessing-risk.html>
<https://healthcanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/58638a-eng.php>

APPENDIX 10. Data extracted from device-specific documents

Document	Purpose	SGBA+ Content			SGBA+ Flags
		Sex	Gender	Intersectionality	
BREAST IMPLANTS Natrelle 410 Truform Microcell Silicone-Filled Breast Implants Class IV (new licence) Approved 2018-06-19	Purpose of application, information reviewed by Health Canada, decision issued, date of decision	Relevant to sex only because biological females use breast implants Revision of previous breast augmentation or reconstruction to correct or improve the results of the previous surgery	---	A woman must be at least 22 years old for breast augmentation	No details about SGBA+ For example, information reviewed by Health Canada: "Safety and effectiveness was supported by conformity to applicable standards, physical and mechanical bench testing such as gel bleed testing, similarities to previously approved 410 Biocell implants, and worldwide marketing history data with comparison between the subject device and the predicate"
Potential Risk of Cancer (Breast implant associated anaplastic large cell lymphoma) Issued: 2019-05-30	Includes key messages, overview, safety review findings, conclusions and action and references	Relevant to sex only because biological females use breast implants	---	---	No details about SGBA+ For example, no information about patient characteristics in studies or post-market surveillance data reviewed
Identified in Drug & Health Product Register (summary safety review) Memory Gel Cohesive III (Mentor Medical Systems) Class IV (annual update with conditions) Issued 2017-10-10 68 incidents	Includes date of approval, hazard severity and description of incident	---	---	---	No details about SGBA+ Hazard Severity: I (potential for death/injury) 2019-06-26 E2303 - Capsular Contracture A0101 - Patient-Device Incompatibility A0406 - Material Deformation A0412 - Material Rupture Capsular contracture associated with breast
Identified in Drug & Health Product Register (medical device incidents)					

<p>Natrelle 410 Truform Microcell Silicone-Filled Breast Implants (Allergan) Class IV (new) Approved 2018-06-19</p> <p>Identified in Recalls and Safety Alerts</p>	<p>Includes starting date, posting date, communication type, hazard classification, reason and affected products</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No details about SGBA+ Recall 2019-05-30 Hazard Severity: II (may cause temporary adverse health consequences) Health Canada has suspended the licenses for Allergan's Biocell textured breast implants (the only macro-textured implants available in Canada), based upon the rare but serious risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). Allergan is voluntarily recalling Biocell breast implants as a precautionary measure.</p>
<p>Biocell breast implants June 2019 Issue</p> <p>Identified in Health Product Infowatch (monthly newsletter on product advisories and other safety information aimed primarily at healthcare professionals)</p>	<p>Includes possible complications, indications and link to <u>Summary Safety Review</u></p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No details about SGBA+ Health Canada's safety review evaluated the risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). This safety review found that there was an increased risk of BIA-ALCL with the use of highly textured (macro-textured) implants, in comparison with those having less textured or smooth implants. Biocell breast implants made by Allergan are the only macro-textured implants currently available in Canada. Health Canada has suspended the licences held by Allergan for their Biocell textured breast implants. Health Canada will work with all breast implant manufacturers to strengthen the instructions for Use of all breast implants regarding the risk of BIA-ALCL. Health Canada has also communicated this information to Canadians</p>

MESH			---		
<p>Gynecare Gynemesh (Ethicon) Class III Approved 2009-11-20 Public release 2019-08-29</p> <p>Clinical Evaluation Report (111 p) provided by Ethicon with redacted sections</p> <p>Identified in Clinical Information on Drugs & Health Products (data on tests and trials used to evaluate safety and efficacy released upon completion of regulatory review)</p>	<p>Includes literature review, clinical data, post-market surveillance data and benefits versus risk analysis (includes redacted sections)</p>	<p>Relevant to sex only because used to treat pelvic issues among biological females</p> <p>Contraindications:</p> <ul style="list-style-type: none"> Should not be used in infants, children, pregnant women, or in women planning future pregnancies, because the mesh will not stretch significantly as the patient grows Should not be used in the presence of active or latent infections or cancers of the vagina, cervix, or uterus 		<p>Critical analysis of literature</p> <p>“Two factors were repeatedly cited as risks for vaginal graft exposure: increasing patient age and concomitant hysterectomy and/or rectocele repair at the time of vaginal prolapse repair...” (p 86)</p>	<p>Little detail about SGBA+ Literature review of equivalent products</p> <p>No details about participant characteristics or statistical data (only notes if product is similar or different)</p> <p>Clinical data on safety/efficacy For each of 50 included studies, lists total number of patients and results with statistics, but no patient characteristics or overall sub-analyses by those characteristics. Complications or safety concerns also noted across studies, but further sub-analyses by patient characteristics not provided.</p> <p>Post-market surveillance data</p> <p>No details about the characteristics of women who experienced problems: 473 complaints from 2010-2012 involving 467 serious injuries</p> <p>Benefits versus risk analysis</p> <p>No details about gender or intersectionality</p> <p>Conclusion: “The literature review data, taken together with previously available clinical and preclinical data, are sufficient to demonstrate State of Art compliance with the essential requirements covering safety and performance of GYNECARE GYNEMESH™ PS under normal conditions of use.”</p>

<p>Gynecare Gynemesh (Ethicon) Class III Approved 2009-11-20 Public release 2019-08-29 50 incidents</p> <p>Identified in Drug & Health Product Register (medical device incidents)</p>	<p>Includes date of approval, hazard severity and description of incident</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Hazard severity: II (may cause temporary adverse health consequences)</p> <p>2019-07-10 (injury) Blood loss (Retired - use 234) E2324 - Incontinence E2326 - Inflammation Injury (Retired - use 636) Revision surgery (Retired - use 1257) A040503 - Material Erosion B12 - Trend Analysis B14 - Analysis of Production Records B17 - Device Not Returned C20 - No Findings Available D15 - Cause Not Established</p>
<p>Capio Vaginal Support System 2018-02-15</p> <p>Identified in Recalls and Safety Alerts</p>	<p>Includes starting date, posting date, communication type, hazard classification, reason and affected products</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Hazard severity: II (may cause temporary adverse health consequences)</p> <p>Increasing trend in reports regarding the Capio suture breakage and/or detachment of the Capio suture darts from both the Capio suture and the pelvic floor kit mesh assembly</p>
<p>Surgical mesh products made from polypropylene for repair of pelvic organ prolapse</p> <p>Identified in Drug & Health Product Register (summary safety review)</p>	<p>Includes key messages, overview, safety review findings, conclusions and action and references</p>	<p>Relevant to sex only because used to treat pelvic issues among biological females</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p>

<p>Surgical mesh products (for repair of pelvic organ prolapse)</p> <p>Identified in Health Product Infowatch (monthly newsletter on product advisories and other safety information aimed primarily at healthcare professionals)</p>	<p>Includes possible complications, indications and link to <u>Summary Safety Review</u></p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No details about SGBA+</p> <p>This safety review evaluated the risk of complications associated with non-absorbable synthetic surgical mesh for the transvaginal repair of pelvic organ prolapse (POP). Health Canada's safety review found that, compared to other treatment options, the transvaginal implantation of non-absorbable synthetic surgical mesh to treat posterior compartment prolapse poses a greater risk of complications. Health Canada's review also found that the use of non-absorbable synthetic mesh for the transvaginal surgical repair of anterior and/or apical prolapse should only be used for patients who have significant risk factors for recurrence of POP, patients that have recurrent POP, or for whom alternative surgical treatments are not appropriate. Health Canada is working with the manufacturer to remove synthetic surgical mesh devices indicated for the transvaginal repair of posterior compartment POP from the Canadian market. Health Canada has also communicated this safety information to Canadians.</p>
<p>IUD</p> <p>Cut 380A QL Intrauterine Device (Mona Lisa) Class III</p> <p>Approved 2011-11-22 Public release 2019-08-23</p>	<p>Analysis of an existing literature review published in 2010</p>	<p>Relevant to sex only because prevents pregnancy among biological females</p> <p>Contraceptive failure The overall risk of ectopic pregnancy is decreased in</p>	<p>---</p>	<p>Contraceptive failure Several studies have demonstrated that younger women are more likely to experience contraceptive failure with a copper IUD</p>	<p>Little detail about SGBA+</p> <p>Document provides no detail on the characteristics of women included in reviewed studies, thus the range of gender and inter-sectional factors are largely not addressed</p>

<p>Pre-Market Review (27 p)</p> <p>Identified in Clinical Information on Drugs & Health Products (data on tests and trials used to evaluate safety and efficacy released upon completion of regulatory review)</p>		<p>women using a Copper T-380A. (p 4)</p> <p>Contraindications There are five distinct categories of contraindications: infection, pregnancy, uterine factors, gynecologic cancer, and adverse reactions to copper. (p 6)</p> <p>User acceptability Bleeding and dysmenorrhea are the most frequent reasons for copper IUD discontinuation. (p 7)</p> <p>Special groups: Concern about future fertility should not be a deterrent to copper IUD use in nulliparous women. (p 9)</p> <p>Insertion of IUDs in the postabortion and postpartum setting is ideal. Women are highly motivated to use contraception at this time and are often in a health care setting with clinicians capable of inserting the devices. (p 10)</p>		<p>than older women. However, it should be noted that the copper IUD is still more efficacious than other contraceptive methods in this age group. (p 3)</p> <p>Special groups: With this paucity of data, it is difficult to comment on the use of the Copper T-380A in adolescents. (p 9)</p>	<p>Approved 2020-05-19</p>
<p>Flexi-T Intrauterine Device (Prosan International)</p>	<p>Date of device approval</p>	<p>---</p>	<p>---</p>	<p>---</p>	

<p>Class III (amendment) Approved 2020-05-19</p> <p>Identified in Drug & Health Product Register (regulatory decision summary)</p>					<p>No SGBA+ details</p> <p>Hazard severity: 1 (potential for death/injury)</p> <p>Details not specified</p>
<p>Cut 380A QL Intrauterine Device (Mona Lisa) Class III Approved 2011-11-22 5 incidents</p> <p>Identified in Drug & Health Product Register (medical device incidents)</p>	<p>Includes date of approval, hazard severity and description of incident</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Safety Review Findings</p> <ul style="list-style-type: none"> 24 published studies about women who were breastfeeding and using LNG-IUS products were reviewed. The studies concluded that the use of LNG-IUS provides highly effective birth control and that these products do not affect breastfeeding. At the time of the review, Health Canada had received 19 Canadian reports of decreased breast milk production in breastfeeding women using LNG-IUS. All the reports were for Mirena. For 13 reports, it was considered that the use of LNG-IUS may have played a role in breastfeeding difficulties. For 3 of these reports, it was considered that the LNG-IUS was probably associated with breastfeeding difficulties, as
<p>Birth control hormone (levonorgestrel, LNG)-releasing IUDs (Mirena, Jaydess and Kyleena) Issued 2017-09-21</p> <p>Identified in Drug & Health Product Register (summary safety review)</p>	<p>Includes key messages, overview, safety review findings, conclusions and action and references</p>	<p>Relevant to sex because only biological females use these devices</p> <p>Decreased breast milk production</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Safety Review Findings</p> <ul style="list-style-type: none"> 24 published studies about women who were breastfeeding and using LNG-IUS products were reviewed. The studies concluded that the use of LNG-IUS provides highly effective birth control and that these products do not affect breastfeeding. At the time of the review, Health Canada had received 19 Canadian reports of decreased breast milk production in breastfeeding women using LNG-IUS. All the reports were for Mirena. For 13 reports, it was considered that the use of LNG-IUS may have played a role in breastfeeding difficulties. For 3 of these reports, it was considered that the LNG-IUS was probably associated with breastfeeding difficulties, as

<p>Levonorgestrel-releasing intrauterine systems</p> <p>Identified in Health Product Infowatch (monthly newsletter on product advisories and other safety information aimed primarily at healthcare professionals)</p>	<p>Includes possible complications, and link to <u>Summary Safety Review</u></p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>breast milk production returned to normal when the LNG-IUS was removed. The remaining 3 reports did not have enough information to conclude that the LNG-IUS affected breast milk production.</p> <p>Conclusions and action</p> <ul style="list-style-type: none"> Health Canada's review concluded that there is currently limited evidence to suggest a link between LNG-IUS products and the risk of decreased breast milk production. <p>No SGBA+ details</p> <p>This safety review evaluated the risk of suppressed lactation associated with levonorgestrel-releasing intrauterine systems (Mirena, Jaydess and Kyleena). Health Canada's review concluded that there is currently limited evidence to suggest a link. Health Canada is considering updating the Canadian product monographs for these products to mention that cases of decreased breast milk production have been reported.</p>
<p>PACEMAKER</p> <p>Micra Transcatheter Pacemaker System (Medtronic) Class IV (new) Approved 2016-10-05</p> <p>Identified in Drug & Health Product Register (regulatory decision summary)</p>	<p>Includes date of approval</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Approved 2016-10-05</p>

Sigma Pacemaker System (Medtronic) Class IV (new) Approved 2019-11-11	Includes date of approval, hazard severity and description of incident	---	---	---	No SGBA+ details Hazard Severity: Potential for death/injury F1903 - Device Explantation F19 - Surgical Intervention E2403 - No Clinical Signs Symptoms or Conditions F1905 - Device Revision or Replacement A1102 - Application Program Problem A072201 - High Impedance A05 - Mechanical Problem F26 - No Health Consequences or Impact B01 - Testing of Actual/Suspected Device C19 - No Device Problem Found D14 - No Problem Detected
ACCOLADE Pacemaker, MRI Pacemaker, VISIONIST CRT-P and X4 CRT-P Identified in Recalls and Safety Alerts	Includes starting date, posting date, communication type, hazard classification, reason and affected products	---	---	---	No SGBA+ details Hazard severity: II (may cause temporary adverse health consequences) Reason: Intermittent oversensing of the Minute Ventilation (MV) sensor signal with certain Boston Scientific pacemaker and cardiac resynchronization therapy pacemaker systems (pacemakers). MV sensor signal oversensing may cause pre-syncope or syncope due to periods of pacing inhibition
TOTAL KNEE IMPLANTS Persona the Personalized Knee System (Zimmer) Class III (amendment) Approved 2020-07-30	Includes date of approval	---	---	---	Approved 2020-07-30

<p>Identified in Drug & Health Product Register (regulatory decision summary)</p>					<p>No SGBA+ details</p> <p>Hazard severity: II (may cause temporary adverse health consequences)</p> <p>2019-12-17 (injury)</p> <p>F12 - Serious Injury Illness Impairment</p> <p>F1905 - Device Revision or Replacement</p> <p>A040101 - Fracture</p> <p>B14 - Analysis of Production Records</p> <p>B20 - Device Not Accessible for Testing</p> <p>C20 - No Findings Available</p> <p>D15 - Cause Not Established</p>
<p>Identified in Drug & Health Product Register (medical device incidents)</p>	<p>Includes date of approval, hazard severity and description of incident</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Hazard severity: III (not likely to cause any adverse health consequences)</p> <p>Potential for intermittent cracks in the raw material batch used to produce the affected products. The cleanliness of the affected products could be compromised if cracks penetrate the surface of the instrument as a result of the raw material issue</p>
<p>Persona the Personalized Knee System (Zimmer) Class III (amendment) Approved 2020-07-30</p> <p>Identified in Recalls and Safety Alerts</p>	<p>Includes starting date, posting date, communication type, hazard classification, reason and affected products</p>	<p>---</p>	<p>---</p>	<p>---</p>	<p>No SGBA+ details</p> <p>Hazard severity: III (not likely to cause any adverse health consequences)</p> <p>Potential for intermittent cracks in the raw material batch used to produce the affected products. The cleanliness of the affected products could be compromised if cracks penetrate the surface of the instrument as a result of the raw material issue</p>