Appendix 1: Key Definitions

	Real-world data	Real-world evidence
FDA[1]	"Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD include data derived from electronic health records (EHRs), claims and billing data, data from product and disease registries, patient-generated data including in home-use settings, and data gathered from other sources that can inform on health status, such as mobile devices. RWD sources (e.g., registries, collections of EHRs, and administrative and health care claims databases) can be used as data collection and analysis infrastructure to support many types of trial designs, including, but not limited to, randomized trials, such as large simple trials, pragmatic clinical trials, and observational studies (prospective and/or retrospective)." *p.4*	"Real-world evidence (RWE) is the clinical evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of RWD." *p.4*
HC[12]	"Real-world data are data relating to patient status and/or the delivery of health care routinely collected from a variety of sources (e.g., data collected from data registries, electronic health records, etc)."	"Real-world evidence is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD (e.g., information derived from multiple RWD sources)."
IMI GetReal[13]	"An umbrella term for data regarding the effects of health interventions (e.g., safety, effectiveness, resource use, etc) that are not collected in the context of highly-controlled RCT's. Instead, RWD can either be primary research data collected in a manner which reflects how interventions would be used in routine clinical practice or secondary research data derived from routinely collected data. Data collected include, but are not limited to, clinical and economic outcomes, patient-reported outcomes (PRO) and health-related quality of life (HRQoL). RWD can be obtained from many sources including patient registries, electronic medical records, and claims databases." *p.27*	"Real-world evidence (RWE) is the evidence derived from the analysis and/or synthesis of real-world data (RWD)." *p.27*

HC = Health Canada; IMI = Innovative Medicines Initiative; RCT = randomized controlled trial.

CADTH

Appendix 2: Survey on the Use of RWE in Device Technology Assessments

Consent Form

Thank you for your interest in contributing to a CADTH report. Your input is both needed and highly valuable as it will inform decision-making on the management of health technologies in Canada. The purpose of this survey is to gather information that will be used to prepare a CADTH Environmental Scan report, which will be published on the CADTH website.

Your participation in this survey is voluntary. You may choose not to participate, or you may exit the survey at any time without penalty. It should take approximately 45 minutes to complete.

Your identifiable private information will be kept confidential. This consent form does not give CADTH permission to disclose your name. If any direct quotes from the survey results are required, respondents will be contacted separately to sign a personal communication form before publishing.

CADTH will summarize your responses in the published report and your organization may be identified as a source. However, you and the organization you represent (if applicable) are not responsible for the analyses, conclusions, opinions, and statements expressed by CADTH in the report. For detailed information on the purpose of this Environmental Scan entitled *"The Use of Real-World Evidence for Medical Device Assessment: An Environmental Scan,"* please see the invitation email from Yan Li (yan.li@cadth.ca).

ELECTRONIC CONSENT: Please select your choice.

By clicking on the Agree button you indicate that:

- you have read the aforementioned information
- you voluntarily agree to participate
- you authorize CADTH to use the information provided by you for the purpose as stated in this form.

If you do not wish to participate in the survey, please decline participation by clicking on the Disagree button.

☐ Agree ☐ Disagree

Name: _____

Title: _____

Province: _____

Phone (optional): _____

Date: DD/MM/YYYY _____

A. Context

1. **What organization do you represent?**
2. **Can RWE be included in the assessment of medical devices to answer questions of clinical effectiveness and/or safety in your organization?**

☐ Yes ☐ No

You can enter any additional comments here:

If you answered NO to this question, then this is the end of the survey. Thank you for your responses.

B. Use and Eligibility of RWE

Please answer based on your organization's perspective and current or accepted use of RWE.

3. **What gaps does RWE fill in the assessment of medical devices in terms of effectiveness and safety?** (Check all that apply.)

☐ Establish the effectiveness of the intervention in the absence or isolation of RCT evidence

☐ Supplement the RCT evidence on effectiveness of therapy

☐ Establish the safety of the intervention in the absence or isolation of RCT evidence

☐ Supplement the RCT evidence on safety

☐ Validate surrogate outcomes

☐ Inform cost-effectiveness and utilization

☐ Other purpose (please specify)

4. Please select the circumstances in which RWE brings significant added value and should be given more weight relative to conventional situations where the evidence base consists of RCT data of sufficient quality and quantity. (Check all that apply.)

☐ Rare condition

☐ Population not well-studied in RCTs (few and/or small RCTs)

☐ Significant unmet clinical need

☐ Innovative or breakthrough technology

☐ Potentially large budget impact

☐ RWE with superior external validity relative to the population of interest

☐ Not applicable; no circumstance can influence the weighting of clinical evidence

☐ Other (please specify)

5. Please choose the RWE study designs eligible for inclusion for assessments. (Check all that apply.)

	Effectiveness	Harms and Safety
Cross-sectional studies	☐	☐
Case-control studies	☐	☐
Prospective cohort studies	☐	☐
Retrospective cohort studies	☐	☐
Pragmatic trials[a]	☐	☐
Uncontrolled single-arm studies	☐	☐
Other (please specify)	☐	☐

[a] Large simple trials designed to test the effectiveness of an intervention in broad routine clinical practice.

6a. What data sources can be used to generate eligible RWE? (Check all that apply.)

☐ EHR / EMR

☐ Hospital database

☐ Homecare database

☐ Patient safety and learning system

☐ Data registry

☐ Physician database

☐ All-payer claims database

☐ Private health insurance plan claims database

☐ Supply chain database

☐ Patient-generated data

☐ Electronic or paper-based patient file managed by a clinician or health care facility

☐ Other (please specify)

6b. Are there circumstances that would allow exceptions to the acceptability of a data source?

7a. Does your organization request RWE from manufacturers to complement an assessment?

☐ Yes ☐ No

7b. If yes, are there mandatory requirements regarding study design and data sources?

☐ Yes ☐ No

7c. If yes, what are the requirements?

7d. If yes, what are the consequences (if any) of non-conformity?

8. Where eligible RWE is accepted, does it need to be captured from individuals treated in your jurisdiction?

☐ Yes ☐ No

9a. Does your agency have any plans to change its current approach relative to RWE in the future?

☐ Yes ☐ No ☐ Uncertain

9b. If yes, please share the rationale and briefly summarize any concrete plan of action?

10. According to your perceptions, what are the added benefits of using RWE for device assessments, in comparison to, for example, RCT evidence?

11. According to your perceptions, what are the challenges of using RWE for device assessments? What are possible solutions to such challenges?

12. How do you reconcile conflicting results from RWE and RCT evidence? Please describe your decision-making processes, if any.

C. Case Example

To better understand the use of RWE in practice, please provide an example of a device assessment in which RWE was included, appraised, considered, and had an impact on either the regulatory decision or HTA.

13. Please provide information on a device that was reviewed by your organization using RWE. (Please limit to RWE submitted for the purpose of addressing questions of safety and/or effectiveness.)

Device name: _____

Manufacturer name (if applicable): _____

Target population: _____

Year of review: _____

Indication reviewed: _____

14. What types of study designs, including RWE, were eligible for inclusion for the assessment? (Check all that apply.)

☐ RCT

☐ Cross-sectional studies

☐ Case-control studies

☐ Prospective cohort studies

☐ Retrospective cohort studies

☐ Pragmatic trials

☐ Uncontrolled single-arm studies

☐ Other (please specify)

15. What data sources were used for the RWE? (Check all that apply.)

☐ EHR/EMR

☐ Hospital database

☐ Home care database

☐ Patient safety and learning system

☐ Data registry

☐ Physician database

☐ All-payer claims database

☐ Private health insurance plan claims database

☐ Supply chain database

☐ Patient-generated data

☐ Electronic or paper-based patient files managed by a clinician or health care facility

☐ Other (please specify)

16. What aspect(s) of the device review did the RWE help inform? (Check all that apply.)

☐ Effectiveness (relative to control, baseline health states, or a comparator)

☐ Safety (relative to control, baseline health states, or a comparator)

☐ Adherence to treatment

☐ Validity of surrogate outcomes

☐ Utilization data (e.g., resource use, hospitalization data)

☐ Coverage or payment information

☐ Other (please specify)

17. In your opinion, in what way and to what extent did the RWE add value to the device review and/or did it influence the regulatory decision or HTA recommendation?

18. If required, would you be open or willing to participate in a follow-up email or phone interview regarding this survey and its content?

☐ Yes ☐ No

Appendix 3: Information on Survey Respondents

National

CADTH
Location: Ottawa and Toronto
Type of Organization: National (pan-Canadian)
Canadian Jurisdictions Served: All (with the exception of Quebec)
Website: https://www.cadth.ca/

Health Canada
Medical Devices Directorate Offices: Cardiovascular Device Evaluation, Digital Health Device Evaluation, Post-Market Evaluation
Location: Ottawa
Type of Organization: National
Canadian Jurisdictions Served: All
Website: https://www.canada.ca/en/health-canada/corporate/about-health-canada/branches-agencies/health-products-food-branch/medical-devices-directorate.html

Alberta
Institute of Health Economics (IHE)
Location: Edmonton
Type of Organization: Provincial
Canadian Jurisdictions Served: All
Website: https://www.ihe.ca/

British Columbia
British Columbia Health Technology Assessment Office (BC-HTAO)
Location: Vancouver
Type of Organization: Provincial
Canadian Jurisdictions Served: British Columbia
Website: https://www2.gov.bc.ca/gov/content/health/about-bc-s-health-care-system/partners/health-authorities/bc-health-technology-assessment

Ontario
Ontario Health (Quality)
Location: Toronto
Type of Organization: Provincial
Canadian Jurisdictions Served: Ontario
Website: https://www.hqontario.ca/Evidence-to-Improve-Care/Health-Technology-Assessment

Quebec
Institut national d'excellence en santé et en services sociaux (INESSS)
Location: Montréal
Type of Organization: Provincial
Canadian Jurisdictions Served: Quebec
Website: https://www.inesss.qc.ca/

Appendix 4: Eligibility Criteria for Inclusion of RWE in Device Assessments

Survey question	Response	Number of responses (% of total)	
		HC (N = 5)	HTA agencies (N = 5)
Can RWE be included in the assessment of medical devices to answer questions of clinical effectiveness and/or safety in your organization?	☐ Yes	5 (100%)	5 (100%)
	☐ No	0 (0%)	0 (0%)
Please specify the RWE study designs eligible for inclusion for the assessment of effectiveness. (multiple answers were accepted)	☐ Cross-sectional studies	4 (80%)	3 (60%)
	☐ Case-control studies	5 (100%)	5 (100%)
	☐ Prospective cohort studies	5 (100%)	5 (100%)
	☐ Retrospective cohort studies	5 (100%)	5 (100%)
	☐ Pragmatic trials	5 (100%)	5 (100%)
	☐ Uncontrolled single-arm studies	5 (100%)	3 (60%)
	☐ Other	2 (40%)	1 (20%)
Please specify the RWE study designs eligible for inclusion for the assessment of harms/safety. (multiple answers were accepted)	☐ Cross-sectional studies	2 (40%)	4 (80%)
	☐ Case-control studies	4 (80%)	4 (80%)
	☐ Prospective cohort studies	4 (80%)	5 (100%)
	☐ Retrospective cohort studies	4 (80%)	4 (80%)
	☐ Pragmatic trials	3 (60%)	5 (100%)
	☐ Uncontrolled single-arm studies	4 (80%)	3 (60%)
	☐ Other		
What data sources can be utilized for the generation of eligible RWE? (multiple answers were accepted)	☐ EHR/EMR	5 (100%)	4 (80%)
	☐ Hospital database	5 (100%)	4 (80%)
	☐ Home care database	4 (80%)	3 (60%)
	☐ Patient safety and learning system	4 (80%)	4 (80%)
	☐ Data registry	5 (100%)	4 (80%)
	☐ Physician database	4 (80%)	2 (40%)
	☐ All-payer claims database	4 (80%)	2 (40%)
	☐ Private health insurance plan claims database	4 (80%)	2 (40%)
	☐ Supply chain database	4 (80%)	2 (40%)
	☐ Patient-generated data	4 (80%)	1 (20%)
	☐ Electronic or paper-based patient files managed by clinician(s) or health care facility	4 (80%)	2 (40%)
	☐ Other	2 (40%)	1 (20%)
Does your organization request RWE from manufacturers to complement an assessment?	☐ Yes	3 (60%)	1 (20%)
	☐ No	2 (40%)	4 (80%)
If yes, are there mandatory requirements regarding study design and data sources (if any)?	☐ Yes	1 (33.3%)	0 (0%)
	☐ No	2 (66.6%)	1 (100%)
		(N = 3)	(N = 1)

Survey question	Response	Number of responses (% of total)	
		HC (N = 5)	HTA agencies (N = 5)
Where eligible RWE is accepted, does it need to be captured from individuals treated in your jurisdiction?	☐ Yes ☐ No	1 (20%) 4 (80%)	1 (20%) 4 (80%)
Does your agency have any plans to change its current approach relative to RWE in the future?	☐ Yes ☐ No ☐ Uncertain	3 (60%) 0 (0%) 2 (40%)	1 (20%) 0 (0%) 4 (80%)

EHR = electronic health record; EMR = electronic medical record; HC = Health Canada; RWE = real-world evidence; pragmatic trials = large simple trials designed to test the effectiveness of an intervention in broad routine clinical practice.

Appendix 5: Use of RWE in Device Assessments

Survey question	Response	Number of responses (% of total)	
		HC (N = 5)	HTA Agencies (N = 5)
What gaps does RWE for effectiveness and safety fill in the assessment of medical devices? (Multiple answers were accepted.)	☐ Establish the effectiveness of the intervention in absence or isolation of RCT evidence	3 (60%)	3 (60%)
	☐ Supplement the RCT evidence on effectiveness of therapy	4 (80%)	5 (100%)
	☐ Establish the safety of the intervention in absence or isolation of RCT evidence	3 (60%)	3 (60%)
	☐ Supplement the RCT evidence of safety	4 (80%)	5 (100%)
	☐ Validate surrogate outcomes	3 (60%)	1 (20%)
	☐ Inform cost-effectiveness and utilization	0 (0%)	5 (100%)
	☐ Other purpose	2 (40%)	0 (0%)
Please select the circumstances in which RWE brings significant added value and should be given more weight, relative to conventional situations where the evidence base consists of RCT data of sufficient quality and quantity. (Multiple answers were accepted.)	☐ Rare condition	5 (100%)	5 (100%)
	☐ Population not well-studied in RCTs (few and/or small RCTs)	5 (100%)	5 (100%)
	☐ Significant unmet clinical need	3 (60%)	1 (20%)
	☐ Innovative/breakthrough technology	3 (60%)	3 (60%)
	☐ Potentially large budget impact	0 (0%)	3 (60%)
	☐ RWE with superior external validity relative to the population of interest	1 (20%)	3 (60%)
	☐ Not applicable: No circumstance can influence the weighting of clinical evidence	0 (0%)	0 (0%)
	☐ Other	0 (0%)	0 (0%)

HC = Health Canada; RCT = randomized controlled trial; RWE = real-world evidence.