

Rapid Response Systematic Review & Meta-Analysis Process

CADTH Evidence
Driven.

REVISION HISTORY

Periodically, this document will be revised as part of ongoing process improvement activities. The following version control table, as well the version number and date on the cover page, is to be updated when any updates or revisions are made.

Section	Revision Number	Date	Description/Changes Made

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ABBREVIATIONS

AGREE II	Appraisal of Guidelines for Research and Evaluation II Instrument
CADTH	Canadian Agency for Drugs and Technologies in Health
Director	Director, Health Technology Assessment and Rapid Response
HTA	Health Technology Assessment
KM	Knowledge Mobilization
NIHR CRD	National Institute for Health Research, Centre for Reviews and Dissemination
PDO	Program Development Office(r)
QUADAS	Quality Assessment of Diagnostic Accuracy Studies

1. INTRODUCTION

1.1. About Product

CADTH's Rapid Response Service offers Canadian health care decision-makers quick and efficient access to health technology information that is based upon the best available evidence.

A Rapid Response Systematic Review and Meta-Analysis responds to specific stakeholder research questions through a comprehensive review of the published evidence meeting predetermined inclusion criteria. If sufficient homogeneous studies meeting the inclusion criteria are identified, a meta-analysis is performed. The meta-analysis combines the data from selected studies and provides a statistical summary of outcomes such as safety and/or efficacy. As well as identifying and summarizing existing/published evidence on a topic, these reports also include possible implications for decision-making.

Systematic Review and Meta-analysis reports attempt to be as comprehensive as possible and follow standard methodological guidelines for the production of systematic review and meta-analysis reports. When appropriate, evidence retrieved is appraised using standardized, internationally recognized appraisal instruments such as AGREE II and QUADAS.

1.2. Scope

In order to meet short timelines, the scope of research questions used in Systematic Review and Meta-Analysis reports tends to be narrower than the scope of questions used in CADTH Health Technology Assessment and Optimal Use projects (i.e., may have no economic analysis or specific patient input process).

Topics suitable for Rapid Response Reports include evaluations of medical, surgical and dental technologies such as:

- drugs
- devices
- diagnostic tests
- medical, surgical and dental procedures.

Please talk to the [Liaison Officer](#) in your jurisdiction to clarify if a topic is suitable for Rapid Response or is better suited to another product line offered by CADTH.

1.3. Audience

1.3.1. Primary Audience

Decision-makers from participating* Canadian publicly funded jurisdictions are eligible to request a Rapid Response Report from CADTH. These include the following stakeholders:

- federal, provincial, and territorial health ministries
- health authorities
- hospitals
- national health care programs and regional health care programs.

* *Quebec and Ontario do not participate in CADTH's Rapid Response service.*

Rapid Response requests are made in confidence, and no identifying information is included when the reports are made public on cadth.ca.

1.3.2. Secondary Audience

Like all Rapid Response reports, Systematic Review and Meta-Analysis reports are freely available for review by anyone on cadth.ca.

1.4. Purpose and Application for Decision-Making

The purpose of Rapid Response Systematic Review and Meta-Analysis reports is to provide detailed evidence-based support to policy and health care decision-makers by identifying and summarizing existing, published evidence on a topic, and describing possible implications for decision-making. Systematic Review and Meta-analysis reports attempt to be as comprehensive as possible and follow standard international methodological guidelines. An overview of possible implications for decision- or policy-making is always included to help inform stakeholders.

Systematic Review and Meta-Analysis reports summarize available existing evidence in the most comprehensive manner possible given resources and timelines, however they should not be construed as a recommendation for or against the use of a particular health technology, nor are they intended to replace professional medical advice. Readers are also cautioned that a lack of good-quality evidence does not necessarily mean a lack of effectiveness, particularly in the case of new and emerging health technologies, for which little information can be found, but which may in future prove to be effective.

1.5. Transparency

CADTH makes every reasonable attempt to be as transparent and reproducible as possible within Rapid Response time constraints. At the start of each project, CADTH produces and registers a protocol documenting the report's methods. Every Systematic Review & Meta-Analysis includes the research questions, selection criteria, selection of included studies, evaluation tools used, methods, and search strategy. Within timelines every attempt is made for external feedback and review, including the following:

- A content expert reviews the included studies.
- The report is externally peer-reviewed by content experts and, if applicable, manufacturers (see section 2.3.1).
- A draft report is posted for stakeholder comment.

CADTH identifies evidence for possible inclusion in a Systematic Review and Meta-Analysis using all reasonable efforts within time constraints. The following are the main avenues used to identify evidence for these reports:

- Published literature is identified by searching major biomedical bibliographic databases using an internally peer-reviewed search strategy. Bi-weekly search updates are run for the duration of the review.

- Grey literature (literature that is not commercially published) is identified by searching relevant sections of the Grey Matters checklist (<http://www.cadth.ca/resources/grey-matters>). Internet search engines are used to identify additional web-based materials.
- For technologies such as drugs and devices, Canadian manufactures are contacted and given the opportunity to send studies and other relevant information.
- A content expert is engaged and given the opportunity to suggest evidence to be reviewed.
- Authors may hand-search the references of included studies.

Rapid Response Reports are freely posted on [cadth.ca](http://www.cadth.ca) although in exceptional circumstances, embargo periods may be considered. All drafts, search strategies, and working documents used to produce Rapid Response Reports are archived for 15 years and may be requested if required, with the exception of copyright-protected documents and information provided in confidence by customers, manufacturers or other agencies.

1.6. Timelines

Exact timelines will be negotiated between a CADTH representative and the customer at the time of topic refinement.

Product Type	Deliverables	Approximate turnaround time
	Report finalized.	4-5 months from point of topic refinement
Knowledge Mobilization Tools <i>(if requested)</i>	Tools finalized. <i>(if requested)</i>	5-6 months from point of topic refinement

1.7. Roles and Responsibilities

Product Type	Role	Responsibilities
Systematic Review & Meta-Analysis	Liaison Officer	Submits requests on behalf of customers, facilitates uptake of CADTH products and gathers evaluation and impact data on completed reports.
	Clinical Research Manager	Provides general oversight of project timelines, workload, contract approvals, and risk management. Also reviews the content and quality of the report.
	Program Development Officer	With lead author and Clinical Research Manager, the Program Development Officer prioritizes, scopes, and refines the topic. The PDO also seeks Director approval for the project.
	Project Manager	Once a project moves to production, the project manager monitors timelines and deliverables. He or she also coordinates the following: <ul style="list-style-type: none"> • requests for information from Canadian manufacturers (if necessary)

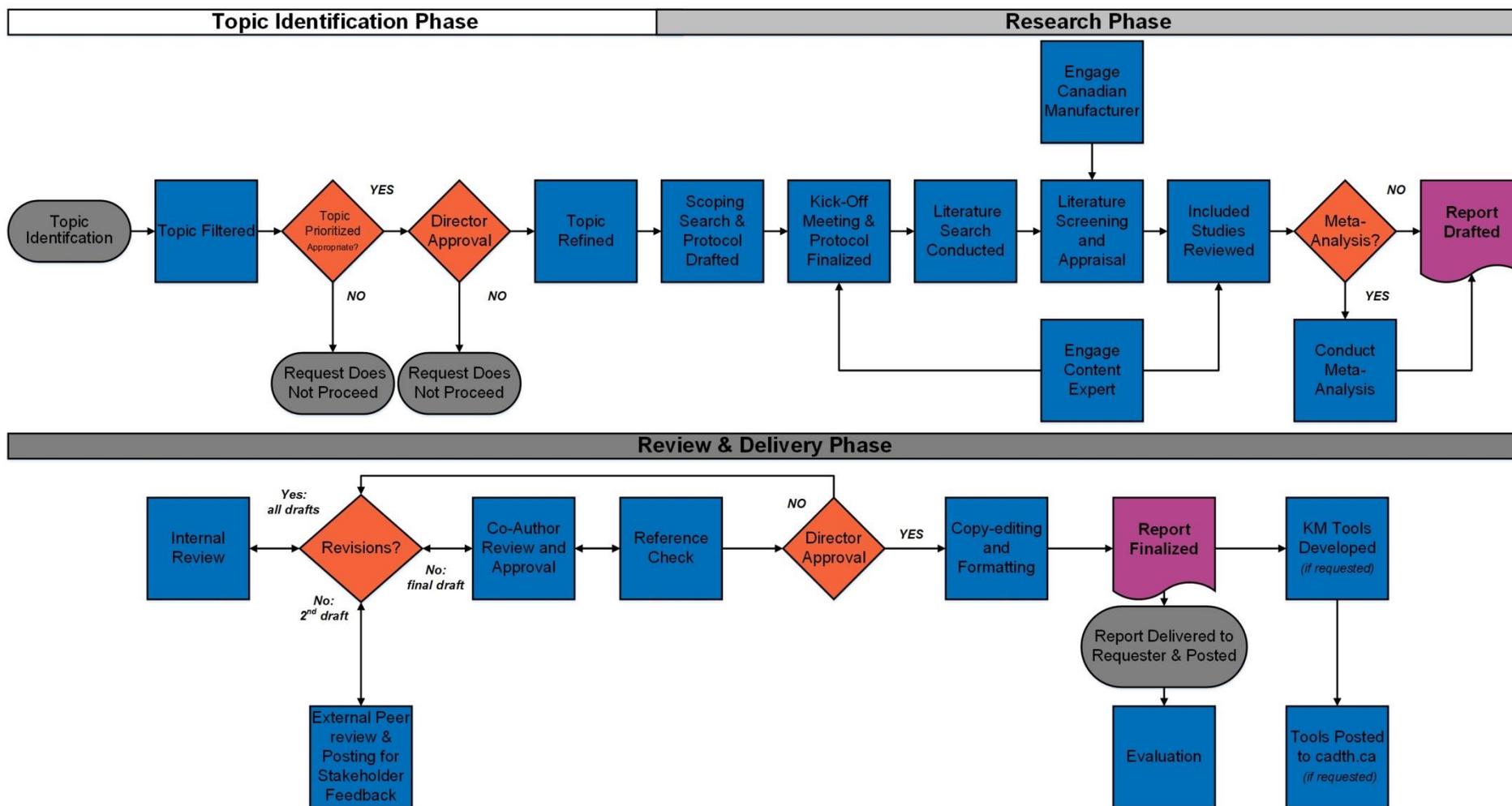
Product Type	Role	Responsibilities
		<ul style="list-style-type: none"> • team meetings • peer reviews • stakeholder feedback • posting reports.
	Information Specialist (lead)	Writes the draft search strategy and literature search methods for the protocol and final versions for the report. Conducts literature search and coordinates search alerts for duration of review. Ensures reference citations are accurate and follow Citing Medicine standards. Assigns medical subject headings and keywords to report metadata. If necessary, helps Project Manager identify Canadian Manufacturers to be contacted for input.
	Information Specialist (second)	Internally peer-reviews the search strategy for the lead Information Specialist.
	Information Technician	Retrieves selected references and delivers the full text to authors according to CADTH's Access Copyright license terms.
	Content Expert	Provides subject matter expertise throughout the production phase, including a review of the included studies selected by the authors.
	Canadian Manufacturers/Suppliers	May provide input for appraisal during the initial evidence-gathering stage and are given the opportunity to comment on the report draft.
	Author (lead)	Drafts protocol, co-screens literature, evaluates evidence, drafts report, addresses both internal and external review comments and makes revisions when needed. If possible the primary author also extracts data from included studies to conduct a meta-analysis.
	Author (second)	Co-screens literature and helps the primary author evaluate the evidence and draft both the protocol and the report.
	Internal & External Reviewers <i>(includes stakeholders when draft report is posted for comment)</i>	Review draft report and make suggestions for revisions.
	Knowledge Mobilization Officer	Participates in project meetings in order to represent the customer perspective.
	Scientific Advisor	Attends team meetings as needed to offer scientific advice on methods, quality, and standards.

Product Type	Role	Responsibilities
	Publishing Team	Responsible for copy-editing, formatting, and translating the following into French: <ul style="list-style-type: none"> • title • key findings • research questions • keywords for metadata.
	Director, Health Technology Assessment and Rapid Response	Approves project initiation and signs off on completed reports.
Knowledge Mobilization Tool(s) <i>If requested</i>	Knowledge Mobilization Officer	Develops knowledge mobilization tools for report as per customer requests.
	Clinical Research Manager	Reviews and approves knowledge mobilization tools.

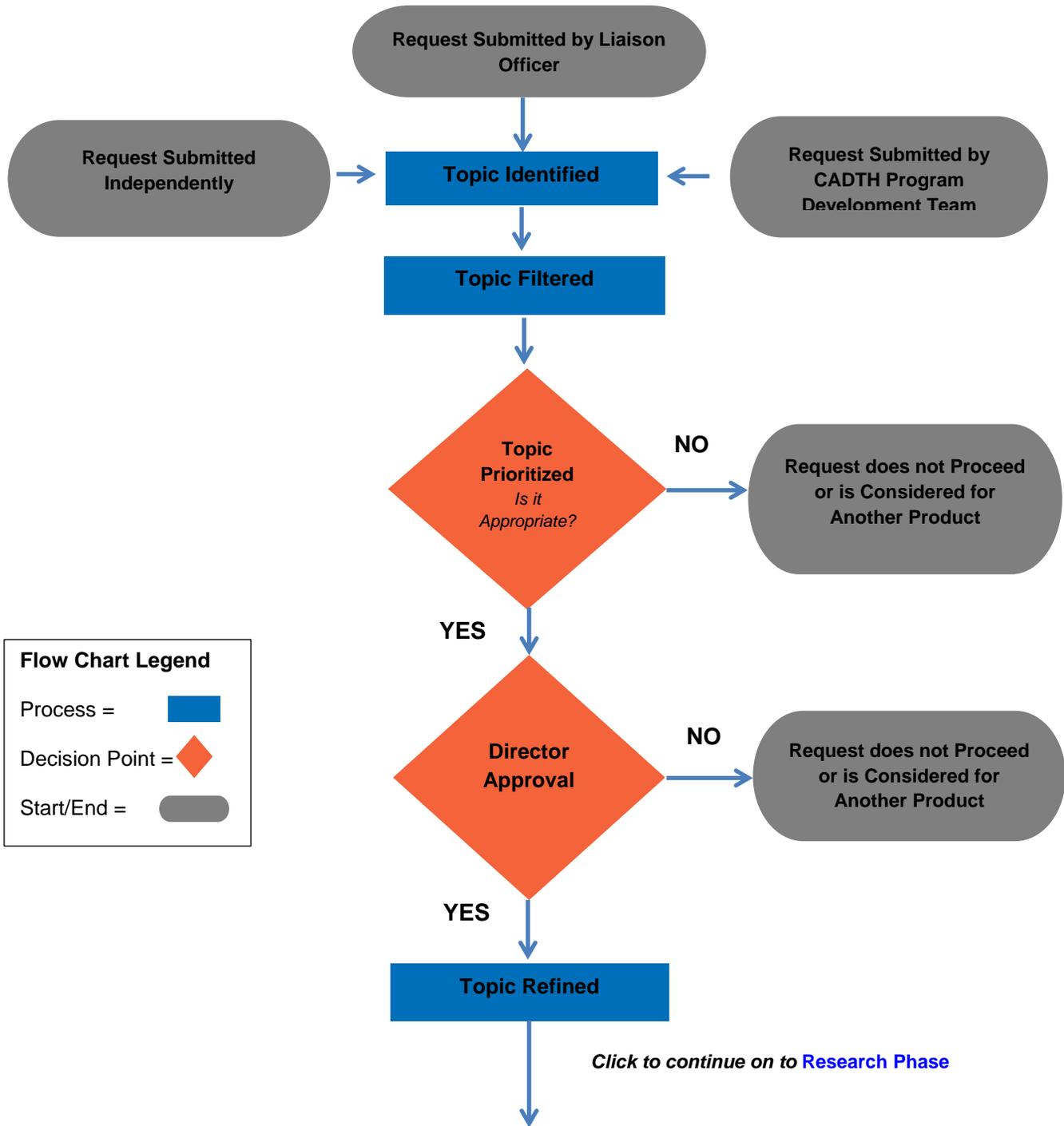
All Rapid Response products are supported by the Web team.

2. PROCESS

Process Flow Chart



2.1. Detailed Process: Topic Identification Phase
Ctrl click on individual processes for details



2.1.1. Topic Identified

Canadian publicly funded health care decision-makers (see “1.3 Audience”) can submit topics for Rapid Response Reports by contacting a CADTH [Liaison Officer](#) or by independently [submitting a request](#) on cadth.ca. Topics for Systematic Review and Meta-Analysis can also be suggested by CADTH’s Program Development Office in conjunction with stakeholder feedback.

2.1.2. Topic Filtered

Once a topic has been identified as a possible candidate for a Systematic Review and Meta-Analysis, it is sent to the Program Development Office to filter. A Program Development Officer (PDO) determines if the topic meets CADTH’s mandate (health technology, patient outcomes, CADTH customer). Topics that do not meet CADTH’s mandate do not proceed, otherwise they are prioritized.

2.1.3. Topic Prioritized

Information is gathered to determine if the topic is appropriate for a Systematic Review Meta-analysis product. The PDO organizes a meeting with Liaison Officers, requestor(s), experts, and the CADTH Director, to help judge the following appropriateness criteria for this higher-level product:

- existing evidence
- not a duplication of reviews completed by other agencies
- relevant to the Canadian health care context
- significant disease burden
- significant impact
- jurisdictional interest.

Topics determined to be highly relevant (see above criteria) are sent to the Director, Health Technology Assessment and Rapid Response for approval. If approved, the topic goes to the production phase, otherwise it does not proceed (see “2.1.5 Request Does not Proceed”).

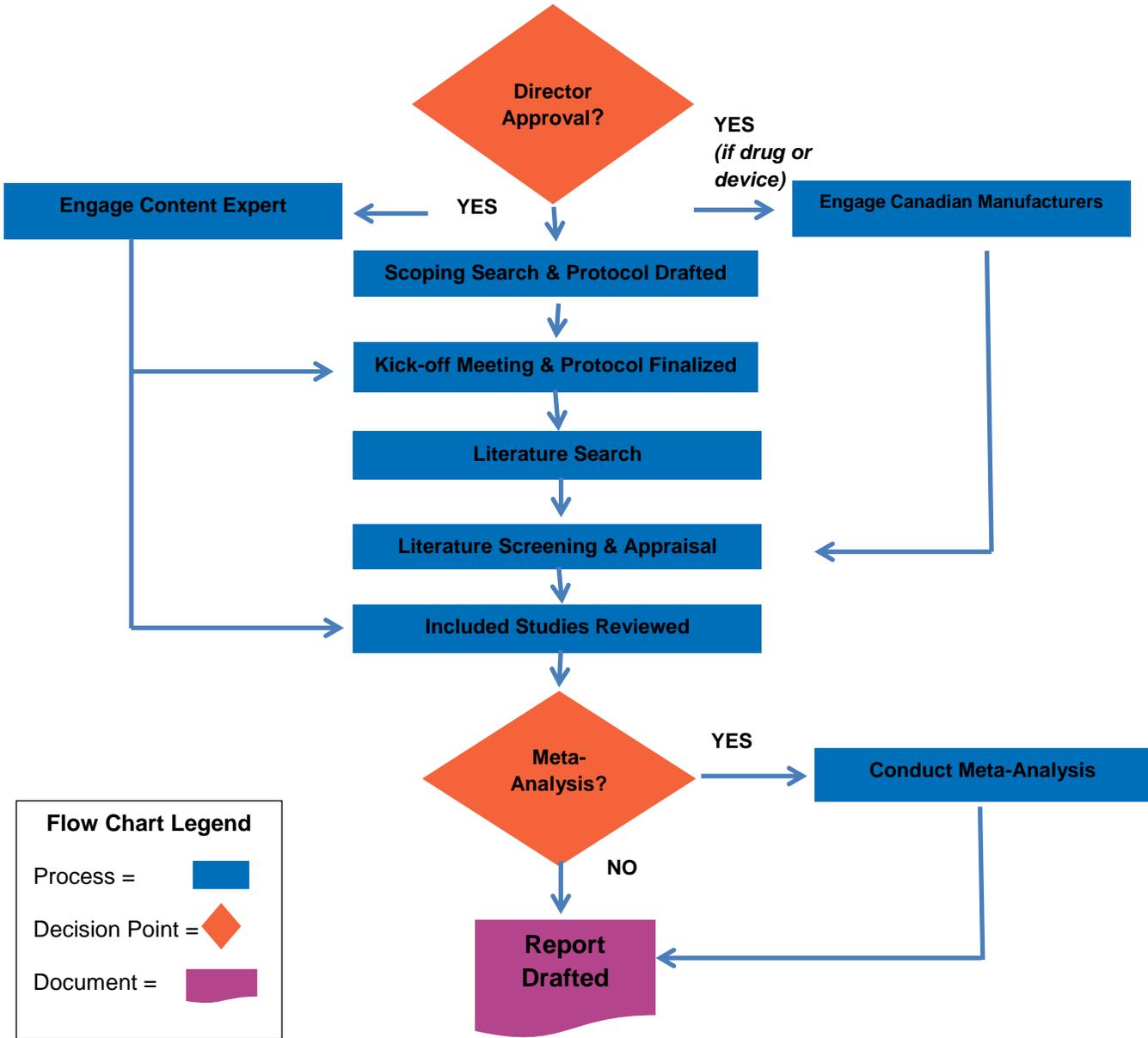
2.1.4. Topic Refined

Approved topics are refined by the PDO and the assigned Clinical Research Manager who set up a meeting with the customers and stakeholders (including the appropriate Liaison Officers). The meeting is used to determine any issues, and to define clear research questions and timing (taking into account when the information is required to most effectively support health care and policy decisions).

2.1.5. Request Does not Proceed

If the topic is not appropriate for a Systematic Review and Meta-analysis (see sections 2.1.2, and 2.1.3), or a previously published report answering the customer’s research needs is identified, the request does not proceed, but it may be considered for another CADTH product line.

2.2. Detailed Process: Research Phase
Ctrl click on individual processes for details



2.2.1. Engage Canadian Manufacturers/Suppliers

If the technology being reviewed is a drug or a device, Canadian manufacturers/suppliers are identified. The Project Manager prepares and sends emails or letters requesting industry input for the review. Any input received (i.e., studies or reports) is sent to the authors to screen and evaluate (see 2.2.6 Literature Screening & Appraisal).

2.2.2. Engage Content Expert

The Clinical Research Manager identifies and selects a content expert to provide subject matter expertise throughout the project. The Project Manager coordinates the engagement of the expert and ensures that a conflict of interest form is filled out.

2.2.3. Scoping Search & Protocol Drafted

The Information Specialist conducts a scoping search of the literature and sends the results to both authors to review. In consultation with the PDO, the lead and secondary authors draft the project protocol using the PDO-created briefing note and the supplemental scoping search. Occasionally a Reference List report is created on the topic as part of the prioritization phase, in which case it will also be used to inform the protocol.

2.2.4. Kick-off Meeting and Protocol Finalized

The Project Manager schedules a kick-off meeting with all team members including the Clinical Research Manager, PDO, authors, Information Specialist, and content expert. At this meeting the protocol is reviewed by all team members and the authors are responsible for making revisions. The Clinical Research Manager approves the final version of the protocol and the lead author is responsible for registering it in the PROSPERO international database.¹

2.2.5. Internally Reviewed Literature Search

An internally peer-reviewed literature search is conducted using key resources, including PubMed, Medline, Embase, The Cochrane Library, NIHR Centre for Reviews and Dissemination (CRD) databases, as well as topic-specific databases when appropriate. Bi-weekly search alerts are set up until the final report is published. A focused grey-literature search is also conducted by searching relevant sections of the Grey Matters checklist (<http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters>). Literature searches are limited to published English-language articles in the human population. Rapid Response searches may also be limited by evidence-based study type, including some or all of the following, as negotiated with the customer:

- systematic reviews, meta-analysis, or health technology assessments
- randomized controlled trials
- non-randomized studies
- economic evaluations
- evidence-based guidelines.

The results of the literature search are sent to the project authors to screen and appraise (see 2.2.6 Literature Screening & Appraisal)

¹ *PROSPERO is an international database of prospectively registered systematic reviews in health and social care.*

A brief overview of the literature search is detailed in the Methods section, and the search strategy is pasted into the appendix of each individual Rapid Response Systematic Review and Meta-Analysis.

From the terms used in the literature search, the Information Specialist assigns French and English medical subject headings and keywords to the document metadata to facilitate retrieval in both official languages once the document is posted on cadth.ca.

2.2.6. Literature Screening & Appraisal

Once the results of the literature search are received, the two authors independently screen retrieved titles and abstracts and come to a consensus on what literature to order (if not freely available). Article orders are sent to the Information Technician who retrieves and delivers the full text articles to authors according to CADTH's Access Copyright license terms. Both authors independently review the full-text articles selected as well as any unique information received from industry (if applicable, see "2.2.1 Engage Canadian Manufacturers") and come to a consensus on which studies meet the inclusion criteria for the project, as documented in the protocol.

2.2.7. Included Studies Externally Reviewed

The agreed-upon included studies list is sent to the content expert on the team to review and to offer suggestions if necessary. A chart detailing the studies selected is documented in each Rapid Response Systematic Review and Meta-Analysis.

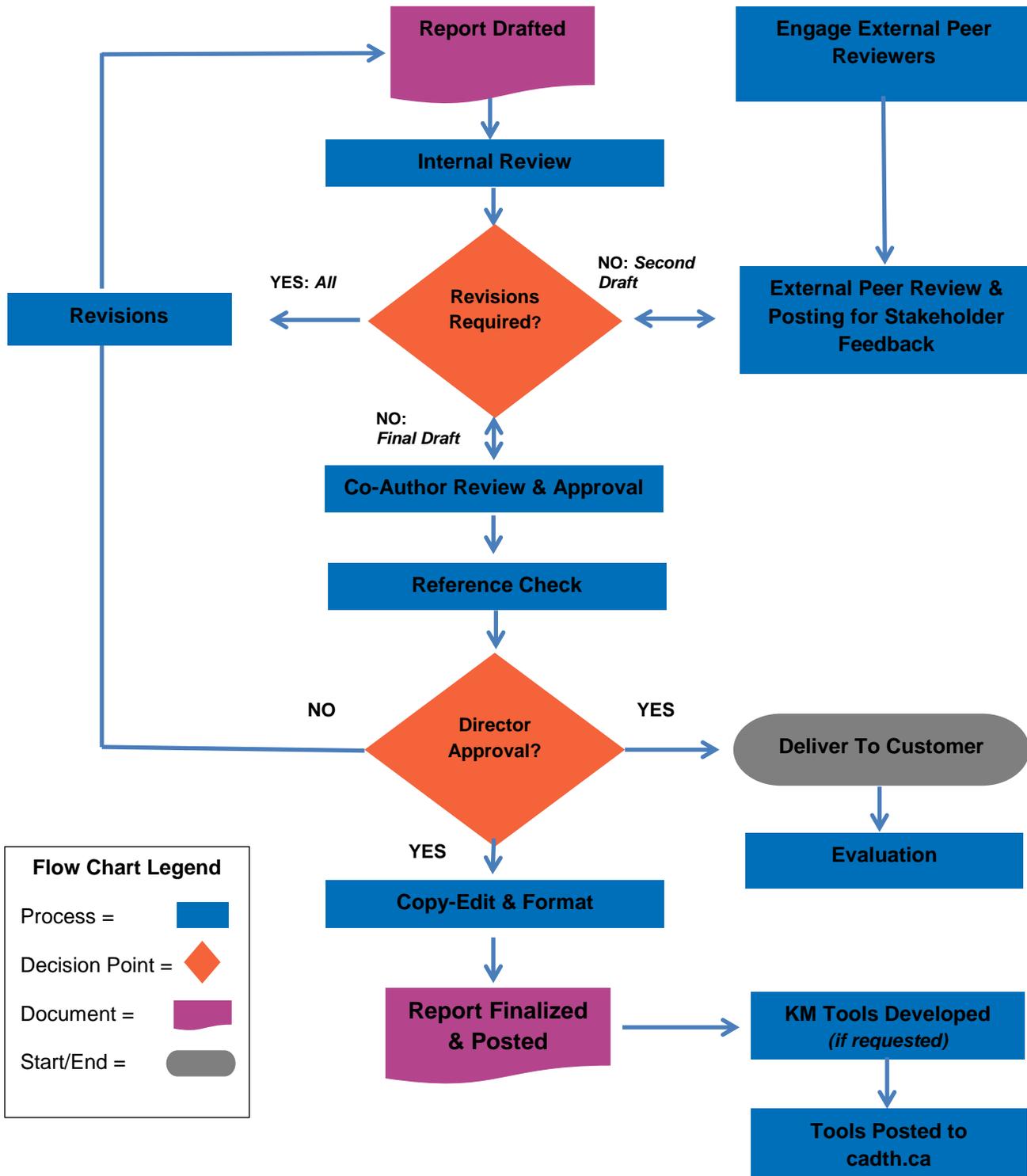
2.2.8. Conduct Meta-Analysis (optional)

If sufficient studies are found meeting inclusion criteria with similar populations and outcomes, the primary author extracts data from the included studies to conduct a meta-analysis. The meta-analysis is a statistical summary of the selected studies that tests the pooled data for statistical significance. Once completed, the included study details, the data extraction strategy, measures and outcomes, and data extraction form template are typically included in the appendix.

2.2.9. Report Drafted

Authors draft the report using a standardized template, CADTH's writing style guide and specific author guidelines for Systematic Review and Meta-Analysis reports. Any limitations and potential biases identified are reviewed in the Discussion section of the report. Report examples can be found on cadth.ca.

2.3. Detailed Process: Review and Delivery Phase
Ctrl click on individual processes for details



2.3.1. Internal Review

Draft reports are sent to the Clinical Research Manager for review. Comments and revisions are sent back to the authors and are incorporated. The revised draft is sent to the Information Specialist to ensure references are correct and all copyright guidelines are followed. If personal communications (oral or unpublished information) have been included in the report, the Information Specialist ensures all the required “permission to publish” forms have been received. These steps are repeated until the report is deemed fit to be sent for external peer review.

2.3.2. Engage External Peer Reviewers

The Program Development Officer prepares a list of potential external peer reviewers. The Clinical Research Manager reviews the list and selects two content experts to peer review the draft report. The Project Manager coordinates the engagement of the reviewers and ensures that a “conflict of interest” form is filled out.

2.3.3. External Peer Review & Posting for Stakeholder Feedback

Once the document is ready for external peer review it is sent to the Project Manager. The Project Manager coordinates the posting of the draft report for stakeholder input. Identified stakeholders are alerted and a general electronic alert is released announcing that the draft is available for comment. CADTH allows 10 working days (two weeks) to submit comments. At the same time, the Project Manager sends the draft to the previously identified peer reviewers (see “2.3.2 Engage External Peer Reviewers”) for their feedback. Comments from all external reviewers and stakeholders (may include manufacturers) are forwarded to the Clinical Research Manager who reviews the feedback and then discusses required revisions with the author. The disposition form is filled out by the author, documenting feedback and CADTH’s response. The Scientific Advisor reviews the disposition form and scans the newly revised draft to ensure external feedback has been accurately addressed. Once the Scientific Advisor, Clinical Research Manager and the author are satisfied with the final draft, it is sent to the whole team for a co-author review and approval.

2.3.4. Co-Author Review & Approval

All project team members – including the Clinical Research Manager, authors, and Information Specialist – review and approve the final draft. Revisions are incorporated as needed. Once everyone’s approval is given, the Project Manager collects signed “authorship”, “acknowledgement” and “conflict of interest” forms.

2.3.5. Reference Check

A final reference check is completed on the report by the Information Specialist, ensuring that the references follow Citing Medicine standards and that copyright guidelines have been followed.

2.3.6. Director Approval

The final draft is sent to the Director, Health Technology Assessment and Rapid Response to review and approve.

2.3.7. Copy-Edit & Format

After approval has been received, the report goes to the Publishing team to copy-edit and format using the Rapid Response Systematic Review and Meta-analysis template with the appropriate disclaimers. The title, key findings, research questions, and keywords in the meta-data are translated into French.

2.3.8. Report Finalized & Posted

The finalized report is posted on cadth.ca. If requested by the customer or other stakeholders, knowledge mobilization tools such as “reports in brief” are created to help disseminate findings. Monthly “New at CADTH” alerts are sent to those who have subscribed, including a list of all CADTH reports finalized during the previous month. Liaison Officers also help to disseminate report findings to the appropriate stakeholders within their jurisdictions.

2.3.9. Evaluation

The Liaison Officer for the jurisdiction contacts the customers to get their feedback on the report and to gather data on how the report was used. Customer feedback is entered into a database and shared with all project team members and the Rapid Response Manager to inform lessons learned.

APPENDIX 1: DEFINITIONS

Business Day: Any day (other than a Saturday, Sunday, statutory holiday or company holiday) on which the CADTH office is open for business during normal business hours.

CADTH: The Canadian Agency for Drugs and Technologies in Health is an independent, not-for-profit agency funded by Canada's federal, provincial and territorial governments. CADTH's role is to deliver reliable, timely and credible evidence-based information and impartial advice to Canada's health care leaders and decision-makers through a variety of customized products and services.

Customer: A CADTH customer is an entity or organization that requests CADTH's products or engages CADTH's services. (The customer is most often the first point of contact and requests knowledge from CADTH. The customers' needs may vary with specific topics, and they may request and/or choose between different products, services and suppliers. By expressing their needs, the customers drive the knowledge CADTH produces.)

External Peer Reviewer: Identified subject matter experts independent of/external to CADTH who are selected to provide comments and feedback on CADTH products as required.

Health Technology: A device, medical procedure, or surgical procedure, and the administrative and supportive system in which health care is delivered.

Jurisdictions: These include the federal, provincial and territorial health ministries from across Canada.

Manufacturer: A company that researches, develops and markets drugs and various medical devices to consumers and the health care system.

Meta-Analysis: A quantitative statistical analysis that is applied to separate but similar experiments of different and usually independent researchers and that involves pooling the data and using the pooled data to test the effectiveness of the results.

Product: A deliverable that is provided to a client. An artifact that is produced, is quantifiable, and can be either an end item in itself or a component item.

Report in Brief: A report that summarizes the findings of the systematic review and meta-analysis.

Request: In the context of this document, a request is a question, suggestion or submission received from a stakeholder external or internal to CADTH (reactive or proactive) in any format. A request could be a simple inquiry or result in a large project.

Stakeholders: Stakeholders for the Rapid Response processes may include organizations, institutions or individuals who have a strong and vested interest in specific Rapid Response products. Stakeholders may include:

- federal, provincial and territorial ministries of health
- hospitals and health institutions
- health regions
- patients, consumers and caregivers
- health professionals
- industry.

Systematic Review: A review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (see meta-analysis) may or may not be used to analyse and summarise the results of the included studies.

Topic: A health technology or clinical or disease area that is being, has been, or will be investigated by CADTH to determine the suitable product or service to be provided. Essentially, it is project idea that is being developed. The topic investigation could result in multiple products, projects or requests.