Drug Safety and Effectiveness Network

Guidance Document for Submitters of DSEN Queries

Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Version - April 2012

This guidance document has been prepared to assist stakeholders in submitting DSEN Queries for prioritization by the DSEN Steering Committee (SC). It is intended to provide an overview on the process and make tools available in the form of standardized procedures and templates. This, in turn, is expected to promote efficiencies in the overall process and facilitate the submission of queries.

DSEN has prepared a second document entitled: Framework for the Management of DSEN Queries, which provides additional details on the handling of Queries submitted.

Contact Information

Please contact us for additional information about the DSEN Initiative, the management of the Queries or on how to submit a Query at:

- dsen@cihr-irsc.gc.ca
- 613-948-2786

or visit our website at http://www.cihr-irsc.gc.ca/dsen.html

The Drug Safety and Effectiveness Network (DSEN) has been established primarily to increase the evidence on the post-market safety and effectiveness of drugs available to public drug plan managers, policy-makers, health technology assessors and regulators to support their decision making. In order to achieve its goals, DSEN will address DSEN Queries received from a number of stakeholders.

A DSEN Query is defined as:

> *A focused, well defined question identified by healthcare decision-makers, as a gap in evidence on the safety and effectiveness of prescribed drugs on the Canadian market, that can be addressed through DSEN sponsored research and that could result in increased knowledge in ensuring the ongoing safety and effectiveness of these medicines in a "real world" environment*

1. Scope

This document applies to potential DSEN Queries on the safety and/or effectiveness of prescribed drugs on the Canadian market. Although information and datasets generated in an international context could be considered while conducting the research in this area, this document does not apply to potential queries or research topics on drugs marketed outside Canada.

DSEN attends to the gap in information on the safety and effectiveness of Prescription Drugs (biologics and pharmaceuticals) used in the real-world. Over-the-counter Drugs, Medical Devices and Natural Health Products (including vitamins and minerals, herbal remedies, homeopathic medicines, traditional medicines such as traditional Chinese medicines, probiotics, and other products such as amino acids and essential fatty acids) are presently not addressed under DSEN's mandate.

***DSEN Queries could include (but are not limited to) topics seeking information on**:*

- *Comparing two (or more) existing drugs (effectiveness and/or safety issues)*
- *Full target population for the marketed drug*
- *Long-term outcomes*
- *Drug interactions*
- *Inputs for pharmacoeconomic models*
- *Support for "willingness to pay" models*

2. Query Submission

Identification of a potential research question is not sufficient in and of itself to be submitted directly to DSEN. At present, DSEN Queries are those potential research questions submitted by high level decision makers working within the Federal Regulator, a Federal, Provincial or Territorial (F/P/T) drug plan or organizations mandated to support F/P/T decision making with respect to drugs (e.g. CADTH).

Stakeholders identifying a potential DSEN research question should complete to the best of their ability, the template available in ***Appendix 1 – DSEN Query Summary***, summarizing the various elements of the issue(s) relating to their potential DSEN research question.

The template asks a series of questions to capture the relevant information on a DSEN Query that will be subsequently used in the prioritization process (refer to *Appendix 2*) and ultimately used as a reference source of information for DSEN affiliated researchers in conducting the research on the topic.

At various points in the process, clarification and/or additional information from the Query Submitter may be needed on their DSEN Query. As such, it is important that a contact be clearly identified for the potential research topic (as specified in *Appendix 1*).

To minimize delay in processing your Query, please complete this form to the best of your ability within a maximum of 5 pages (not including any references you deem pertinent).

Once completed, the DSEN Query Summary is to be submitted to the DSEN Coordinating Office:

by e-mail to: DSEN-RIEM@cihr-irsc.gc.ca

by mail to: Drug Safety and Effectiveness Network
Canadian Institutes of Health Research
160 Elgin Street, 9th Floor
Address Locator 4809A
Ottawa, ON
K1A 0W9

Parties eligible to submit a DSEN Query:

- Federal regulator
- F/P/T drug plan
- Organizations mandated to support F/P/T decision making with respect to drugs (e.g. CADTH)

Parties not eligible to submit a DSEN Query at the moment:

- Voluntary Health Organizations
- For profit enterprises (*e.g.* drug manufacturers, private insurance providers)
- Individual practitioners
- Community pharmacies
- Public (*e.g.* patients, advocacy or consumer organizations)

Expedited procedures

Mechanisms will be established to identify and expedite DSEN Queries of an urgent nature (*e.g.* typically relating to drug safety issues). As such, Query Submitters are requested to identify their potential DSEN Query according to one of the following categories (as outlined in the template provided in *Appendix 1*):

- Safety
- Comparative Effectiveness
- Urgent Request

3. Examples of Strong and Weak Queries

	Queries	Why
	Study the safety of second-generation antipsychotics in seniors	The question isn't defined well enough, the population is very large, and there are many drugs that need to be considered
	Study of second-generation antipsychotics in the management of dementia in institutionalized seniors	The question provides a defined population, and a dataset that will enable a reasonable answer to be provided
	Does *Drug A* have similar cardiotoxic effects and mechanism of action as *Drug B* using the same animal model?	Not within scope of DSEN as research would require animal studies (i.e. it is not a clinical study)
	How does *Drug A* compare to *Drug B* in terms of effectiveness and safety for anticoagulation in atrial fibrillation?	The question refers to specific drugs for a defined health problem

4. Query Management Process

This section outlines the various steps of the management of the DSEN Queries where the Query submitter may be engaged. A schematic is available illustrating the flow of these steps and procedures (see *Appendix 2*).

4.1 Initial Evaluation

The DSEN Coordinating Office will conduct an initial evaluation of the DSEN Query to determine if sufficient information has been provided to allow for an appropriate understanding of the issue(s) for subsequent steps. If additional information is warranted, the CO will seek clarification/additional information from the Query Submitter.

4.2 Feasibility Assessment

Under the Feasibility Assessment, Query Submitters will engage with the researchers to allow for a dialogue between the future user of research evidence and researchers, who have expertise in several disciplines and methodologies from across the DSEN network. This dialogue will facilitate the assessment of the scientific feasibility of each Query (*i.e.,* determine the possible approaches for responding to Queries including methodologies, project duration, availability of data, costs).

4.3 Prioritization

The DSEN Coordinating Office will inform the Query Submitter of the status of their Query following receipt of the final recommendations by the DSEN Steering Committee (SC) on the Query being advanced to the *prioritized research agenda* (*e.g.,* proposed query has/has not been accepted for the prioritized research agenda).

4.4 Research

Once the DSEN Research Teams (RTs) have started work on a specific Query, it is possible that they will contact with the Query submitter during the course of their research for further clarifications. Made up of existing data centres, teams and networks from across Canada, the RTs create the research capacity to respond in a timely manner to the drug safety and effectiveness queries of decision makers. (see *Appendix 3*).

4.5 Dissemination

Dissemination of research results immediately upon conclusion of a research investigation back to those who originally proposed a DSEN Query is of paramount importance and an agreed principle of DSEN affiliated researchers.

DSEN research results will remain the intellectual property of the researchers who developed the evidence.

Appendix 1 – Template for Summarizing Information on DSEN Queries

DSEN QUERY SUMMARY	
DSEN Query Title:	
DSEN Reference Number:	
Submitted by (organization):	
Contact Information: • **Name**	
• **Phone**	
• **E-mail**	
Proposed DSEN Query Category(ies):	[ ] Safety
	[ ] Comparative Effectiveness
	[ ] Urgent Request

DSEN Query Proposal	
1.	**What is the specific DSEN Query (in the form of a research question)?** (If possible, please state the question in terms of specific & measurable objectives, including any pre-specified hypotheses. Ideally, the research objectives would define the intervention(s), clinical problem, population and outcome.)
2.	**What is the relevant information regarding the drug product(s) for which the DSEN Query is being proposed?** *Please provide the:* *2.1 name (brand/generic)* *2.2 product class* *2.3 indication(s) or use(s) of the product and severity of the underlying condition/clinical problem considering risk of death, pain and psychological effects.* *2.4 anticipated number of patients that are using or will use the drug* *2.5 other noteworthy information about the drug product as appropriate*
3.	**What is the knowledge gap that is going to be addressed with this DSEN Query?** *Please consider the:* *3.1 degree of urgency for decision makers to obtain new information,* *3.2 usefulness of information to decision makers, and* *3.3 number of decision makers who could use this information.*
4.	**What is the current level of evidence available on this issue?** *Considering previous research in the particular area:* *4.1 how critical is the evidence gap to be filled, and* *4.2 the likelihood of findings to lead to change in patient health status including safety, effectiveness and comparative effectiveness?*
5.	**How might the information generated by DSEN research be used by your organization?** *What is the potential of research findings to:* *5.1 be translated into new regulatory, clinical or health service practice* *5.2 contribute to cost effective management of the condition or health problem*
6.	**Are there broader implications of generating the information through DSEN research?** *(e.g. are there any legal, ethical, equity, political or social implications related to the Query)*

To minimize delay in processing your Query, please complete this form to the best of your ability within a maximum of 5 pages (not including any references you deem pertinent).

DSEN Query Summaries should be submitted:

by e-mail to: DSEN-RIEM@cihr-irsc.gc.ca

by mail to Drug Safety and Effectiveness Network
Canadian Institutes of Health Research
160 Elgin Street, 9th Floor
Address Locator 4809A
Ottawa, ON, K1A 0W9

Appendix 2 – Process for the Management of DSEN Queries

DSEN Query
Queries can arise from multiple sources Federal Regulator, Federal, Provincial or Territorial (F/P/T) drug plan or organizations mandated to support F/P/T decision making with respect to drugs (e.g. CADTH)) and identify needed research intended to increase evidence available to support decision-making.

DSEN Coordinating Office
Established within CIHR as the hub of the network to facilitate and coordinate network operations.
Responsible for managing and administering the DSEN grants and awards.

Feasibility Assessment
Conducted by DSEN's Advisory Committees to determine the best approach(es) for responding to the research questions (including methodologies, data, project duration, costs and Research Teams involved).

DSEN Steering Committee
Provides strategic direction to the DSEN, sets priorities for needed research through the development of a prioritized research agenda, and promotes the translation of research knowledge into actions.

DSEN Collaborating Centres(CC) and Research Teams
Coordinated national network of researchers in post-market drug safety and effectiveness committed to the highest excellence in research thereby creating a dedicated research capacity for the DSEN program.

Key Activities:
Research ♦ Capacity Development ♦ Networking ♦ Knowledge Translation

- **CC for Observational Studies:**
  - Canadian Network for Observational Drug Effect Studies
- **CC for Network Meta-Analysis (3 teams):** KSRU, NETMAN, TNMA
- **CC for Prospective Studies (3 teams):**
  - Active Surveillance (SEARCH)
  - Pharmacogenomics of Adverse Drug Reactions (PREVENT)
  - Comparative Effectiveness (CAN-AIM)

Project-Funded Research
Additional funds made available to undertake the required research to respond to specific queries identified on the prioritized research agenda

Decision Makers & End-Users
DSEN will increase the evidence on drug safety and effectiveness available to regulators, policy-makers, health care providers and patients; and increase capacity within Canada to undertake high-quality post-market research in this area.

Appendix 3 - Relevant Research Areas of the DSEN Collaborating Centres (CCs) and Research Teams (RTs)

Within their own research area, the CCs and RTs may, for example, undertake studies on the following:

Collaborating Centre for Observational Studies:

- Perform drug safety and effectiveness research using epidemiological approaches and existing national healthcare databases
- Analyze, link, and develop electronic health data for research

Collaborating Centre for Prospective Studies:

- **Active Surveillance**
  - Active safety surveillance of post-market drugs using valid epidemiologic study designs
  - Working with established disease, or patient registries to assess the benefit to harm profile for drugs of interest in a "real world" context
  - Active surveillance by gender and/or in different patient subpopulations such as ethnic and racial minority population, children or seniors

- **Pharmacogenomics of Adverse Drug Reactions (ADRs)**
  - Assessments on the potential role of pharmacogenomics relating to the impact on reduction of incidence of ADRs
  - Validation of surrogate outcome measures and real world studies
  - Identification of predictive genomic biomarkers of drug risks
  - Compare incidence of ADRs by gender and/or in different patient subpopulations such as ethnic and racial minority population, children or seniors
- **Comparative Effectiveness**
  - Performing studies comparing the clinical effectiveness, risk and benefits of treatment options in different patient subpopulations or circumstances
  - Developing strategy, best practices and methods for comparative effectiveness research in the "real world"

Collaborating Centre for Network Meta-Analysis:

- Indirect comparisons (e.g. mixed treatment comparisons) of drugs of interest using data from previously completed RCTs
- Innovative methods for systematic reviews