Drug Safety and Effectiveness Network

CIHR IRSC

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Modernization of the Drug Regulatory Framework: Training for the Future

6th semi-annual Drug Safety and Effectiveness Network Meeting

The Lord Elgin Hotel

100, Elgin Street, Ottawa, ON

Meeting Report

March 21st 2014, Ottawa

Background

The Drug Safety and Effectiveness Network (DSEN) convened its sixth semi-annual Network meeting on March 21st, 2014 in Ottawa to bring trainees together with DSEN funded teams, provincial/territorial decision-makers; and, organizations mandated to support F/P/T decision making with respect to drugs (e.g. Health Technology Assessment organizations), to gain common understanding on the evidence needs on post-marketed drugs in Canada.

According to Health Canada's Regulatory Roadmap for Health Products and Food (2012):

> "*The regulation of food and health products is based on the principle that the product's benefit must exceed any potential harm, with a reasonable degree of certainty. Benefit may be loosely defined as any intended useful, positive effect obtained, whereas harm is any unintended effect that may cause injury or diminish human health in any way. Benefit and harm are not absolute, and regulators recognize that uncertainties exist with respect to both the benefit and harm that may result from being exposed to a food or health product. Tolerance for harm and uncertainty is inextricably linked with the benefit that a product may provide*". (http://www.hc-sc.gc.ca/ahc-asc/activit/strateg/mod/roadmap-feuillederoute/rm-fr-eng.php)

DSEN's mandate is to reduce uncertainties in post-market information about drugs and to better define the clinical benefits and harms of marketed products. In Canada and worldwide, more information is needed on the safety and effectiveness of drugs used by diverse patient populations in real-world settings, i.e., outside the controlled experimental environment of clinical trials. DSEN has been established at CIHR to collaborate with Health Canada and with stakeholders from across Canada. DSEN is actively working to increase evidence on drug safety and effectiveness available to regulators, policy-makers, health care providers and patients; and to increase capacity within Canada to undertake high-quality post-market research in this area.

In 2009, HC commissioned the study: "*Human Resource and Educational Inventories to Support the Life Cycle Approach to the Regulation of* Therapeutic *Product".* The report was published in March 2010 and is authored by Judith A. Soon *et al.* http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/reshum-eng.php Some of the key recommendations of the report were: to develop more collaboration between academia and government; to focus, in collaboration with CIHR, on developing a new generation of post market drugs researchers; and finally, that access to health data be facilitated in Canada.

It is of primary importance for DSEN to continue working to develop the next generation of researchers and assist in positioning them to help reduce uncertainty around prescription drugs in Canada. Therefore the principal objectives of this meeting were to:

- Engage Network members in discussion on the advancement of training in post market drug research
- Present work from Past and Current DSECT-DSEN trainees
- Provide network-wide interactions between DSEN funded researchers, trainees, and decision makers
- Update participants on recent developments and upcoming plans and activities
- Support a culture of knowledge translation within the DSEN program

Meeting Summary

This 6th semi-annual meeting, held by DSEN on March 21st, 2014 at The Lord Elgin Hotel, was attended by 59 participants from the research and the decision making communities (Agenda is attached in *appendix 1* and Attendees list in *appendix 2*).

Robert Peterson, the DSEN Executive Director gave welcoming remarks and explained the objectives of the meeting. He then updated the participants on work done by the DSEN Coordinating Office (DSEN CO) and the network of researchers in the past few months.

The morning session focused on different post market drug research career paths with presentations from: CADTH's Vice-President, Strategic Initiatives, and Chief Scientist, **Tammy Clifford**, **Suzanne Cadarette**, Assistant Professor at the University of Toronto, **Daniel McLean**, Policy Analyst for Health Canada, and **Christine Voggenreiter,** Director**,** Economic Analysis division, British Columbia Ministry of Health. **Lisa Dolovich** introduced the CIHR funded Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT), following which seven DSECT and DSEN trainees (**Erin MacDonald, Wendy Teft, Cristiano Moura, John Lee, Joanne Ho, Erika McDonald, Richard Morrow**) made short presentations on their research work.

The lunch keynote presentation was made by **David K. Lee**, Director, Office of Legislative and Regulatory Modernization at Health Canada, who presented elements of the regulatory renewal taking place in Canada.

The afternoon session was devoted to the work accomplished by the Network teams and Collaborating Centres in integrating and developing trainees with presentations from CCNMA, CNODES, CAN-AIM, KSRU, SEARCH, NETMAN, and PREVENT. After the break, a panel of experienced trainees addressed the question of what was needed to improve post market drug research training for the future.

Dr. Peterson concluded the meeting. A tentative date for the next semi-annual Network Meeting was given for October 17th, 2014 and the meeting was adjourned.

<u>The AM session:</u>

After a round table introduction from the participants, **Robert Peterson** gave an overview of the different projects the DSEN CO has been working on since the last Network meeting in October 2013.

At the time of the meeting, DSEN had funded 55 research projects, 17 of which have been completed, and had invested over $5.5 million in capacity building (New Investigators Awards, Bridge Funding, Fellowships, Doctoral Research Awards), and taken over the funding of the Strategic Training Initiative in Health Research (STIHR program), DSECT.

Dr. Peterson also provided an update on the status of the evaluation of the implementation phase of the DSEN. He informed participants that the evaluation has been completed and the draft report will be submitted to the DSEN Steering Committee members in the spring for feedback and suggestions.

The two draft recommendations of the report were that:

- the DSEN CO, in consultation with its partners and stakeholders, examine key design and delivery features of the DSEN to identify areas where increased efficiency and effectiveness may be possible. Example features included :
    - expectations on key DSEN concepts (e.g., reporting, prioritization of queries), and

- timelines between query submission and the delivery of research results

- it was also suggested that the DSEN CO, should review the current performance measurement strategy to determine what changes could better position the DSEN to monitor how it fulfills its mandate.

The DSEN CO will spare no efforts to fully address the recommendations of the final report.

Dr. Peterson also told participants that in a view to making the pharmaceutical industry and the healthcare system more accountable and transparent, the Minister of Health proposed, last December, new powers for Health Canada in the monitoring of post market drugs through an amendment to the Food and Drugs Act. The new Bill, called the Protecting Canadians from Unsafe Drugs Act (Vanessa's Law) will allow Health Canada to recall a drug already on the market and impose fines for promoters of unsafe products. This new Bill, which requires strong post market surveillance, will probably result in an increased number of questions coming to DSEN.

Dr. Peterson then invited **Tammy Clifford**, **Suzanne Cadarette**, **Daniel McLean**, and **Christine Voggenreiter** to present their views to developing a career in post market drug research.

Tammy Clifford, Vice-President, Strategic Initiatives, and Chief Scientist at CADTH presented the views of an established researcher and explained that in terms of career; sometimes the best laid plans are not what actually happen. She talked about her tortuous and fortuitous career path where love, changes of orientations (from medicine to epidemiology), and a chance meeting with David Moher, finally lead to a passion for systematic reviews and a first job at CHEO, then at CADTH.

Suzanne Cadarette, Assistant Professor, University of Toronto, explained her views as a mid-career investigator who juggles many projects, activities, supervision, and mentorships. She was grateful to have been able to use data from the Canadian Longitudinal Study on Aging while she was an undergraduate and is now a strong proponent of data access. She did her Master's in epidemiology and then studied health services before doing a fellowship in Boston in pharmacoepidemiology, where she developed a great interest in methods.

Daniel McLean, Policy Analyst at Health Canada, spoke about transitioning from chemical and bioengineering research to public policy. After being awarded a CIHR Policy Fellowship, Daniel spent six months at the Office of Pharmaceuticals Management Strategy (OPMS) at Health Canada, and was then offered a permanent position. He explained that he learned the importance of being able to summarize an issue in three bullets and that timing is everything in the policy environment where what is important is more that which is influential rather than what is interesting.

Christine Voggenreiter, Director, BC Health Outcomes, Evaluation and Economic Analysis, has been working on economic evaluations for the province for nine years now. Her team supports drug listing decisions and the monitoring policy for the province. The team works closely with pharmacists for decision and modeling. As is the case for other people working in policy, the work is driven by the hot topic of the day.

Right before the morning break, the group welcomed two Human Resources Advisors from Health Canada (HC), **Tandice Wiwchar** and **Leonce Philoctete**, who made themselves available to answer trainees' questions about job opportunities at HC, and to give information about the types of positions available to scientists in a regulatory environment.

After the morning break, **Lisa Dolovich** gave a brief introduction to DSECT, its mentoring program, and its learning and exchange activities. DSECT was holding its two-day Initiation Symposium just preceding the Network meeting so that all the new DSECT trainees were present for the DSEN semi-annual meeting. She then introduced seven of the DSEN and/or DSECT trainees who made presentations summarizing the following items:

- Educational background
- How they became engaged with their research team
- Key aspects of new learning within their research team
- Research they are working on and their role
- Long-term objectives

The presenters were:

Erin MacDonald (CDSERN/DSECT), epidemiology, stimulant use and hospitalization for psychosis.
Wendy Teft (PREVENT/DSECT alumni), pharmacogenomics, Tamoxifen and breast cancer patients, personalized therapies for cancer patients, assessment of NOACs safety and efficacy.
Cristiano Moura (CAN-AIM/DSECT alumni), clinical epidemiology, anti-TNF versus DMARDs in rheumatoid arthritis.
John Lee (SEARCH/DSECT alumni), active surveillance, Cisplatin-induced hearing loss in children.
Joanne Ho (KSRU/DSECT), network meta-analysis, Cognitive Enhancer in Alzheimer's Disease, 5HT3 Receptor Antagonists and cardiac safety.
Erika McDonald (CCNMA), network meta-analysis, Efficacy and Safety of TNF-alpha Inhibitors in IBD
Richard Morrow (CNODES), observational studies, instrumental variable analysis to handle unmeasured/unknown confounding in ADHD phamacoptherapy in children.

Lunch Time:
During lunch time, **David K. Lee**, Director, Office of Legislative and Regulatory Modernization, Health Canada, presented the keynote address: ***"Regulatory Renewal in the Context of Drug Benefits, Harms, and Uncertainties"***.

With the introduction of Bill C-17 (Vanessa's Law) and the Regulatory Roadmap adopted by Health Canada in 2012, the government is taking action to harmonize different frameworks, legislation and regulation. These changes are modifying the drug approval process and their subsequent monitoring. There is a shift in paradigm for drug approval going from simple effectiveness of a drug to the balance of harms and benefits, and the management of uncertainties linked to this drug in a life-cycle model.

Bill C-17, as drafted, would give Health Canada the power to:

- Require information, more tests and/or studies, form the manufacturers
- Promote mandatory reporting of serious adverse events by health care institution
- Require label change
- Recall unsafe products
- Impose increased fines and penalties for unsafe products

In conjunction with these efforts, Health Canada is developing the Orphan Drugs Framework to address the unique challenge of rare diseases and, thus, small populations which are difficult to study. The regulator will increasingly call on DSEN to validate signals and accrue the evidence needed in a life-cycle approach to drug approval.

The PM Session:

After lunch, each of the DSEN teams was invited to give an update on their training efforts. The first presentation was from CCNMA's coordinator, **Shannon Kelly,** on behalf of George Wells. CCNMA's training activities have been revolving around practical and interactive training and mentoring, linkages and partnerships, hands-on workshops, and research rounds. Two hands-on workshops have been held up to now and were attended by approximately 40 people. The four clusters which form CCNMA currently include four trainees.

Ingrid Sketris presented on behalf of Colin Dormuth who is the lead of the CNODES training team. CNODES has developed workshops, conferences, discussion forums, and a journal club, and is planning on doing an evaluation of the training efforts inside the Collaborating Centre. Each year, every single site of the CNODES CC is asked to send one trainee to either the McGill Summer course in phamacoepidemiology or the DSECT training course. CNODES is currently developing online interactive training modules.

Louise Pilote, representing CAN-AIM, underlined the importance of the development of active interdisciplinary research collaborations and joint research training initiatives among the CAN-AIM co-applicants, who are spread over 14 universities in 8 provinces and over several disciplines of methodological and clinical research. The end goal is to enhance and promote state-of-the-art methods for observational, longitudinal, prospective studies of drugs' safety and effectiveness. Up to now, CAN-AIM trainees collaborated in 9 publications/presentations.

Sharon Strauss, KSRU principal investigator, presented the current KSRU trainees and the activities offered to them. As part of KT Canada, KSRU trainees are given opportunities to participate in Seminar Series, Research Operations Seminar Series, Summer Institute, Scientific Meeting, and Pragmatic Trials Course.
KSRU also offers a Systematic review course (online), an End of Grant KT Course, and has participated in the 2013 CADTH Symposium to present knowledge synthesis. Currently, KSRU has six new trainees with different areas of expertise and skill sets.

Bruce Carleton, SEARCH principal investigator, is also a mentor for DSECT and believes that a good mentor gives trainees more responsibilities. SEARCH/PREVENT currently encompass 12 trainees, including two visiting scientists. All the trainees participate in projects and are exposed to all the facets of these projects. They are offered opportunities to collaborate and attend meetings and conferences.

Brian Hutton presented on behalf of David Moher for NETMAN. The team has local trainees as well as visiting international trainees. The team offers a training module and other resources on USB key, and one-on-one meetings. Practical experience is gained at the Ottawa Hospital, where members of the knowledge synthesis program participate in screening, data collection, and writing.

Richard Kim, PREVENT principal investigator, talked about his personalized medicine group at the London Health Sciences Centre. The pharmacogenomics training program at Western has become the largest clinical pharmacology training program in Canada. The group offers inpatient and ambulatory care personalized medicine specialty training experiences. The group helps people with uncommon drug reactions and conducts studies while assesing patients.

Following the DSEN teams' presentations, a panel comprised of **Andrea Tricco** (KSRU), **Shannon Sullivan** (CCNMA), **Tibor Schuster** (CNODES), and **Ricardo Jimenez** (SEARCH), all of them "senior" trainees, exchanged views on training in post-market drug research.

In general, the panelists agreed on the importance of mentoring. Network building and multidisciplinary team work were also extremely important components of their training and were seen as conducive to a better grasp of the "big picture". Interconnected, multidisciplinary teams are essential to tackle complex problems and questions. The need for very strong methods and development of new methods was emphasized. Also noted was the need for more opportunities for informal meetings and discussions, possibly visits between teams. In conclusion, the panelists concurred that more collaboration brought more creative answers and more solutions to complex questions.

Closing Remarks

Robert Peterson adjourned this very dynamic meeting by thanking all participants. In following up on this capacity-building meeting, the DSEN Coordinating Office will be working in collaboration with DSECT to foster a DSEN wide seminar series available to faculty, staff, trainees, decision makers and other stakeholders across the Network. The plan is for each of the teams to co-host a webinar over the course of a year.

DSECT has also offered to link training opportunities and resources available across the Network and the creation of a web page is in the works.

The next Network meeting will be held on October 17th, 2014.

APPENDIX 1 - MEETING AGENDA

6th Semi-annual Drug Safety and Effectiveness Network meeting:
Modernization of the drug regulatory framework: Training for the future
March 21, 2014
The Lord Elgin Hotel, Ontario Room, Ottawa

8:00	Breakfast (provided)	
8:30	Welcome and Introductory remarks	**Robert Peterson**, DSEN, CIHR
8:45	DSEN Update	**Robert Peterson**, DSEN, CIHR
09:15	Views to developing a career in post market drug research	
	• Established researcher	**Tammy Clifford**, VP Strategic Initiatives, Chief Scientist, CADTH
	• Mid-Career Investigator	**Suzanne Cadarette**, Assistant Professor, University of Toronto
	• CIHR-HC Policy Fellow	**Daniel McLean**, Policy Analyst, Health Canada
	• Provincial Drug Plan	**Christine Voggenreiter**, Director, BC Health Outcomes, Evaluation and Economic Analysis
10:15	Break	
10:30	Introduction to DSECT Presentations by DSEN and/or DSECT participants	**Lisa Dolovich**, McMaster University
	Erin MacDonald (CDSERN/DSECT) **Wendy Teft** (PREVENT/ DSECT alumni) **Cristiano Moura** (CAN-AIM/DSECT alumni) **John Lee** (SEARCH/DSECT alumni)	**Joanne Ho** (DSECT/KSRU) **Erika McDonald** (CCNMA) **Richard Morrow**, (CNODES)
12:00	Networking Lunch – Keynote address: ***"Regulatory Renewal in the Context of Drug Benefits, Harms, and Uncertainties"***	**David K. Lee**, Director, Office of Legislative and Regulatory Modernization, Health Canada
13:00	Update on the DSEN training efforts	**Lisa Dolovich**, moderator
	Shannon Kelly (CCNMA) **Ingrid Sketris** (CNODES) **Louise Pilote** (CAN-AIM) **Sharon Straus** (KSRU)	**Bruce Carleton** (SEARCH) **Brian Hutton** (NETMAN) **Richard Kim** (PREVENT)
14:30	Break	
14:45	Panel: Training researchers for the post-market drug research of the future – the trainees' experience	
	Ricardo Jimenez (SEARCH/PREVENT) **Shannon Sullivan** (CCNMA)	**Andrea Tricco** (KSRU) **Tibor Schuster** (CNODES)
15:30	Closing remarks	**Robert Peterson,** DSEN, CIHR

APPENDIX 2 - List of Attendees

Acevedo, Maria	University of British Columbia
Alsabbagh, Wassem	University of Saskatchewan
Amiche, Amine	University of Toronto
Boucher, Michel	CADTH
Brochu, Christian	DSEN
Cadarette, Suzanne	University of Toronto
Cameron, Chris	University of Ottawa
Carleton, Bruce	University of British Columbia
Chapman, Laurie	Health Canada
Clifford, Tammy	CADTH
Czarny, Tomasz	McMaster University
Daly, Caitlin	McMaster University
Delage, Johanne	DSEN
Dolovich, Lisa	McMaster University
Ewusie, Joycelyne	McMaster University
Fatima, Safoora	McMaster University
Forbes, Diane	DSEN
Gehrke, Sebastian	McMaster University
Gulilat, Markus	Western University
Hamid, Jemila	McMaster University
Hersi, Mona	University of Ottawa
Ho, Joanne	McMaster University
Hutton, Brian	University of Ottawa
Jimenez, Ricardo	University of British Columbia
Kelly, Shannon	University of Ottawa
Kilpatrick, Natasha	Health Canada
Kim, Richard	Western University
Lange, Lisa	Health Canada
Lee, John	University of British Columbia
Lee, David K.	Health Canada
Li, Guowei	McMaster University
Loshaj, Shepresa	Health Canada
MacDonald, Erika	University of Ottawa
McDonald, Erin	ICES
McEneny, Alanna	University of Waterloo
McLean, Daniel	Health Canada
Mitchell, Chad	Alberta Ministry of Health
Mizrahi, Corine	McGill University
Morrow, Richard	University of British Columbia

Moura, Cristiano	McGill University
Pang, Menglan	McGill University
Pant, Sirjana	CADTH
Peterson, Robert	DSEN
Pierce, Susan	Health Canada
Pilote, Louise	McGill University
Pirrie, Melissa	McMaster University
Ross, Colin	University of British Columbia
Schuster, Tibor	McGill University
Sherwood, Emma	McMaster University
Sketris, Ingrid	Dalhousie University
Smith, Anne	University of British Columbia
Soobiah, Charlene	University of Toronto
Straus, Sharon	University of Toronto
Sullivan, Shannon	University of Toronto
Teft, Wendy	Western University
Tricco, Andrea	University of Toronto
Voggenreiter, Christine	British Columbia Ministry of Health
Yasari, Siham	DSEN