Orphan Drugs and Rare Disease Policy

Background

A rare disease, by definition, affects only a small number of individuals. However, taking into account that around 7000 rare diseases are currently known, the estimated proportion of people affected by a rare disease in Canada is significant (about 1 in 12). Orphan drugs used in the treatment of rare diseases are typically very expensive. Many of these drugs cost over $500,000 per patient per year, which is too costly for most patients and their families to pay out-of-pocket, and most drugs do not meet standard cost-effectiveness thresholds for publicly-funded drug coverage. Nonetheless, governments routinely cover orphan drugs based on alternative considerations like equity of access, unmet need and perceived societal preference; however, the rational for funding decisions tend to be inconsistent and non-transparent.

While public spending on expensive orphan drugs only accounts for a small proportion of healthcare budgets in industrialized countries, the budget impact is expected to grow dramatically as the number of treatments available and the number of orphan indications increase. However, most countries with government-funded drug programs lack a transparent, evidence-based process for determining coverage of orphan drugs, and are therefore unprepared for the political and budgetary pressures that expensive orphan drugs will put on public payers in the next 10 years. Moreover, the lack of international consistency and transparency in orphan drug reimbursement decision-making has hampered public payers' ability to leverage their market share in negotiating fair prices with the pharmaceutical industry.

Over the past five years, the New Emerging Team for Rare Diseases (wwww.rare-diseases.ca) – a UBC-lead multidisciplinary Canadian Institutes of Health Research (CIHR)-funded team – has made substantial headway in bringing Canada closer to a coherent, national decision-making process for funding orphan drugs. Thus, this 'UBC cluster' is now well positioned to develop international partnerships with stakeholders to establish knowledge mobilization around the globe.

Aims

The research cluster, led by Larry Lynd at UBC Pharmaceutical Sciences, aims to continue to contribute to the development of a consistent, transparent decision-making system for determining coverage of orphan drugs internationally. The UBC research cluster will invite international stakeholders to a roundtable workshop hosted by the cluster at UBC. The aims of the workshop will be to: i) explore current international policies related to reimbursement decisions for drugs for rare diseases; ii) inform and enhance research priorities within Canada; iii) share knowledge obtained by UBC researchers with international rare disease stakeholders; and iv) establish formal international partnerships between the research cluster and leading international experts and stakeholders. The ultimate goal will to develop and submit a collaborative Social Sciences and Humanities Research Council (SSHRC) Partnership Grant to continue to move this research agenda forward on an international scale.

Funds

Vice President, Research and Innovation (VPRI) funding of this research cluster will serve as a catalyst for long-term, international partnerships aimed at establishing explicit and transparent processes to support policy and practice decision-making for orphan drugs. The funds will be used to host leading international decision-makers and researchers to a roundtable workshop at UBC. The funds will also assist the cluster in developing an application for future SSHRC Partnership Development Grant or Development Grant funding.

GOALS – The research cluster will use Grants for Catalyzing Research Clusters (GCRC) funds to build on a previous CIHR-funded project, developing an international group that will work collaboratively to advance the development of orphan drug/disease policy. With VPRI support, the UBC cluster will convene international stakeholders to identify commonalities and differences across countries, lead knowledge translation activities as they pertain to the roundtable, and develop international research priorities. The ultimate goal is to develop a competitive SSHRC Partnership Grant and identify additional funding opportunities to support an international research and policy agenda for multiple countries, as well as inform public debate, and guide policy development and practice pertaining to orphan drug coverage.

SIGNIFICANCE

Research Relevance

Subsection 1: Build on background – why is this relevant now?

This proposal is relevant and timely. New genomic technologies are rapidly facilitating the identification of more rare diseases and stratification of common diseases into rare subtypes. Consequently, there is an increasing number of orphan drugs set to hit the market with an estimated 1800 new treatments in development – in fact, orphan drugs have recently accounted for one third of new molecular entities (NME) approved. Moreover, an increasingly prevalent strategy used by pharmaceutical companies ("indication creep") is to initially obtain approval for an NME for an orphan indication, price it accordingly, and then apply for approval of the drug for more common indications that involve the same molecular mechanism without reducing the price. Indeed, advances in genomic science are likely to turn this last factor into a major health policy challenge. These trends will dramatically expand the number of patients for whom treatment with orphan drugs are indicated. Thus, decision-makers need to be proactive in establishing clear models and processes for drug reimbursement decisions, price negotiation and fiscal management.

Subsection 2: What is the need, where is there a gap?

A recent review of current policies of 20 Organization for Economic Co-operation and Development (OECD) countries indicates that many countries do not have centralized review processes for orphan drug coverage. Rather, these countries have multiple systems in place to determine coverage of orphan drugs, subjecting rare disease patients to uncertain and inconsistent coverage decision-making resulting in significant inequities both within and between countries. Moreover, while the actual cost paid for specific orphan drugs by payers in different jurisdictions varies substantially due to price negotiations with manufacturers, companies usually insist on the final price remaining confidential, which makes it difficult for other payers to develop a negotiation strategy. Furthermore, variation in coverage decision-making criteria undermines payers' ability to leverage their collective bargaining power in price negotiations with the pharmaceutical industry. Thus, having clear, consistent, and transparent international policies would make it easier for public payers to negotiate fair prices for orphan drugs and manage the coming orphan drug policy challenge driven by the genomics revolution.

Subsection 3: Research themes, building on past research.

Research themes to be addressed in the roundtable meeting will build on successful research goals addressed by the Emerging Team for Rare Disease, including value-based decision criteria, creation of priority-setting and decision making frameworks for orphan drugs, as well as discussion of knowledge translation strategies to integrate evidence into policy making, and evaluation of decision-making frameworks. The roundtable will be essential in determining how to adapt these research themes to an international population. Moreover, research strategies for addressing critical gaps in knowledge

necessary to developing a consistent international framework for orphan drug coverage decisions (e.g., how to estimate cross-national differences in prices or "fair prices" for an orphan drug) will be discussed.

Collaborative Partnership:

Subsection 1: demonstrated strengths/skillset of the group

The UBC Orphan Drugs and Rare Diseases Policy Cluster, an expansion of the core CIHR Team, consists of health economists, epidemiologists, health policy experts, social scientists, and ethicists with a track record of orphan drug and rare disease research. Bringing this group together under this cluster will be the catalyst for positioning UBC in an international leadership role in convening international experts and knowledge-users to establish international rare disease policy.

Subsection 2: Secured team members

The research cluster will bring together an interdisciplinary team of leading UBC researchers as listed in the table below. The VPRI funds will be used by the core team to convene an international network of partners and to set the foundation for an ongoing international research collaboration.

UBC Researcher Name	Department/Affiliation
Larry Lynd	Pharmaceutical Sciences
Peter Klein	Journalism
William McKillan	Anthropology
Jan Friedman	Medical Genetics
Lorne Clarke	Medical Genetics
Milan Patel	Medical Genetics, Rare Disease Foundation
Sandra Sirrs	Adult Metabolic Diseases Clinic
Craig Mitton	SPPH, Health Policy
Stirling Bryan	SPPH, Health Economics
Aslam Anis	SPPH, Health Economics
Mike Burgess	Biomedical Ethics
Michael Law	SPPH, Health Policy

SPPH=Medicine, School of Population and Public Health

Subsection 3: Potential collaborators

The research cluster will invite international leading experts and stakeholders in orphan drug policy. Potential collaborators include Dr. Andrew Wilson (Pharmaceutical Benefits Advisory Committee, Australia), Drs. Peter Jackson and Ron Akehurst (National Institute for Health and Care Excellence,UK), Dr. Bruno Sepodes and Ms. Lesley Green (EMA Committee for Orphan Medicinal Products, EU), Dr. Lutz Altenhofen (German Institute for Quality of Efficiency in Health Care, Germany), Bartha Knoppers (Centre for Genomics and Policy, Canada), Dr. Edmond Jessop (National Health Services, UK), Dr. Roberto Giugliani (Federal University of Rio do Sul, Brazil), Dr. Juan Francisco Cabello (University of Chile, Chile), Dr. Maurizio Scarpa (Centre for Rare Diseases, Denmark), Dr. Jim McGill (Lady Cilento Children's Hospital, Australia), David Lee (Health Canada), Dr. Tammy Clifford (Canadian Agency for Drugs and Technologies in Health), Dr. Anne Pariser (Office of Rare Diseases Research, NIH).

The immediate outcomes of the proposed workshop will be to create a formal international partnership in orphan drug policy research, the development of summary publication, and to develop a SSHRC Partnership Grant proposal to secure funding that supports continued collaborative research between Canadian and international partners.

Research Excellence:

Part 1: What is the gap this cluster is trying to fill?

Until now, there has been no model for guiding development of clear and cohesive national orphan drug coverage policy, nor are there consistent international models for funding orphan drugs. The research cluster is in a unique position to build upon its demonstrated achievements in moving Canada toward a national orphan drug policy by partnering with international collaborators for the purpose of developing the best, most consistent, evidence global approach for orphan drug coverage.

Part 2: What are the objective measures of research excellence?

The research cluster will recruit international project participants, partners and stakeholders to develop a research agenda e.g. decision-making processes, price negotiations, orphan drug designation, and to produce a document formalizing an international partnership group for the purposes of pursuing a SSHRC Partnership Grant. The international partnership will aim to mobilize knowledge between academic and non-academic stakeholders to address societal, governmental and economic aspects of funding orphan drugs. Should a SSHRC Partnership Grant be awarded to this research cluster, an opportunity would be created for training UBC students and emerging scholars in a field of great societal importance. The ultimate measure of success will be the acquisition of further funding, and influencing the future development of reimbursement policy.

Research Dissemination:

The goal of this project is to stimulate cross-sector knowledge transmission by bringing in leading stakeholders from other countries facing similar challenges relating to orphan drugs. The meeting will serve both to share current knowledge obtained through the research cluster's past CIHR-funded project, and as a foundation for establishing an ongoing, international collaboration with the goal of furthering research and developing consistent orphan drug policy around the globe.

Collaboration with cross-sector knowledge-users is a strong and valuable characteristic of this research cluster. Previous projects included collaborations with Eric Lunn (Pharmaceutical Service Division, BC Ministry of Health) and Barry Jones (Strategic Policy Branch, Health Canada). Both Canadian and international knowledge-users will be invited to attend the roundtable, and will be consulted throughout the duration of the cluster's work.

Partnership with UBC's Graduate School of Journalism and the Global Reporting Centre (Peter Klein) will make the outcomes of this project available in a public forum. The award-winning online reporting project *Million Dollar Meds (http://www.milliondollarmeds.com/)* uses journalistic storytelling to highlight the challenges arising from a lack of clear policy on orphan drugs, and offers insight into the processes required to develop coherent national frameworks for funding rare disease treatments. Should the cluster gain additional funding, *Million Dollar Meds* will be expanded to include an international component, thus creating further education and research opportunities at UBC.

The Global Reporting Centre will also organize a public engagement event to mobilize knowledge about expensive drugs for rare diseases, utilizing some of the global experts attending the workshop.

BUDGET JUSTIFICATION

The cluster is requesting $100,000 to establish a formal partnership between the research cluster and international stakeholders with the intent of applying for a SSHRC Partnership Grant in February 2019. The VPRI funds will cover the cost of **partnership development** (UBC cluster meetings and a 2-day roundtable workshop), **public engagement** (public event) and **administration** (part-time staff to coordinate partnership development and SSHRC proposal preparation).

1. **Partnership Development** TOTAL ESTIMATE: $ 57,500

   UBC Research Cluster Meetings *Subtotal:* $3,000

An initial meeting with the local UBC research cluster will be held in January 2018, followed by two subsequent meetings: one to be held before the Roundtable Workshop (March 2018) and one cluster meeting to be held after the Roundtable Workshop (June 2018). Catering costs for each meeting (breakfast, lunch and coffee breaks) will be approximately $1000 ($1000 x 3 meetings = $3000).

2. **Roundtable Workshop at UBC** *Subtotal:* $54,500

Cluster members will be invited to attend a two-day Roundtable Workshop at UBC in person or via videoconference to be held in April 2018. Cost per traveler is estimated to be $2200 ($1600 per person for international flight roundtrip, $600 per person for 3 nights hotel, x 22 people = $48 400). Transportation costs (taxi fare) to UBC for attendees, if required, is estimated to be $1500 ($68 x 22 people). Catering costs for two days (breakfast, lunch and coffee breaks) will be $4600.

3. **Public Engagement Event** TOTAL ESTIMATE: $17,500

Utilizing some of the workshop attendees and a variety of stakeholders (patients, advocates, clinicians, payers, etc), the Global Reporting Centre will organize a public event to address the research, findings and future investigations of the cluster. Space rental is estimated to be $1000 and catering costs are $~8000 (coffee break, breakfast or lunch). Travel costs for speakers within BC are estimated to be $7000 ($500 per flight per person, plus one night hotel at $200 per night, x 10 people= $7000) Advertising for the event through the Vancouver Sun is $1500.

4. **Administration** TOTAL ESTIMATE: $25,000

A part-time research coordinator will oversee planning and implementation of cluster meetings and international roundtable, the public event, and preparation of the SSHRC Partnership Grant proposal. The research coordinator/assistant will assist in scheduling, travel booking, document preparation, and general communications.

TOTAL REQUEST: $ 100 000

TIMELINE

January 2018 to December 2018

	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sep	Oct	Nov	Dec
I. Partnership Development												
Identify and invite new partners	*	*	*									
UBC Cluster meetings	*					*				*		
Roundtable Workshop					*							
Public Event									*			
II. SSHRC Partnership Grant												
Grant preparation						*	*	*	*	*	*	*
Grant submission (February 2019)												
SSHRC decision (June 2019)												