The Future of Scientific Advice in Canada

CADTH Symposium 2017
Panel Objectives

• Explain the current Scientific Advice process and benefits to those involved

• Explore the future of HTA Scientific Advice through the lens of various stakeholders including CADTH, Health Canada and the pharmaceutical industry

• Discuss a recently completed innovative pilot project for providing Scientific Advice for products already in phase 3
Panel Participants

Moderator
• Don Husereau, Senior Associate, Institute of Health Economics

Panelists
• Dr. Amy Sood, Scientific Advisor and Lead, Scientific Advice Program, CADTH
• Dr. Cathy Parker, Director General, Biologics and Genetic Therapies Directorate, Health Canada
• Dr. Jens Grueger, Vice-President, Head of Global Pricing & Market Access, Hoffmann-La Roche
• Simon Yunger, Group Manager, Market Access and Health Economics, Hoffmann-La Roche
CADTH Scientific Advice: What?

- Program launched in January, 2015
- Advice on early drug development plans from a Canadian health technology assessment (HTA) perspective
- Non-binding, confidential, cost-recovery
- Eligibility: pre-Phase III
CADTH Scientific Advice: Why?

Help generate complete and relevant evidence for a Canadian reimbursement recommendation

For Industry
- Reduce uncertainty

For Drug Plans
- Recommendations based on more relevant evidence

For Patients and Clinicians
- Timely access for patients

4 weeks

Online Application

14 weeks

Briefing Book*

Scientific Advice Meeting

4 weeks

Record of Scientific Advice

*May submit a Briefing Book prepared for another agency to reduce workload
CADTH Scientific Advice: Who?

Record of Scientific Advice

- Health Economist
- Clinical Expert 1
- Clinical Expert 2
- Patient Interview
- CADTH Staff
## Type of Advice Requested

<table>
<thead>
<tr>
<th>Clinical Topics</th>
<th>Economic Topics</th>
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<tbody>
<tr>
<td>Target trial population and subgroups</td>
<td>Population</td>
</tr>
<tr>
<td>Trial Design and duration</td>
<td>Choice of comparators</td>
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<td>Choice of comparators</td>
<td>Choice of economic model</td>
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<tr>
<td>Primary and secondary endpoints; surrogate outcomes</td>
<td>Data to populate the model</td>
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<td>Health-related quality of life measures</td>
<td>Utility values</td>
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<td>Time horizon and extrapolation hypotheses</td>
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<td>Resource utilization data</td>
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Opportunities for Improvement?

- Semi-structured interviews conducted July to October, 2016
- Participants: 16 companies
  - 4 small
  - 6 large U.S.-based
  - 6 large internationally-based
Interview Findings: Key Themes

Perceptions on the opportunities for improvement:

- Scope
- Flexibility
  - Timing
  - Fees
- Parallel or joint advice with Regulatory or other HTA agencies
Post-Phase III Experience

Benefits:
• Economic model is much more developed at this time
• Great opportunity to give advice on specific aspects of the economic evaluation and adapt it to the Canadian setting

Challenge:
• Need to differentiate and separate Scientific Advice from CDR and pCODR processes
• Eligibility after initiation of Phase III trials is still under review
Launch of New Program Offerings

- **Increased flexibility** to better meet the needs of applicants. Talk to us about a potential product.

- Applicants may inquire about:
  - customized timelines
  - more timely advice for smaller requests
  - advice at multiple touch points

- We welcome your inquiries:
  requests@cadth.ca or scientificadvice@cadth.ca
Future of CADTH Scientific Advice

Initiatives underway:

• Health Canada participated as an observer at a Scientific Advice meeting in 2016

• Plans for Health Canada in 2017:
  • Attend CADTH Scientific Advice teleconferences and observe at the Scientific Advice meeting

• Collaboration with NICE
cadth.ca/scientificadvice

scientificadvice@cadth.ca
requests@cadth.ca
The Future of Scientific Advice in Canada

Catherine Parker
Director General, Biologics and Genetic Therapies Directorate
Health Products and Food Branch

2017 CADTH Symposium
April 24, 2017
Existing scientific advice processes

(1) Pre-Clinical Trial Application (CTA) consultation meetings

**Purpose/benefits** - provides an opportunity for the sponsor to present relevant data, discuss concerns and issues regarding drug development and obtain guidance on acceptability of proposed trial(s).

**Process** – sponsors are asked to suggest possible meeting dates ~ 3 months in advance due to volume of requests and submit an information package that contains a list of questions to be raised, brief summary of data, global clinical development plan, details of the proposed clinical trials to be conducted in Canada, summary of significant quality data.

**Timing** – can be requested prior to any CTA; however, majority are requested prior to pivotal trial(s)

Note: CTAs only required for trials conducted in Canada
Existing scientific advice processes

(2) Pre-Submission meetings

**Purpose/benefits** - sponsor can discuss data in support of a specific submission; help Health Canada prepare for and become familiar with forthcoming submission; uncover any major unresolved issues that can be managed early on.

**Process** –

- Meetings to be requested at least one month in advance; however, in reality meetings are being booked at least 3-4 months in advance due to volume of requests.
- A meeting package is submitted that contains a list of specific issues, brief summary of the drug product, proposed strengths and dosages, overview of the market history, summary of the development of the product, a summary of the clinical development plan, identification of the indication(s) for which approval is sought, brief summaries of the safety and efficacy data relating to the drug (e.g. draft product monograph)

**Timing** – generally months in advance of filing a submission; required as part of requests for Priority Review and Notice of Compliance with Conditions pathways
Other consultation processes

• Health Canada also encourages earlier engagement with sponsors
  – Pipeline meetings
    • Useful for workload planning purposes and identifying expertise needed for upcoming submissions
  – Biosimilars Scientific Advice Meeting Pilot; earlier engagement for complex or novel drugs

• All meetings are voluntary, upon request by the sponsor, and no specific user fees apply.
Experience

- Health Canada is seeing an increase in the number of requests for consultation meetings. There is significant workload associated with these meetings.

- Do sponsors follow through on advice given?
  - Sponsors generally do follow the advice provided. If the sponsor cannot abide by the advice given, a rationale must be provided upon filing.
  - Recommendation to put mechanisms in place to quantify this

- Sponsors often seek advice from other (larger market) jurisdictions and some may not seek advice from Health Canada in advance of filing a submission

- Do pre-submission meetings improve the quality of drug submissions and facilitate more timely reviews?
  - Positive feedback received from sponsors. Early discussions may help decrease the number of negative decisions issued.
Collaboration with CADTH - Past, present and future opportunities

- Past and present pilots between Health Canada and CADTH
  - CADTH-TPD Priority Review pilot
  - CADTH as observer to pre-submission consultation meetings for new product types, such as biosimilars
  - Exploring collaborations related to orphan drugs

NEW

- CADTH-TPD Oncology pilot (alignment of processes)
A look to the future….

Healthcare system collaboration and scientific advice

Providing early parallel advice by Health Canada and HTA
✓ Enable earlier interaction on development programs
✓ Increase the quality and appropriateness of information submitted by sponsor for regulatory decision making and HTA assessment
✓ Help identify data collection across product life cycle

Health Canada as observer/participants in CADTH’s Scientific Advice meetings

Press release

31/03/2016

Early dialogue with regulators and HTA bodies

Parallel scientific advice at EMA helps to reconcile different data requirements in one development plan to improve timely patient access to new medicines

The European Medicines Agency (EMA) has published today a report on its pilot on parallel scientific advice with health-technology-assessment (HTA) bodies that finished at the end of March 2016. This initiative that allows developers of new medicines to receive simultaneous feedback on their development plans from both regulators and HTA bodies is being continued.
“Then we’ve agreed that all the evidence isn’t in, and that even if all the evidence were in, it still wouldn’t be definitive.”

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Key reference documents

- Health Canada Guidance for Sponsors: Management of Drug Submissions
- Health Canada Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications
The Future of Scientific Advice in Canada: Experience in a global pharmaceutical company

Jens Grueger, PhD
Head of Global Pricing & Market Access

CADTH Ottawa, April 24, 2017
Pharma Pipelines have shifted to new disease areas

Roche pipeline includes products in diseases like:

- Alzheimer’s Disease
- Spinal Muscular Atrophy
- Autism
- Geographic Atrophy
- Rare cancers
Need to balance evidence expectations of regulators and HTA

• Regulators created new pathways for accelerated approval in areas of high unmet need

• HTA and payers remain concerned about reimbursing potentially costly therapies in the absence of robust data on outcomes

• Scientific advice can facilitate alignment between regulatory and HTA evidence expectations before finalization of clinical development program
Scientific advice has become standard

There are many sources of scientific advice

- **Advisory boards**
  - Internal vs external
  - Scientific Experts and patients

- **Scientific advice from HTA**
  - Single vs multiple agencies
  - Without or without participation from regulators

- **How early? How often?**
Roche experience

- Single Agency HTA Advice:
  - NICE (UK), HAS (France), GBA (Germany), AIFA (Italy), TLV, (Sweden), PBAC (Australia), CADTH, (Canada)

- Multiple agency HTA advice:
  - EUnetHTA, SEED

- With and without regulatory agencies
Implications for Roche

• **Aligned with internal decision tools (Access Evidence Metric) for late stage portfolio investments**

• **Has resulted in changes to clinical development program:**
  • Design of phase III studies (comparators, endpoints, study population, ...)
  • Acceptance and validation of surrogate endpoints and biomarkers
  • Relevance of medical affairs and real world evidence studies
  • Scope of health economic and budget impact models

• **Has given additional weight to internal access evidence guidance**
  • Similar to scientific and protocol advice from regulatory agencies
Experience with scientific advice

- Participation of clinical experts and patient representatives is important
- Focused questions and clear briefing documents are critical
- There are no simple answers
- Single agency advice is often more technical, multi agency advice more strategic
- Jointly agreed written minutes are very helpful
- Not every agency has competencies in every disease area
- Advice is often transferable within disease areas
- Scheduling is an art
Summary and recommendations

- Scientific advice has become standard practice
- Few products made it to market, difficult to assess final impact
- Agencies could specialize in certain disease areas, increases competency, allows for consistent guidance
- Consider disease specific written guidance documents similar to what regulators are providing
- Always include the regulator
Doing now what patients need next
Scientific Advice

A Canadian Pharmaceutical Affiliate Perspective

Simon Yunger

Group Manager, Market Access and Health Economics
Why is Scientific Advice Important?

WE HAVE INCOMPLETE DATA, SO I’LL NEED TO USE MY INTUITION AND EXPERIENCE TO MAKE THE DECISION.

BECAUSE MAGICAL THINKING FIXES IGNORANCE?

HUSH! I THINK I HAVE SOMETHING.

I THINK SO TOO.
## What Clinical Data would CADTH Prefer?

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<tr>
<th>Criteria</th>
<th>Sub-Criteria</th>
<th>Sub-Criteria Definitions</th>
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<tbody>
<tr>
<td>Overall Clinical Benefit</td>
<td>Effectiveness (systematic review in the Clinical Guidance Report)</td>
<td>The potential health impact of the drug compared to the other drug and non-drug alternatives, measured in terms of relevant patient outcomes such as mortality, morbidity, quality of life. Magnitude, direction and uncertainty of effect should be considered.</td>
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<tr>
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<td>Safety (systematic review in the Clinical Guidance Report)</td>
<td>Frequency and severity of adverse effects associated with the new drug compared to other drug and non-drug alternatives.</td>
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<td></td>
<td>Burden of Illness (Clinical Guidance Report, patient advocacy group input)</td>
<td>Incidence, prevalence or other measure of disease burden on the population.</td>
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<tr>
<td></td>
<td>Need (Clinical Guidance Report, patient advocacy group input)</td>
<td>Availability of an effective alternative to the drug technology.</td>
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Unified Advice from Experts

Target population

Choice of comparator

End points for reimbursement

Statistical issues (stratification, subgroups)

Trial design and duration

Current and ex CDR and pCODR Reviewers

Health Economists

Patient Representatives

Data used to populate model

Population

Choice of economic model

Utility values

Choice of comparator

Resource utilization data

Time horizon and extrapolation hypothesis
CADTH Scientific Advice Pilot

*Product Already in Phase III*

- Sought Scientific Advice for a product already in phase 3

- Provides clarity on key issues that may arise during CDR/pCODR review

- Provide HTA advice on a clinical trial design developed to meet regulatory approval

- Development and further refinement of the economic model
Advice on Development Plan Outside of Pivotal Trial

- Burden of Illness Studies
- Extension Studies
- Phase 3B studies
- Utility Generation
- Natural History of Disease
- PRO Validation
- Post Approval Registries
Utility of Scientific Advice

Clinical/Medical
- Future study design
- Future Ph. IV and RWD studies
- Inform publication and education around patient-centered measures for new therapeutic area

Global and Local Health Economics
- Utility study and CE Model structure

Local Affiliates
- Inform local HTA strategy (i.e. which data cut-off is most appropriate for HTA)
- Provided insights on areas of focus for HTA review, which will help tailor submission to CADTH
- Provide stronger probability of HTA success to enable commercialization at local level
Challenge for a Canadian Affiliate

Sources: 2016 ITA Pharmaceuticals Top Markets Report; IMS Health Study,
Health Canada and CADTH Collaboration

- Support collaboration between Health Canada and CADTH in areas where it would be beneficial to all parties involved and speed/improve access to patients
  - Scientific Advice is one of these key areas
What would advice from Health Canada and CADTH look like?

Phase II Clinical Evidence in Canadian Oncology Health Technology Assessment Recommendation. R Milenkovski, S Yunger, D Shum. CADTH Symposium 2017
Conclusion – Recommendations for the future

• Scientific Advice is a highly valuable process to gain HTA insights during the development process

• Future Opportunities
  – Parallel/Joint Scientific Advice with Health Canada
  – Joint Scientific Advice with other HTA Bodies
  – “Targeted Scientific Advice”
  – Flexible timelines to meet changing clinical trial dynamics
Doing now what patients need next