Harmonization and Alignment of HTA Reimbursement and Regulatory Processes for Non-pharmaceutical Health Technologies

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Background: Existing Paradigm in Obtaining Market Access

Class I & II Devices

- Discovery + Ideation
- Invention + Prototyping
- Preclinical
- Clinical
- Regulatory Decision
- Product Launch
- Post-market Monitoring

Class III & IV Devices

- Quality, safety, efficacy
- Risk-benefit profile

Market Authorization

- Yearly licensing renewal

Assessment Focus

Key Stakeholders

- Industry/Manufacturers
- Regulators
- Payers

Unknown: may/may not be evidence-based

HTA

Advocates/Stakeholders

Relative efficacy/effectiveness
Economic and budget impact

Market Access?
# Regulatory Approval vs. HTA/coverage

<table>
<thead>
<tr>
<th>Decision</th>
<th>Regulatory Approval</th>
<th>Reimbursement (based on HTA)</th>
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<tbody>
<tr>
<td></td>
<td>Does the product do more good than harm? Should this technology be available?</td>
<td>Does product offer useful, appropriate (and affordable) benefits for patients compared to what is most commonly used in the disease area? Should we buy this technology at the current price?</td>
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<table>
<thead>
<tr>
<th>Type of Evidence</th>
<th>Safety</th>
<th>Efficacy</th>
<th>Quality (e.g. good manufacturing practices)</th>
<th>Safety</th>
<th>Effectiveness and quality of life</th>
<th>Economics and budgetary impact</th>
<th>Social, ethical, legal, organizational impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence considered</td>
<td>Pre-launch: RCT (usually placebo-controlled)</td>
<td>Post-launch: Relative efficacy or effectiveness</td>
<td>Pragmatic RCT, observational studies</td>
<td>Relative effectiveness and costing studies</td>
<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>Validity</th>
<th>Internal validity</th>
<th>Internal &amp; External validity</th>
</tr>
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<thead>
<tr>
<th>Endpoint</th>
<th>Laboratory findings and surrogate endpoints</th>
<th>Quality of life</th>
<th>Final clinical ‘hard’ outcomes (e.g. mortality)</th>
</tr>
</thead>
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<tr>
<th>Comparator</th>
<th>Placebo</th>
<th>Active control, ideally standard of care</th>
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| Time horizon | Trial duration | Life-time; or at least the time needed to capture all risks and benefits of treatment |
Criticism of Existing Paradigm

- Disjointed and poor alignment between regulatory and HTA/reimbursement has resulted in:
  - Delayed patient access:
    - Inefficiencies that are time- and resource-intensive due to:
      - Dual clinical development track
      - Duplicated, sequential assessment
  - Increased uncertainty for manufacturers:
    - Different decisions between regulators and payers
Objectives

The purposes of this study were to:

- To identify and evaluate proposed and existing strategies to harmonize regulatory and HTA/reimbursement processes.

- To contextualize the findings into the Canadian health-care system by predicting potential implementation and operational challenges to harmonization.
Methods

- Systematic literature review:
  - Captured literature published up to September 4th, 2012
  - Database searched: OVID Medline, EMBASE, Cochrane, HEED, PubMed, BIOSIS
  - Grey literature: agency websites, policy documents, commissioned report, working papers
  - Both articles on pharmaceuticals and non-pharmaceuticals were included

- Interviews
  - Semi-structured
  - Snow-ball sampling approach
Results

PRISMA flow diagram

- Records identified through database searching (n = 2824)
- Additional records identified through other sources (n = 51)
  - Records after duplicates removed (n = 2659)
    - Records screened (n = 2659)
      - Records excluded (n = 2545)
        - Full-text articles excluded, with reasons:
          - Not relating to HTA/reimbursement process (n = 13)
          - Not on harmonization of HTA and regulatory activities (n = 38)
          - Not primary literature (n = 3)
      - Full-text articles assessed for eligibility (n = 114)
        - Studies included in qualitative synthesis (n = 60)
Results: Interviews

- 14 interviews
- Individuals from:
  - Canada (57%)
  - United States (15%)
  - United Kingdom (14%)
  - The Netherlands (7%)
  - International perspective (7%)
- HTA, regulatory, academic, and consulting
Results: Harmonization Strategies

- The following strategies were identified with an intent in harmonizing HTA/reimbursement-regulatory processes:

1. Alignment of evidentiary needs
2. Tripartite early dialogue
3. Parallel Submissions
4. Pre-market evaluation
5. Adaptive licensing
Our Classification System of Harmonization Approaches

- Passive
  - Aligning Evidentiary Needs
    - Alignment of Evidentiary Needs
  - Harmonizing Timeframes (Logistics)
    - Early Dialogue
    - Parallel Licensing
    - Pre-market evaluation
    - Adaptive Licensing

- Active
Alignment of Evidentiary Needs

- Conceptual papers and interviews focused on modernizing regulator’s evidentiary standards
  - Expansion to new evidentiary criteria:
    i) Active-comparator relative efficacy (comparative-effectiveness)
    ii) Cost-effectiveness
  - Alignment of study methodology to meet both agencies’ need:
    • Choice of comparator
    • Timing: Long-term vs. short-term assessments
    • Choice of outcome: surrogate vs. final clinical outcome
Tripartite Early Dialogue Processes

- Early and continued interaction between regulators, payers and manufacturers
  - Benefits:
    - Manufacturer: Supports single clinical trial program to provide relevant evidence to meet requirements of both assessment bodies
      - Clarifies needs of each agency (e.g. measurement and analytic tools for outcomes, trial design)
    - Assessment agencies: Promote mutual understanding of the other’s methods and requirements
  - May involve input from clinician and patients
Objective: reduce time between regulatory and reimbursement decision by aligning the assessment processes of both agencies.
Pre-market Evaluation

➤ Application Phase

Submission
Applicants complete an application form and submit it to MaRS

Screening
MaRS collaborates with applicants to fine tune the application

Review
The OHTAC Subcommittee reviews the applications and makes recommendations

Selection
The EXCITE Management Board selects and prioritizes the successful candidates

➤ Consultation/ Evaluation Phase

Health Tech Innovators

Application
Consultation
Evaluation/ Execution

Good Fit?
Robust Study Design?
Strong Data?

EXCITE Involvement

Regulatory
Adoption
Patient Use

Reference: http://excite.marsdd.com
Adaptive Licensing

Two activities that may work concertedly:

- Regulatory: broadening of license
- Reimbursement: coverage with evidence development
Adaptive Licensing

General Challenges

- Requires a culture of value in which innovation is rewarded
- Lack of tools and legal structure to ensure continued compliance by manufacturers in gathering additional data
  - Introduction of a different reward structure and progressive policies
- Infrastructure: how to support data collection?
- Earlier evidence = lower evidence standards?
RECURRING GENERAL CHALLENGES
Environment of Trust and Mutual Understanding

- Requires open and continued dialogue:
  - To promote mutual understanding on each other’s purposes, remits and processes
    - Limits will likely exist on the extent of harmonization possible and over-ambitious goals should be avoided
  - To increase confidence that existing roles will remain and avoid ‘protecting turf’ mentality

- Dialogue may extend beyond to include manufacturers, patients and prescribers
Confidentiality

- In Canada, legislation exist limiting what and when information can be disclosed
  - Requires manufacturer’s consent

- A method is needed to handle and share confidential information
  - What was studied?
  - How were decisions made?

- However, manufacturers often concerned with security of sharing proprietary information since each agency handles such information differently
Operational Issues

- Project management requires the existence of a secretariat or agency
- Appropriate personnel support needed to prevent short-staffing
- Strong leadership
- Appropriate financing
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- Active
Conclusion

- Complex web of interactions presently impact the introduction and diffusion of a health technology into the market.

- Harmonization of evidentiary requirements may increase effectiveness of the decision-making process and may provide other benefits to the stakeholders involved in the healthcare system.
Conclusion

Various theoretical models on harmonization have been put forth with a number of practical attempts made so far demonstrating its feasibility.

Approaches to harmonization have focused on:

• (i) Aligning procedures to reduce uncertainty and knowledge gaps
• (ii) Aligning timeframes and other logistical aspects of the review process
Conclusion

➢ The main challenges of harmonization:
  • Greater interaction and open dialogue between regulators and HTA/payers with buy-in from other stakeholders
  • System to share and handle proprietary information
  • Operational issues
Acknowledgements

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➢ The views presented here are solely that of the presenters and do not necessarily reflect official views of Health Canada.
Thank you

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Supplementary Slides
Strategy Specific Challenges
Alignment of Evidentiary Needs

Challenges

- Non-pharmaceutical health technologies have a more prominent organizational impact than drugs, which may be evaluated in an HTA.

- “Protecting turf” resistance:
  - Concern that this may lead to a single regulatory-HTA process.
Tripartite Early Dialogue Processes

Challenges

- Value of advice depends on its stability:
  - R&D is a long-term process, difficult for manufacturers to reverse decisions once trial begins
  - But, advice is dependent on the existing evidence, which may change over time
  - Solution: Iterative early-dialogue process

- Confidence in advice provided
  - Written advice provides greater confidence but may not always be provided
Parallel Submissions

Challenges

- Less rigid data requirements for device licensing
  - Solution: Concurrent framework to align evidentiary data needs and ensure appropriate data collection prior to submission

- Potential waste of resources and time if HTA conducted on products that ultimately fail to obtain regulatory license
  - Could certain components of the HTA be completed that aren’t resource intensive but would reduce the time delay?
  - Could technologies be screened/ prioritized to identify those with the greatest likelihood of obtaining regulatory approval?
Pre-market Evaluation
Opportunities & Challenges

Several factors must exist for this program to be successful:

• Academic centers with experience with field evaluation and coverage-with-evidence-development activities

• Mutual understanding between stakeholders, especially in aligning different interests between manufacturers and academic centers