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

Lisa Masucci, Bernice Tsoi, Kaitryn Campbell, Daria O’Reilly, Mike Drummond, Ron Goeree

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Background: Existing Paradigm in Obtaining Market Access

Class III & IV Devices

Discovery + Ideation → Invention + Prototyping → Preclinical → Clinical

Class I & II Devices

Regulatory Decision → Product Launch

Market Authorization

Yearly licensing renewal

• Quality, safety, efficacy
• Risk-benefit profile

• Relative efficacy/effectiveness
• Economic and budget impact

HTA

Unknown: may/ may not be evidence-based

Advocates/Stakeholders

Industry/Manufacturers

Regulators

Payers

Assessment Focus

Key Stakeholders

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>
</tr>
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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>
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<table>
<thead>
<tr>
<th>Validity</th>
<th>Internal validity</th>
<th>Internal &amp; External validity</th>
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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>
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<tr>
<th>Comparator</th>
<th>Placebo</th>
<th>Active control, ideally standard of care</th>
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<tr>
<th>Time horizon</th>
<th>Trial duration</th>
<th>Life-time; or at least the time needed to capture all risks and benefits of treatment</th>
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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
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

ACTIVE
- Harmonizing Timeframes (Logistics)
  - Early Dialogue
  - Parallel Licensing
  - Pre-market evaluation
  - Adaptive Licensing

Aligning Evidentiary Needs

Harmonizing Timeframes (Logistics)
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
Parallel Submissions

- Objective: reduce time between regulatory and reimbursement decision by aligning the assessment processes of both agencies.

**Existing Process:**
- Regulatory Decision
- Product Launch
- HTA/Reimbursement
- Market Access
- Post-market Monitoring

**Harmonized Process:**
- Regulatory Decision
- Product Launch
- HTA/Reimbursement
- Market Access
- Post-market Monitoring
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

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
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
Our Classification System of Harmonization Approaches

**PASSIVE**
- Aligning Evidentiary Needs
- Harmonizing Timeframes (Logistics)
  - Early Dialogue
  - Parallel Licensing
  - Pre-market evaluation
  - Adaptive Licensing

**ACTIVE**
- Alignment of Evidentiary Needs
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

Contact
lisamasucci@hqontario.ca
masucl@mcmaster.ca
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
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?
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