EVALUATING OUR CURRENT PREMARKET DEVELOPMENT PROCESS FOR PERSONALIZED MEDICINE TECHNOLOGIES

The uptake of market-approved technologies is often delayed due to the absence of the right kind of evidence and information on how these tools meet the needs of the healthcare system. One solution to this problem is to re-draft the pre-market development process to include an integrated evaluation approach that develops both the evidence required for product licensing and for payer and market adoption. The objective of this document is to provide a framework for developing a pre-market development process in Ontario that can address the particular aspects of personalized medicine technologies. This will help enhance the competitiveness of Ontario’s premarket development process, improve Ontario’s reputation as a destination for personalized medicine product development, and increase the quantity and quality of products accepted adopted for use in Ontario, amongst other benefits.

WHAT IS THE PROBLEM?

Personalized medicine (PM) is a healthcare model based on the use each patient’s molecular characteristics to better inform clinical decisions. PM technologies have the potential to better diagnose a patient’s disease, guide treatment, and even predict disease onset and guide prevention. In Ontario and elsewhere, significant research dollars have been spent on developing personalized medicine technologies. However, such technologies have not had the anticipated impact on patient health or on industry success (Crawford and Aspinall, 2012). Problems include the fact that payers have resisted uptake due to unclear clinical utility and cost effectiveness, and clinical labs struggle with regulatory issues, payment and with rapidly changing technologies. PM technologies present unique policy challenges for payers due to the type of information a PM test can provide. For example, predictive genetic tests (those that predict future onset of disease) present the following challenges in generating the appropriate supportive evidence:

- Cost, length and complexity of studies are prohibitive – would pre-and post-disease onset of archive pathology specimens be suitable approach; what is the role for surrogate or intermediate outcomes?
- How is the predictive test threshold determined for recommending preventive approaches following a positive test in asymptomatic individuals? This information could be generated in different ways; what are the respective policy approaches if:
  - People who are being tested following identification of an index case (e.g. hypertrophic cardiomyopathy evaluation in family members of an affected individual)?
  - People are identified through opportunistic or population-based screening?
  - Where the test was not requested but formed part of an array or genome study (i.e. “incidental findings”)
- How is the relative contribution to outcome of environmental versus genetic factors determined?
We propose that a better premarket development process, following the example of the process central to the MaRS EXCITE program, would improve the quality and uptake of PM technologies.

### ABOUT MARS EXCITE

MaRS Excellence in Clinical Innovation and Technology Evaluation (“EXCITE”) was formed to help get health technologies to market faster with the expectation of improved health outcomes. The program is designed to provide not only the evidence base but the economic analysis needed to demonstrate that the technology meets the needs of the healthcare system. EXCITE “helps companies increase the likelihood of success for their breakthrough technology-based health innovations through a more effective approach to navigating the required approvals, adoption and uptake. EXCITE unifies Ontario’s best-in-class approach to medical technology testing, bringing together a broad spectrum of research under one harmonized platform based on relationships brokered with academic health research facilities across the province.”

MaRS EXCITE works with companies during the pre-market development stage, bringing in the “health technology assessment” (HTA) process early in product development to guide product development and expedite product adoption. This helps innovators, by faster and more probable adoption and uptake, investors, by reducing risk, the health system, by matching innovation with needs, enabling smooth adoption and improving healthcare at a lower cost, and Ontario, by growing companies and providing jobs.

### Features

- Removes the requirement for post-market, evidence-based analysis
- Presents an integrated evaluation approach that combines the evidence required for product licensing and market adoption
- Innovators get feedback earlier in the development process, when there is time to make any required adjustments to meet the needs of the medical system and increase the likelihood of adoption and uptake of their breakthrough health technologies
- Provides companies with valuable evidence and business requirements — key information for regulatory reviews, reimbursement reviews and competitive positioning
- Funders/investors can have more confidence that investments will pay off
- Health care providers can prepare appropriately for new technologies and make better use of them once adopted – making a direct and positive impact on health outcomes

### APPLYING THE MARS EXCITE PROCESS TO PERSONALIZED MEDICINE TECHNOLOGIES

Examples of specific aspect of premarket HTA that need to be considered for PM technologies:

- The perceived health burden associated with PM technologies
  - Prevalence and severity of the targeted disease
• Availability of intervention for those with a positive test
  • Likelihood of inappropriate use

• Practical issues
  • Availability of the test,
  • Relevance to health-care providers and consumers
  • Potential clinical or public health impact

• If a pharmacogenomics test:
  • Who pays for the test
    • When the test is bundled with the drug by Health Canada?
    • When the test is not bundled with the drug?
  • Who oversees the Quality Assurance component of the test?
    • When the test is bundled with the drug
    • When the test is not bundled with the drug
  • What might drive market creep (e.g. targeted therapeutics for a specific mutation associated with a particular tumour used for patients with a different type of tumour yet bearing the same mutation)

• If a predictive test:
  • Weighing harms and benefits:
    • Ability to mitigate risk? (e.g. BRCA, newborn screening)
    • Complications from interventions following a positive test (e.g. screening for prostate cancer)
  • Will test lead to appropriate changes in behavior?
  • What will impact be on budget based on:
    • Prevalence
    • Pedigree to be tested
    • Costs attributed to the test including counseling, immediate and lifetime additional diagnostic tests, physician visits and interventions
    • Effectiveness determined by disease avoided, modifications of the natural history, quality of life, changes in mortality rates
  • Consistency with societal/ethical values

WHAT IS THE DESIRED OUTCOME?

• Higher success rate of market adoption of Ontario PM technologies both in Ontario and internationally
• Faster market adoption of Ontario PM technologies both in Ontario and internationally
• International PM technologies attracted to Ontario for premarket development including clinical trials plus premarket HTA
• Better access of Ontarians to latest technology either through clinical trials or as MOHLTC-approved technology
Better alignment of policy with needs of PM technologies both from perspective of developers and payers

WHAT ARE THE BARRIERS TO ACHIEVING THIS OUTCOME?

The following are important factors that are considered to be potential barriers to developing an effective pre-market HTA for PM technologies:

- **Inconsistency in evaluating evidence**: There is limited consensus among stakeholders about the types of evidence needed, outcomes to be assessed, and thresholds to be set for determining clinical benefit of genomic tests (i.e. how is the predictive test threshold determined for recommending approaches following a positive test in asymptomatic individuals? How is the relative contribution to outcome of environmental versus genetic factors determined?)

- **Lack of a robust regulatory infrastructure/policy**: There are inadequate decision frameworks that provide transparent, consistent, fair, and equitable policy that are consistent with societal/ethical values for genomic tests (i.e. effects of a negative test, privacy and insurance, affected costs attributed to test, counseling, and interventions)

RECOMMENDATIONS

The following are recommendations to mitigate the barriers to achieving an effective pre-market HTA for PM technologies:

- **Look into the major challenges in evaluating evidence** for PM technologies and determine an appropriate methodology that would be acceptable to most of the stakeholders in the healthcare system (i.e. associate with the Evaluation of Genomic Applications in Practice and Prevention [EGAPP] initiative)

- **Gather stakeholders to establish a working group to identify key societal/ethical issues** in PM technologies and develop a regulatory framework that is transparent, consistent, fair, and equitable (i.e. involvement of members in the Ontario Personalized Medicine Network throughout this process is vital)

Resources


Much of this document is derived from a presentation by Dr. Les Levin “Personalized medicine – the alignment between great expectations, evidence and policy”. Genome BC 2012 Winter Symposium.