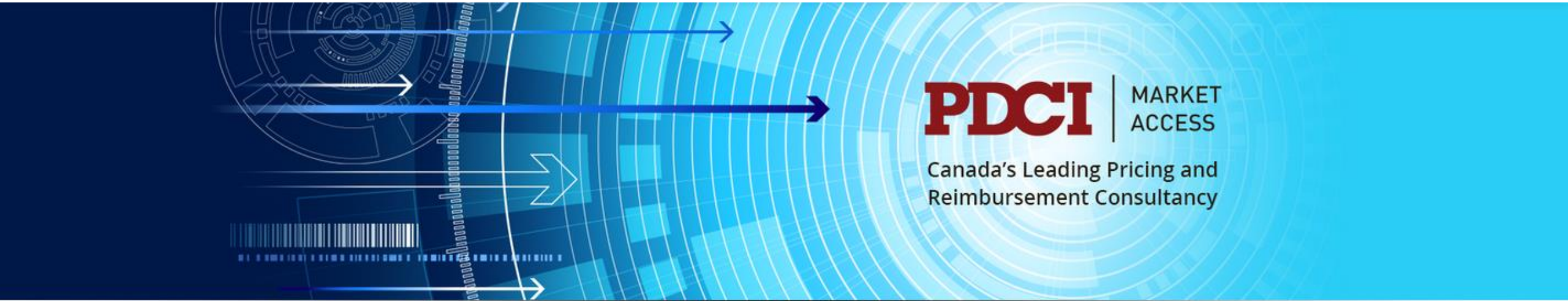
Overview, Impact and Implications of PMPRB 2019 Price Reforms

Neil Palmer

December 4, 2019



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Outline

- Brief History and Overview
- Current PMPRB Price Review Process
- Overview of Amended Regulations & Draft Guidelines
- Impact & Implications
- Next Steps

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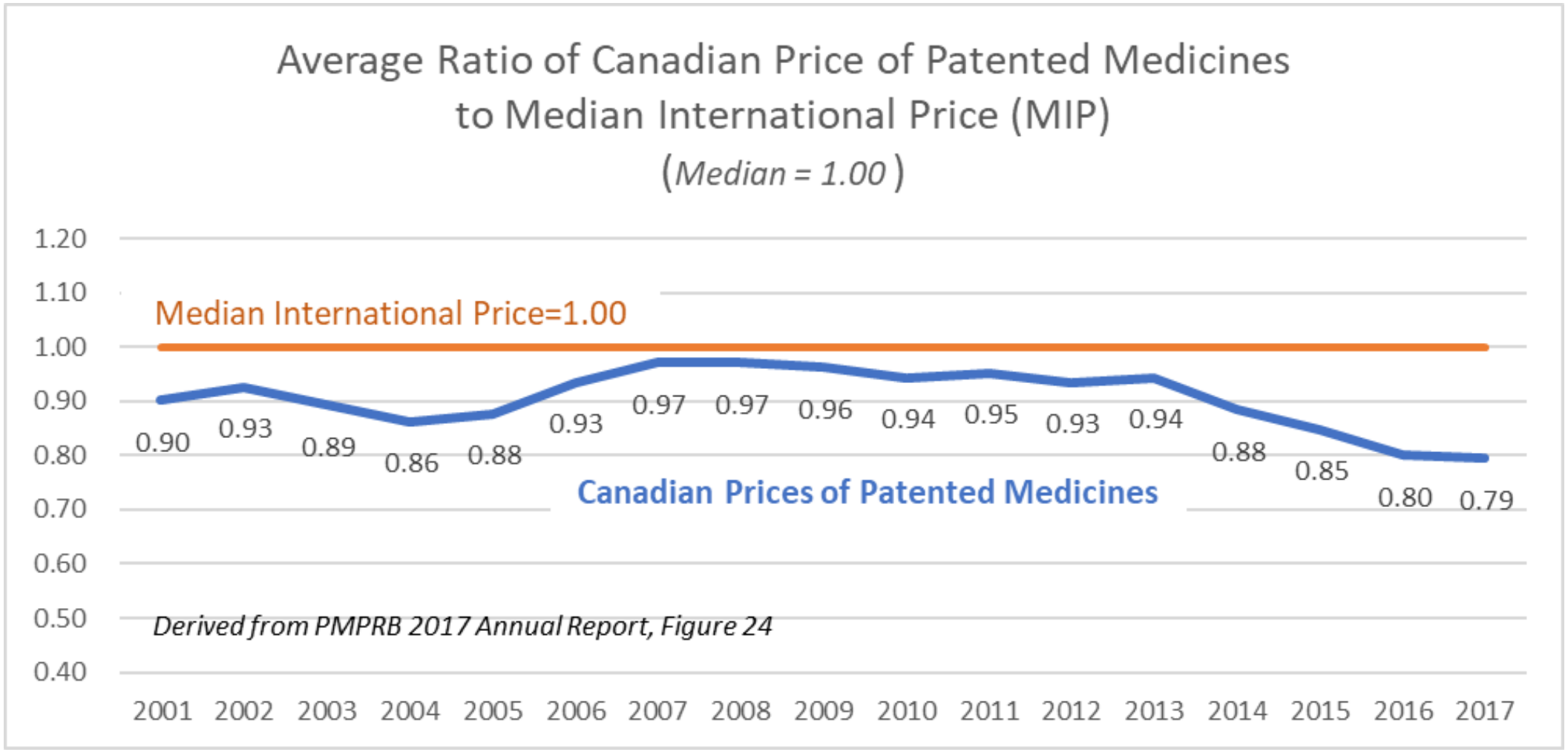
PMPRB Overview

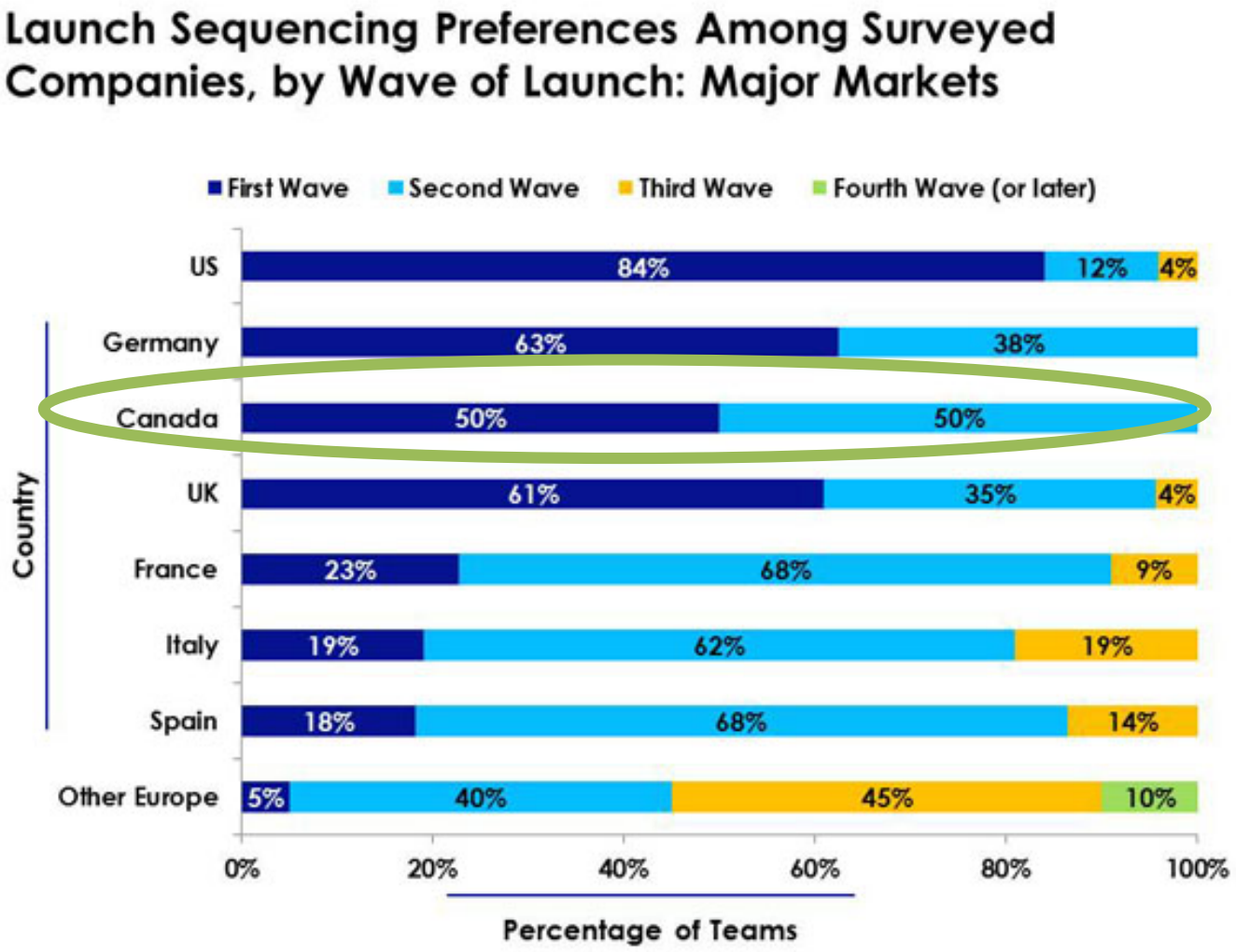
- Created in 1987, the PMPRB is a federal regulatory agency with a statutory mandate
  - To ensure prices of patented medicines are not “excessive”
  - To report to Parliament on price trends and research spending in the pharmaceutical industry
- PMPRB regulates the maximum “factory gate” prices that can be charged in Canada for patented medicines by considering the excessive price factors in the Patent Act:
  - Prices of other drugs in the same therapeutic class
  - Prices in other countries
  - Changes in inflation (as measured by the Consumer Price Index or CPI)
- PMPRB carries out its price review mandate by applying its Excessive Price Guidelines as part of its compliance and enforcement policy

PMPRB Policy:

Canadian prices, on average, should not exceed median international price..



Canada is currently a 1st or 2nd wave launch country

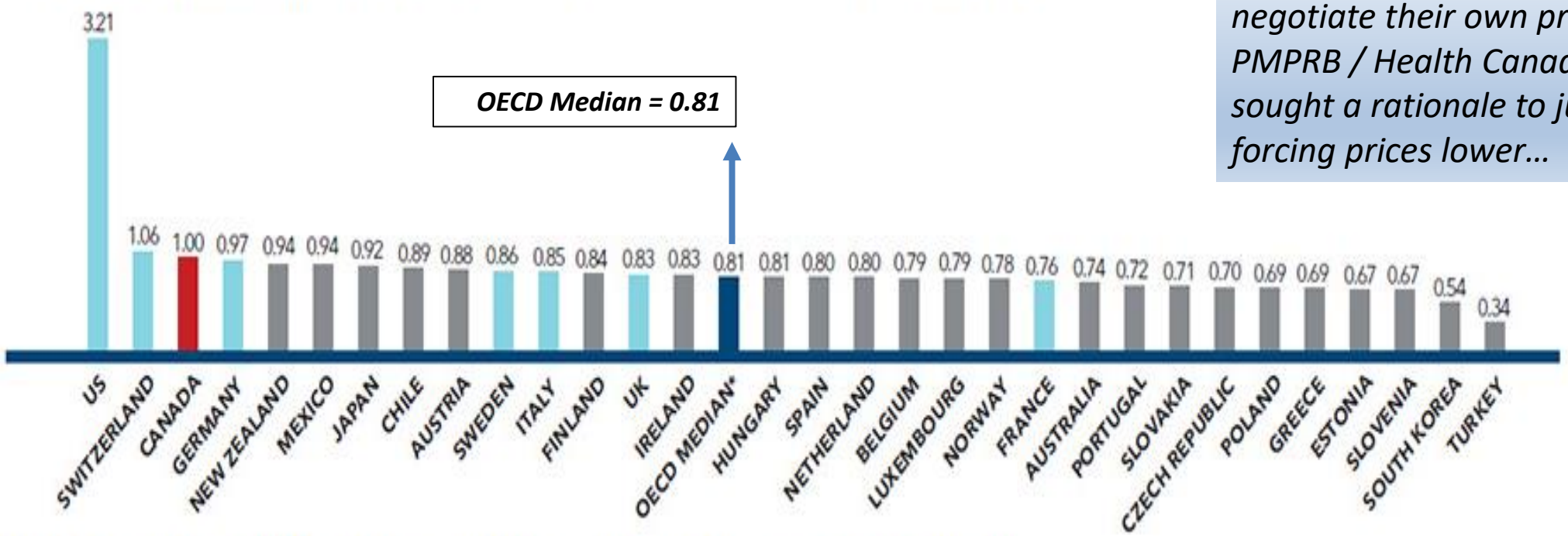


Source: Cutting Edge Information, 2016

IQVIA: OECD Median Price ~20% Below Canadian Prices (on average)

PMPRB had become less relevant to payers (that negotiate their own prices) so PMPRB / Health Canada sought a rationale to justify forcing prices lower…

Figure 21. Average Foreign-to-Canadian Price Ratios, Patented Medicines, OECD, 2017



* Calculated at medicine level for medicines with prices available in at least three foreign markets

Source: MIDAS™ database, 2017, IQVIA. All rights reserved.

PMPRB Reforms Timeline

June – Oct 2016	PMPRB Discussion Paper Rethinking the Guidelines
May 16- Jun 28 2017	Federal Health Minister proposes new excessive price factors in regulations that would target OECD Median Price
Sept 8, 2017	Health Canada Cost Benefit Analysis published
Dec 2, 2017	Canada Gazette 1 pre-publication of Regulations
Dec 11, 2017	PMPRB Scoping Document (conceptual description of new guidelines)
Jan 29, 2018	PMPRB Outreach Session
June 25, 2018	Steering Committee established, **Guideline Guidance Document issued**
December 2018	PMPRB publishes Case Studies of new Category 1 drugs
August 2019	Canada Gazette Part 2 **Regulations enacted**
November 2019	**Draft Guidelines released, 60-day consultation period**
February 2019	**Policy Forum, Working Groups to be established**
July 2020	**Earliest Expected Implementation Date**

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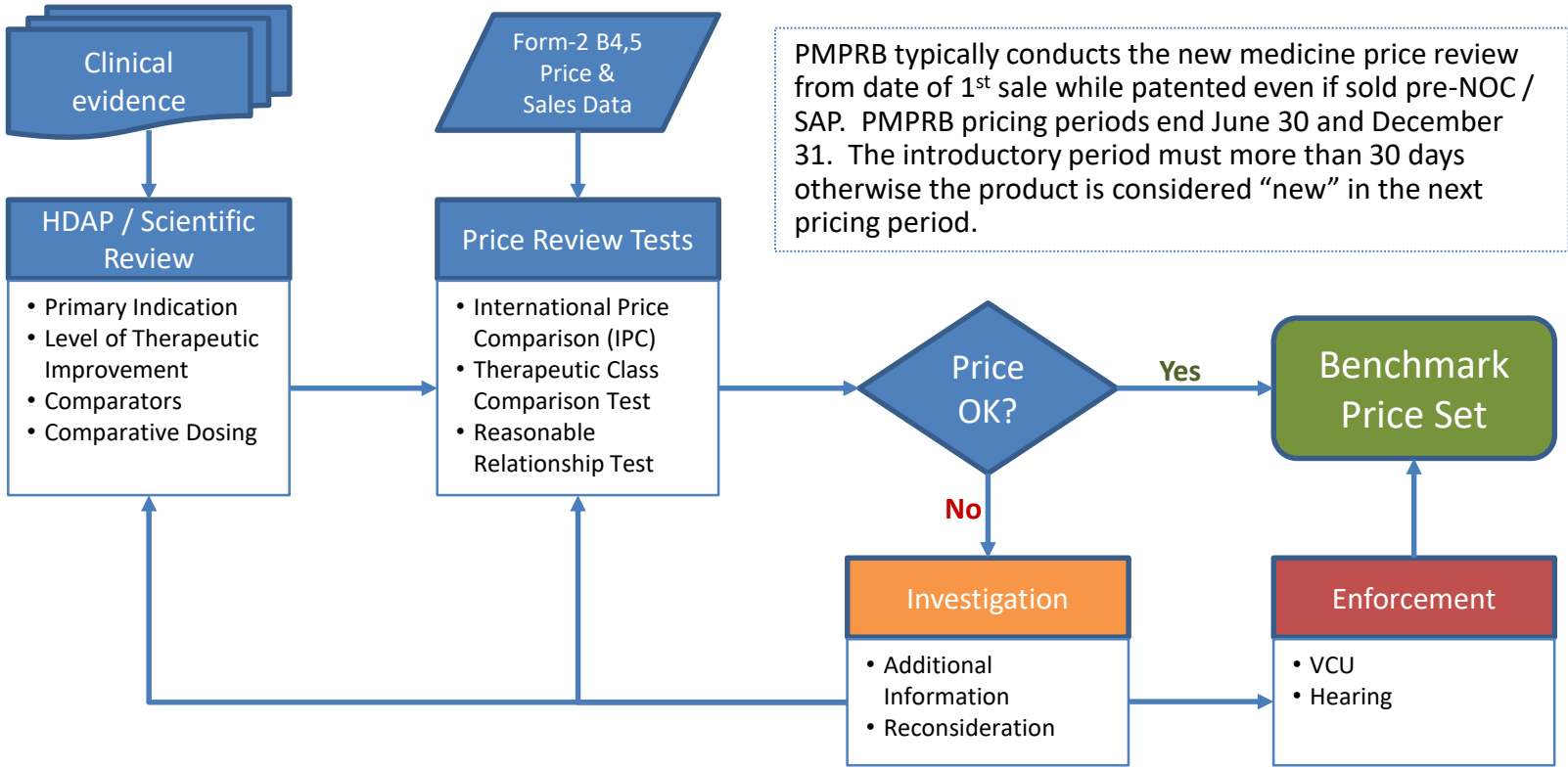
Current New Medicine Price Review Process informed by Clinical Evidence



PMPRB typically conducts the new medicine price review from date of 1st sale while patented even if sold pre-NOC / SAP. PMPRB pricing periods end June 30 and December 31. The introductory period must more than 30 days otherwise the product is considered "new" in the next pricing period.

Underlying principle

The Guidelines anticipate higher prices for drugs that offer therapeutic improvement, and the same, or lower prices for drugs that do not.

- Recommendations of the HDAP (an independent therapeutics committee) determine the "primary indication" level of therapeutic improvement and comparators for therapeutic class comparison tests
- The level of therapeutic improvement determines which prices test are applied

PMPRB Level of Therapeutic Improvement and Price Tests

Level of Therapeutic Improvement	% of New Medicines*	New Medicines Price Tests	Existing Medicines Price Test	All Patented Medicines HIPC Price Test
Breakthrough	2%	MIPC	CPI 3-year methodology	Patented medicines, new and existing, may never exceed the highest international price (PMPRB-7)
Substantial	3%	Higher of: TCC & MIPC		
Moderate	13%	Midpoint of: TCC & MIPC (but not lower than TCC)		
Slight or No	82%	TCC or RRT		

IPC = International Price Comparison MIPC= Median IPC HIPC= Highest IPC
TCC = Therapeutic Class Comparison RRT = Reasonable Relationship Test CPI = Consumer Price Index
* % of new patented medicines introduced between 2010 and 2017 as categorized by PMPRB HDAP

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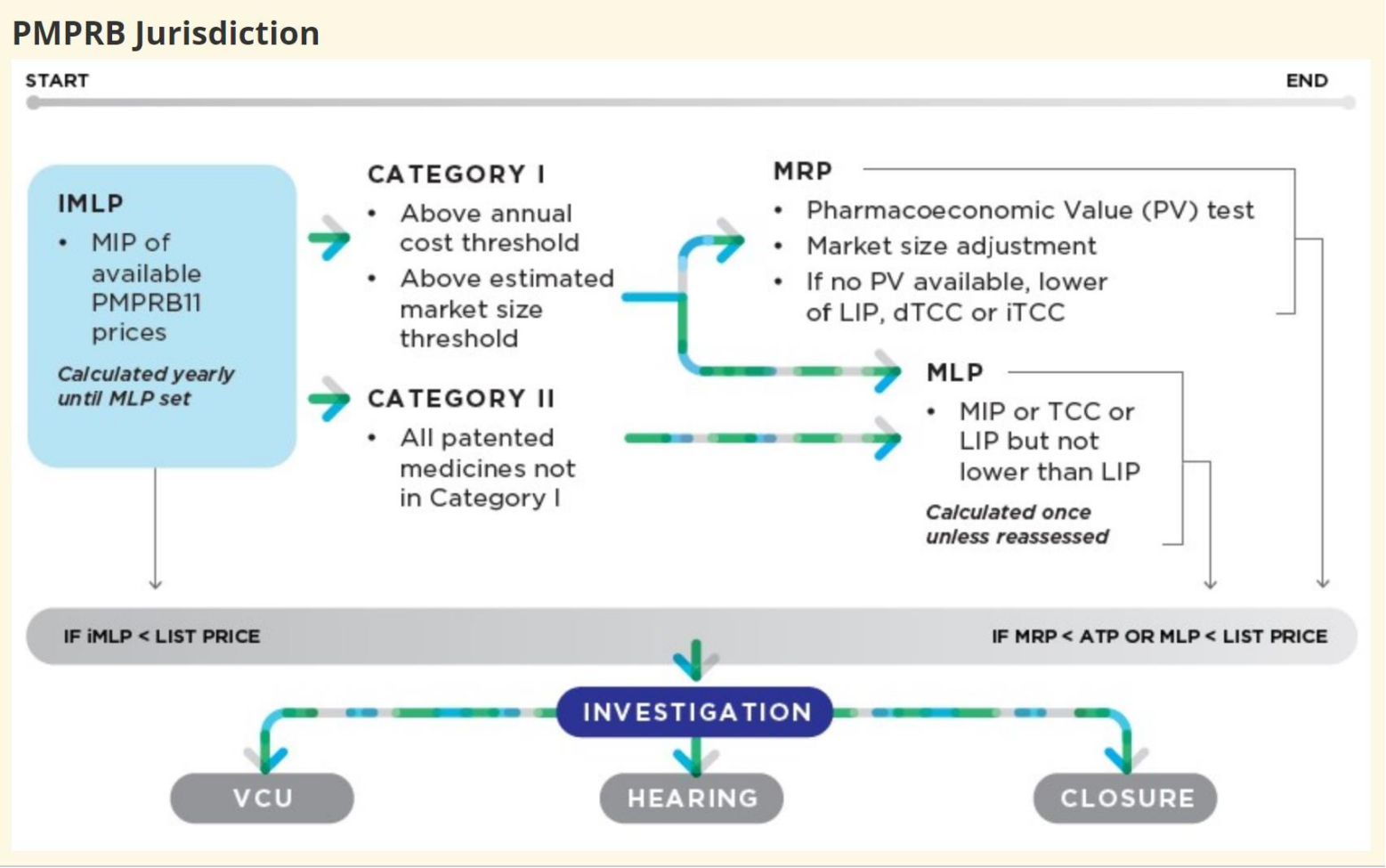
New Guidelines: Process for setting Maximum List & Rebated Prices

(Clinical Evidence need not apply!)



- *Interim Max List Price (IMLP) set by median international price (PMPRB-11) (for 3 years or 5 countries)*
- *Final Maximum List Price (MLP) set by lower of MIP and dTCC but not lower than LIP*
- *Maximum Rebated Price (MRP) is the List Price adjusted for Market Size and PV, or if no PV, the lower of LIP, dTCC, iTCC*
- *TCC calculated as the median price in the therapeutic class*

MIP= Median International Price LIP=Lowest international Price

TCC= Therapeutic Class Comparison dTCC= domestic TCC iTCC-=international TCC

Formulaic Application of Pharmacoeconomic Factor

For medicines that provide health benefits relative to current care, the PEP is calculated as:

$$PEP = \frac{P_1 (PVT * \text{Incremental QALYs} + \text{Treatment Cost} - \text{Incremental Costs})}{\text{Treatment Cost}}$$

For the purpose of this calculation:

- **PVT** is the Pharmacoeconomic Value Threshold of $60,000/QALY;[17]
- **P_1** is the list price of the medicine used in the agency's reporting;
- **Incremental QALYs** are the point estimate of incremental QALY gains of the medicine over the comparator in the agency's base case cost-utility analysis model, expressed in present value;
- **Incremental Costs** are the point estimate of incremental costs of the medicine over the comparator, expressed in present value; and
- **Treatment Cost** is the point estimate of the costs per patient of the medicine over the time horizon studied by the agency's report, expressed in present value. This value is limited to the medicine being assessed and excludes the cost of other medicines used jointly with the medicine being assessed or of medicines used to treat side effects.

Category I: Calculating Maximum Rebated Price (MRP)

Market size adjustment for Category I medicines

Annual revenues	Incremental adjustment factor	MRP	
		Medicines with a PEP	Medicines without a PEP
<$25M	0%	PEP	Lower of dTCC, iTCC
$25M–$50M	-10%	PEP adjusted by applicable factor	Lower of LIP, dTCC, iTCC adjusted by applicable factor
$50M–$75M	-20%		
$75M–$100M	-30%		
$100M–$125M	-40%		
$125M+	-50%		

- There is no lower limit to how far the rebated prices can fall –
  - Generics and older drugs may be included in the calculation of the median TCC prices (domestic & international)
  - Price reductions based solely on CADTH cost per QALY assessments can exceed 90%

Category I: Calculating Maximum Rebated Price (MRP) – Rare Disease Drugs

Market size adjustment for Category I rare disease or disorder patented medicines

Annual revenues	Incremental adjustment factor	MRP	
		Medicines with a PEP	Medicines without a PEP
<$12.5M	+50%	1.5 * PEP	Lower of LIP, dTCC, iTCC
$12.5M-$25M	0%	PEP	
$25M–$50M	-10%	PEP adjusted by applicable factor	Lower of LIP, dTCC, iTCC adjusted by applicable factor
$50M–$75M	-20%		
$75M–$100M	-30%		
$100M–$125M	-40%		
$125M+	-50%		

- Prevalence of no more than 1:2000 (across all approved indications)
- MRP based on Pharmaco-economic price (PEP) increased by 50% (if annual revenues less than $12.5M)
- Again, there is no lower limit to how far the rebated prices can fall –
  - Generics and older drugs may be included in the calculation of the median TCC prices (domestic & international)
  - Price reductions based solely on CADTH cost per QALY assessments can exceed 90%

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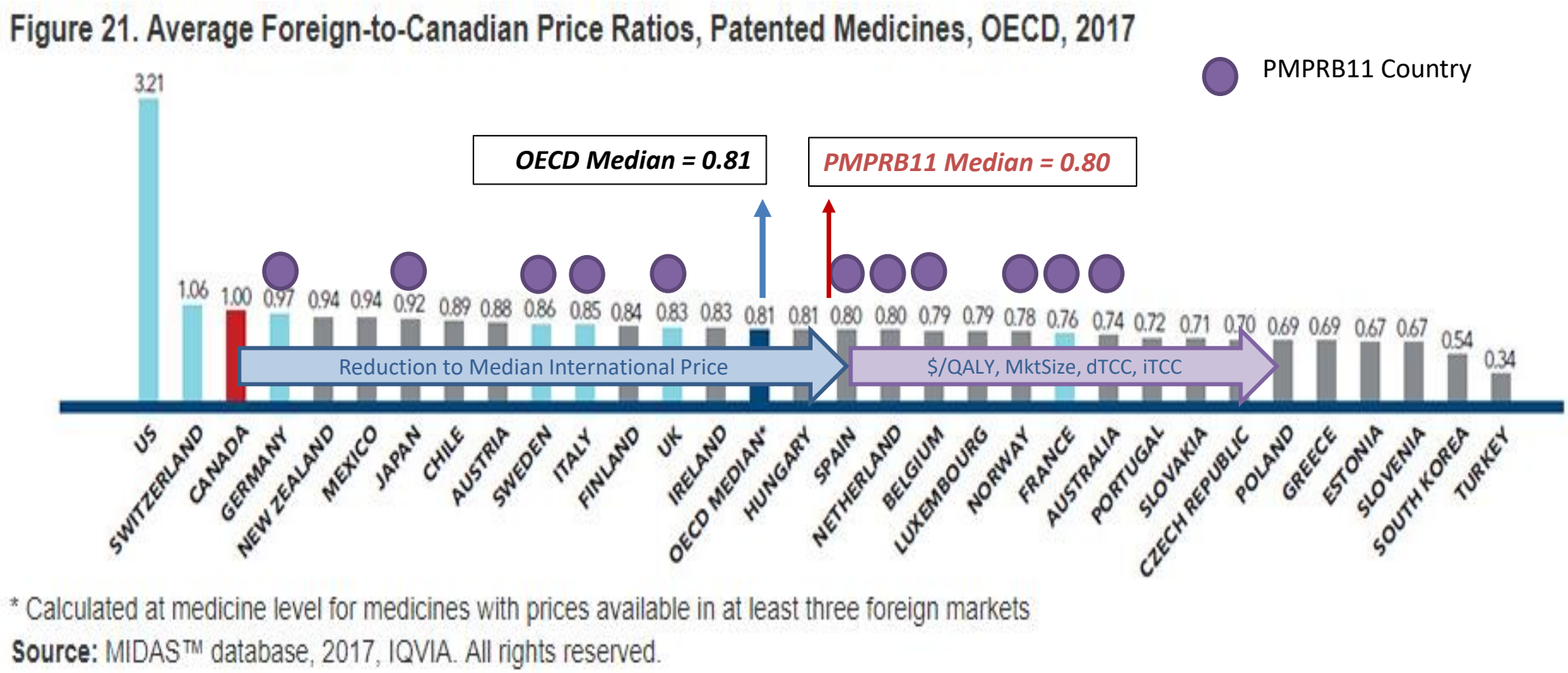
Impact of New Guidelines: Heading to lowest international price and beyond…

Annotated by N Palmer / PDCI



* Calculated at medicine level for medicines with prices available in at least three foreign markets

Source: MIDAS™ database, 2017, IQVIA. All rights reserved.

Impact of External Reference Pricing (2017)

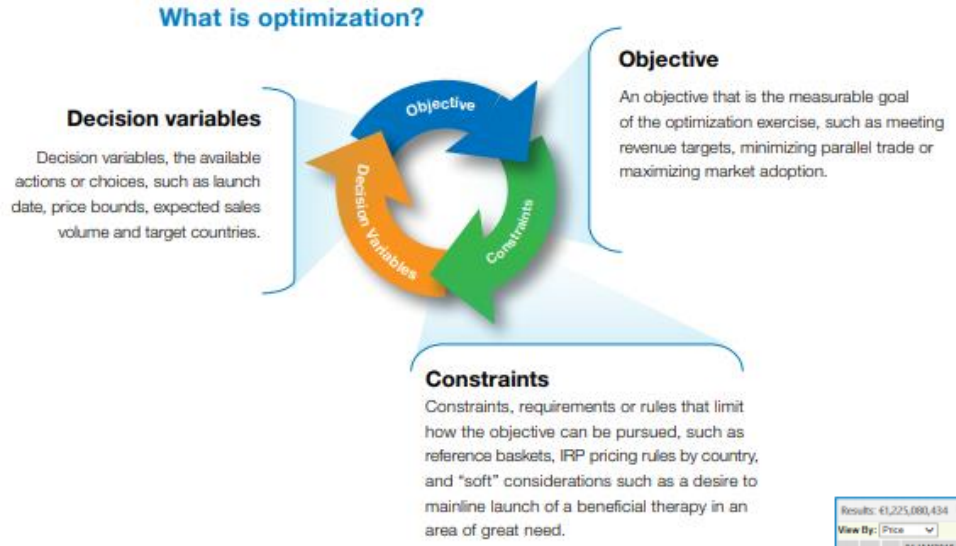
The Impact of External Reference Pricing within and across Countries

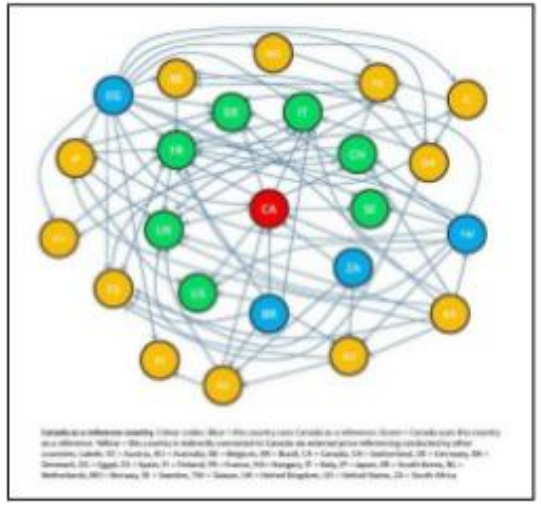
Panos Kanavos
Anna-Maria Fontrier
Jennifer Gill
Olina Efthymiadou
Nicola Boekstein

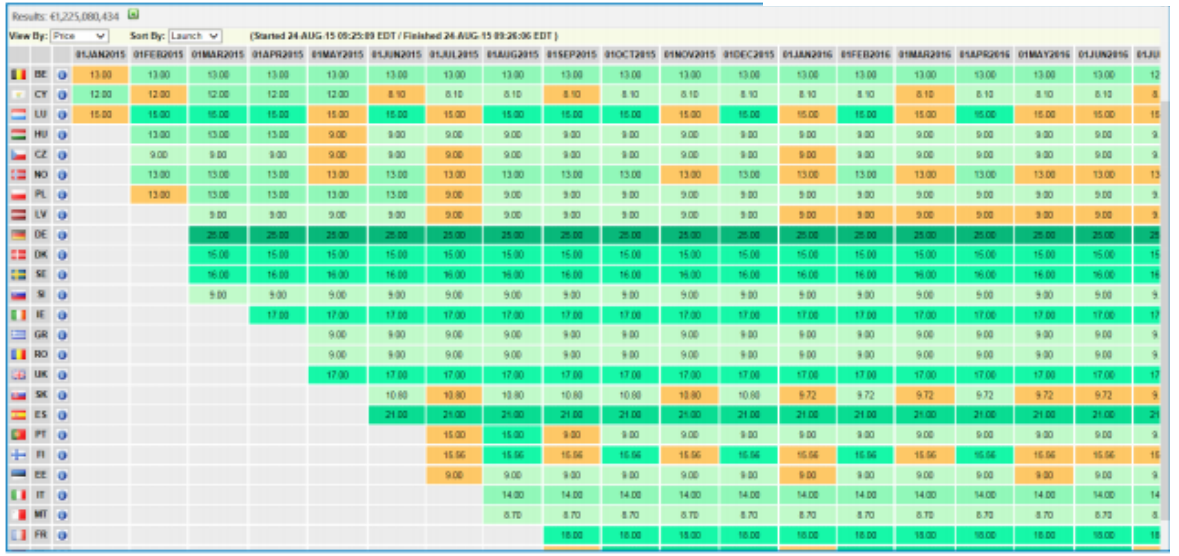
- Systematic Literature Review of Impact of External Reference Pricing (ERP)
- Trends observed from ERP:
  - health expenditures can be reduced at least in the short-term because prices are more likely to decrease
  - **availability of pharmaceuticals, equitable access to medicines and the stimulation of industrial policy can be undermined**
  - **the impact of ERP on the affordability of medicines is ambiguous**.

- ERP can trigger spillover effects, resulting in
  - **price instability, leading to launch delays**
  - **unwillingness of manufactures to launch in low price countries,**
  - promoting price convergence towards the international average

Manufacturers seek to optimize global launch sequencing, primarily based on price





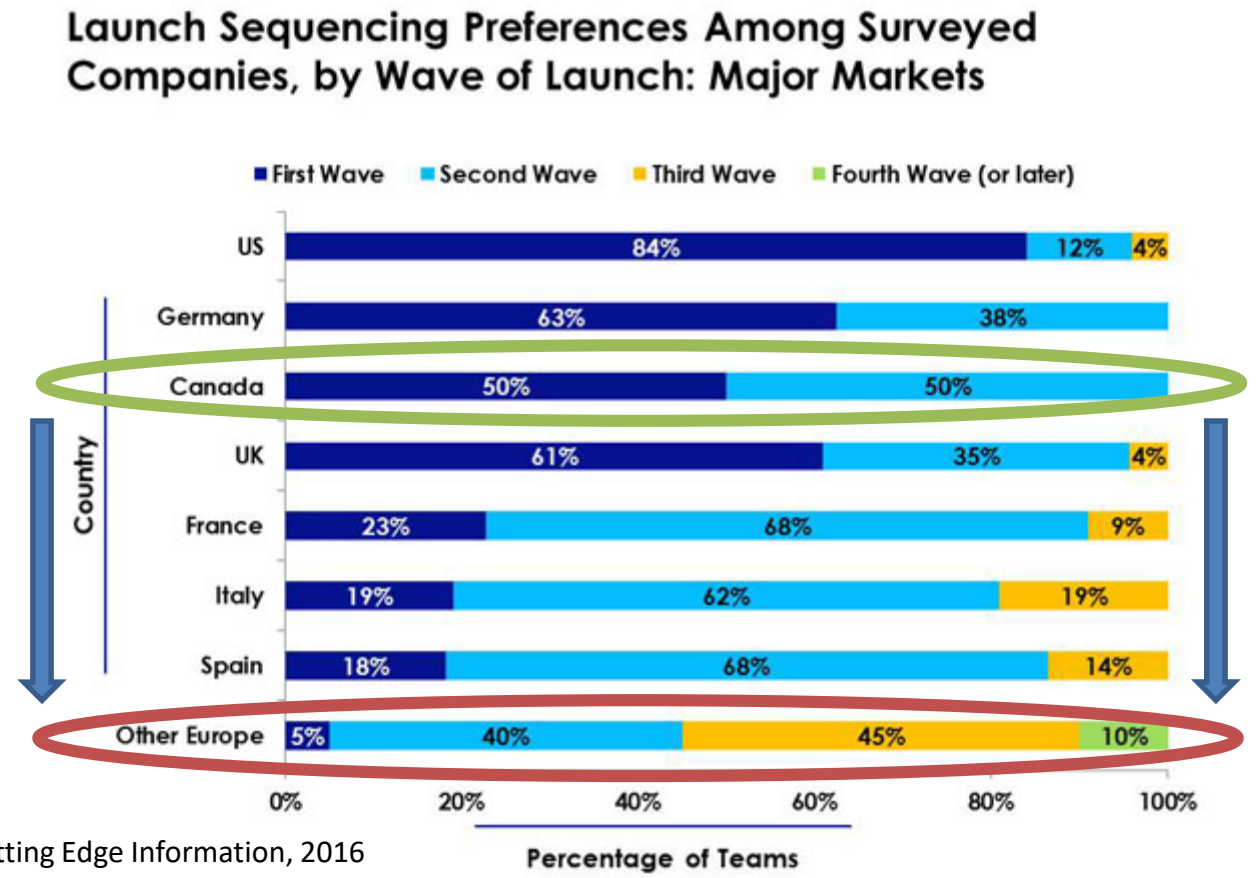


sas
THE POWER TO KNOW.

Optimize Your Launch Sequence Strategies

Maximize global revenue from international pharmaceutical product launches

Canada risks moving to 3rd or 4th wave of product launches



Source: Cutting Edge Information, 2016

Potential Impact on Clinical Trials

- Manufacturers are reluctant to conduct clinical trials in a specific country unless they are confident they will be able to commercialize the drug in that country.
- *Helsinki Declaration*: *"At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study"*
- Manufacturers are ethically bound to provide study patients with the study drug (if effective) at no cost until reimbursement is available
- Accordingly, manufacturers are less likely to conduct clinical trials in countries where:
  - Price controls force prices below the global pricing corridor
  - Reimbursement is unlikely
  - There is sufficient uncertainty as to whether an acceptable price / reimbursement can ultimately be achieved.

Potential Impact to Patient Support Programs

- PMPRB price reductions (combined with provincial policies limiting wholesale / pharmacy markups) may jeopardize these programs
- Origins with outpatient biologics – a lack of available infusion facilities within hospitals and health clinics spawned the development of specialty pharmacy, private infusion clinics and patient support services
- Manufacturers typically establish patient support programs for expensive and rare disease drugs
- Patient support programs typically provide among other things:
  - Specialty pharmacy services
  - Infusion services (if infused)
  - Nurse support and self care training (eg SC injections)
  - Reimbursement coordination
  - Copay assistance
  - Compassionate access for patients with no drug insurance coverage

Summary of Impact of PMPRB Reforms on Drug Prices

- PMPRB11 will potentially impact older existing drugs the most – depending on implementation prices could fall by more than 20% on average
  - An earlier analysis suggested ~25% of medicines would have no price reductions, but ~75% would have price reductions averaging ~30%

- PMPRB11 median may be less impactful for drugs for rare diseases and high cost drugs
  - Strict adherence to international pricing corridors

- $/QALY and "market size" likely to be the most impactful for new rare disease drugs
  - Rare disease drugs almost always significantly exceed traditional cost effectiveness thresholds - in all markets
  - RIAS: Rare disease drugs would require a 33% reduction in price on average (base case scenario) – PMPRB Guideline proposals have been even more severe

- Overall impact is that the average transaction price of rare disease drugs will be forced significantly lower: approaching the lowest international price

- Significantly lower prices (and pricing uncertainty) will likely result in launch delays in Canada

- Clinical trials will be impacted (unlikely that manufacturers will conduct clinical trials in countries they don't expect to enter)

- Patient support programs for new drugs could be at risk

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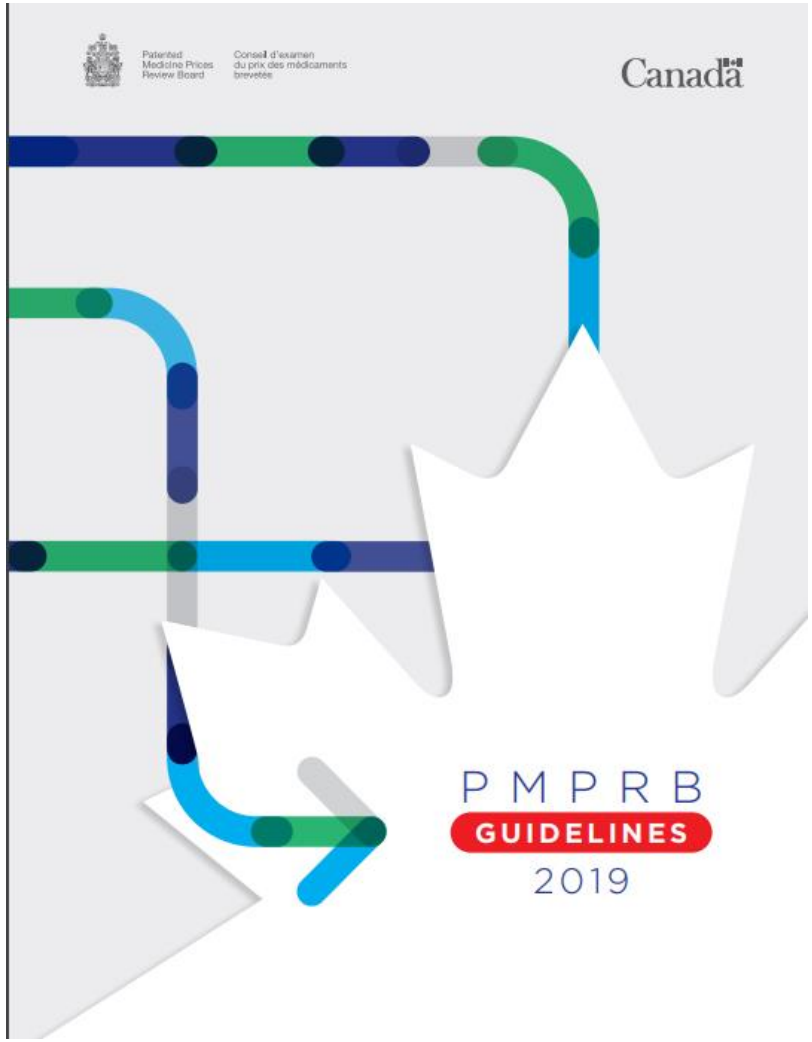
PMPRB Draft Guidelines



- "Draft" Guidelines released Nov 22 2019
- 60 day consultation period – comments by January 20 2020
- PMPRB travelling road show to meet with "stakeholders" beginning December 2 2019 in Western Canada
- "Civil Society Forum" ("third sector" of society, distinct from government and business) December 10, 2019 in Ottawa
  - Open to patient groups and academics
  - Closed to industry
- Policy Forum in New Year (by invitation)
- New Guidelines to come into effect July 2020 – likely with transition measures such that full effective date is January 2021

What can you do.....?

- Get involved!
- Register for PMPRB Dec 10 “civil society” session in Ottawa and/or upcoming regional events to have your voice heard: PMPRB.Consultations.CEPMB@pmprb-cepmb.gc.ca
- Compile written responses to PMPRB by Jan 20, 2020 deadline and/or participate in one of the umbrella organization submissions https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/draft-guidelines.htm
- Ensure the Federal Government hears your concerns

EXTRA

PMPRB Legal Framework

- **Patent Act** (*Parliament*)
  - Empowers the PMPRB as a quasi-judicial agency
  - Outlines the excessive price factors the PMPRB must consider plus secondary factors it may consider
  - Empowers the PMPRB to roll back prices and recover "excess revenues"
- **Patented Medicines Regulations** (*Federal Cabinet aka "Governor-in-council"*)
  - Outlines the reporting requirements for patentees (prices, sales, R&D expenditures)
  - Lists the countries for which international prices must be filed by patentees
  - Lists additional "excessive price factors" the PMPRB must / may consider (ie, in addition to those in the Patent Act)
- **Excessive Price Guidelines** *(PMPRB)*
  - Describes the PMPRB's compliance and enforcement policy
  - Outlines the price tests for new and existing medicines
  - The price tests reflect the methodologies the PMPRB will employ to apply the excessive price factors listed in the Patent Act and the Regulations

Health Canada: *Objectives of Proposed Regulatory Changes*

1. Introduce new, economics-based price regulation factors that would ensure prices reflect Canada's willingness and ability-to-pay for drugs that provide demonstrably better health outcomes;
2. Update the list of countries used for price comparison so that it is more aligned with the PMPRB's consumer protection mandate and median OECD prices;
3. Formalize a move to a complaints-based system of oversight for patented generics products that are at lower risk of excessive pricing, reducing regulatory burden for patentees;
4. Set out the pricing information required of patentees to enable the PMPRB to operationalize the new pricing factors; and
5. Require patentees to provide the PMPRB with third party information related to rebates and discounts on domestic prices.

Based on international best practices, the proposed amendments would provide the PMPRB with new regulatory tools and information to better protect Canadian consumers from excessive prices while reducing regulatory burden on patentees.

Source: Health Canada "Protecting Canadians from Excessive Drug Prices: *Consulting on Proposed Amendments to the Patented Medicines Regulations",* Ottawa May 2017

Other Issues briefly (details for another day…)

- Relevant indication (replacing primary indication, relying primarily on “prevalence”)
  - There is rarely a single agreed upon prevalence figure for diseases / conditions – often a range
  - May not exist for contingent indications (eg, stroke prevention in statin experienced patients)
  - CADTH may be considering only a subset of approved indications, PMPRB will consider all
- Criteria for selecting comparators for dTCC, iTCC (generics, older low cost drugs?)
  - PMPRB comparators and CADTH comparators will often not align (different selection criteria)
- Estimating market size
  - there will be a form requiring BIA like methodology, projections…
- Reasonable relationship test
  - per mg pricing only – no more flat pricing
- Reassessments: Cat II can move to Cat I, but can Cat I move back to Cat II?
- Information required to calculate the Pharmaco-Economic Price (PEP)
  - Some elements are not currently in CADTH reports
  - Weighted average of sub-populations (are the weights readily available?)
- Alternative PEP for products with no incremental health benefits (compared to standard of care) may force prices lower than standard of care