Everything you always wanted to know about industry's practice and reality in reimbursement

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Frédéric Lavoie, MSc, PhD
Director, Patient Access
Pfizer Canada

Situational Analysis

- >100 submissions produced by manufacturers have been reviewed
  - Measuring industry's performance by the proportion of positive recommendations = 51%
  - Publications, guidelines and presentations have provided industry with signals of what is expected of them:
    - Standard set of evidence as required by regulatory agencies (placebo controlled trials supporting efficacy and safety)
    - Experimental evidence reducing uncertainty as to the medicine's performance in real-life clinical context
      - Comparative data
      - Reliance on validated surrogate markers
      - Morbidity / mortality outcomes data
      - Objective outcomes vs subjective

Situational Analysis

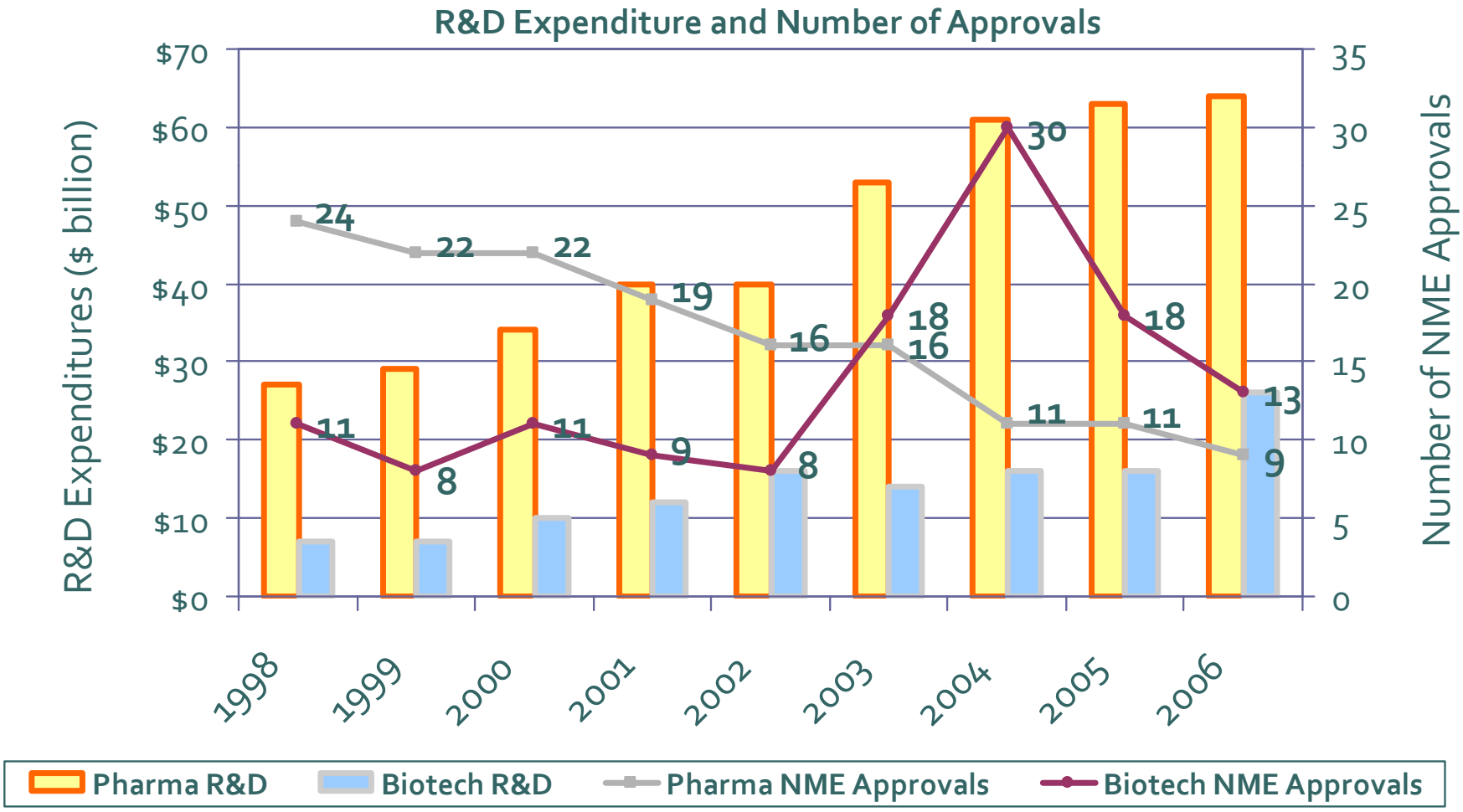
- Two elements appears to be key drivers of CDR decision making – Evidence and drug price

The evidence…

- Predominantly defined by regulatory agencies which offer relative predictability
  - Pre-determined risk/benefit thresholds
  - ↓
  - informed R&D investment decisions
  - ↓
  - relatively high certainty on Pr(NOC)
- Evidence is increasingly expensive to gather with decreasing returns for the risks undergone

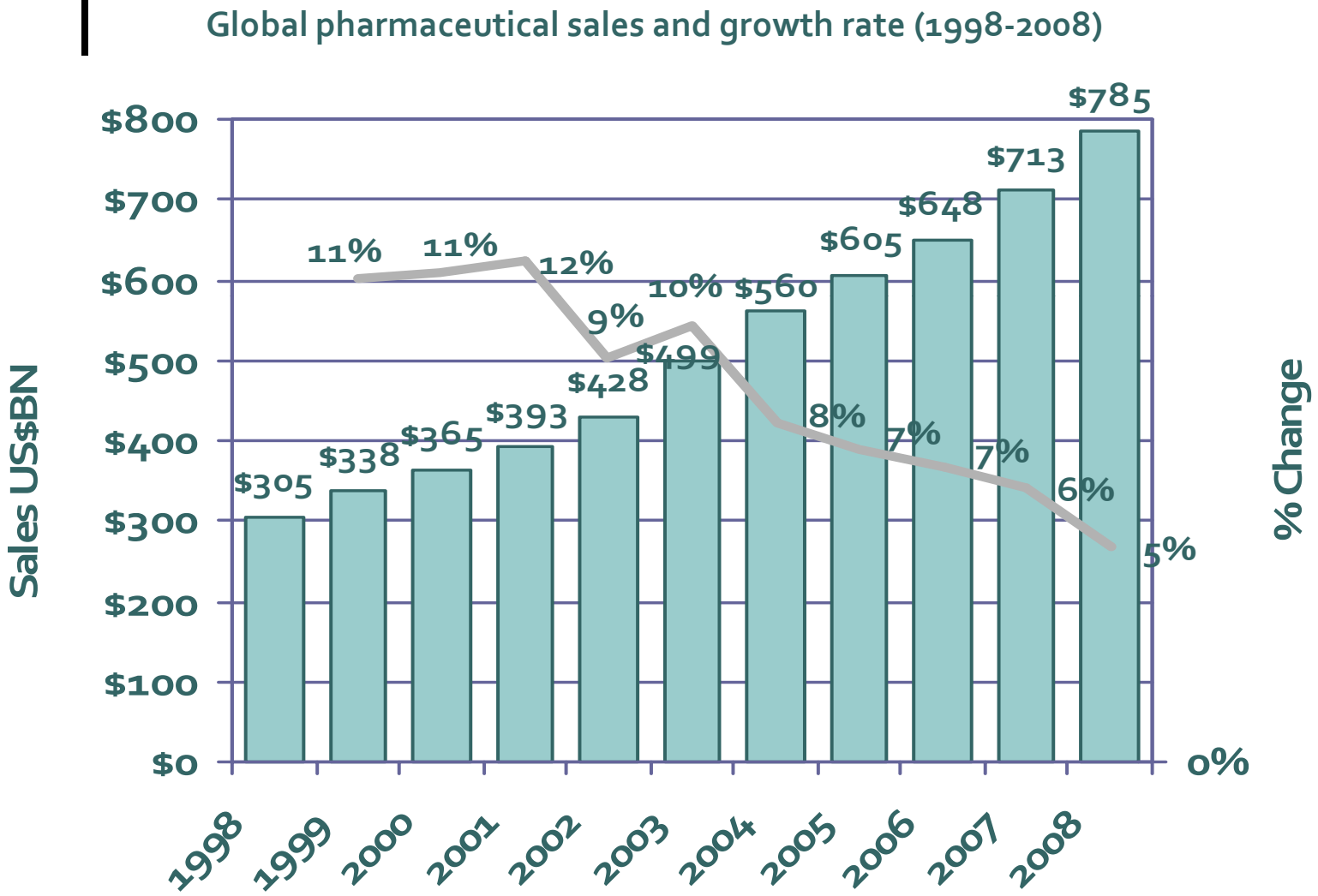
Despite higher R&D spending, the number of drug approvals has been decreasing

- Pharma Research & Development increased 137%
- Pharma New Molecular Entity (NME) approvals were down 63%



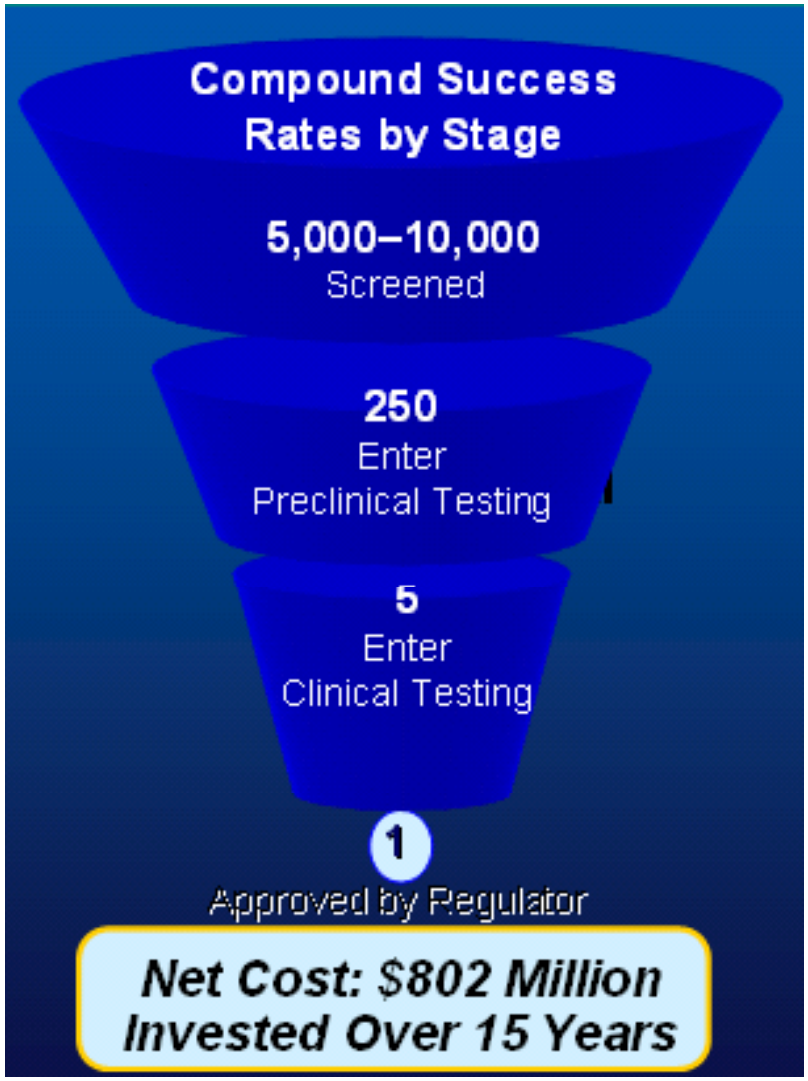
Source: Tim Anderson, Bernstein Research, Bernstein estimates and analysis

Pharma growth has slowed significantly



Source: IMS Health, Market Prognosis

The evidence…



Source: DiMasi, JA, Hansen, RW, Grabowski, HG. The Price of Innovation: new estimates of drug development costs. *Journal of Health Economics*. 2003; 22:151-185.

The evidence…

Year of CDR reviews	# of reviews	Publications: Peer-reviewed, presentations, guidelines	Trial period	Phase III start
2004	14		[1988 - 2003]	1997
2005	12	Laupacis et al.	[1989 - 2004]	1998
2006	31	Laupacis et al. & CDR	[1990 - 2005]	1999
2007	34		[1991 - 2006]	2000
2008	16	Mann et al. & Rocchi et al.	[1992 - 2007]	2001

Assumptions

* 15 years of experiment before NDA
* Phase III starts 6 years pre-NDA
* 1.5 years of HC and CDR review

Laupacis A. Incorporating economic evaluations into decision-making: the Ontario experience. *Med Care.* 2005;43:15-19.

Laupacis A. Economic evaluations in the canadian common drug review. *Pharmacoeconomics.* 2006;24:1157-1162.

http://www.cadth.ca/media/cdr/process/CDR_Submission_Guidelines_2008Apr.pdf

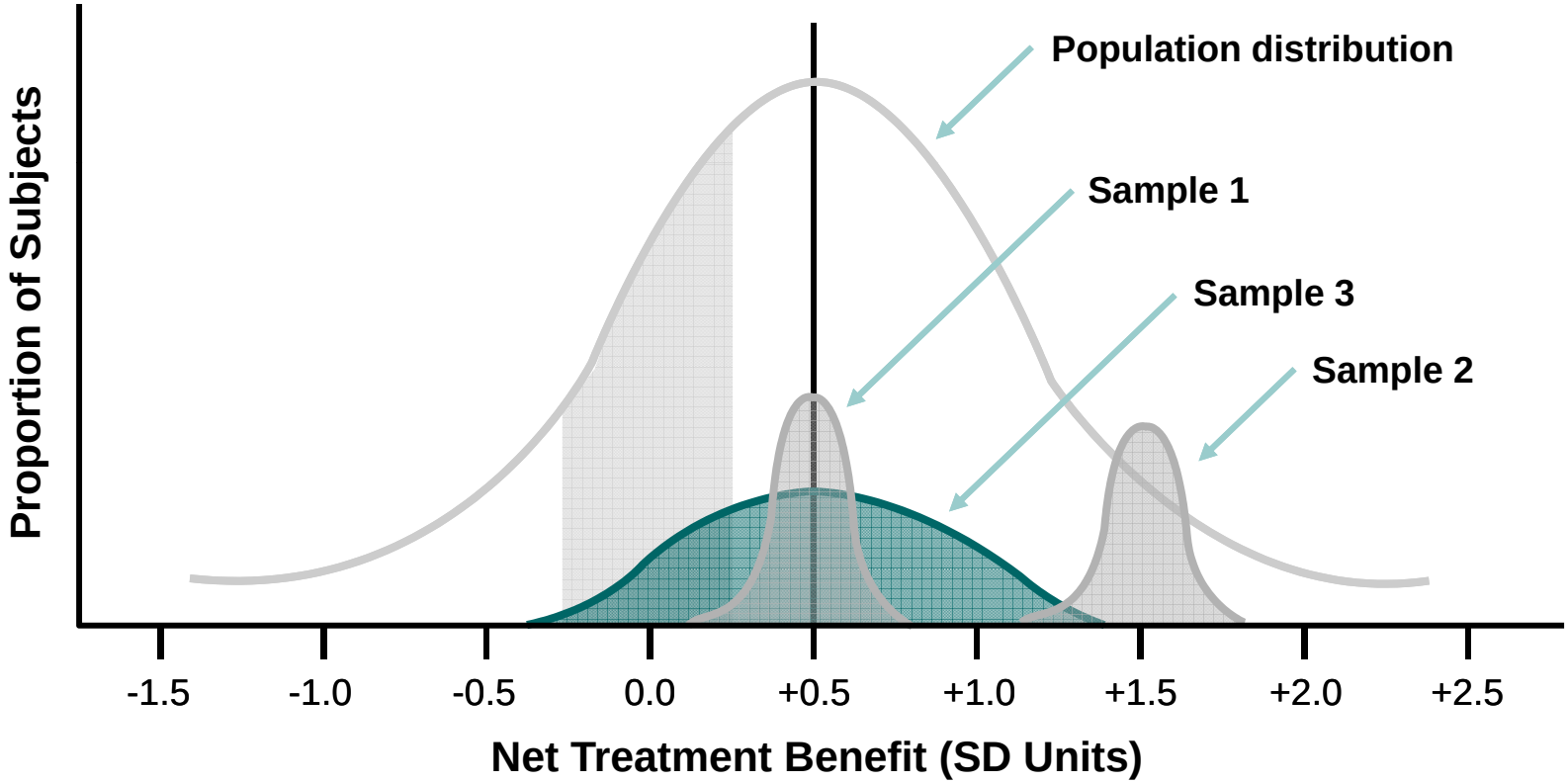
http://www.cadth.ca/index.php/en/events/sympos-2008/speakers-presentations-day-1

The evidence…

- Other trial design constraints:
  - Ethical considerations
  - Minuscule patient populations
  - Biases and experimental rigidity in a naturalistic setting
  - Time trade off between reducing uncertainty and providing benefits to patients
  - Narrow down where the ideal level of risk benefit & C/E resides

How much are you like the average?

Heterogeneity of treatment effect in the sample



Kravitz RL, Duan N, Braslow J. Evidenced-based medicine, heterogeneity of treatment effects, and the trouble with averages. *The Milbank Quarterly*. 2004; 82: 661-687

How do we fill the evidence gap?

- Pre-submission guidance: realistic & reliable advice to manufacturers (as regulators do)
- Consideration of other types of evidence & special patient populations
  - Indirect comparisons in meta-analysis
  - Observational studies
  - Treatment effect in sub-population
- Consistency in decision making = predictability = reliability of return on investment
  - Multi-criteria Decision Analysis

The Price…

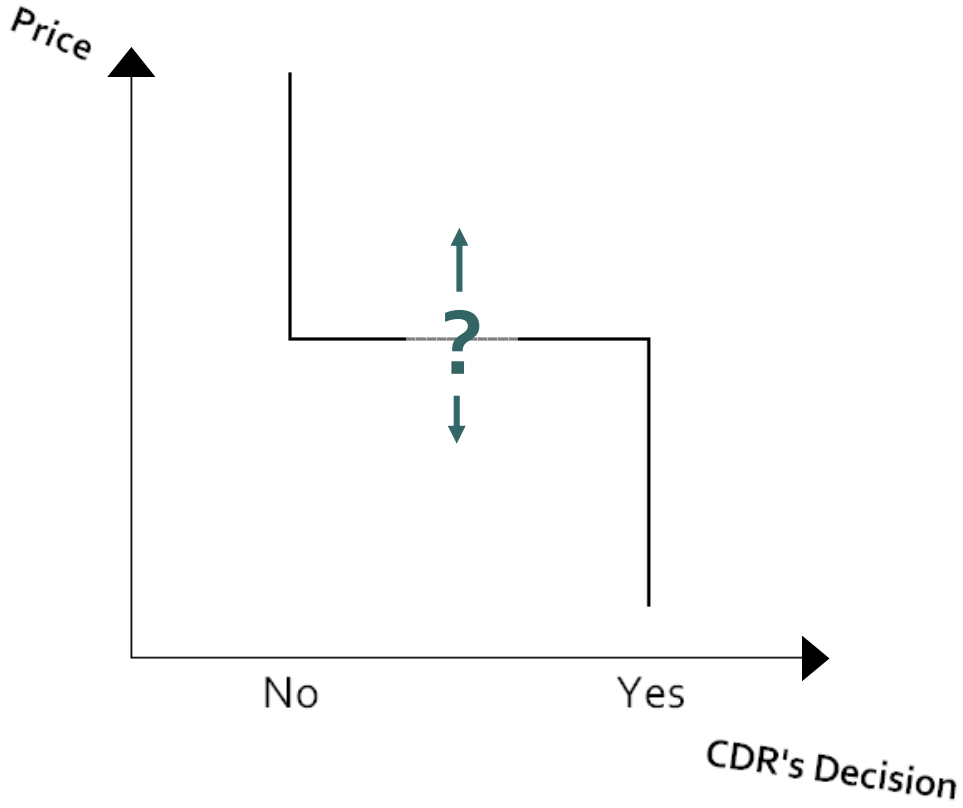
- The price that we set is subject to an optimization under constraints
  - The rules set by the PMPRB (CLEAR)
  - The likelihood of achieving success with HTA bodies and other reimbursement authorities
    - CDR (UNCLEAR) = Provinces (UNCLEAR)
    - Private Sector (CLEARER)

Funding Source	($ 'million CDN)	%
P/T governments	$8,048.8	39%
Federal Programs	$620.4	3%
WCB & Social Security	$812.2	4%
Total Public Funding	$9,481.4	46%
Private Insurers	$7,101.1	34.4%
Household (Out-of-pocket)	$4,033.6	19.6%
Total Private Sources	$11,134.7	54%

* Balancing Supply and Demand of Medicines: Lessons from the Canadian Experience, CADTH, July 13, 2006

The Price…

- A reflection of imprecise signals from CDR on its acceptability given level of data certainty – Price elasticity



- How can we make the right pricing decision with information asymmetry
- This dilemma * number of member plans

Conclusions

- Signals need to be made clearer
  - On the industry side - clinical trial.gov + submission which includes unlocked copies of PE
  - On the CDR side - With the current level of transparency and consistency in decision making, It is difficult for us to advocate effectively internally in the development process
    - No one can predict with enough certainty what will be acceptable to CDR
- When the CDR does not say yes, the entire system is failing
  - It challenges the incentives provided to innovators as it relates to building a strong knowledge based economy and bringing patient benefits
- Industry produces most of the supporting evidence
  - Therefore we are an important stakeholder
  - Industry's R&D will continue to be driving the CDR agenda challenging the evaluation framework with different technologies in the very near future
  - Therefore, the system, its principles and its values need to evolve
  - We must work together to pave the way for a system of success and excellence for all parties (patients, authorities, industry, government…)