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The Seven-Star Pharmacist
الأدوار السبعة للصيدلي

نقابة صيادلة لبنان
ORDER OF PHARMACISTS OF LEBANON

Are Regulations the Problem or the Solution?

The Reality of Localized Risk Analysis

It’s Complicated

Are regulations the problem or the solution?

- Countries around the world are struggling to adequately monitor the quality of medicines available to their citizenry.
- From more regular manufacturing inspections, to risk-based investigations into the sourcing of ingredients, to a rethinking of post-marketing surveillance, there isn’t one single solution – and efforts to reach international “harmonization” are part of the problem.

The dangers of “regulatory imperialism”

- Advising and training countries to adopt the standards and practices of the USFDA or the EMA is unrealistic.
- It often results in the cutting-and-pasting of western rules and guidances to satisfy international institutions, taking the place of real advances in quality and safety oversight.

Not Potemkin Pharmacovigilance but "Regulatory Democracy"

- We need programs for "Regulatory Democracy" that provides both a path for convergence with global best practices and immediate tactical programs that can address the true situation on the ground.
- Regulatory Democracy is tactical, pragmatic regulation that recognizes the asymmetries inherent in an evolving regulatory ecosystem.

An Expedited Pathway

- Regulatory Democracy a philosophy of multi-variant inputs and the potential leapfrog impact of technologies such as mobile apps and artificial intelligence opportunities that result in shortening the reporting-to-action continuum.
- Regulatory Democracy means collaborative programs to enhance communications between regulatory agencies and physicians, hospitals, pharmacists, and patients to drive more timely post-marketing reports of both adverse events and substandard pharmaceutical outcomes.

It’s a problem all over the world

According to a new EU report:

- ADRs account for 5% of all hospital admissions, cause around 200,000 deaths per year in the EU, and cost roughly €80 billion
- “A key solution identified by the report is to put in place awareness raising programmes aimed at both patients and healthcare professionals to increase knowledge about medicinal safety and highlight the role it can play to ensure public health.”

Action, not Theory

- In the real world Regulatory Democracy means using any means available from mobile apps to traditional paper reporting. Leadership + Collaboration = Speed to Action.
- Regulatory Democracy understands that the perfect mustn't get in the way of the good. "Good" is a highly worthwhile goal.
- "Good" recognizes the need for continuous improvement. Data from every source is important – but is not necessarily equal.

Signals vs. Noise

- Which are the “signals” and which the “noise?” Rather than letting this important question stymie progress, Regulatory Democracy suggests a more tactical, risk-based decision-making process that ranks information, by source on a reliability scale. Such a strategy recognizes the inherent inconsistency of quality reporting while also understanding the value of quantity as a predictive tool.

The best way to avoid questionable data ...
... is the question the data!

- Regulatory Democracy recognizes the importance of not only acting faster based on imperfect evidence, but also understanding the real-world impact those actions have on both the lives of patients and (more broadly) the quality of medicines within any nation's borders.

The Power of Predictive Evidence

- The lack of signals is an important signal to take into regulatory consideration. This requires regular monitoring of other reporting sources (via bilateral national information sharing) and international repositories such as the World Health Organization’s Uppsala database for global adverse event reporting.
- Should certain medical products be required to submit prospective pharmacovigilance predictions upon approval?

Regulatory Check .. or Checkmate?

- The world's greatest chess players understand that every variable (analytic, contextual, social) is interdependent and relevant.
- Regulatory Democracy means creative intelligence for *impact*. It means smarter ways of utilizing existing intelligence in order to achieve enhanced public health for patients *faster*.

Regulatory Freedom

- Regulatory Democracy frees developing nations from the bondage of regulatory systems developed for advanced needs.
- Lock-step harmonization with “best western practices” are likely pointless considering the profound differences in regulatory staffing levels, overall budgetary limitations, and physician, pharmacist, and patient education.
- Expecting other nations with less experience and resources to “harmonize” with the FDA or the EMA isn’t the right approach. Just as every nation has it’s own unique culture and cuisine, so too must it design it’s own pharmacovigilance philosophy and structure.

Enhanced Predictability

- Less mission creep
- Greater predictability
- More creative use of data and data analytics
  - Implantable biomaterials
- More partnerships with industry
- More intramural programs
  - biomarker validation, etc.

21st Century Cures Act

- **Health Care Economic Information.** Clarify ability of manufacturers to discuss pharmaco-economic data with payers, formulary committees and others. Timeframe: Immediate
- **Real World Evidence.** Require FDA to establish a framework for use of real-world evidence to approve supplemental indications and satisfy post-approval requirements. Timeframe: Within 2 years

Real World Evidence

- Real World Evidence (clinical outcomes data not collected in conventional randomized controlled trials) is the new star on the precision medicine horizon.
- In the 21st century the heatlthcare revolution will shift from the generation of data to figuring out the meaning and purpose of the data with the patient's perspective in mind.

Defining the Value of Real World Evidence

- “Big Data” and “Valid Evidence” are not the same thing. It is an important distinction that illuminates a crucial difference
- Requires 21st Century Regulatory Science

Patient-Focused Drug Development

- Patients who live with a disease have a direct stake in the outcomes of the drug review process and are in a unique position to contribute to the entire medical product development enterprise. The FDA will increase patient participation in medical product regulation
- Provide a more systematic and expansive approach to obtaining the patient perspective on disease severity or the unmet medical need in a therapeutic area to benefit the drug review process
- The patient perspective will provide context in which regulatory decision-making is made, specifically the analysis of the severity of the condition treatment and the current state of the treatment armamentarium for a given disease

The Global Market Access Environment

- More options and less money
- Should licensing be contingent on pricing?
  - Bifurcated vs. Unitary models
- NICE and “risk sharing” => “expanded access
  - Velcade
- Where is HTA going?
  - Former NICE Chairman,Sir Michael Rawlins told the House of Commons that the QALY, “is based on the collective judgment of the health economists we have approached across the country. Measuring value is “elusive.”

Partner in Innovation

Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics

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The Appropriate Use of Expedited Pathways

- A rethinking of 21st Century Regulatory Science

New Review Pathway Designations

- Fast Track
- Breakthrough Therapy
- Accelerated Approval
- Priority Review
- Special Medical Need

Expedited Review Criteria

… The potential to address unmet medical needs

… Preliminary clinical evidence that the drug may demonstrate substantial improvement over existing therapies

… An effect on a surrogate endpoint or a clinical endpoint

… Elimination or substantial reduction of a treatment-limiting adverse reaction

… Evidence of safety and effectiveness in a new subpopulation

Value-Based Insurance Design (VBID)

- Value as measured in clinical outcomes
- “Effectiveness” vs. “Efficacy”
- Real World Evidence
  - What if this evidence is for off-label usage?
- Phase IV trials and registries
- Electronic Health Records
- Impact of therapeutic switching and interchangability
  - Generics, Biosimilars and NBCDs

An FDA Quality Revolution

"The spark that ignited the flame was when we asked ourselves, *Do we know enough about the quality of drugs that are sold in the United States?*"

"In the 21st Century the FDA mustn't operate under a two-dimensional system of safety and efficacy, but a three-dimensional approach that includes quality."

-- Dr. Janet Woodcock

Office of Pharmaceutical Quality

- Integrated unit in CDER dedicated to product quality
  - - Across all drug products (new, generic, biosimilar, OTC)
  - - Across all sites of manufacture (domestic and foreign)

- “One quality voice” throughout drug product lifecycle - Integrates review, inspection, surveillance, policy and research - Spans pre- and post-approval for new and generic drugs - Strengthens pharmaceutical quality on a global scale

FDA Office of Pharmaceutical Quality

- “One quality standard” for all medicines

Steve Jobs

"Innovation distinguishes between a leader and a follower."

Innovation is a Continuum

- Basic Research
- Applied Research
- Regulatory Science
- Procurement and Manufacturing

Price vs. Value

- When patients have access to more effective medications, their overall health improves, even as their overall medical expenses go down. That, in turn, reduces national health-care spending and boosts the economy.
- Value must be measured in patient outcomes.
- Positive patient outcomes are impossible without quality medicines.

Regulatory Convergence

"Globalize the evidence, localize the decision."

-- Former Director of the Agency for Healthcare Research and Quality (AHRQ) JM Eisenberg who suggests,

The Devil is in the details, but so is salvation.

(Hyman Rickover)

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