Transparency and Predictability

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From Innovation to Globalization: The Regulatory Gateway

Session Objectives

- To define “Transparency and Predictability” in the context of public health needs
- To recognize different approaches to Good Regulatory Review Practices around the world
- To appreciate the value that Good Regulatory Review Practices can bring to regulatory outcomes

Our Speakers Today

- **Importance of Predictability**
  Alberto Grignolo, PhD
  Corporate Vice President, Global Strategy
  PAREXEL Consulting, USA

- **Good Review Practices – A Common Regulatory Language – Influenced by the CTD**
  Justina A. Molzon, JD, MPharm, Capt. USPHS
  Associate Director for International Programs,
  Center for Drug Evaluation and Research (CDER),
  FDA, USA

Our Speakers Today

- **Good Regulatory Practices (GRP) – Agency Consultation, Transparency**

  Jerry Stewart, JD

  Regulatory Policy Head, Emerging Markets, Pfizer, Inc., USA

- **Good Regulatory Practices –Updates from Cuba**

  Dr. Celeste Sánchez, MSc., Ph.D. Principal Adviser.
  CECMED, Cuba

Session Structure

3:30 **Introduction** (Grignolo)

3:40 **Importance of Predictability** (Grignolo)

4:00 **Good Review Practices – Common Regulatory Language – Influenced by the CTD** (Molzon)

4:20 **Good Regulatory Practices (GRP) – Agency Consultation, Transparency** (Stewart)

4:40 **Good Review and Regulatory Practices – Updates from Cuba** (Sanchez)

5:00 **Panel Discussion; Audience Q&A**

5:30 **Session Ends**

Importance Of Predictability

Predictability

The ability to foretell the future
on the basis of
observation,
experience,
or scientific reason

Merriam-Webster Dictionary

Unpredictable (Japan Tsunami, March 2011)

Predictable: Disciplined Behavior of Japanese Citizens In Line for Water After Tsunami (March 2011)

Predictability in Regulatory Affairs

- Observation
  - What has happened to others
- Experience
  - What has happened to me
- Scientific Reason
  - The persuasiveness of data

A set of government “rules”, behaviors and expectations should help improve **predictability** for innovators

Predictability is an Adventure…

- …not a destination
- Even Agencies with established Processes and Practices do not guarantee outcomes
- **Innovation** can be global, but **predictability** is local and variable
- Industry has an important role in promoting predictability of outcomes in drug development

Things That Go Wrong*

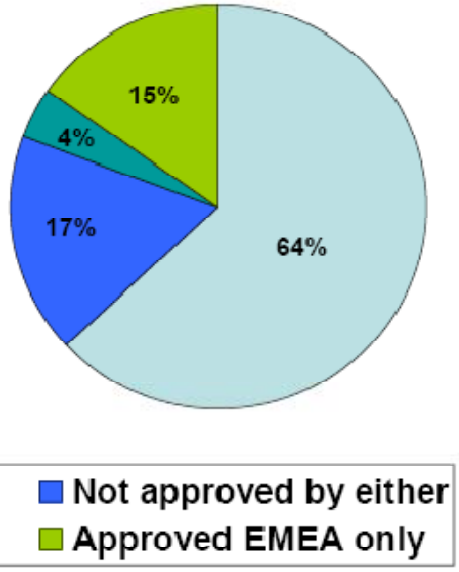
- A Phase 3 study fails to show efficacy after a successful Phase 2 study
- An FDA Advisory Committee votes 18-0 against approving a new drug
- A New Drug Application is rejected
- A manufacturing plant fails GMP inspection
- A new medicine receives approval in EU but not in US

**"The Team has not done its homework"*

New Molecular Entities Having Outcomes in ***both*** FDA and EMEA**

(Jan 2006 – October 2008) *n = 46*

Regulatory Outcome	#
Approved by both Authorities	29
Not Approved by either Authority	8
Approved by FDA only	2
Approved by EMEA only	7



** Preliminary FDA analyses

Source: FDA data and EMEA published information (EMEA annual reports, published lists of refusals and withdrawals, published CHMP Monthly Plenary Meeting reports). These figures only include drugs that would be considered NMEs based on CDER's definition for New Molecular Entities.

Reasons given for negative outcomes

Period: January 1995 to March 2009

- 31 products were approved in the US but had negative outcome in Europe
- 24 products were approved in Europe but had negative outcome in the US

Reason for negative outcome	EU negative cases	US negative cases
Further data request	12	15
Quality	3	1
Nonclinical Safety	4	1
Clinical safety	14	11
Clinical Efficacy	16	9
Clinical trial study design	7	1
Comparators	4	0

Source: Paul Huckle, GSK

Good Regulatory Review Practices: Behavioral Drivers of (Some) Predictability

	Authority	Industry
Early and Frequent Sponsor-Agency Communication	√	√
Focus on Scientific **Data** and Local Relevance	√	√
Technical Competence	√	√
Risks	√	√
Accuracy and Precision	√	√
Overall Assessment and Conclusions	√	√
Timeliness	√	√
Fairness	√	√

The Goal of Interactions with Health Authorities is to Ensure that a Worthy Innovative Product is Available to Patients

Readily,

Affordably,

Safely,

Effectively,

Profitably

Health Authority Interactions Today Are More Challenging

Increasing Product Development Complexity

- New types of product development challenges / requirements cause uncertainty for both sponsors and regulators about what to do
  - Comparative effectiveness, biosimilars, etc.

Product Globalization Targets Many "New" Countries

- Sponsors must interact effectively with Health Authorities and systems with whom they may have little experience and few relationships
- Some Health Authorities, particularly in emerging markets, lack experience and resources for effective sponsor interactions and product assessment

Health Authority Capacity Constraints

- Current resources are limited, resulting in slower response times and delays in granting meeting requests and product approvals (in both developed and emerging markets)
- Instability and evolution at several Agencies (Russia, India, China, Mexico)

Emerging / Innovative Practices to Improve Predictability of Outcomes

A number of innovative practices are emerging that help companies deal effectively with today's increased development / regulatory complexity

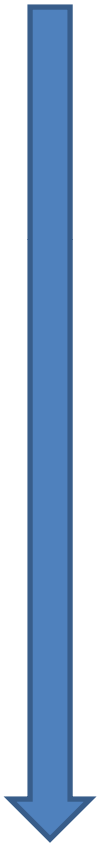
- **Global Prioritization**: Re-think commercialization strategy and consider pursuing development / registration of products in emerging markets before developed markets
  - Requires active engagement with Health Authorities in target emerging markets, some of whom may not have experience dealing with certain product types (e.g., biologics)

- **Regulatory and Commercial Alignment**: Engage multiple stakeholders and decision makers (e.g. regulators, payers, KOLs, etc.) earlier in the drug development process
  - Understand how to address the needs of these stakeholders individually as well as holistically; this is uncharted territory in the age of Comparative Effectiveness Research

Global Differences in Health Authority Interactions: A Challenge to Predictability

- US FDA
- EU EMA/CHMP
- Japan (MHLW, PMDA)
- Latin America
  - ANVISA: Brazil
  - COFEPRIS: Mexico
  - DIGEMID: Peru
- China (SFDA, CDE)
- India (DCGI)
- Russia (MoH)

More Structured



Less Structured

Optimizing Health Authority Interactions

- Build and maintain *trust* -- always, invariably, worldwide
- Nurture professional personal relationships
  - *"A good lawyer knows the law; a great lawyer knows the judge"*
- Combine substance (*what*) and style (*how*)
  - Facts and data are substance
  - Communication is style
- Promote favorable regulatory outcomes

What are “regulatory outcomes”?

- Good-quality, data-based decisions reached in timely fashion, according to a **predictable**, well-documented process
- Decisions that promote and protect the **public health**
- Decisions that promote **innovation**

What “regulatory outcomes” are NOT

- “Regulatory outcomes” are not necessarily “regulatory approvals”
  - Rejections can protect the public health

- Regulatory outcomes are not necessarily the same across regions
  - Different benefit-risk perspectives
  - Differences in medical practices

What *Should* be Predictable?

- Format of applications
- Type, depth, style of regulatory review
- Timelines of Authority responses
- Regulators' expectations
- Industry's ethical behavior

What Is Less Predictable?

- The final result of the regulatory review
- Random human behavior

Why is Predictability Important?

- To promote the public health through innovation
- To promote innovation through discovery and medicines development
- To promote investments and economic growth
- To reduce costs, inefficiency and delays

Making accurate predictions is very difficult; especially predictions about the future.

¡Gracias!

Obrigado!

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