Global Regulatory Strategy

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Abbott Quality & Regulatory Strategic Deployment

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Overview

Thank you for this opportunity to share my perspectives on points to consider for Global Regulatory Strategy.

This presentation represents my perspectives as a Regulatory Professional with 26 years experience in Industry and 10 years in healthcare/public health.

My perspectives have been shaped by multifunctional experience (R&D, Clinical, Operations, Quality & Regulatory) primarily in Medical Devices Businesses and less in Pharma and Nutrition

Abbott

Abbott is a global, broad-based health care company with >90,000 employees.

Our products span the continuum of care, from nutritional products and laboratory diagnostics through medical devices and pharmaceutical therapies.

Abbott has announced that we will separate into two publicly held companies by the end of 2012:

- **Abbott:** a global diversified medical products company (medical devices, established pharmaceuticals and nutritional products)
- **AbbVie**: a global research based pharmaceutical company (current proprietary pharmaceuticals)

Overview – Global Regulatory Strategy

- Points to consider
- Today and looking forward
- Dynamic environment - constant change
- Challenges

We Share Objectives

- Apply the best science to therapeutic areas where there is an unmet need – focus on our patients
- Protect and improve the public health
- Increase access to healthcare
- Support innovation in products, processes, and healthcare delivery
- Provide value and achieve appropriate return on investment

Emerging Market Challenges

Established Market Challenges

Emerging Markets - A Very Dynamic Environment

Drivers ↑

Inhibitors ↓

Emerging Markets:
- Average annual growth rates = 12 – 18 % over next five years
- Growing middle class
- Disposable income
- Advancing healthcare policies
- Population demographics

- <u>Uncertainty</u>
  - Pricing/reimbursement
  - Regulatory pressures/changes
  - Economic environment
  - Patent protection

Many of the forces at work are **both** Synergistic and Conflicting;

Having potential for positive & negative effects

Economic development

Healthcare reform

Government plans and initiatives

Evolving Regulatory framework

Provide affordable care - value driven, not just low cost

Drive Innovation - Benefits versus Risks

Attract MNCs AND build local Industry

“Pharmerging Markets” as an example . . .

- Investment continues in emerging markets by pharmaceutical industry with increased revenues – (e.g. Brazil, Russia, India, China, and now more are being added...Turkey, Mexico, Korea and so on…)
- Over next 5 years, emerging markets expected to **double** their spending on medicines.
- Market demand for more effective products and widening healthcare access.
- In contrast, European and US spending on pharmaceutical products is set to decline 3-5 % over the same period : (EU 24 to19 %; US 36 to 31%).

But some are worried . . . . . .

Is Pharma's Emerging Markets Safety Net About To Burst?

Posted by Anu Bharath · February 17, 2012 ·

"The so called 'pharmerging' markets — e.g. Brazil, Russia, India, China, Russia, Mexico and Turkey — have been forecasted double digit growth of approximately 14% through to 2014, compared to the global pharma market, estimated to have mid-to-high single digit growth over the same period."

Will Emerging Markets Slow Down .. And Impact Pharma?

The regulatory moves in these markets are critical …….the view of many economists is that emerging markets are experiencing a slow down. (This was backed by World Bank and IMF projections….this year, which …downgraded …GDP growth forecasts for these markets, with the former even warning of a possible market recession in some emerging market countries.)

Trends and shifts . . . .

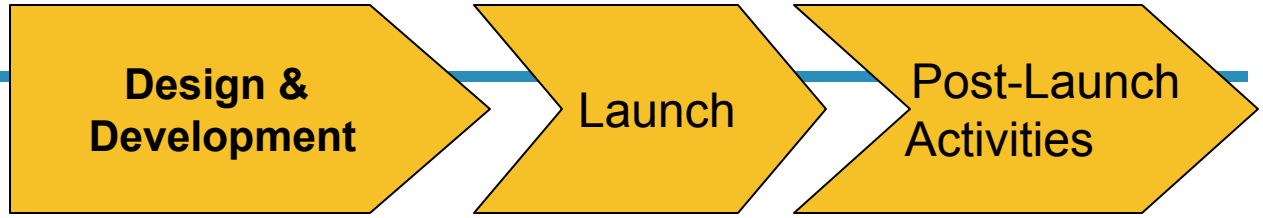
Trends

- Demographic trends are driving fundamental changes in the global economy…high birth rates, aging populations . . .
- Economic trends …e.g. depreciation of $ US with strong adverse effects on economic growth beyond US
- Growing pricing pressures and regulations
- Rapid development of new technologies

Paradigm Shift

- Traditional lines of business, technology, and competition are blurring…many new partners and types of partnerships
- International market continues to grow
- Definition of customer is changing – who selects and pays for the product?
- Increasing regulatory pressures on government and industry
  - scarcity of qualified resources, both human and financial

Typical Device Development Cycle



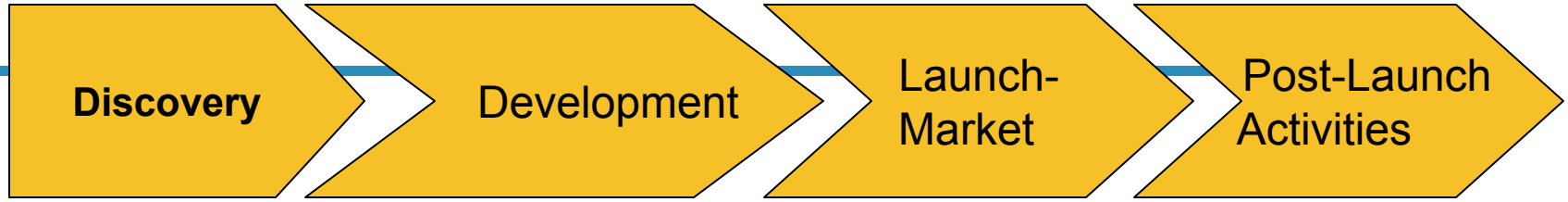
- **Depends on product classification**
- **Design & development more rapid; often involves medical practice innovators**
- **Clinical studies vary**
- **Approval time varies**
- **Iterative process**

2010 report: estimated device 510(k) process could cost a manufacturer **up to $24 million**:

•bench and functional testing,
•human factors,
•environmental engineering,
•biocompatibility testing
•sterilization validations
•Equipment/product validations, etc.
•GMP manufacturing/Quality Systems

•Stanford University researcher Josh Makower, and sponsored by the Medical Device Manufacturers Association (MDMA)

Typical Drug Development Cycle



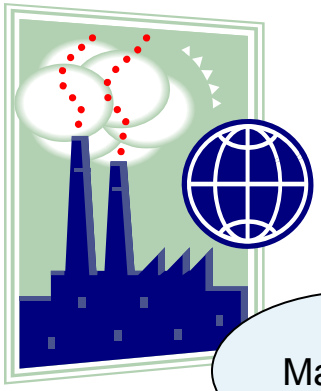
- **Phase I: drug safety** verified by applying increasing doses of the drug candidate to healthy patients.
- **CLINICAL – IND APPROVAL**
- If side effects are acceptable, drug progresses to **Phase II**, in which the efficacy is tested in volunteer patients.
- **Phase III** finally applies the drug to a larger group of patients to detect frequent side effects, and may include other (older) drugs as comparator.
- **REGULATORY APPROVAL**
- **POST MARKET Requirements**

- Drug development success rate = low single digits %
- Time frame 8 -14 years
- Development costs > $Multi Millions to $1Bs
- Large investments in clinical trials pre and post market
- Cost of launching into multiple markets
- Reimbursement/Healthcare payment

What are some critical questions for MNCs?

- What are the unmet needs and where can we make a difference?
- What products can come to market predictably?
- In which markets can these products be sustained and be a good value proposition for all parties?
- Where do we perform manufacturing? R&D? Clinical Trials?
- How do we streamline the processes?
- What partnerships do we need?
- How do can we succeed locally while a Global MNC?
- How do we assure that we have adequately trained resources in an environment of growing complexity?

Industry has a Dual Challenge: Grow with Emerging Markets and Sustain/Build Growth in Established Markets



Achieve the right balance

Local presence

- Marketing
- Manufacturing
- R&D/Clinical

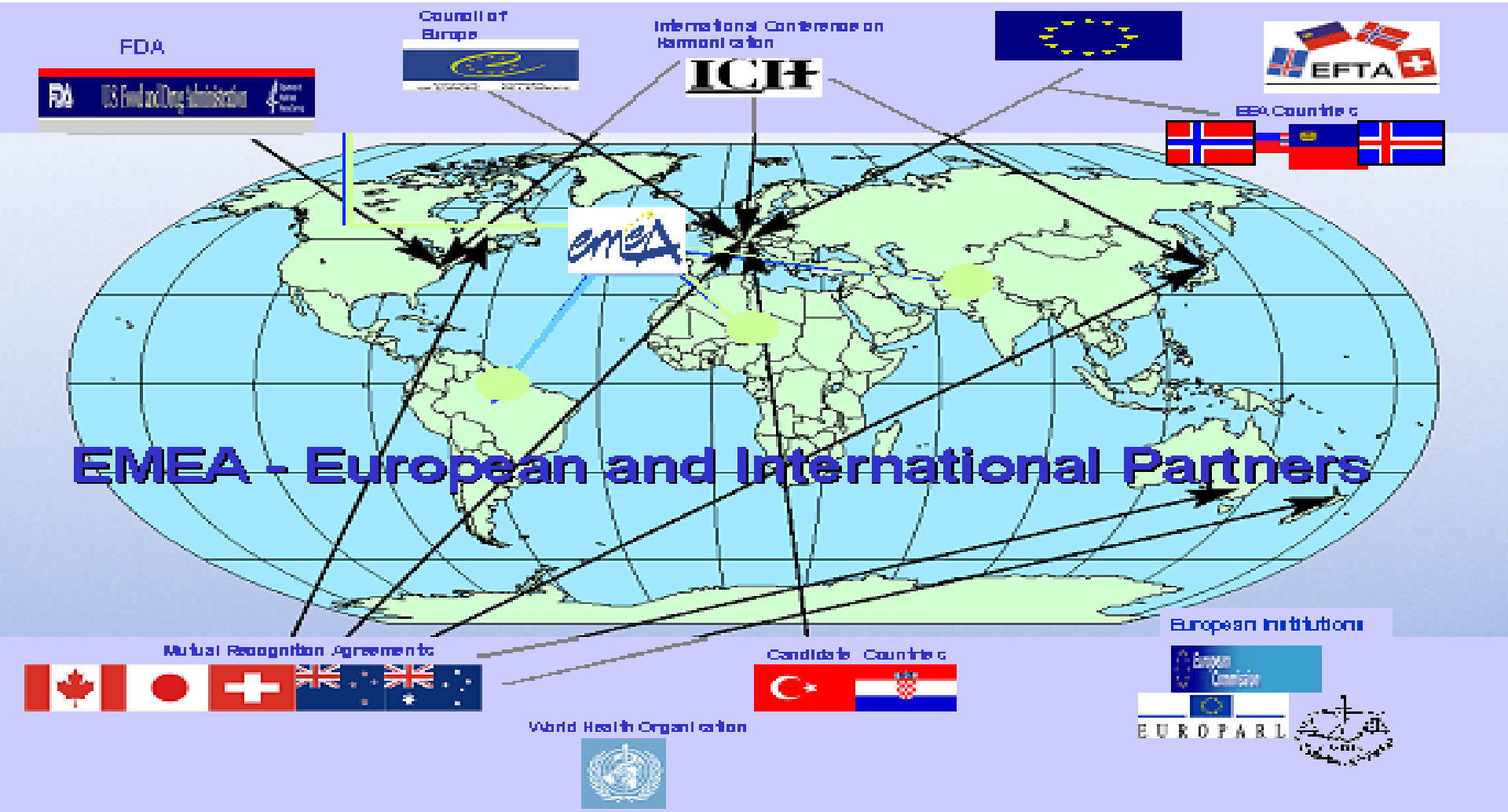
Local partner

- Marketing
- Distribution Manufacturing
- R&D/Clinical

Attracting & Retaining The Best Local Talent

Knowledge & Experience in Regulatory Framework Is ONE Critical Success Factor

Changing Regulatory Landscape ….Regulators are connecting the dots…sharing inspection data, information on product defects, adverse events…



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WHO Regulatory Guidance

"Governments need to put in place policies that will address all elements related to medical devices, ranging from access to high quality, affordable products, through to their safe and appropriate use and disposal. …

Policies will be unsuccessful unless they are translated into **national regulations** that are enforced by legislation and correlating sanctions, and that form an integral part of the overall national health system."

Source: Medical device regulations: Global overview and guiding principles; World Health Organization, Geneva; 2003

(At: http://www.who.int/medical_devices/publications/en/MD_Regulations.pdf)

What is “Harmonization”?

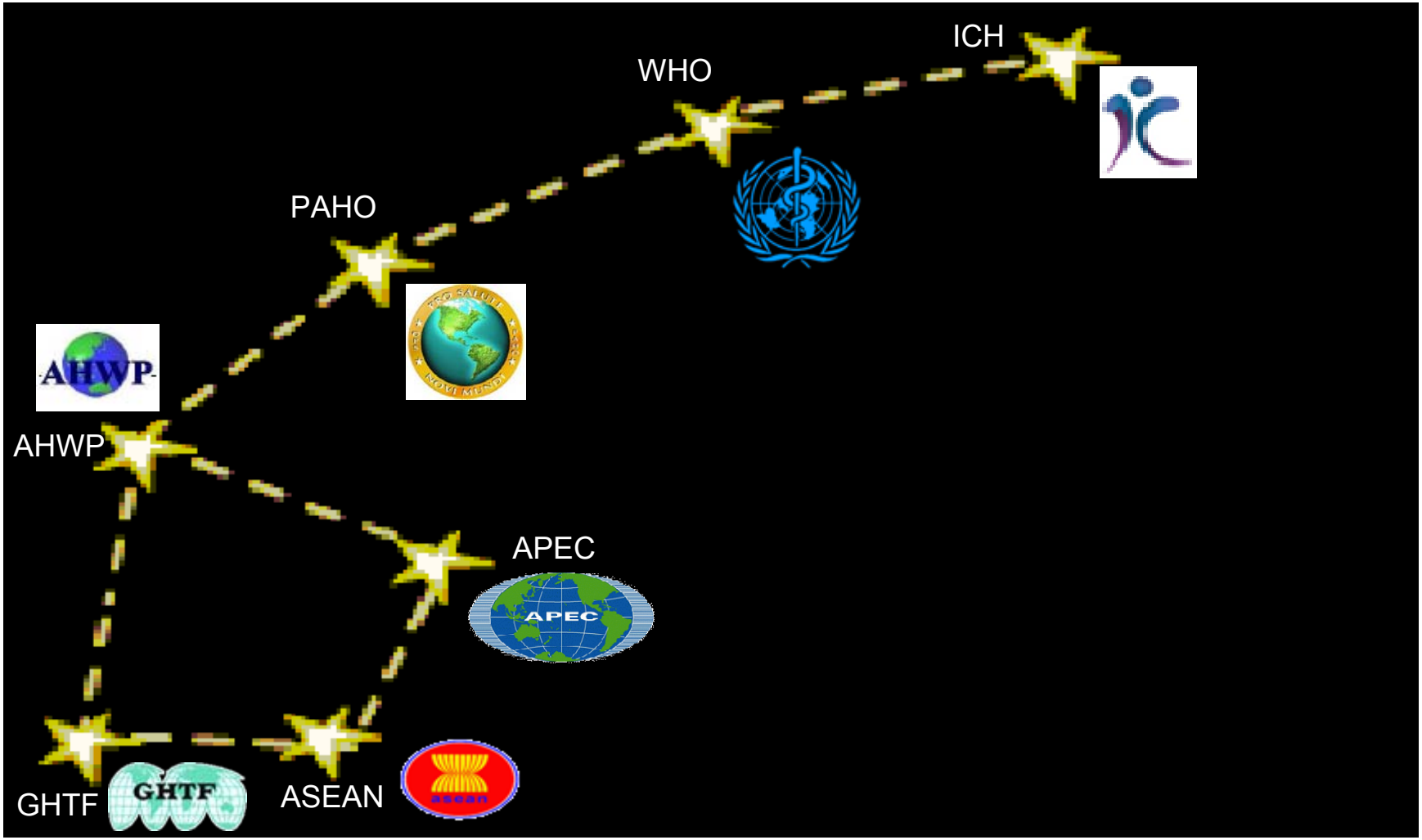
- Harmonization: “to bring into agreement or harmony”
- Harmony: “agreement in ….opinion; accord”

  American Heritage College Dictionary, 3rd edition, 2000

- Medical Device/IVD harmonization: “to encourage convergence in regulatory practices related to ensuring the safety, effectiveness/performance and quality of medical devices, promoting technological innovation and facilitating international trade.”

GHTF, http//www.ghtf.org/about/index.html

Regulatory Harmonization Constellation



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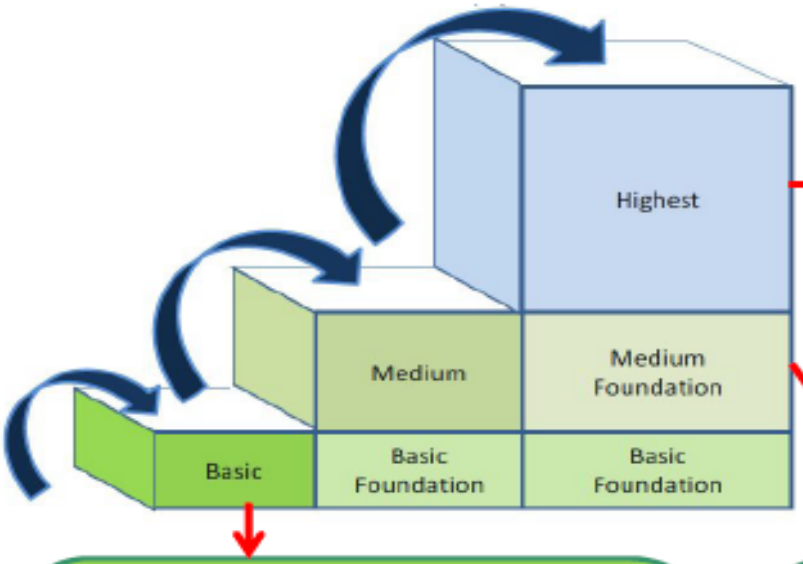
GHTF/(Now IMDRF) – Progressive Regulatory Framework



- Technical Information Review
- Robust clinical trial applications review
- Oversight of conformity assessment of the manufacturer's QMS
- Robust Post-market Surveillance system with Inspection system
- Post-market testing ability

- Risk classification
- Definitions –
  Manufacturer/importer/ distributor/medical device
- Registry for listing
- Post-market Surveillance system
- QMS
- Record keeping
- Labeling

- Compliance with essential principles of safety and performance
- Recognition of International standards
- Clinical trials - oversight
- Special access program
- Advertisement control

Source: GHTF Guidance Implementation, from Dr. Rama S, HSA, Singapore, July 2011 Presentation

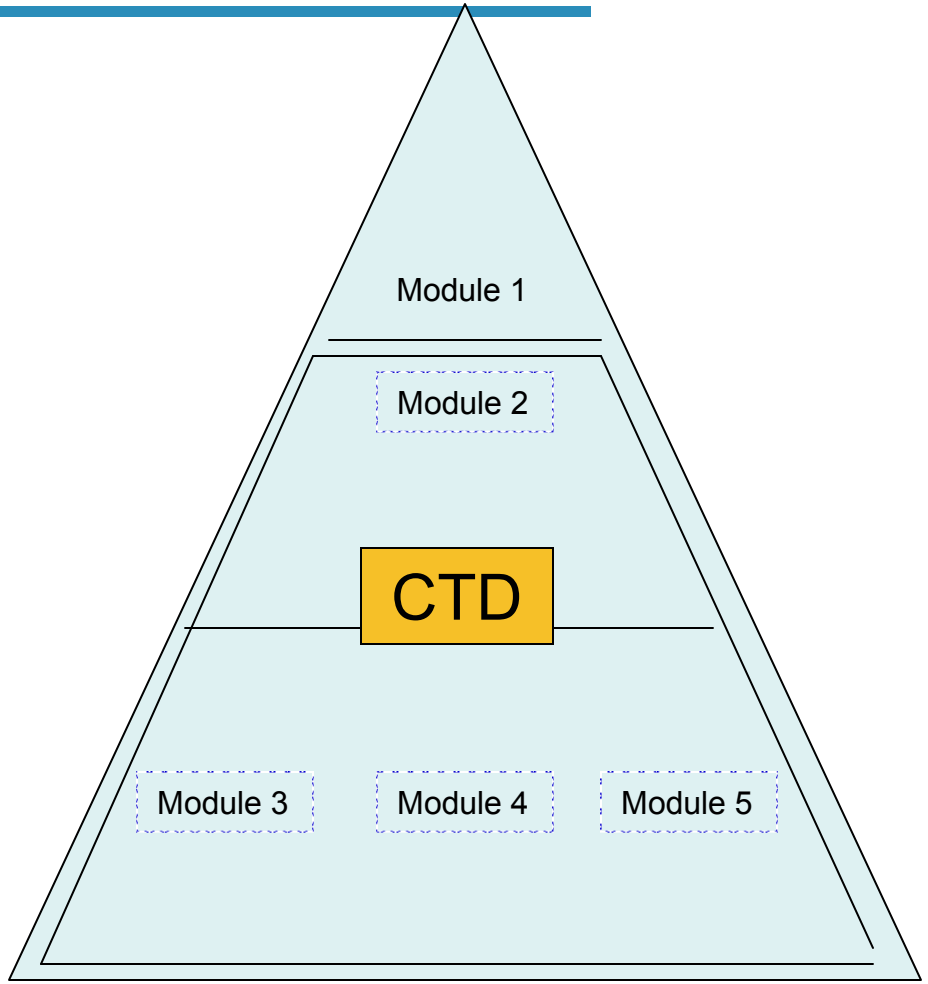
Harmonized approaches/standards help Regulators and Industry

Tremendous value in consistent format: e.g. Common Technical Document.

Module 1(not part of CTD) - administrative information specific to region/agency.
Module 2 :introduction, summaries, overviews.
More complete data are contained in Modules 3, 4, and 5.

Depending on the product, and the situation, countries can focus on modules of interest.

> 50 harmonized guidelines and standards - developed through consensus process with regulatory and industry experts working side-by-side. (safety, quality, CTD (Common Technical Document) and MedDRA (Medical Dictionary for Regulatory Activities).



Advantages of Common Submission Template

- Submission content & formats alignment - country to country
- Manufacturers present data to different countries in a predictable fashion
- “Add on” requirements per country should be/ can be few and well understood early in development
- For both Manufacturer & Regulator this approach can be
  - Time saving
  - Least burdensome
  - Less complex and confusing; more predictable
  - Requires fewer resources & infrastructure
  - Resources gain/build skills & knowledge

How are we doing with Harmonization ?

Dozens of harmonization efforts often work independently, rather than coordinating agendas and communications

- Progress has certainly been made…. but perhaps we can do better ?
  - There are positive initiatives in Asia, Africa and the Americas…regulatory agencies from different nations have developed programs to recognize the rules of others
  - **Despite 20 years of work,** regulatory review/approval times in various parts of the world have not decreased and in some cases, seem to be increasing.
  - As the need for harmonization grows, so do the number of organizations involved. Industry efforts resulted in more bodies working toward harmonization.

Now more than ever, perhaps the various stakeholders need to act together to **"harmonize harmonization"** efforts.

Harmonization Benefits & Challenges

BENEFITS

- Deliver novel technologies that are safe and effective in saving life
- Reduce redundancy and optimize resources
- Reducing overall cost of medical technologies to patients around the world.
- Facilitate exchange of information by speaking the same “technical language” and having common and comparable standards and data.

CHALLENGES

- Long lead times to draft and promulgate guidance documents.
- Difficult for stakeholders to reach consensus on harmonization efforts and agreements.
- Delays inherent in transposition of agreements into laws and regulations.
- Cultural differences can also present barriers to adoption of harmonized practices

How Do We Build A Global Regulatory Network ?

Greater cooperation and consistency between Regulators in different markets will be advantageous both for Regulators and for the Pharma/Medical Device industry

Streamlined development and approval requirements and reduce cost to bring new medical products to market while assuring safety and efficacy of products.

Industry to Agency …..+ …..Agency to Agency Interactions Are Key

Common Approaches

Standards
Guidance
Comparability

Shared Clinical & Scientific Data

Dialog

Data Review

"Totality of Evidence"

CTDs; STEDs;

Pre-Clinical and Clinical Data; Vigilance data; etc.

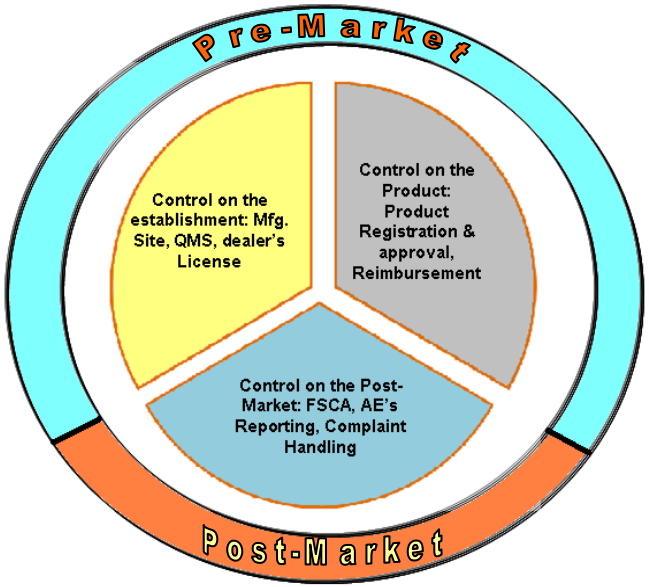
Predictability

Clear expectations

Communications

A Great Need For More Trained Regulatory Professionals throughout the Industry Around the Globe

Able to give direction, evaluate complex technologies and data, communicate with Regulators, Customers, Clinicians, R&D, Marketing, etc., and make Risk/Benefit decisions throughout the Product Life Cycle

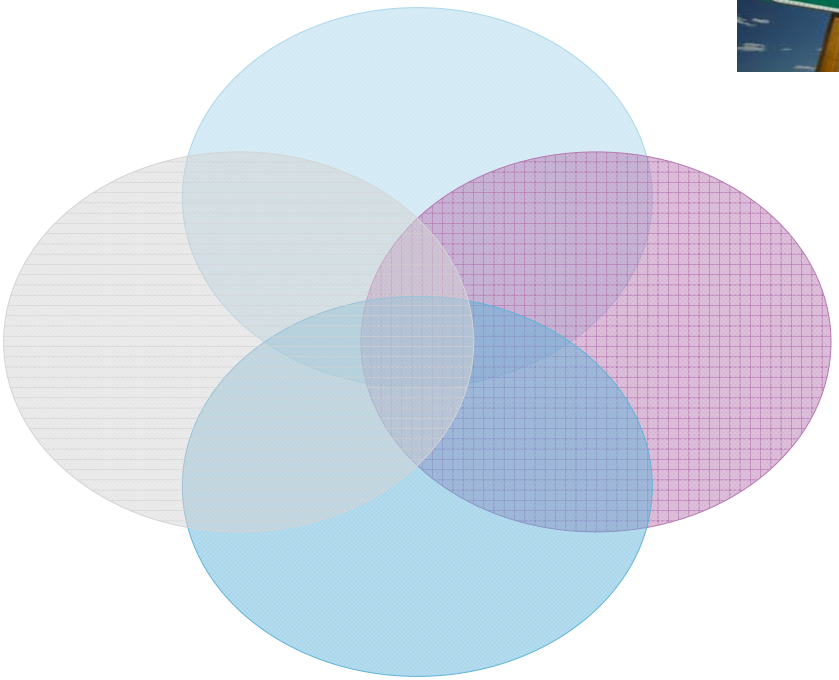


In summary: Many factors affect Global Regulatory Strategy … very dynamic

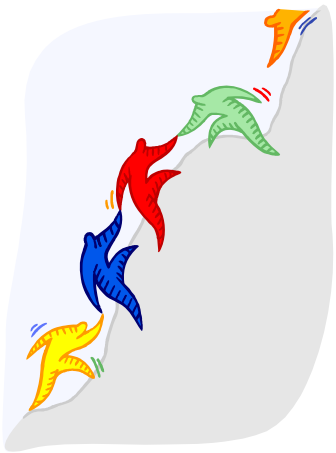
Product Classification

Approval Pathway

Studies?



Reimbursement



Manufacturing/Supply Chain/Distribution

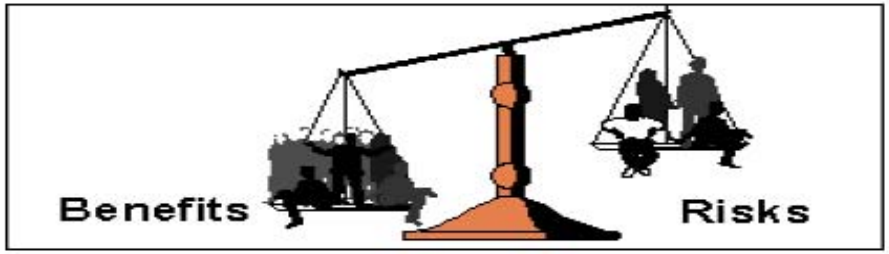
Which products?

- countries ?
- order?
- customers?

Developing A Global Regulatory Strategy

Understanding Risk Management Through Different Lens

Regulator
evaluates
benefits/risks
for the population



Provider
evaluates
benefits/risks
for a patient

Patient
evaluates
benefits/risks
in terms of
personal values

Source: Managing the risks from medical product use; Creating a risk management framework; Report to the FDA commissioner; May 1999 (Adapted)

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To Achieve Our Common Objectives

- Apply the best science to therapeutic areas where there is an unmet need – focus on our patients
- Protect and improve the public health
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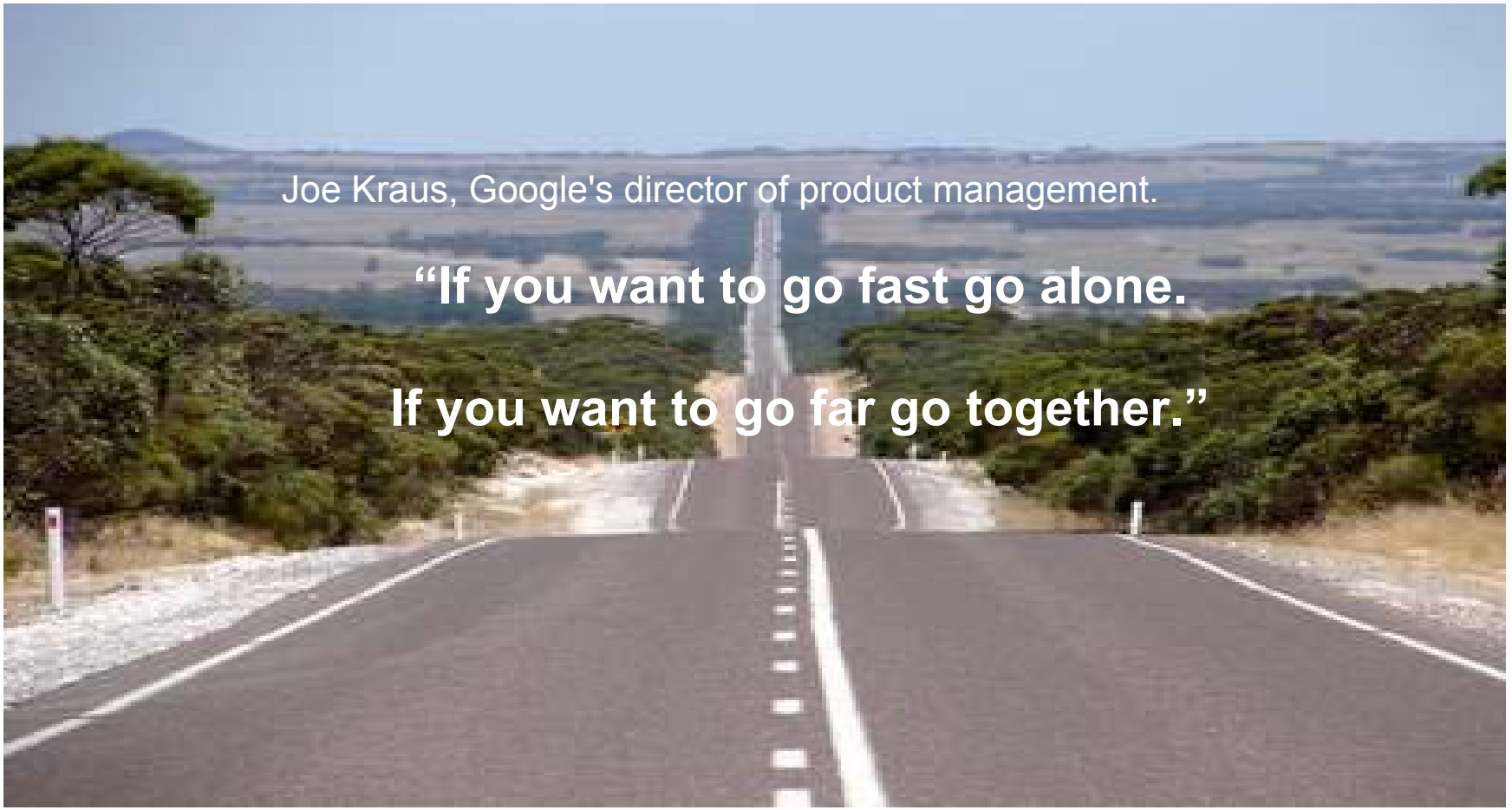
Greater collaboration (internal and external) will help to build successful Global Regulatory Strategies going forward

- Agencies, Countries, Regions,
- Non-governmental organizations and Academia
- Industry and its multiple functions/areas of expertise
- Payers

Opportunities for **collaboration** are many

- Training and recognition of Regulatory Professionals
- Technical guidance, standards, clinical study approaches
- Alignment of formats, processes, electronic information sharing

Some thoughts . . .



My thoughts . . .

Thank You