

Review Policies for Global Drug Development: Singapore's Perspective

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Outline



- Overview of the Health Sciences Authority
- Biomedical Sciences Initiative
- Regulatory Framework & Review Policies
- Summary

Vision



To be the **LEADING**
INNOVATIVE AUTHORITY
protecting and advancing **NATIONAL HEALTH** and **SAFETY**

Mission

- To **wisely regulate** health products
- To **serve** the administration of justice
- To **secure** the nation's blood supply
- To **safeguard** public health




Health Products Regulation Group • Health Services Group • Applied Sciences Group



Health Products Regulation

Applied Sciences



- Health Products
- Quality Analysis

- Drugs & Devices**
- Product Risk Assessment
 - Quality Systems Audit
 - Clinical Trials Regulation
 - Licensing
 - Vigilance & Surveillance
 - Enforcement

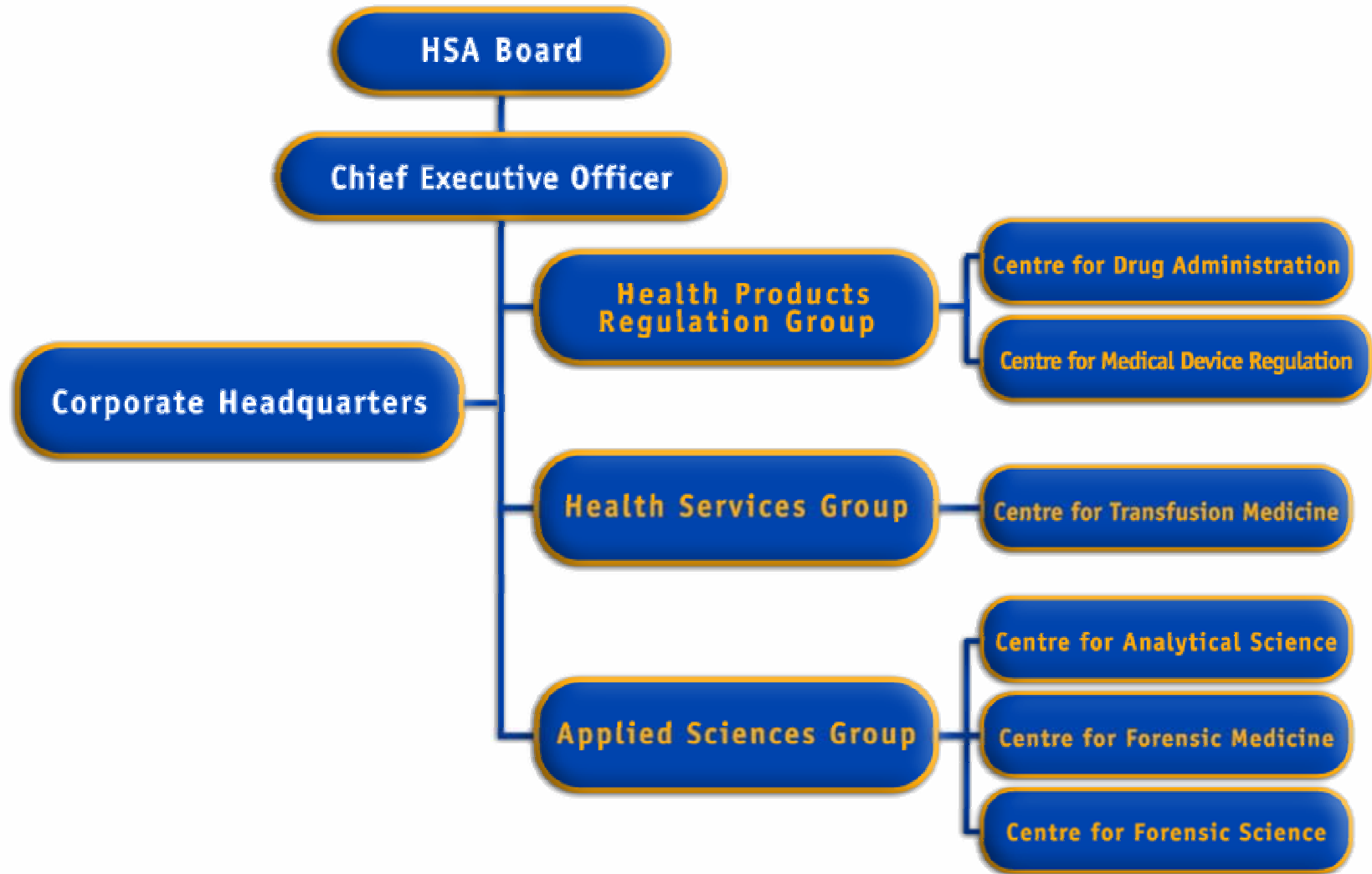


Health Services

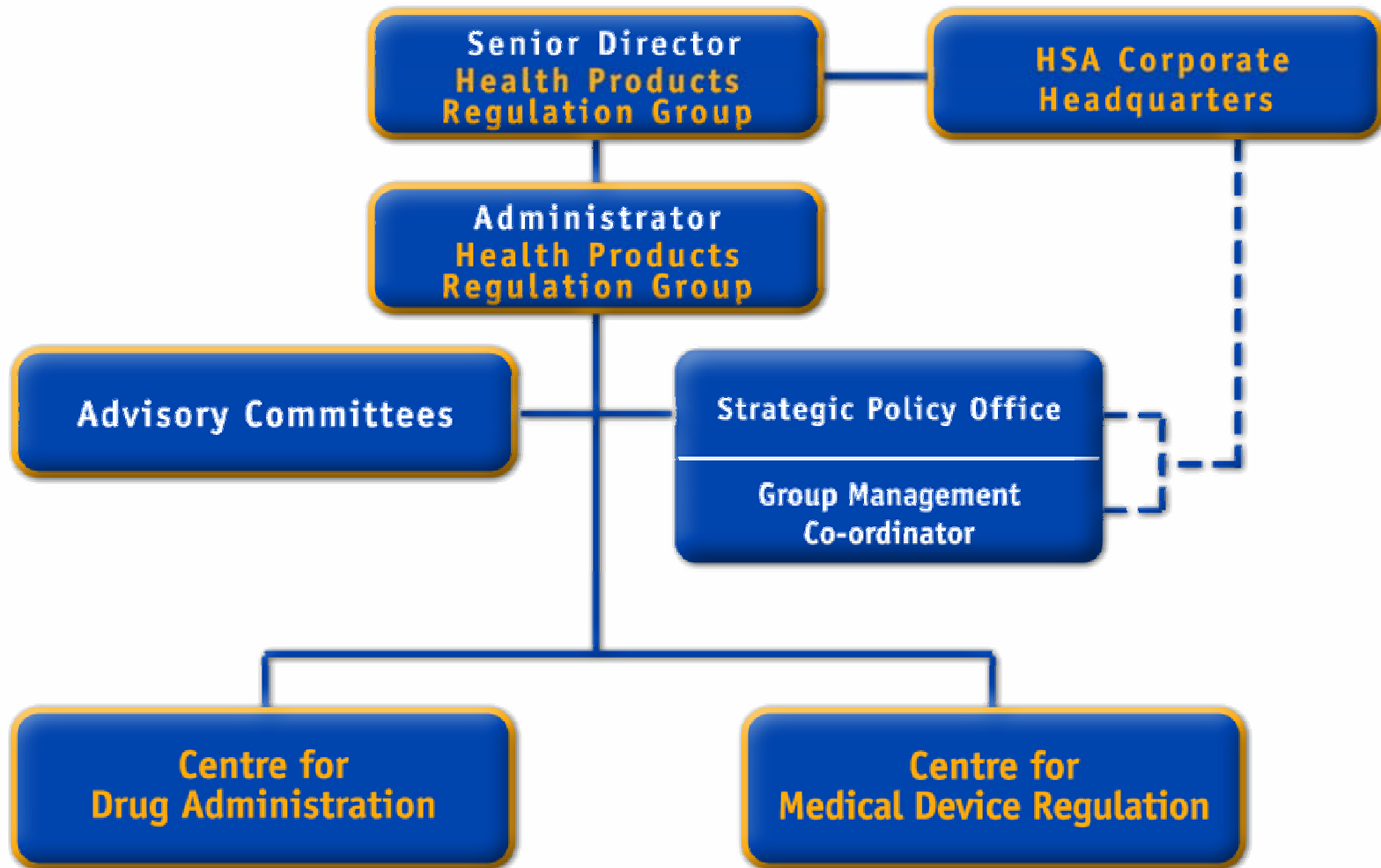
- Blood Banking & Transfusion Services
- Hemovigilance

Options for new & greater synergies across Groups

HSA Organisation Chart



Health Products Regulation Group



As of 2 April 2007

Biomedical Sciences Initiative in Singapore

Health Sciences Authority • To be the leading innovative authority protecting and advancing national health and safety

Singapore

- Total Population: 4.48 million (in 2006)
- Singapore Residents: 3.6 million
- Ethnic composition:
 - Chinese : 75.2%
 - Malay : 13.6%
 - Indians : 8.8%
 - Others : 2.4%

Source: Ministry of Health, Singapore

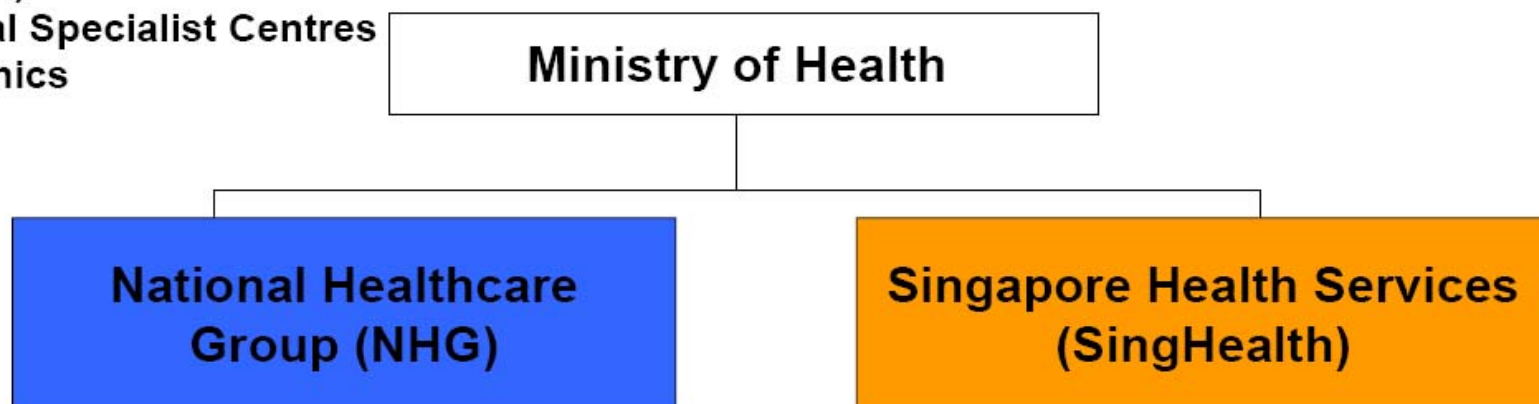
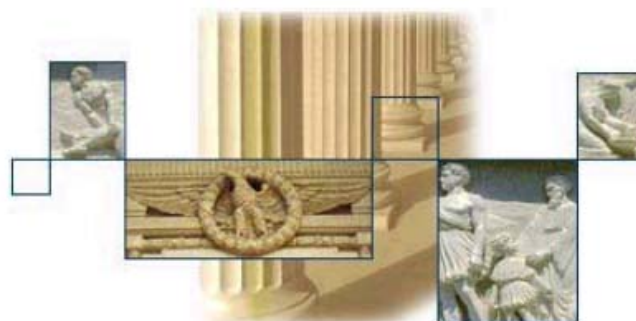
Healthcare Delivery System

- Public healthcare system managed by Government
- Private system provided by GPs & private hospitals
- Primary Healthcare
 - Private GPs (2,000 clinics) : 80%
 - Public outpatient polyclinics (18) : 20%
- Secondary/Tertiary specialist care
 - Private hospitals : 20%
 - Public hospitals/specialist centres : 80%

Public Healthcare Delivery System

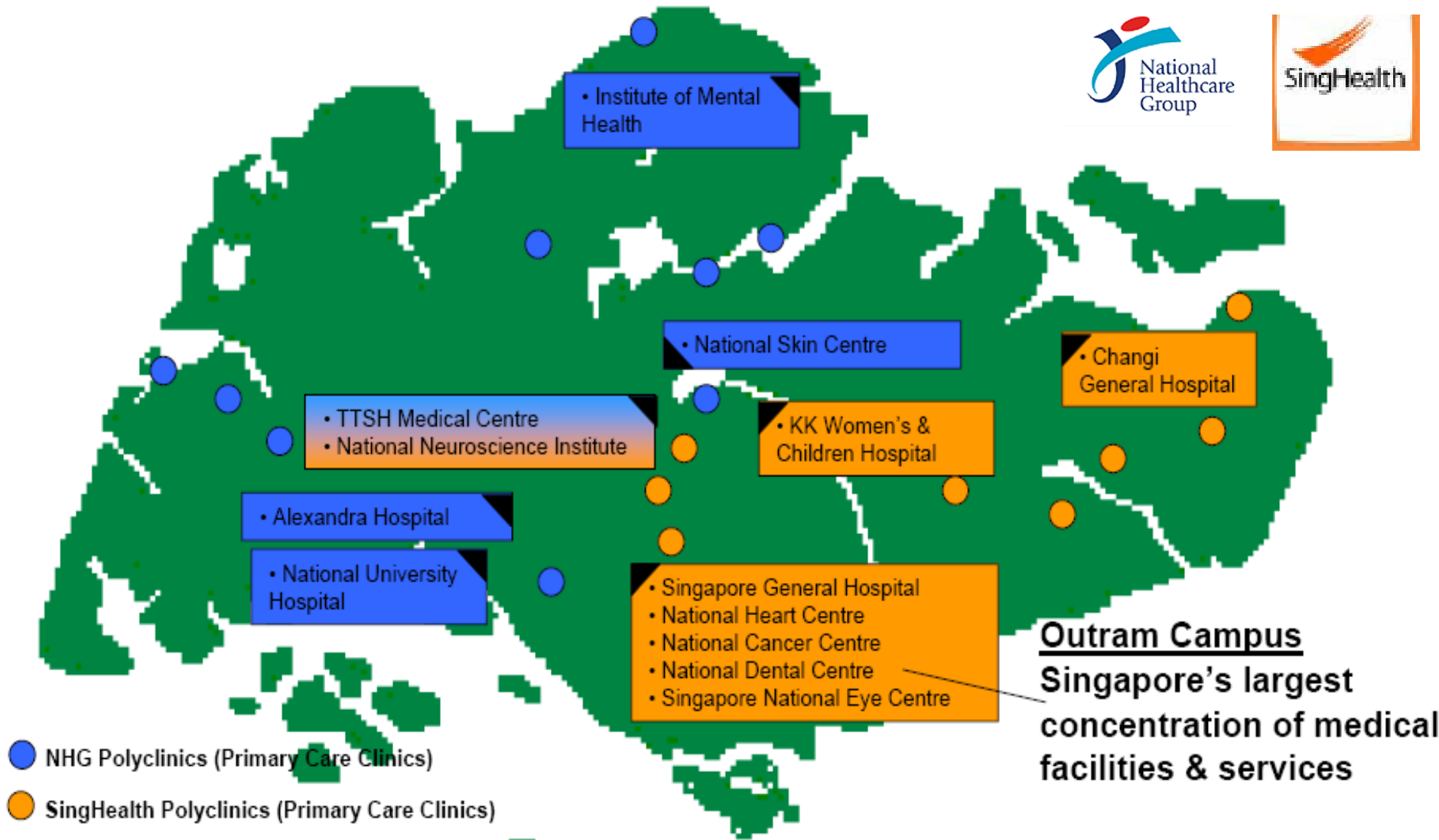
- In Apr 2000, all public healthcare institutions were divided into 2 integrated healthcare delivery networks comprising:

- Hospitals (tertiary and regional)
- National Specialist Centres
- Polyclinics



Aim: Greater integration with better quality healthcare services among public sector healthcare providers

Public Healthcare Delivery System



Biomedical Sciences Initiative

Government Support & Commitment
Substantial Investment, Long-Term & Coordinated



***Industry
promotion & facilitation***



***Public research &
manpower training***



***Strategic investments
for developmental &
financial returns***



Public Hospital Clusters



MINISTRY OF HEALTH
SINGAPORE

Regulators



Biomedical Sciences Initiative

- ▶ One of the key strategic initiatives in Singapore's drive towards a knowledge-based, innovation-driven economy
- ▶ Strengthening basic research capabilities as it strongly supports clinical research and clinical trials with the necessary capabilities, talent and infrastructure
- ▶ Emphasis on Early Phase and 'Proof of Concept' studies - key in enabling MNCs to set up dedicated phase I centres to conduct **Global Drug Development** in Singapore

Hub for Clinical Trials and Regional Clinical Research Management



- 60-man team
- 41 beds
- Phase 1 unit



- 60-man team
- 31 beds
- Phase 1 unit



- Phase 2-4 trials
- Data management



- 14-man team
- Phase 1-4 trials



GSK Biologicals

- 25-man team
- Phase 2-4 trials



- Phase 3 trials
- Results used in NDA submission



- Phase 2-3 trials
- Results used in NDA submission



- 20-man team
- Phase 2-4 trials
- Data management



- 12-man team
- Phase 2-4 trials



- 12-man team
- Phase 2-3 trials
- Centralized data



- 8-man team
- Phase 2-4 trials



- Japanese CRO
- 2nd largest in Japan



- Clinical Trial Management
- Regional HQ
- Central Lab Services



Shaping Solutions

- Clinical Trial Management
- Central Lab Services



- Clinical Trial Management
- Data Management



- Clinical Trial Management

CROs in Singapore



- Clinical Trial Management
- Clinical Trial Supplies
- Central Lab Services
- Regional Training



Shaping Solutions

- Clinical Trial Management
- Central Lab Services



- Clinical Trial Management
- Central Lab Services
- Data Management



- Central lab



- Clinical Trial Management
- Central Lab Services



- Taiwanese CRO
- Large Presence in China



- Japanese CRO
- 2nd largest in Japan



- Clinical trial management



- Clinical Trial Management
- Site Management
- Biometrics
- Bioequivalence



- Clinical Trial Management
- Data Management (EDC)



- Clinical Trial Management



- Clinical Trial Management
- Regulatory Affairs Consultation
- Drug Development Planning



- Clinical Trial Management



- Local Start-up Central Lab
- Partnership with LabCorp

Growing Base of Drug Discovery



- 60 RSEs
- Drug discovery for neuro-degenerative diseases
- Medicinal chemistry



- 40 RSEs
- In-vivo pharmacology
- Target validation



- 20 RSEs; 200 RSEs by 2008
- Chemistry process development R&D



- 55 RSEs
- Genomics & small molecule technologies-based drug discovery



- 85 RSEs
- Drug discovery for TB, Dengue and Malaria



- 62 RSEs
- Natural products research for drug discovery



- 15 RSEs
- R&D in stem cell expansion



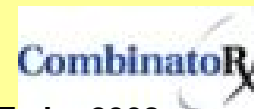
- 80 RSEs (projected)
- R&D in biocatalysis

Pharmaceuticals Research (PLR)

- 21 RSEs
- Focus on breast cancer
- Chugai-Biostar (Mitsui/CIEA) JV

LILLY

- 150 RSEs
- Oncology biomarker research & genomic data analysis
- Drug Hunting Teams for cancer and metabolic diseases
- Integrated computational science research



- 15 RSEs by 2008
- Drug development for infectious diseases



- 13 RSEs
- Neuroscience R&D



- 60 RSEs by 2008
- Development of vaccines for infectious diseases prevalent in Asia

Strategic Global Manufacturing Site



- >S\$1.3 bil, 800 emp by 2010
- 5 Chemical Bulk Actives Plants
- Technical Centre
- Chemical Pilot Plant
- Paediatric Vaccines Plant



- S\$600 mil, 260 emp
- Chemical Bulk Actives Plant



- S\$360 mil, 470 emp
- Infant Formula Plant



- S\$10 mil, 70 emp
- Biologics process devt and contract manufacturer

Biopharmaceuticals



- >S\$1.5 bil, 800 emp
- 3 Chemical Bulk Actives Plants
- Steroids Plant
- Tablet Facility
- Dry Powder Inhalers
- Biologics Fill & Finish
- Chemical Process R&D Centre



- >S\$1 bil, projected 400 emp
- Formulation Plant



- S\$190 mil, 140 emp
- Chemical Bulk Actives Plant

GENENTECH

- S\$210 mil, 100 emp
- Microbial bulk biologics facility



- >S\$1 bil, 280 emp
- Chemical Bulk Actives Plant
- Tablet Facility
- Tablet Facility Expansion



- S\$450 mil, several hundred emp projected
- Nutritional Powder Plant



- S\$200 mil, 88 emp
- Antibiotic Intermediates Plant



GENENTECH

- Large scale bulk biologics manufacturing
- 1st plant operational by 2010
- 2nd plant operational by 2011

Strategic Global Manufacturing Site

Medical Devices, Research & Clinical Tools Providers



- 500 emp
- Blood Bag & Catheters



- 520 emp
- Hearing Aids



- Projected 140 emp
- Microarray chips



- Projected 100 emp
- Cell analysis systems and mass spectrometers



- 800 emp
- Centre of Competence for Needles & Syringes
- Critical Care Systems



- 250 emp
- Contact Lenses & Global Distribution Centre



- Partnership with Solectron
- High performance liquid chromatography systems



- 400 emp
- Atomic absorption system, Auto liquid dispensing system, Bioassay reader



- 1800 emp
- Largest IV Sets, CAPD Solutions, Infusion Pumps



- 180 emp
- Interventional Cardiology & Critical Care products



- 130 emp
- Thermal Cyclers & Sequence Detection System



- 90 emp
- Electrochemistry meters & Thermometry Products



Edwards Lifesciences

- Projected 400 emp
- Tissue heart valves



- 18 emp
- Microfluidic biochips & analysis instruments
- Global Product Devt Ctr for microfluidic biochips & analysis instrumentation

Regulatory Framework & Review Policies

Biopolis

HELIOS

- Health Sciences Authority
- GSK
- ES Cell Int'l
- RIKEN Office
- British High Comm S&T Office

NANOS

- Institute of Bioengineering & Nanotechnology (IBN)
- Johns Hopkins
- Singapore Tissue Network

MATRIX

- Bioinformatics Institute
- Science & Engineering Research Council
- Exploit Technologies

CHROMOS

- Novartis
- REDI Centre

CENTROS

- A*STAR
- BMRC
- EDB BMS Group
- Bio*One Capital
- Bioprocessing Technology Institute

PROTEOS

Institute of Molecular & Cell Biology

GENOME

- Genome Institute of Singapore
- Singapore Cancer Syndicate
- Swiss House

Shared Facilities

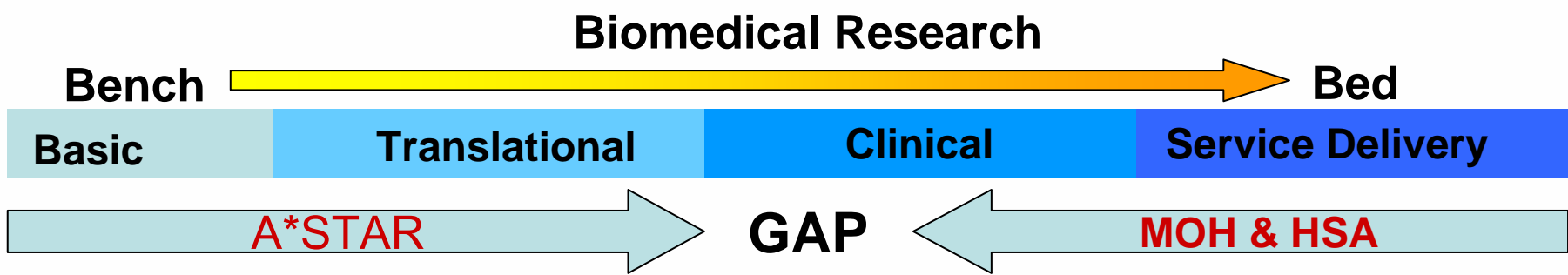
- Shared scientific services and resources (e.g. NMR, flow cytometry, x-ray crystallography, glassware washing, media prep)
- Shared facilities and amenities (e.g. lecture theatres, auditorium, F&B outlets, laundry, childcare, shuttle bus)

Expanding Regulatory Roles

- Controller & Regulator
- Nurturer & Facilitator
- Convenor & Aggregator

Keeping Up with Scientific Developments

- Rapid development in translational research
- Emergence of new products & modalities
 - ▶ Biologicals, biotech products, human cell & tissue therapy products, devices, delivery systems, diagnostic products
 - ▶ Innovative, complex or combination products



Whole Life-Cycle Approach

← Pre-market activities →

← Post-market activities →

Drug/
Product
design

Investigational
Testing/
Clinical Trial

Product
approval for
sale

Product
manufacturer

Pdt available
for sale/
supply

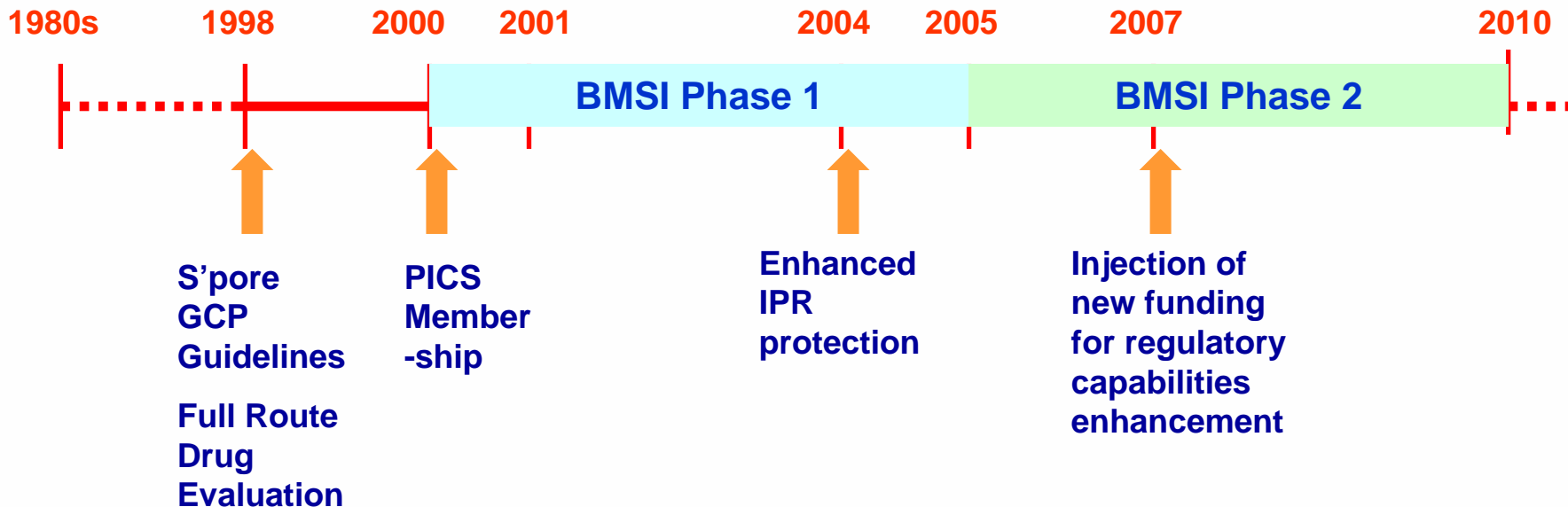
Product
purchase/
use

Regulatory Framework

- ▶ Compliance to International Regulatory Standards
- ▶ Rigorous intellectual property framework
- ▶ Active promotion of Good Clinical Practice
- ▶ New Drug Approval Systems
- ▶ Continually enhancing capabilities to manage emerging technologies and therapies

Regulatory Infrastructure Development

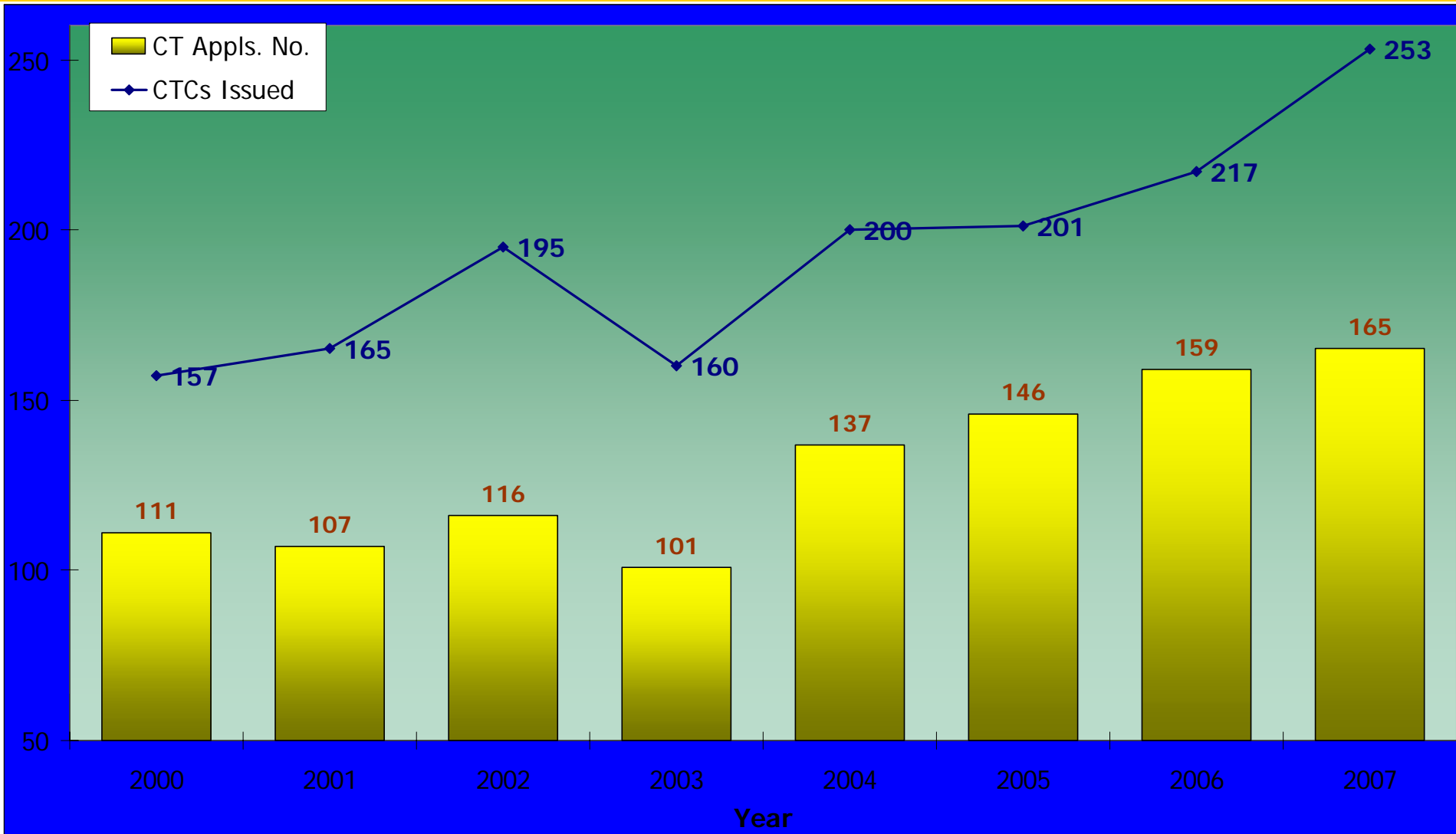
HSA Formed



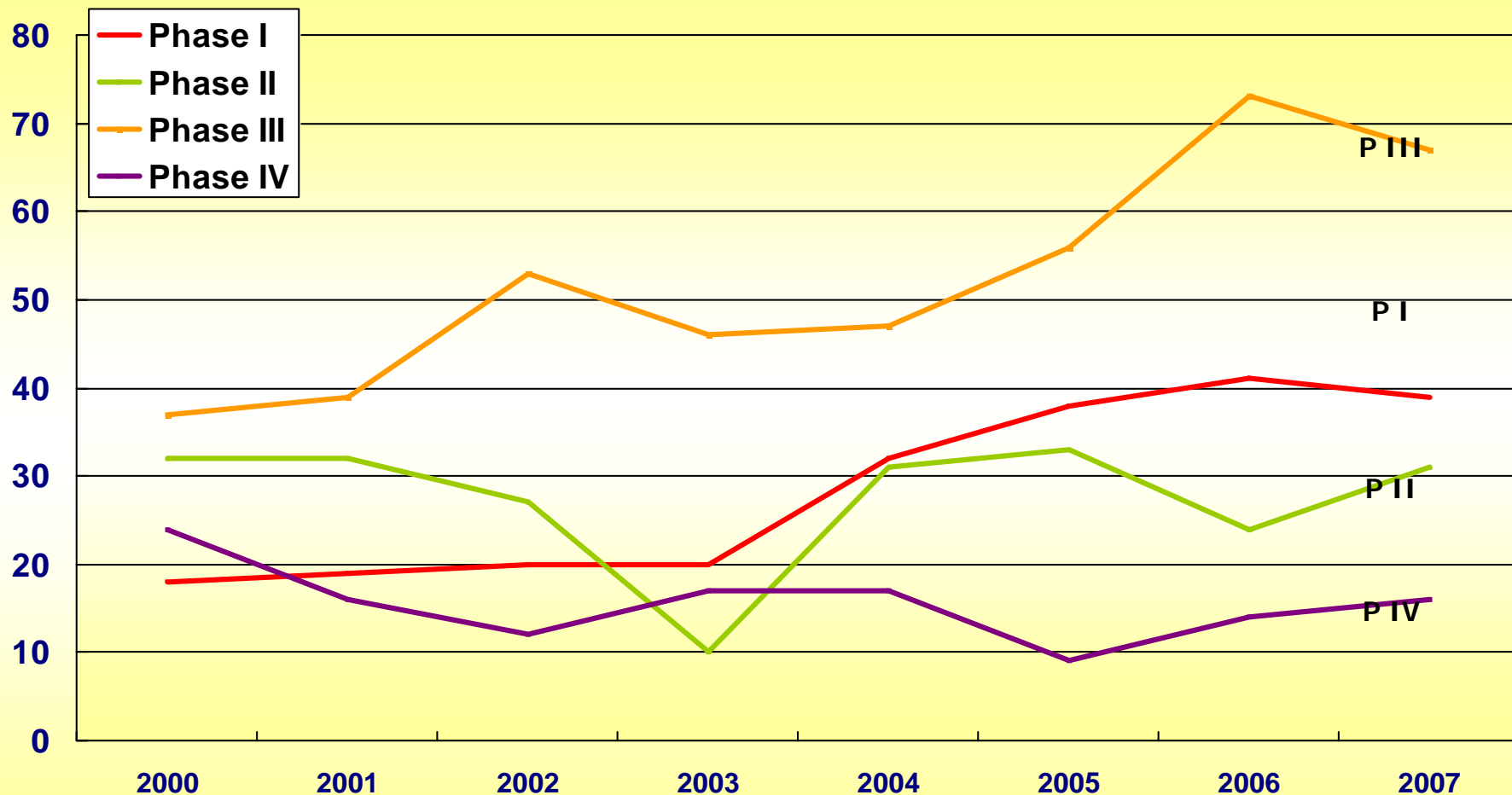
No. of Clinical Trial Certificates

Phase	2000	2001	2002	2003	2004	2005	2006	2007
I	21	19	20	24	31	44	48	47
II	44	50	52	19	49	50	35	45
III	63	68	97	91	88	90	116	135
IV	29	28	26	26	32	17	18	26
	157	165	195	160	200	201	217	253

No. of CT Applications & CTCs Issued



No. of Approved CT Applications

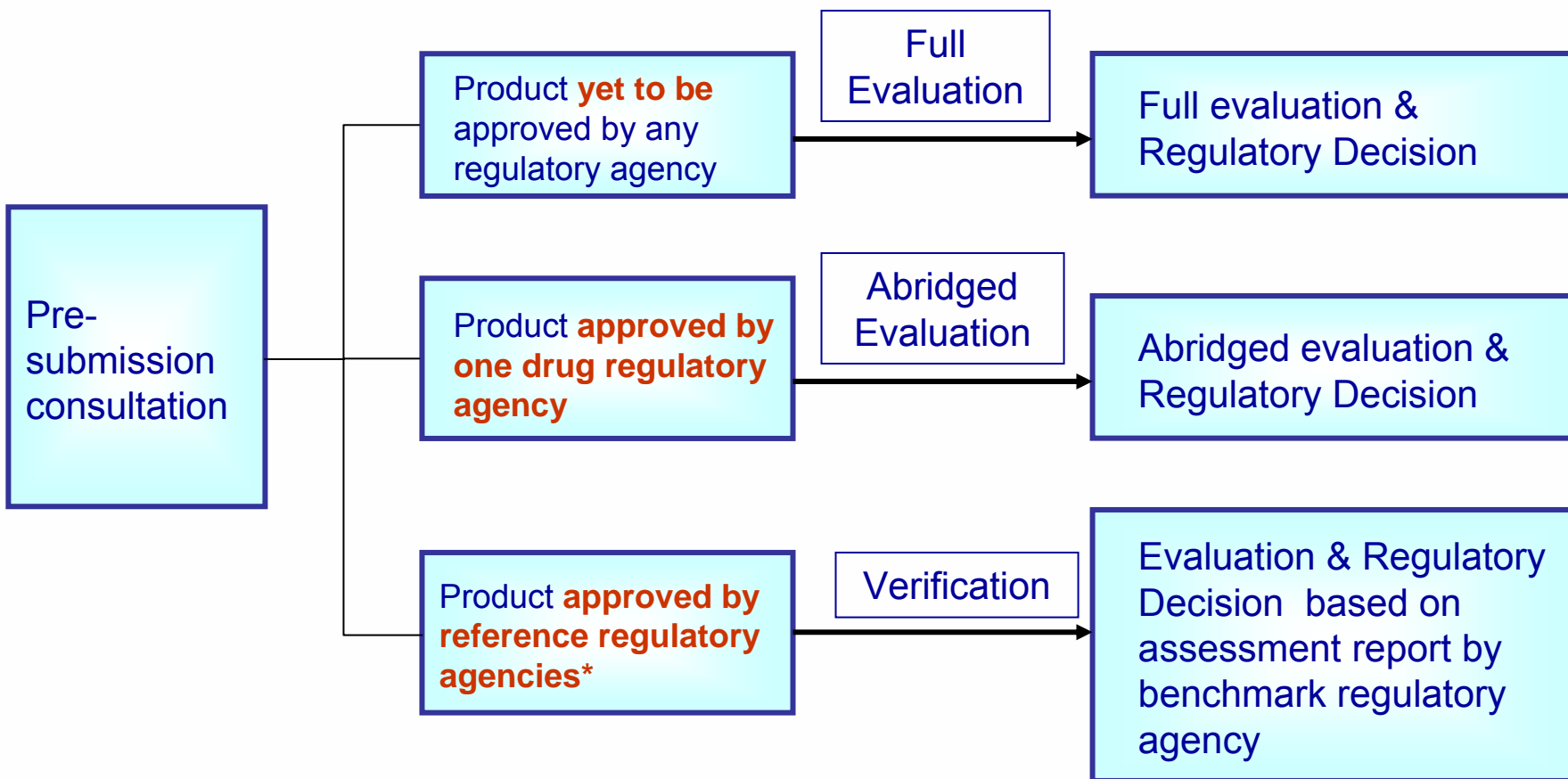


NDA: Risk-based Assessment

Since 2003, three “confidence-based” pathways allow companies to opt for route potentially expediting access to market for new medicine in Singapore

- Full (1998)
 - First-in-world evaluation of innovative products, with focus on innovative therapies for disease predominant in region and those originating from Singapore
- Abridged (Original)
 - Original pathway, following other agency approval
- Verification (2003)
 - ‘Safest’ applications (based on benchmark agency approvals)
 - ⇒ quick review and regulatory outcome

NDA: Risk-based Assessment



* Reference regulatory agencies refer to US FDA, Health Canada, UK MHRA, Australian TGA, EU EMEA

NDA: Features of the 3 Evaluation Pathways

- Employs risk-stratification strategy
- Different risk-based evaluation routes take account of product's international registration status & provides flexibility for companies in planning submissions
- Includes regular review to align with international best practice & meet local needs
- Allows optimal allocation of limited resources
- Dynamic flexibility caters for change in route of evaluation

Risk-based Vigilance

Ongoing vigilance activities to ensure that marketed products continue to be safe.

Process



International Regulatory Cooperation



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration



Inter-Agency Cooperation covers range of possible activities:

- Harmonisation of regulatory technical requirements
- Exchange of information
- Mutual recognition
- Joint inspection

Summary

Health Sciences Authority • To be the leading innovative authority protecting and advancing national health and safety

- **Wise Regulation**

Science based & judiciously adapting good international regulatory principles/practices to meet Singapore's unique situation

- **Regulatory Balance**

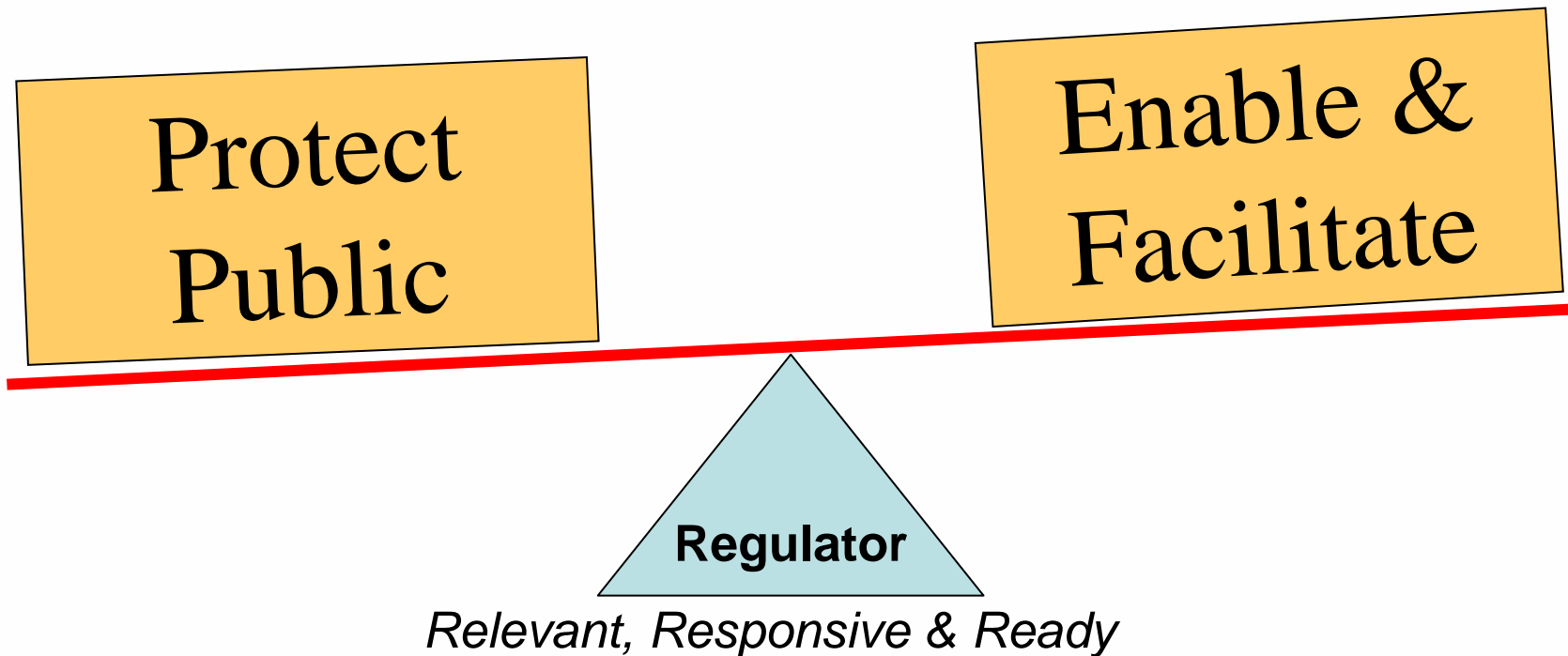
Protecting public health & expediting access to new medicines

- **Increasing Collaboration**

Strategic Partnership at all levels (local, regional & international) with research institutes, academics, industry & regulatory agencies is key to make process efficient



Finding the Right Balance



Thank You

www.hsa.gov.sg