Regulatory Overview and Considerations of Biologics & Biosimilars

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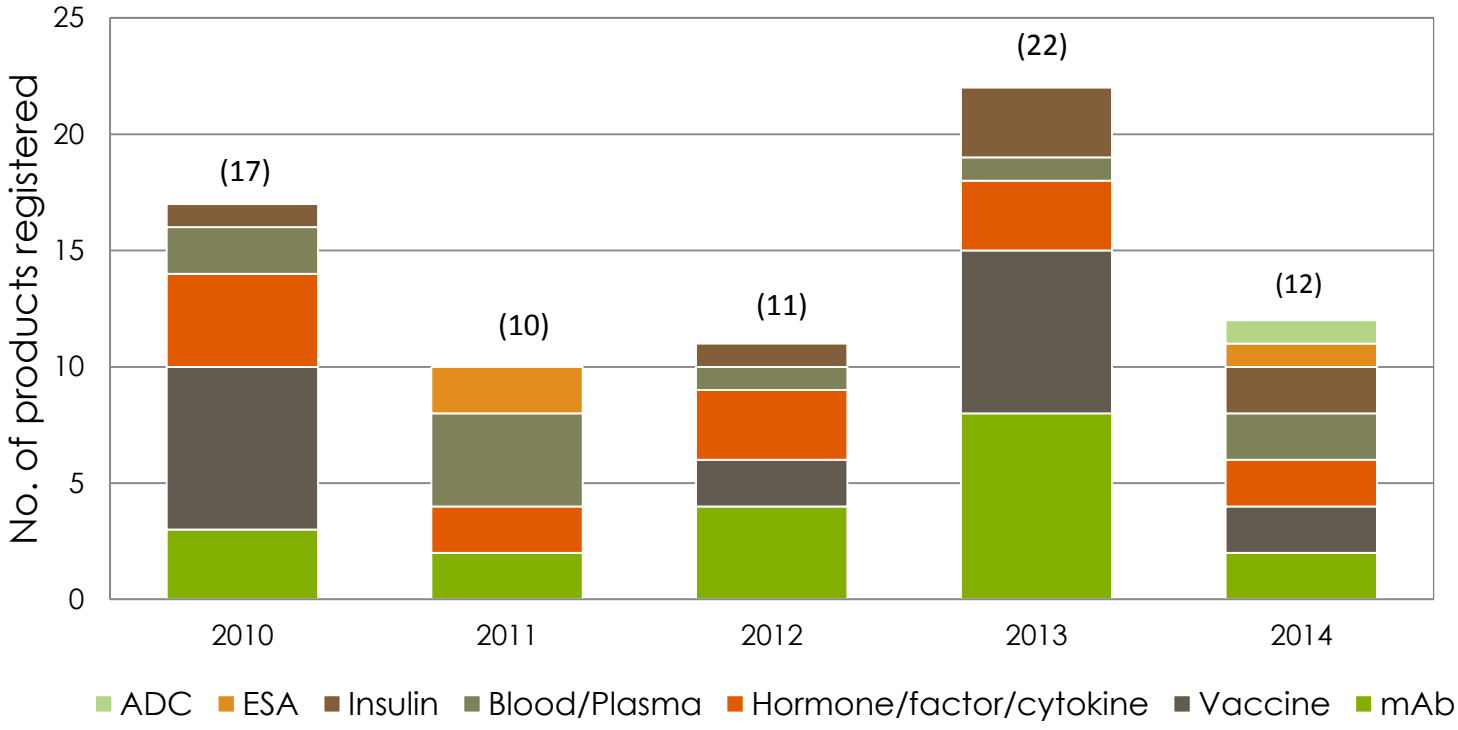
Petaling Jaya, 5th August 2015

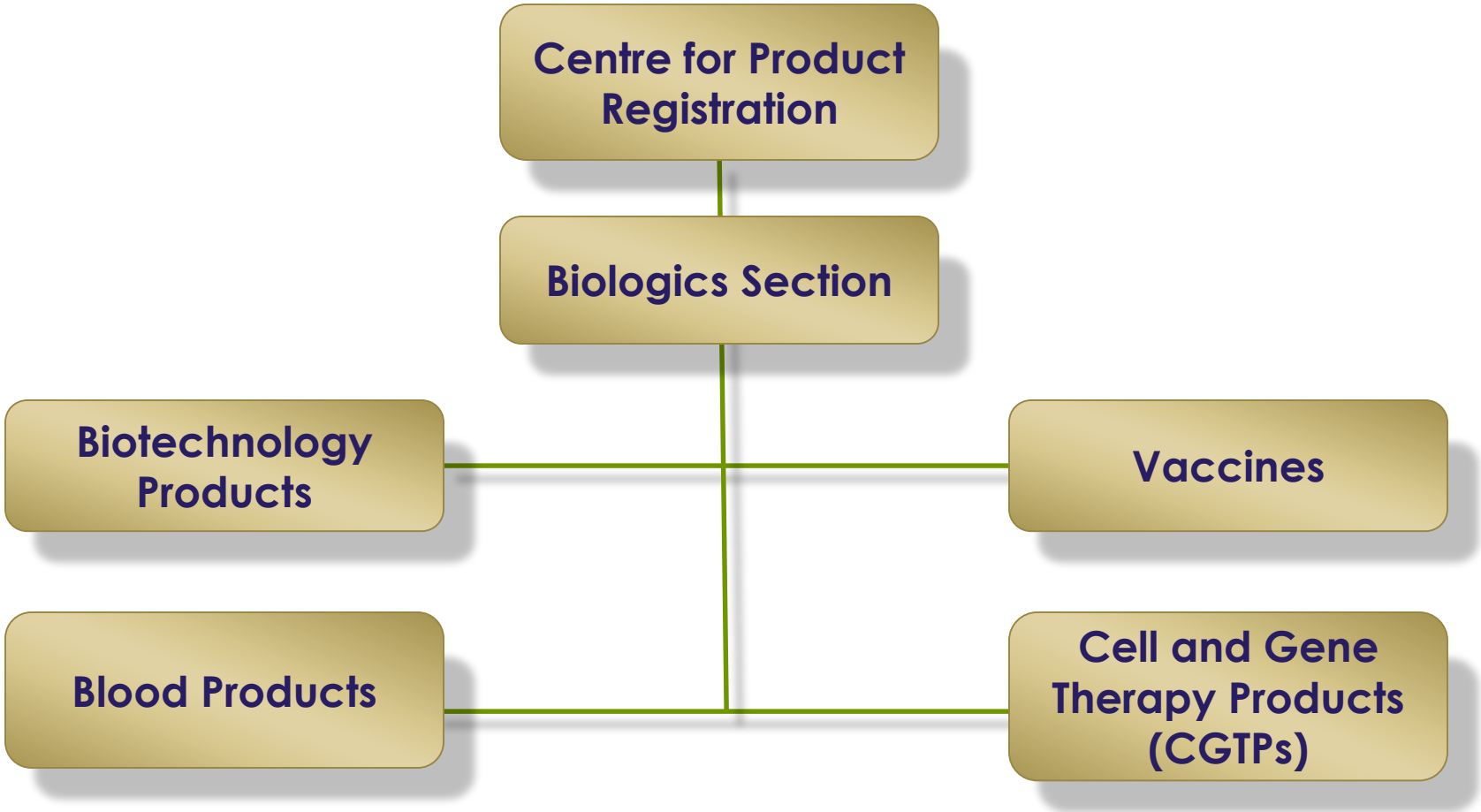
**The opinions expressed by this presenter does not always represent the opinions of NPCB*

Registration of Biological Products in Malaysia, 2010-2014

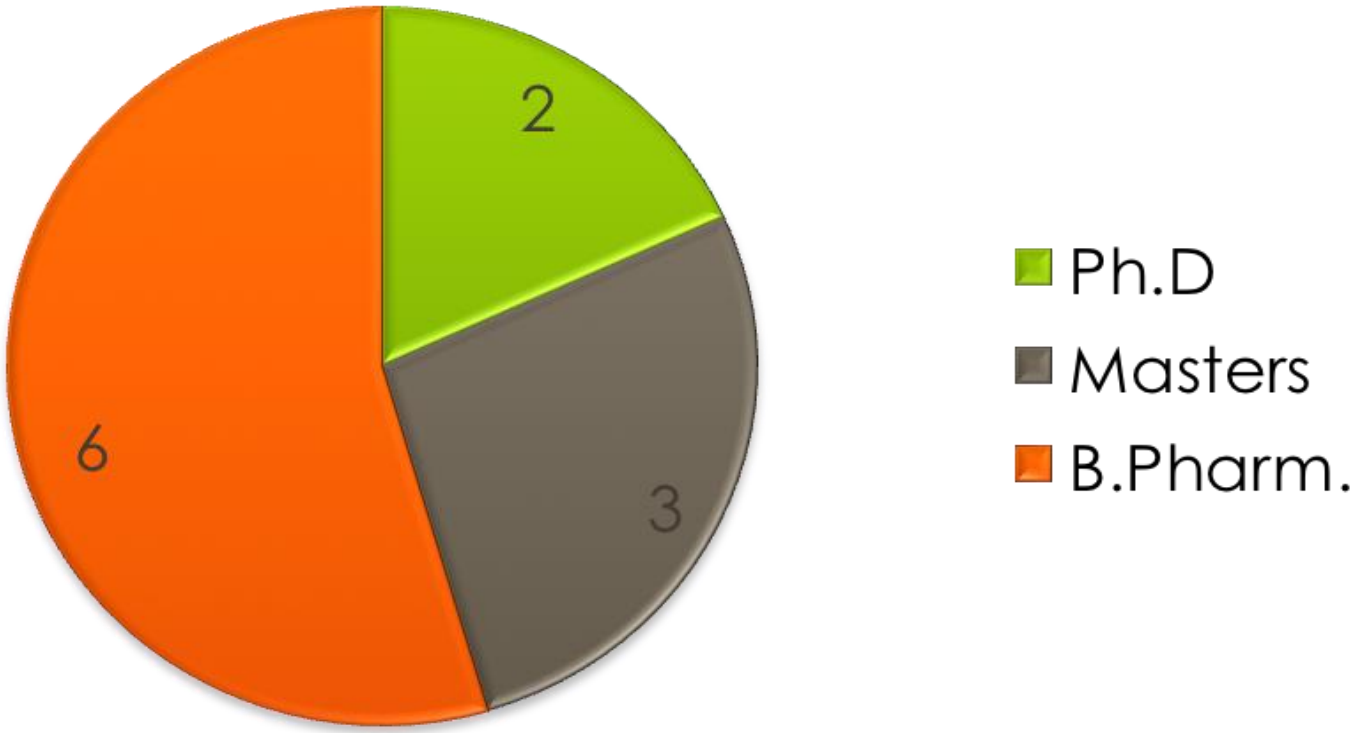


Abas A and Khoo YSK, GaBI Journal 2014, 3(4): 193-198 [figure updated]

Biologics Product Registration Section

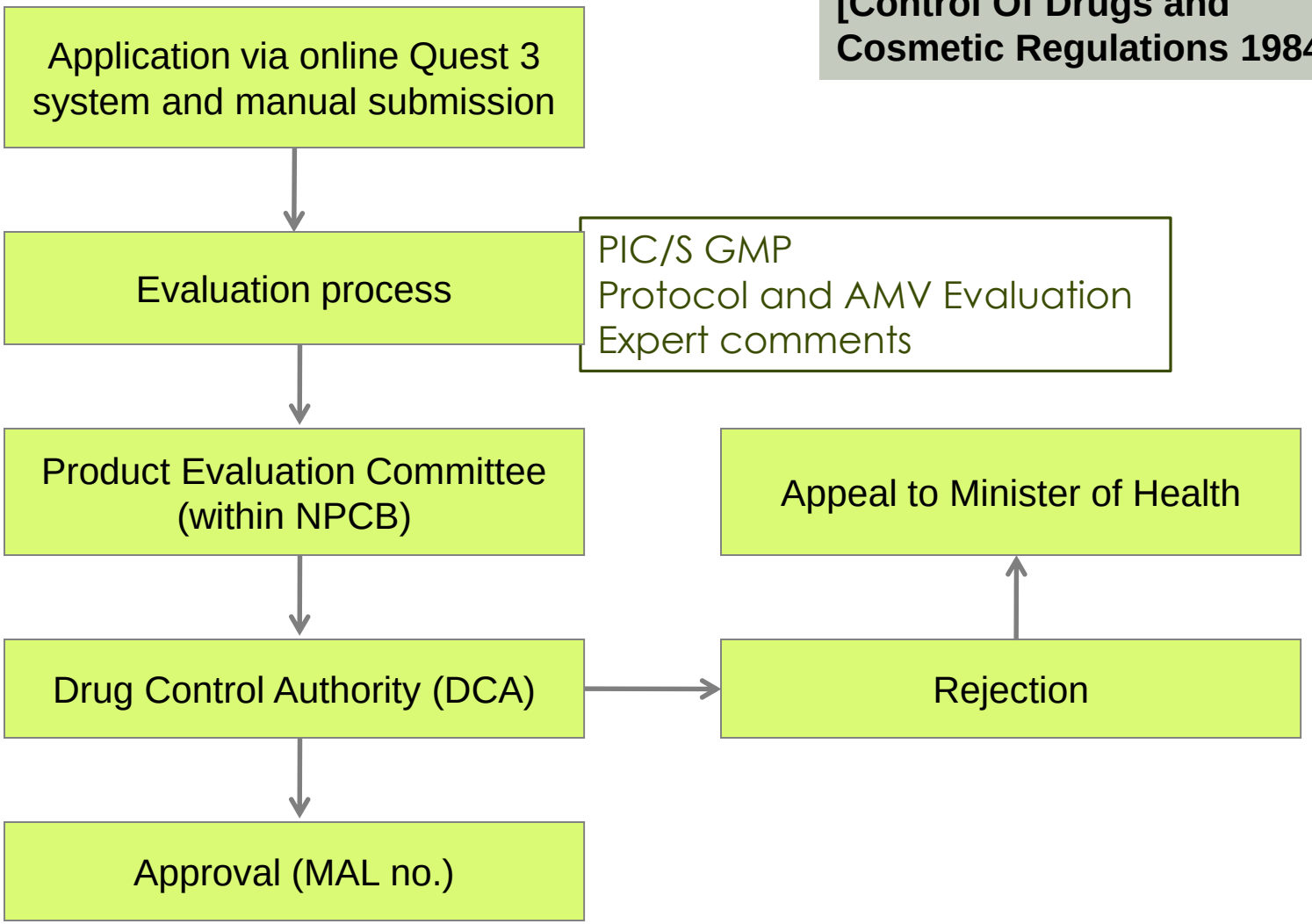


Biotechnology Product Registration Section



Registration Process

Legal Framework:
Sales of Drugs Act 1952
[Control Of Drugs and Cosmetic Regulations 1984]



Review Process

- New product (245 working days)
  - Line extension
  - 2nd source
- Priority review (90 – 120 working days)
  - Unmet medical need
  - Pandemic and emerging threats (e.g. influenza A H1N1 vaccine)
  - Country-specific needs
- Additional indication (~ 3 / 6 months)
- Variations (20 – 60 working days)

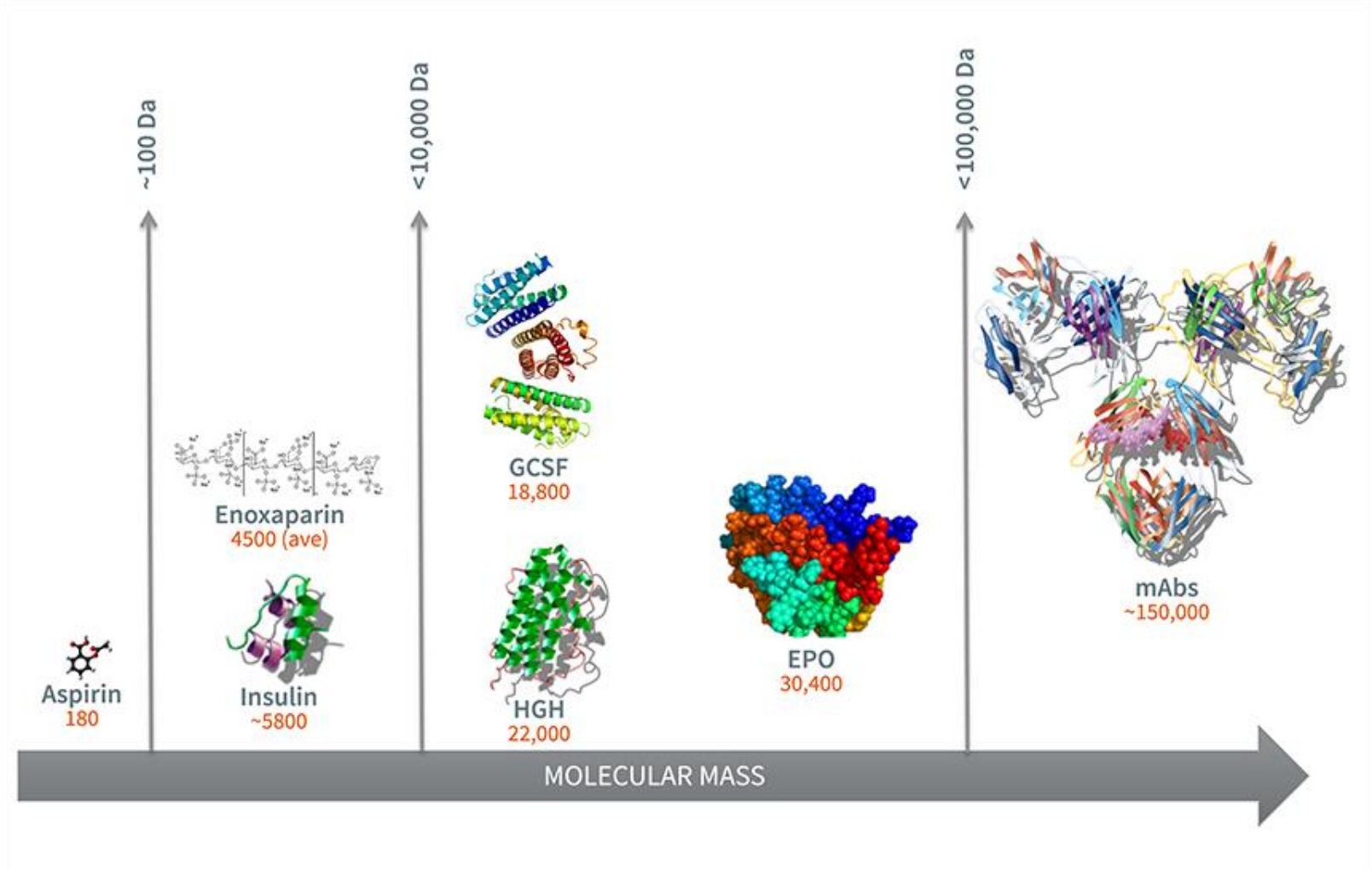
General Requirements

Organisation of product registration dossier	ICH - CTD	ACTD
Part I	Country-specific administrative & prescribing information	Table of contents, Common administrative data & Product Information
Part II	CTD summaries	Quality
Part III	Quality	Safety (nonclinical study reports)
Part IV	Safety (nonclinical study reports)	Efficacy (clinical study reports)
Part V	Efficacy (clinical study reports)	Not applicable
Other information	Not applicable	Country-specific administrative data (e.g. label, PI)

Abas A and Khoo YSK, GaBI Journal 2014, 3(4): 193-198

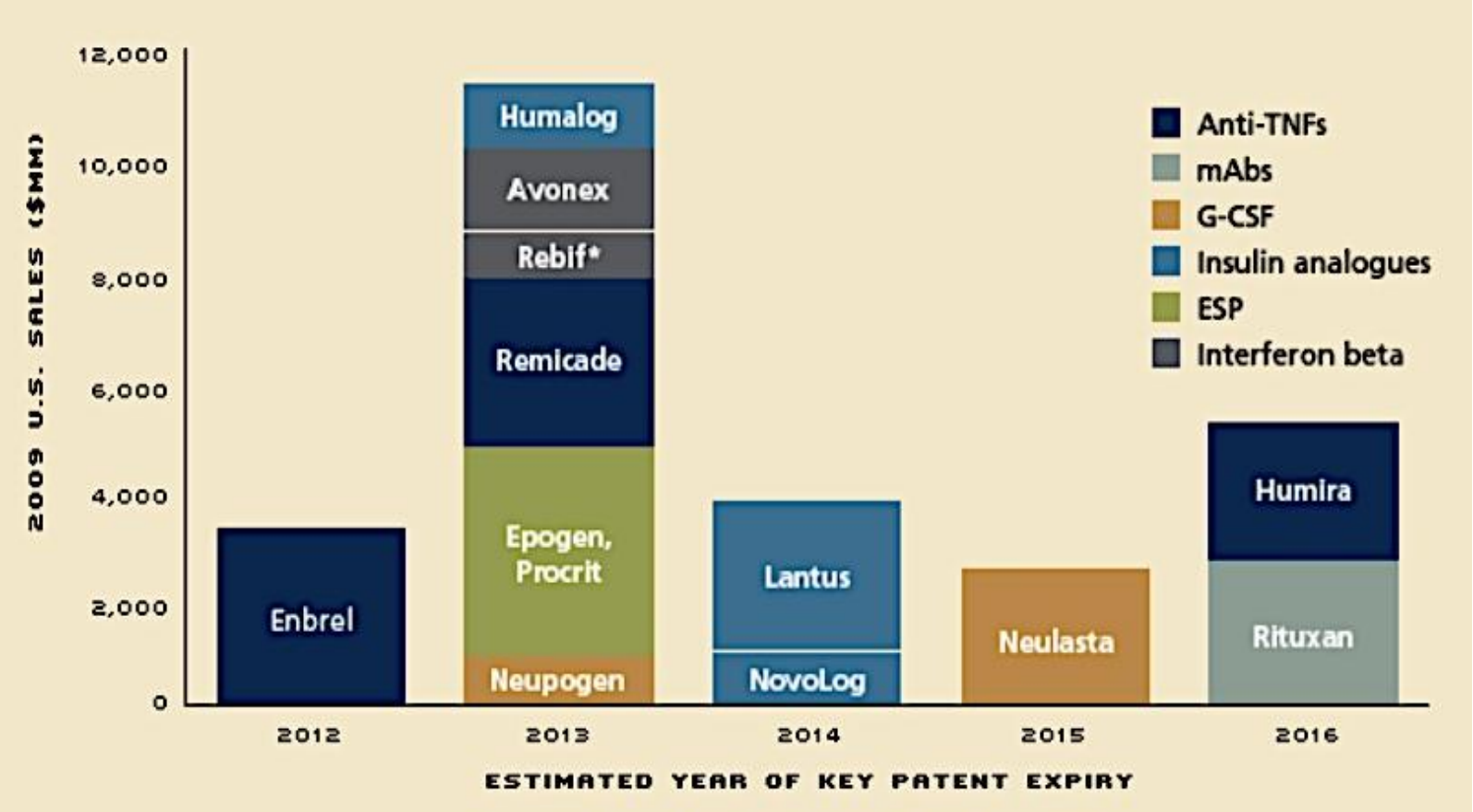
Biosimilar Product Registration

Evolution of medicinal products



http://www.amgenbiosimilars.com/the-basics/the-power-of-biologics/

US Patent Expiry of Reference Products



http://worldofdtcmarketing.com/biosimilars-poised-to-make-dent-in-branded-rx-sales/business-of-the-drug-industry/

Biosimilar products registered in Malaysia

INN	Product brandname	Company	RBP (company)	Date Approved
Somatropin	SciTropin	Sandoz	Genotropin (Pfizer)	August 2010
Epoetin alfa	Binocrit	Sandoz	Eprex (J&J)	March 2011
Filgrastim	Zarzio	Sandoz	Neupogen (Roche)	March 2012
Filgrastim	Nivestim	Hospira	Neupogen (Roche)	August 2013
recombinant Human Insulin	Insugen	Biocon	Actrapid / Insulatard / Mixtard (Novo Nordisk)	January 2014
Infliximab	Remsima	Celltrion	Remicade (J&J)	January 2015

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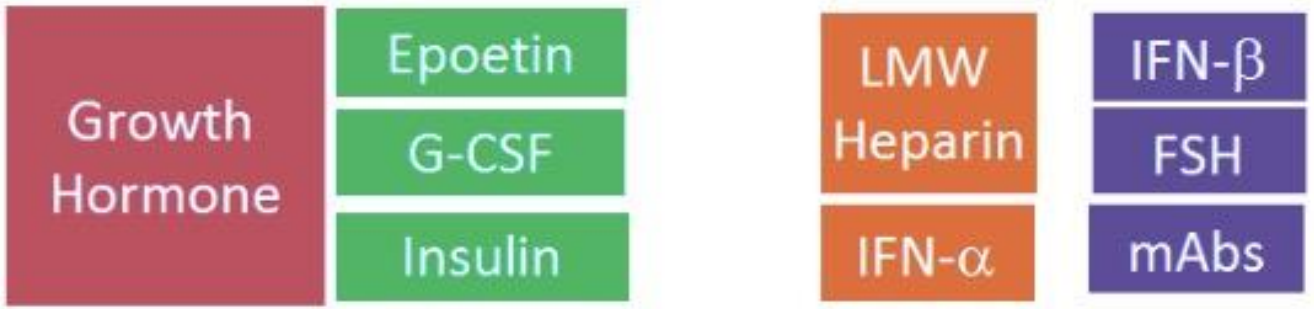
Biosimilar product evaluation

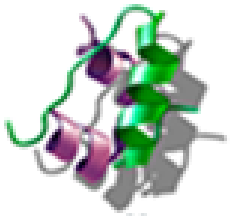
- NPCB Guidance Document and Guidelines for Registration of Biosimilars in Malaysia
- WHO Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs)
- EMA Guidelines for Biosimilars



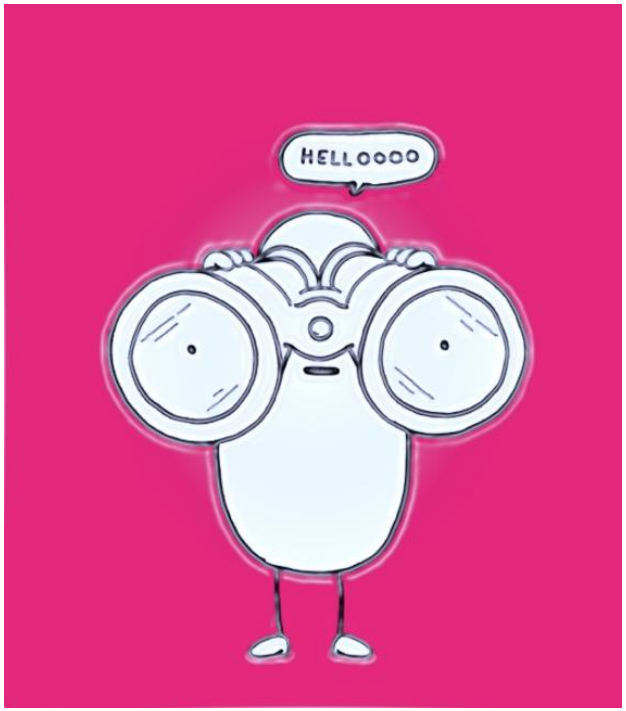
Biosimilar Product Registration Highlights (2014-2015)

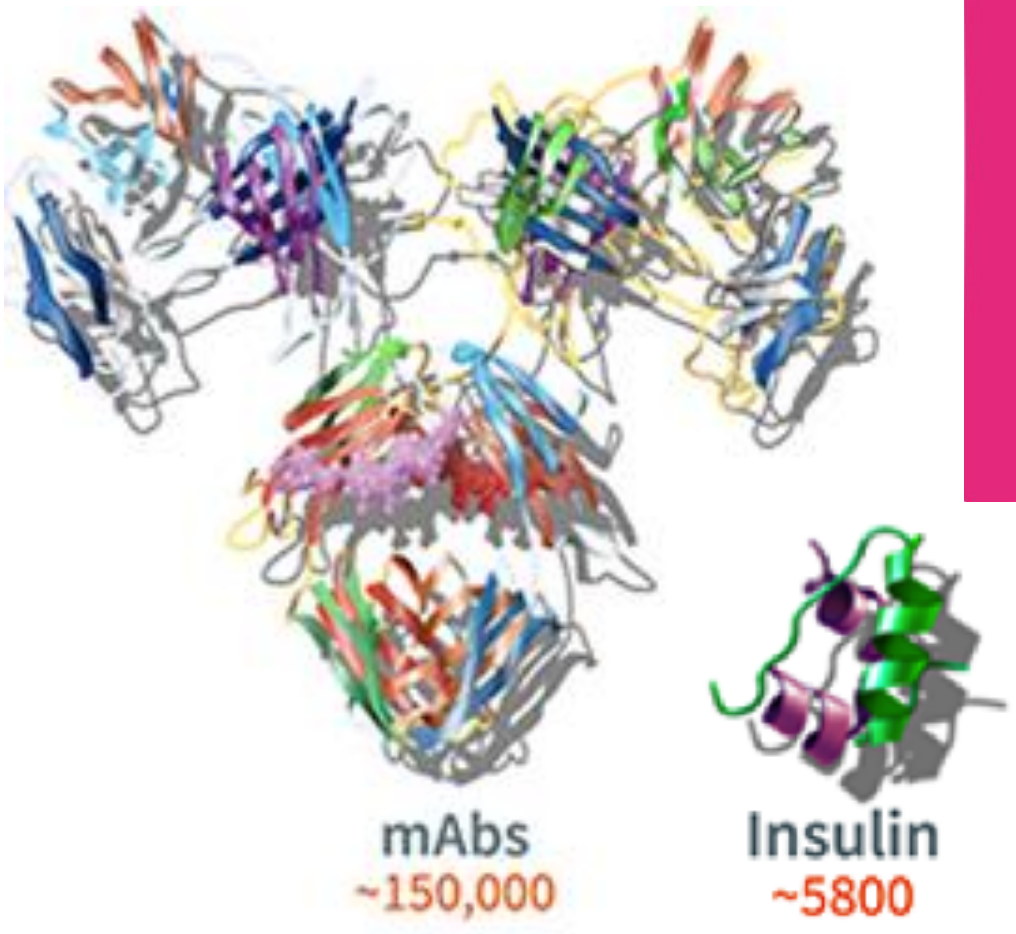
1st biosimilar rHuInsulin registration

- Insugen® (Biocon Ltd, India) – previously registered in India (non-biosimilar pathway)
- NPCB GMP inspection on manufacturing facilities in India
- CMC, nonclinical and clinical comparability studies
- DCA approval with conditions (RMP, PBRER, patient registry, post-marketing surveillance study)
- Biocon Malaysia in Bio-Xcell, Iskandar Malaysia



Protein complexity

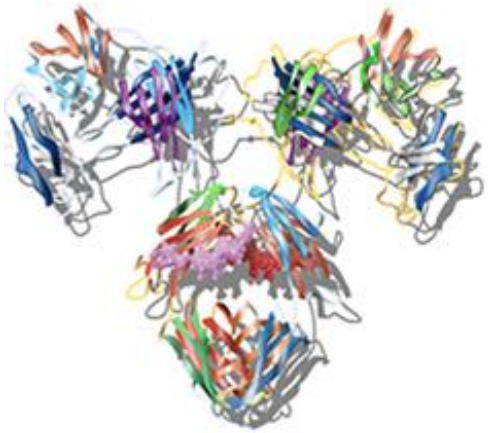




1st biosimilar mAb registration

- Remsima® (Celltrion Inc., Korea)
- CMC, nonclinical and clinical comparability studies (RA & AS only)
- Extrapolation of indication:
  - Psoriasis & Psoriatic arthritis (OK)
  - IBD (Crohn's disease and UC) (not OK)
- DCA approval with conditions

  (RMP, PBRER, patient registry)



What I think would work…

NRA Self-assessment on regulation of vaccines

WHO NRA Assessment System and Institutional Development Plan (IDP), 2013

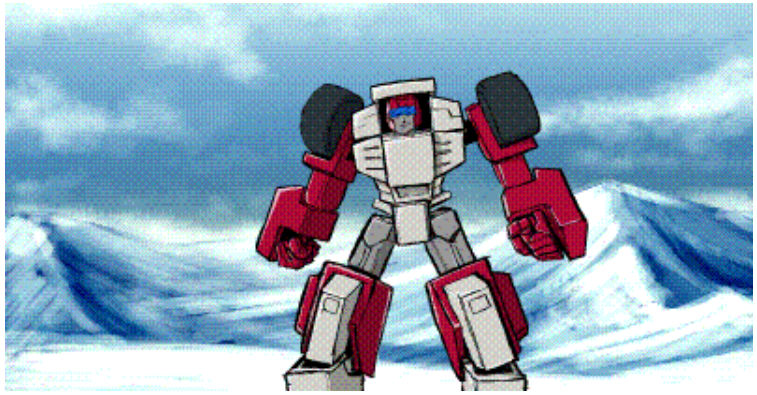
- WHO Workshops for NRAs for vaccines in the Western Pacific Region
  - 2nd Meeting on the Regional Alliance for NRAs for Vaccines in the Western Pacific Region (WPR), 11-15 March 2013 in Manila
  - NPCB has performed a self-assessment on the capacity of its regulatory functions (as a direct procuring country) and determined that its lot release/laboratory access components were non-functional.
  - WHO audit on NRA self-assessment, 25-27 February 2014

WHO NRA Assessment System and Institutional Development Plan (IDP), 2013

Regulatory functions	UN agency	Procure	Produce
Regulatory system	Y	Y	Y
Marketing authorization & Licensing activities	Y	Y	Y
Postmarketing: AEFI	Y	Y	Y
Lot release	Functions undertaken in producing countries with functional NRA	Y	Y
Lab access		Y	Y
Regulatory inspections			Y
Authorization & monitoring of CTs	Y	Y	Y

How did we do?
Passed (100%) for MA & Licensing Activities Function

Criteria	Marketing Authorisation (MA) & Licensing Activities Function
1	System for MA and licensing for manufacturing activities
2	Auditing system documented and implemented
3	Staff training plan developed and implemented
4	Monitoring acquired skills and or competencies of the staff after training
5	Assessment of clinical data (safety & efficacy)
6	Assessment report prepared and used as reference for decision
7	GMP assessment for domestic manufacturers through dedicated inspections on the manufacture site
8	Web site or other official publication with SPC-like information is available and regularly updated
9	Written criteria to cover circumstances in which the routine licensing procedures may not have to be followed



Gearing up for challenges ahead

- As a member in the Dengue Vaccine Initiative (DVI)'s Cooperation among early adopter countries (EACs) for Dengue Vaccines meetings
- As an observer in the Developing Countries Vaccine Regulators' Network (DCVRN) meetings
- As a reviewer for WHO's Guidance on scientific principles for regulatory risk assessment of biotherapeutic products (me-too products)
- Local bio-manufacturing & Novel vaccines lot release, in preparation for WHO functionality assessment audit
- Regulation on CGTPs

- NRA’ s preparation to receive products to address unmet medical needs in Malaysia, e.g. novel vaccines for tropical diseases (dengue, malaria)
- Cooperation of mutual benefit, i.e. MoU with other NRAs
- Opportunities for regulatory convergence – ASEAN and Asia Pacific levels
- Our national commitment to be a biologic producer country

The Future of Biologics

THANK YOU

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