Globalization of Biosimilars

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Outline of the presentation

- Milestones for biosimilar developments
- Current situation
- Benefits of Globalization
- Shiny side vs Grey areas
- Strategies
- Critics of Biosimilars
- Future prospects

How will globalization of biosimilars take place

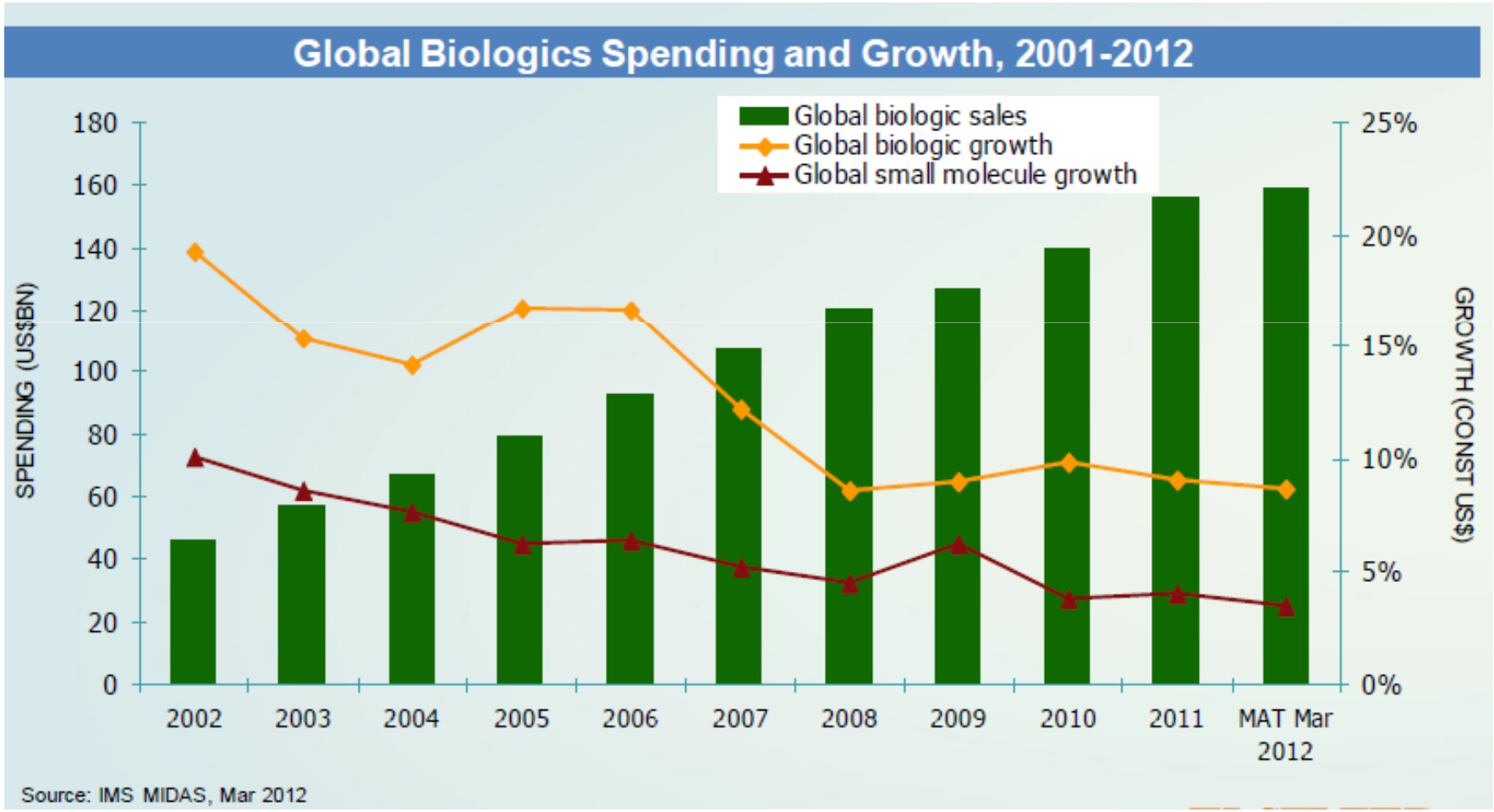
Why Globalization ?

Is it really needed ?

Who will benefit the most ?

What ‘price’ are we ready to pay for development of biosimilars?

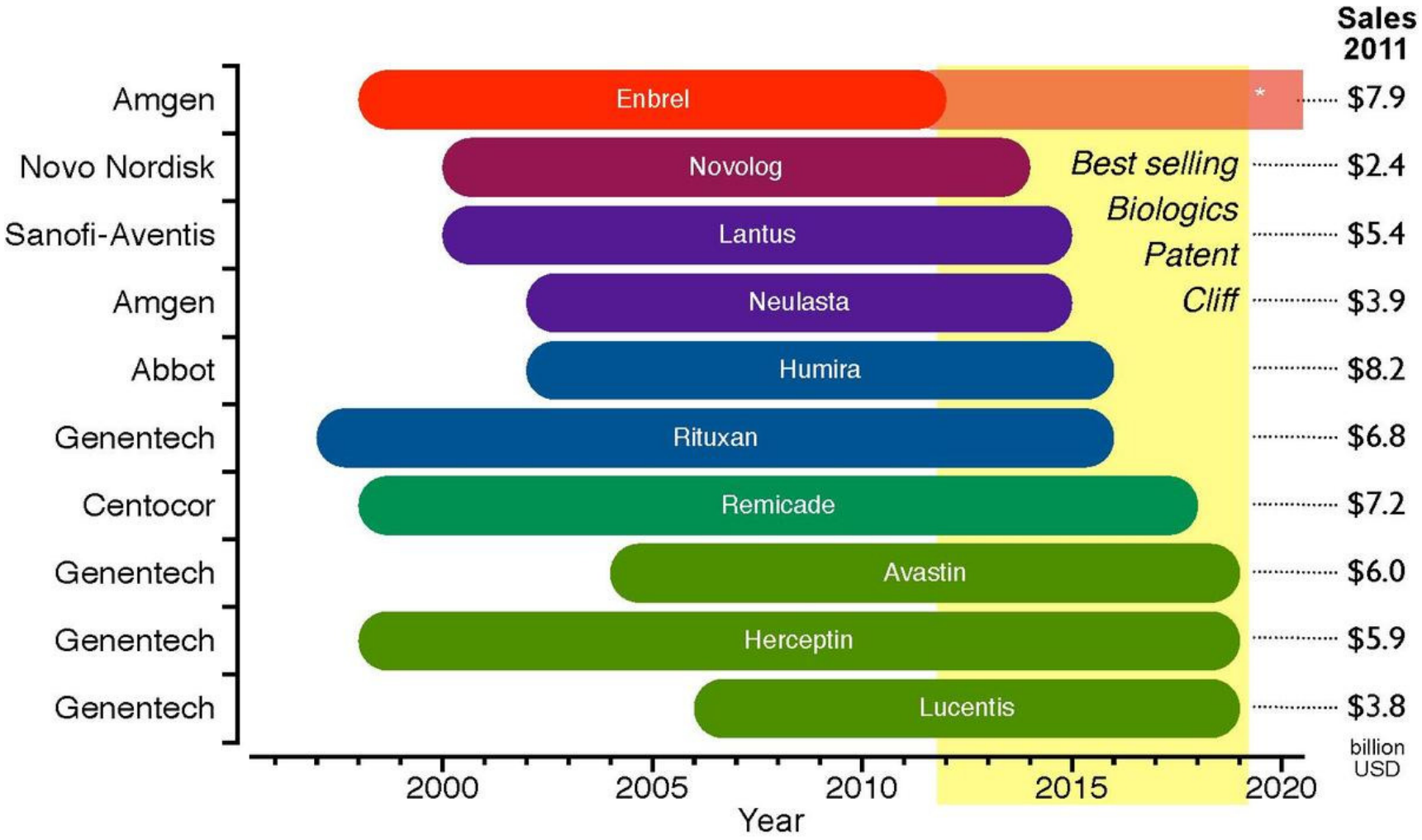
Growth of Biological products



Developmental milestones

- 1996: FDA issued first comparability Guidelines for interchangeability Biologics
- 2004: EMA develops legislation for guidelines on biosimilars
- 2006: First biosimilar available (Omnitrope)
- 2009: BPCIA authorized FDA to oversee an abbreviated pathway for biosimilar approval
- 2010: Canada, S. Africa , Japan biosimilar guidelines
- 2012: Three draft guidelines by FDA in public domain
- 2014 July: FDA accepts first application for Biosimilars
- Sept 2014 : FDA issues purple book

The patent cliff (highlighted in Yellow)



Biosimilars market is highly fragmented

- Top ten players represent< 15% of market
- Market shares of biosimilars is < 5% as compared to innovator biologics
- Distribution unequal

Biosimilar products

1. **Recombinant non-glycosylated proteins**
   - G-CSF), interferon, and human growth hormone (Largest)
2. **Recombinant glycosylated proteins**
   - erythropoietin, monoclonal antibodies, and follitropin.
3. **Recombinant peptides**
   - Glucagon, calcitonin

Monoclonal Antibody , Insulin, and Interferon market will exhibit the fastest growth by 2018

Biosimilar market is segmented

- Oncology, - largest and fastest-growing segment
- Blood disorders,
- Growth hormonal deficiency,
- Chronic and autoimmune disorders, and
- Others (female infertility, hypoglycemia, myocardial infarction, postmenopausal osteoporosis, and chronic kidney failure).

Biosimilars are segmented...cont.d

- Not all that goes off-patent is pursued
- Some like Erythropoietin (EPO) have many takers
  - (In Spain EPO 50% ; while GH around 5%)
- Monoclonal antibodies (Mab) represent a more complex manufacturing pattern

How different regions are greeting biosimilars

Biosimilars available in 50 countries all over the world

Eager

1. Europe (EMA)
2. Asia
3. Australia

Cautious

1. US (FDA)
2. Canada (PBRER ICH)

Non-originator biologics dominate in some countries: termed "Pharmerging Markets"

- Algeria • Argentina • Brazil • China
- Colombia • Egypt • India • Indonesia
- Mexico • Pakistan • Russia • Turkey

What's Red-Hot...



What's Not...

Regulatory points to look out

- FDA proposes to assess applications as
  - Not similar
  - Similar
  - Highly similar
  - Highly similar with fingerprint-like similarity:
- Interchangeability
- Data exclusivity and patents

Purple Book

Lists of Licensed Biological Products

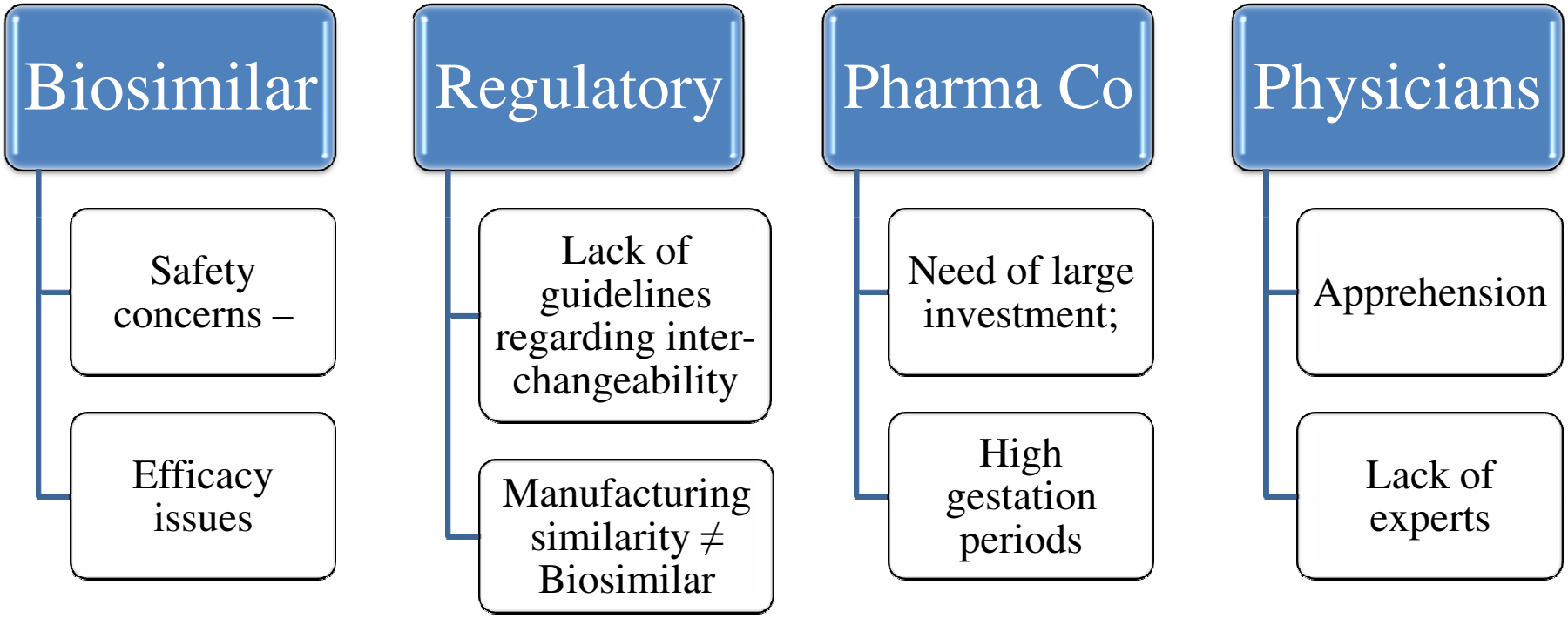
- First edition published by FDA in July 2014

1. Divided in two parts
   - Center for Drug Evaluation and Research (CDER)
   - Center for Biologic Evaluation and Research (CBER)
2. Information on biologic substitutes
   - BLA number
   - Product name
   - Proprietary name
   - Date of licensure
   - Date of First licensure
   - Reference product
   - Interchangeability

Shiny side

- Biologics/ Biosimilars outperforming
- Covers variety of disease
- Offer novel treatment strategy
- Provide revenue in billions
- Overcoming of Patent cliff
- Cover for rising health care costs

Grey areas


Biosimilar
Safety concerns –
Efficacy issues
Regulatory
Lack of guidelines regarding inter-changeability
Manufacturing similarity ≠ Biosimilar
Pharma Co
Need of large investment;
High gestation periods
Physicians
Apprehension
Lack of experts

EMA Biosimilar Applications Rejections & Withdrawals

Biosimilar vs Innovator	Year	Differences	Consequence
Alpheon (interferon alpha 2a) vs. Roferon-A®	2006	•Differences identified between the two medicines (such as impurities) •Non-validated finished product evaluation process •Lack of stability data	•CHMP recommended that Alpheon be refused marketing authorization
Human Rapid Marvel, Human Long Marvel and Human 30/70 Insulins vs. Humulin® S, I and M3 Insulins, respectively	Feb 2008	Clinical differences in rates of lowering blood sugar levels - "Trend in favor of Humulin" • Inadequate submission of active/finished product process • Non-validated manufacturing process	Marvel withdrew its applications for marketing authorizations

Factors deciding growth in a particular market/country

- Policy of Government/ Regulatory body
- Market size
- Distribution: Retail/ hospital
- Scope of incentives
- Physician/consumers

What favors biosimilar growth

- A strategic location- Market
- Favourable economic climate
- Strong government support
- Technological leadership
- A pool of world-class researchers and experts

Positive strategies

- Pharmaceutical co:
  - Investment
  - Marketing skills
  - Partnerships
- Researchers:
  - Clinical development
  - Analytical
- Regulatory bodies: Clear regulatory policies
- Physicians: Awareness among practitioners

Learning from examples

- Taiwan government : unveiled the availability of a $1.9 billion biotechnology venture capital fund

- Sandoz invested & gained
  - shown tremendous growth

- Merck tried to manufacture biosimliar for Enbrel; expecting its patent expiry in 2012.... But Amgen got patent protected till 2028

Indian Scenario

- Draft guidelines for biosimilars announced by Dept of biotechnology in asso with CDSCO
- Over 20 products approved by GEAC
- More than 250 brands available
- Various clinical trials being conducted on biosimilars (GEAC with permission from DCGI approves clinical trials)

Product In India	Company							
	Bharat Biotech	Bio con	DRL	Intas	Lupin	Sanofi	Ran-baxy	Reliance Life
Enbrel							Appr	
EPO		Pipe			Appr			Pipe
G - CSF		Pipe	Pipe	Pipe			Pipe	Pipe
GH	Pipe			Appr				
Insulin		Pipe	Appr		Pipe			
Interferon				Pipe		Pipe		Pipe

Pipe = In Pipeline ; Appr = Approved

Critics of developments of Biosimilars

Viewed as hindrance in new drug development

Abbotts case: petition against biosimilar approval to FDA

Flip-flop policy of Amgen

Concern about Safety issues

Skepticism among physicians

Way forward

- Establish clear pathways for regulatory approval
- Innovation in pharmacovigilance trials
- Investment in market : Huge opportunity
- Establish partnership with international industry leaders
- Export of products

Things to Look forward to...

- FDA approval process to the two biosimilar applications...
- Whether FDA accepts more applications...
- How (& when) Interchangeability is defined..
- After-effects of overcoming patent-cliff...
- Reach to consumers??

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Thank You