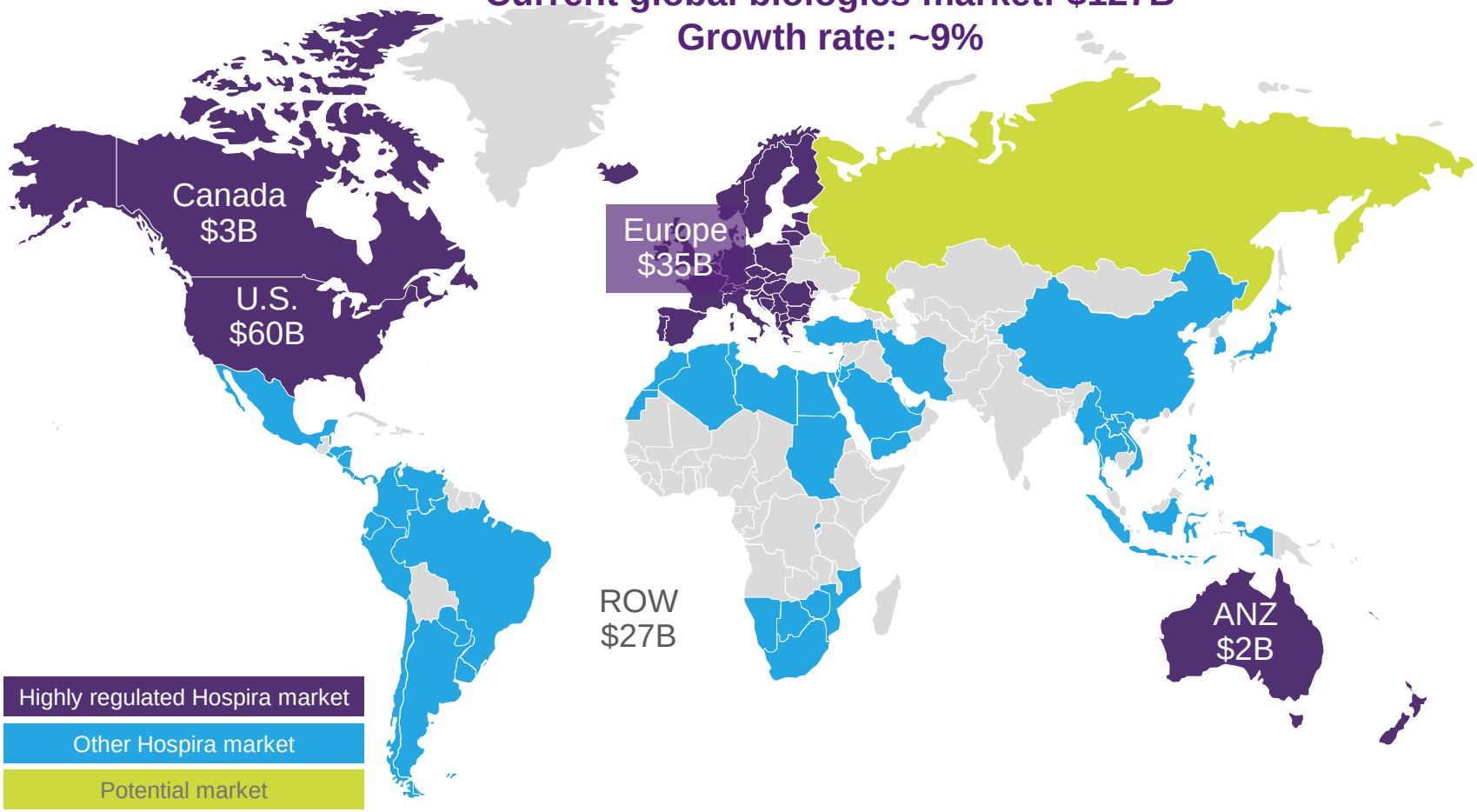
Lessons for the United States: Biosimilar Market Development Worldwide

Sumant Ramachandra, MD, PhD, MBA
Senior Vice President, Chief Scientific Officer
Hospira

Hospira

$67B+ of 2012 LMV is expected to face biosimilar competition by 2020

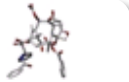
Current global biologics market: $127B
Growth rate: ~9%



*LMV: local market value. LMV is not a forecast of Hospira's expected net sales. ROW: rest of world
Source: Excludes Vaccines; Source PharmaView, Decision Resources, 2013, Regional Figures modified from DataMonitor, 2012.

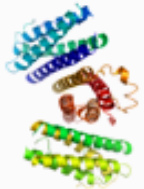
Biosimilars are not generics

Biosimilar development is longer, much more costly and riskier than generic development



Paclitaxel

854 Da*



Filgrastim

18,000 Da

Monoclonal Antibody

145,000 Da

- <$5M and 3-5 years to develop a generic[1]
- >$100M and 8-10 years to develop a biosimilar[1]
- Unlike generics, biosimilars must complete extensive non-clinical and clinical comparability studies

Biosimilars are more costly to develop than generics and require manufacturers to take considerable risk. The relative cost is expected to be higher than generics.

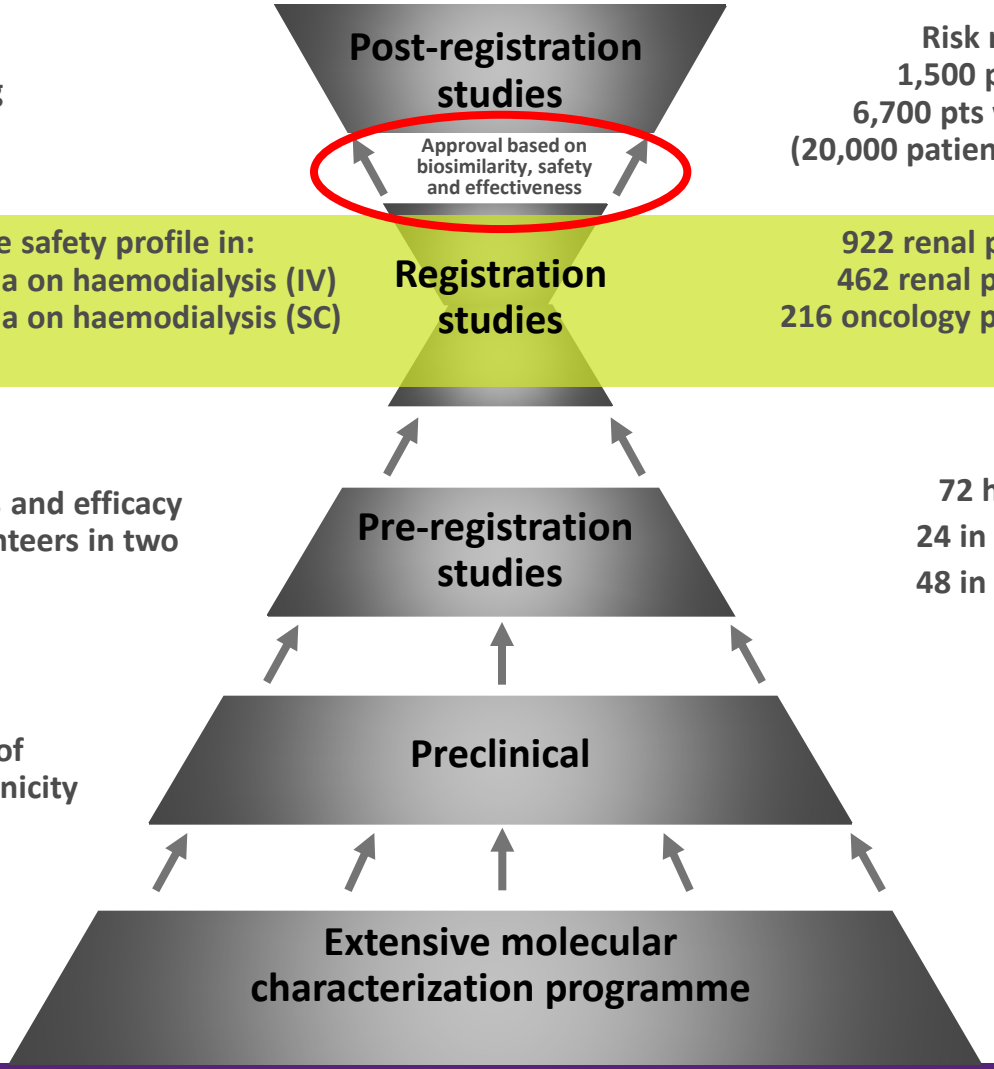
*Molecular weight in Daltons (Da)

1. Federal Trade Commission 2009. Emerging Health Care Issues: Follow-on Biologic Drug Competition. Federal Trade Commission Report June 2009 http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf

Biosimilars will require significant non-clinical and clinical studies

Example: Hospira Biosimilar EPO (Retacrit™) as compared to Originator EPO (Eprex) at each stage

Comparative



Post-marketing surveillance and ongoing safety monitoring

Risk management plan:
1,500 pts with IV Retacrit
6,700 pts with SC for 3 years
(20,000 patient treatment years)

Proven efficacy with comparable safety profile in:
– Patients with CKD and anaemia on haemodialysis (IV)
– Patients with CKD and anaemia on haemodialysis (SC)
– Patients with CIA (SC)

922 renal pts with IV Retacrit
462 renal pts with SC Retacrit
216 oncology pts with SC Retacrit

Comparable pharmacokinetics and efficacy demonstrated in healthy volunteers in two phase I studies

72 healthy volunteers:
24 in 2 period crossover
48 in 3 period crossover

In vivo and in vitro assays confirm biosimilarity in terms of pharmacodynamics and antigenicity

Animal studies

Comparability demonstrated with regard to protein structure and product quality

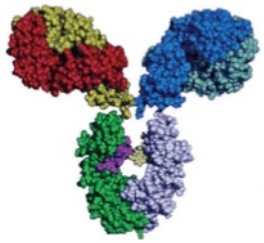
The data required for EC marketing authorization of Hospira's Biosimilar EPO was GREATER than the data for the original EPO. And, Hospira is doing extensive studies for U.S. FDA submission.

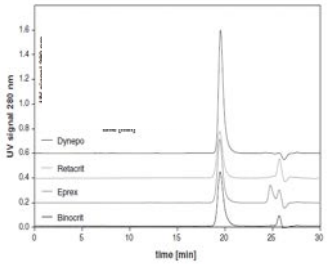
Biosimilars are biologic drugs similar to the originator biologic

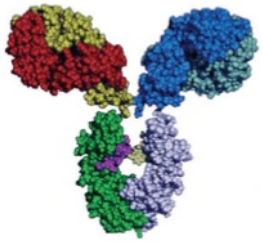
Originator product

Biosimilar product

Analytical similarity[1]



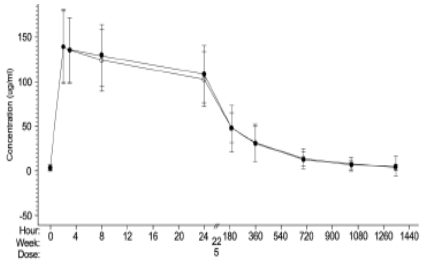




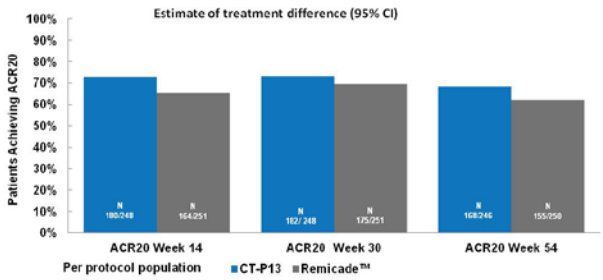
Well-defined physiochemical attributes

Highly similar on physiochemical level

Clinical
Pharmacobioequivalence[2]



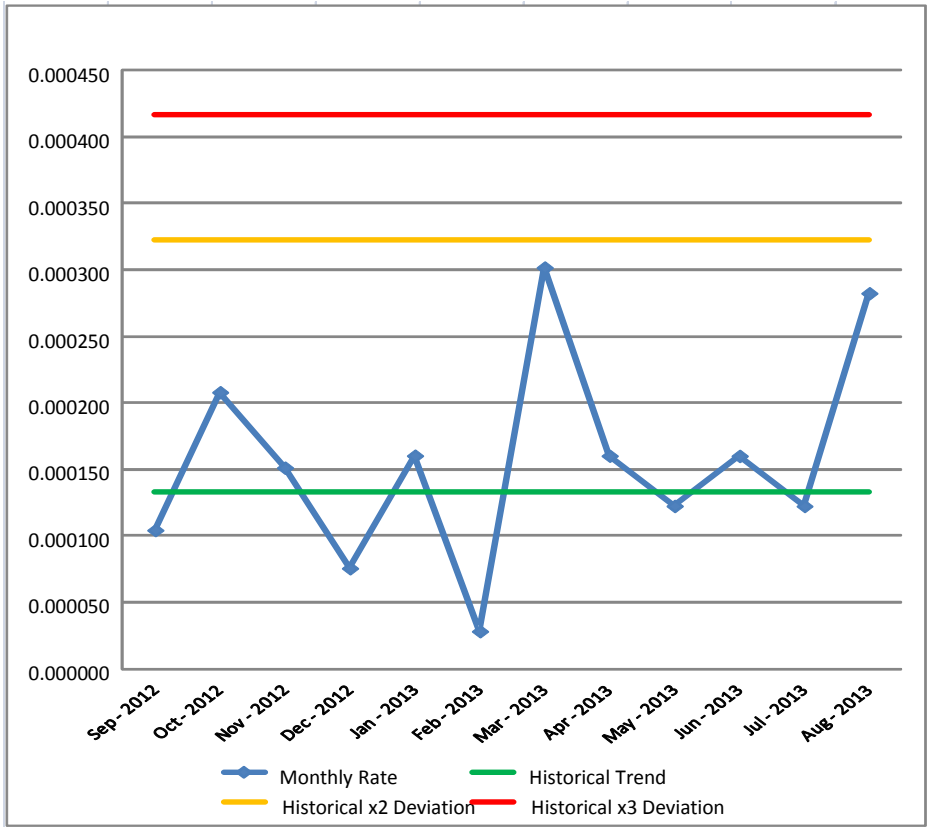
Clinical
Efficacy[3]



1. Brinks et al., Pharmaceutical Research 2011;28:386–393 2011.;
2. Yoo, DH et al, ARD, 2013 Oct;72(10):1613-20;
3. EMA/CHMP/589422/2013; CT-P13 Assessment Report

Continued post-marketing trending data critical for tracking issues

- Issues such as immunogenicity cannot always be predicted.
- May take years to develop
- Must be detected with the minimal latency period
- Key that post marketing trending data is captured for all biologics (both originators and biosimilars)



To date there have been no immunogenicity issues seen with Hospira's biosimilars in Europe[1]

1. Internal Hospira data

Post-approval market surveillance with same name for biosimilars works for identification

Product identification of Retacrit™ (epoetin zeta) and Nivestim™ (filgrastim)

Post-market records created from Dec. 12, 2008 to Oct. 8, 2013

Product	Count	Identifiable as Hospira Product	Not Identifiable	Records Identifiable (%)
Epoetin	820	816	4	99.51%
Filgrastim	289	275	14	95.16%

Biosimilars Do NOT Need a Unique INN for Post-Market Identification as Brand name was used in nearly all cases and, in general, in the U.S., dispensed agents are recorded in the Pharmacy IT systems

Having a different INN to the reference product (Hospira's epoetin zeta) has caused confusion in the EU

Romania

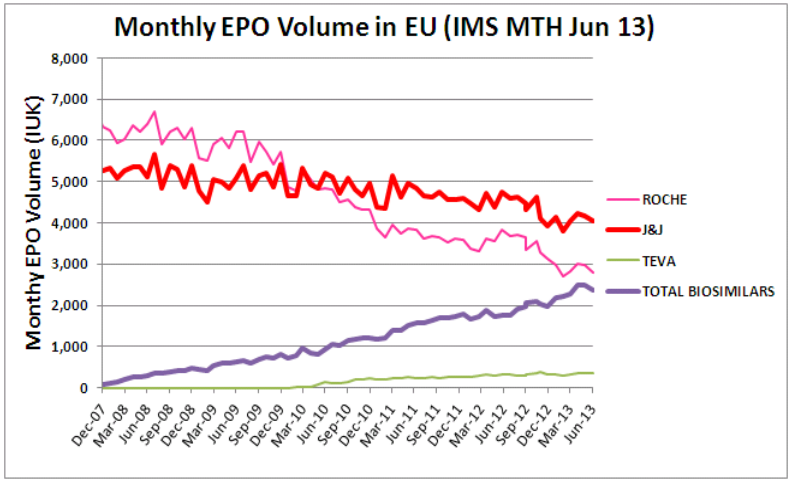
- The Romanian authorities have not approved any new INN categories for reimbursement since 2009.
- Retacrit (epoetin zeta) is still awaiting reimbursement Binocrit (epoetin alfa), which, like Retacrit, is a biosimilar to epoetin alfa, had obtained reimbursement.

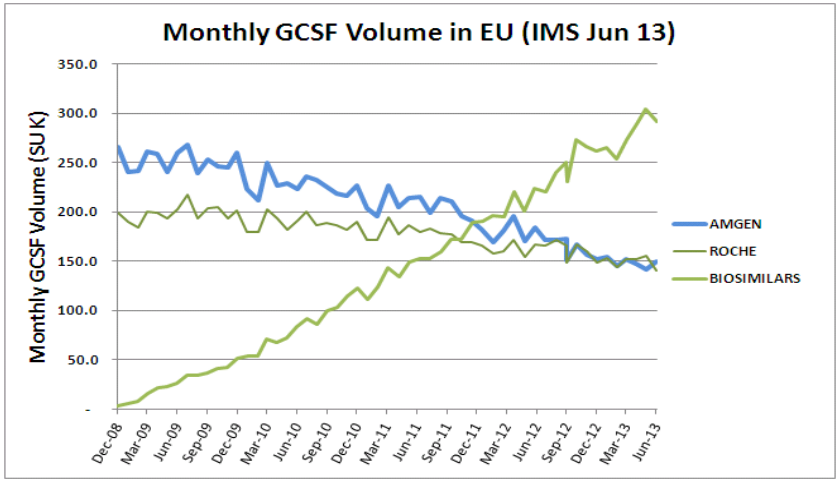
Italy

Spain

- In Italy and Spain, Retacrit (epoetin zeta) has been excluded from tendering in epoetin alfa batches. Lengthy and expensive legal challenges have helped to remove this restriction in most regions in Italy, but it has significantly delayed the uptake of Retacrit in that country. In Spain, despite legal challenges, Retacrit continues to be excluded from epoetin alfa batches in some regions. This is significantly delaying Retacrit uptake in Spain.
- In both Italy and Spain, uptake would have been much more significant if these obstacles were not present.

Trust in and cost savings of biosimilars continues to increase in Europe





Biosimilar EPO Uptake

- **25% of the short-acting EPO market**
- **37% of the epoetin alfa market**

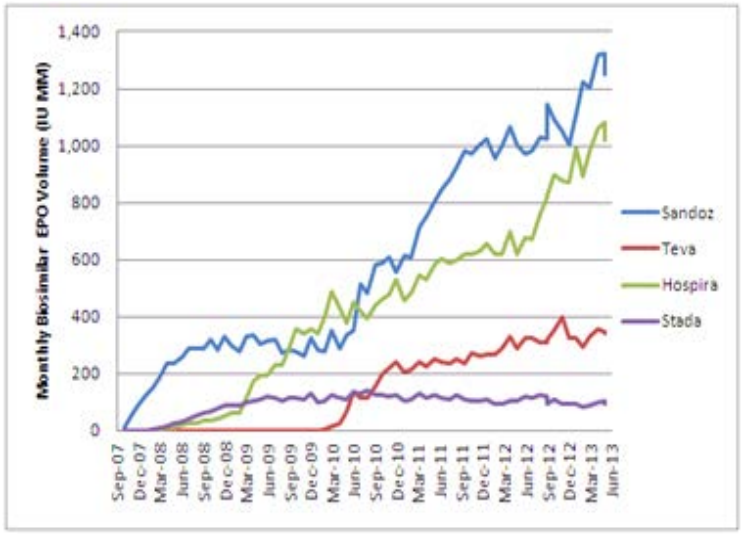
Biosimilar Daily GCSF Uptake:

- **50% of the daily GCSF market**
- **66% of the filgrastim market**

Each molecule uptake is different based on a number of clinical and competitive factors

Source: IMS Midas June 2013

There are three main biosimilars players in Europe



retacrit
epoetin zeta

Hospira's Retacrit™ is one of the largest brands of biosimilar EPO in the EU

nivestim
filgrastim

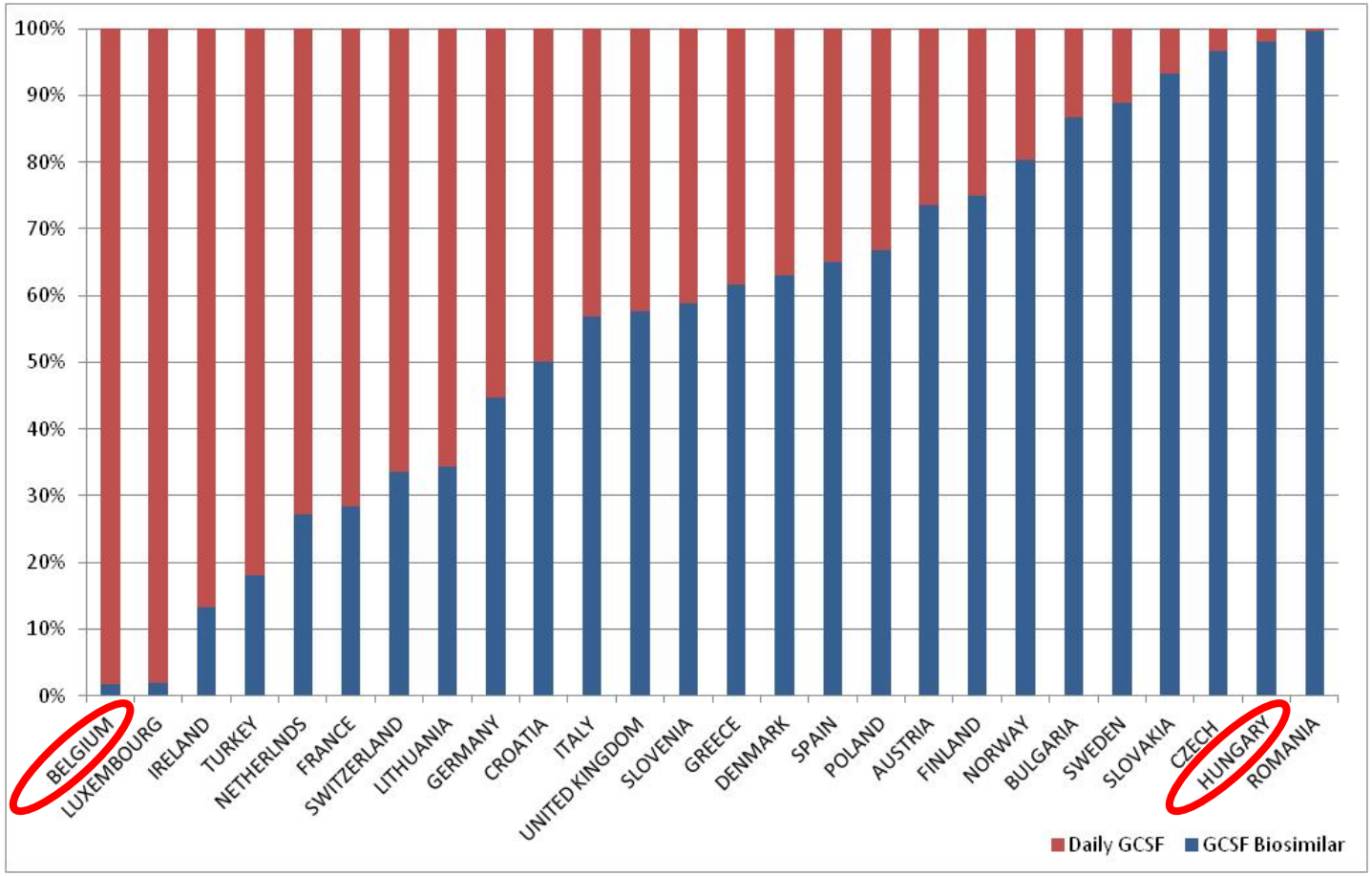
Hospira's Nivestim™ was the 3rd biosimilar GCSF to enter the EU and continues to grow

It is expected that, in addition to the originator biologic, there will be more entrants to biosimilars in the next few years

Source: IMS Midas June 2013

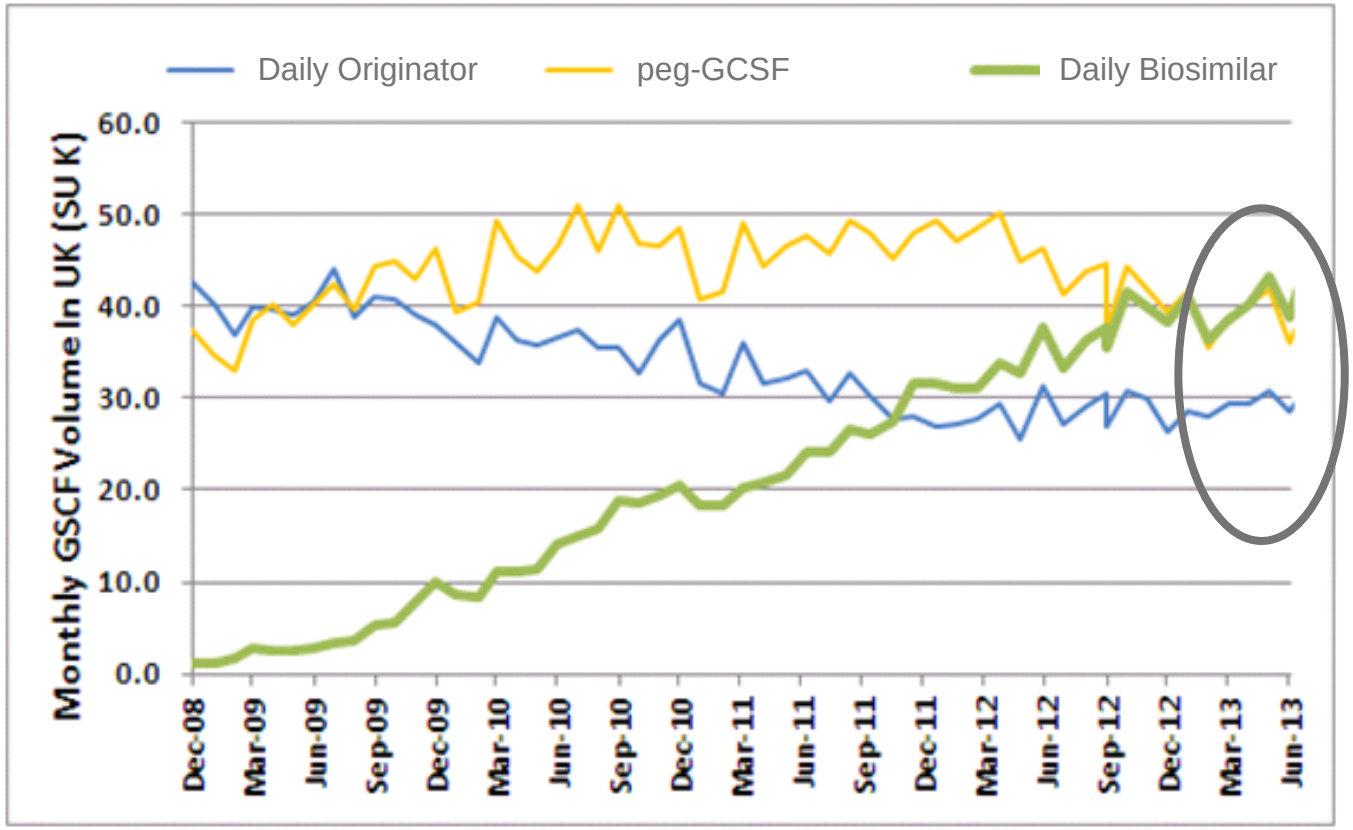
Regional and national policies will drive rate of adoption of biosimilars after approval

Volume uptake of GCSF biosimilars in standard units vs. daily GCSF available market products, %



Source: IMS Health, MIDAS, July 2013 MAT

In the UK, the entry of biosimilar GCSF has increased patient access

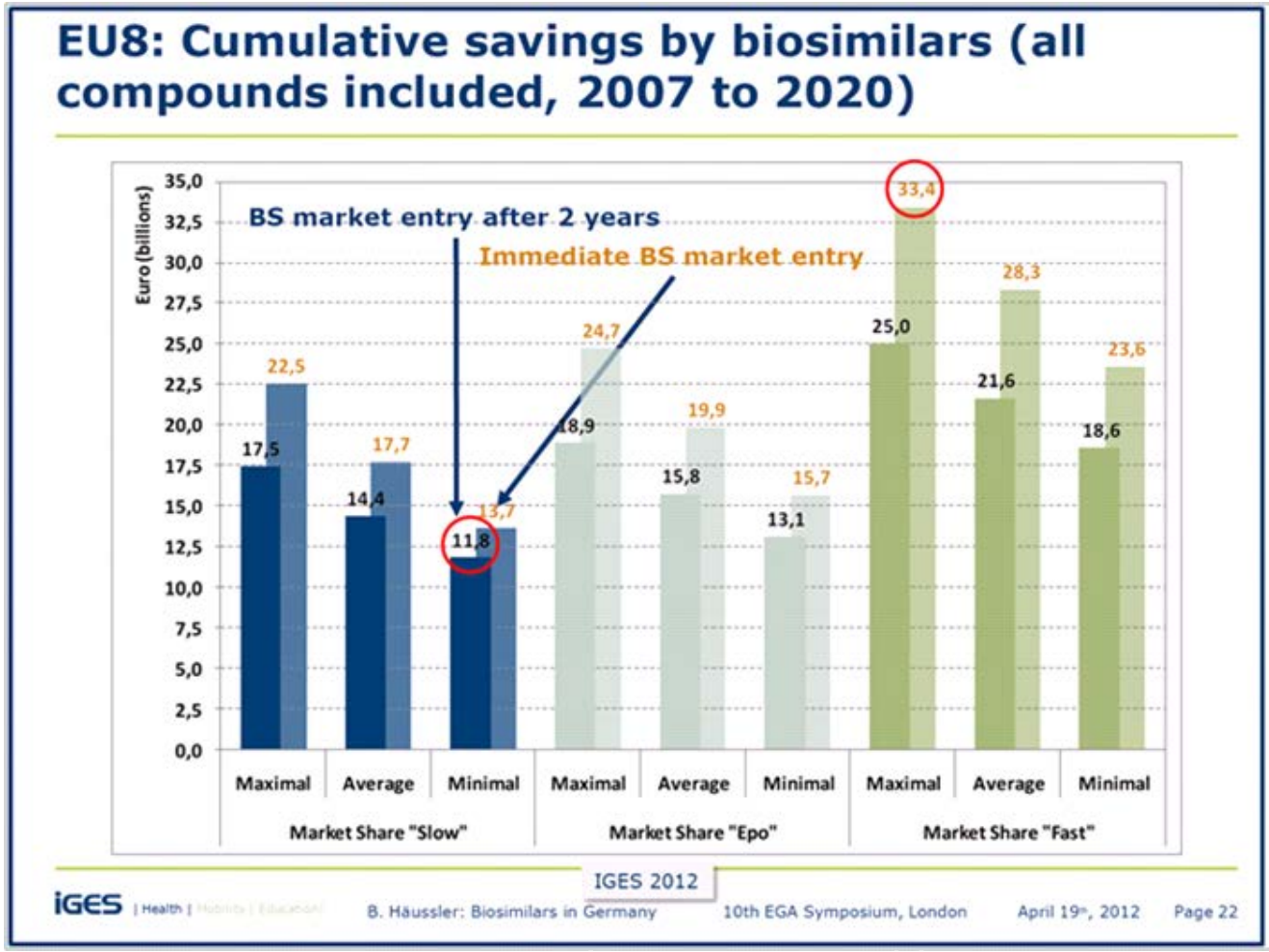


Data : IMS MIDAS to Jun 2013

*** 1 SU of once-per-cycle GCSF (peg-GCSF) is assumed to be equivalent to 11 SUs of daily GCSF (Neulasta SPC)**

Due to increased competition there has been a 50% increase in GCSF volume since biosimilar entry, thereby improving patient access

Biosimilars are producing significant cost savings



Source: EGA International Symposium London, April 19th, 2012 / Bertram Häussler IGES Institut, Berlin Germany

- EU8 = Germany, France, the UK, Italy, Spain, Sweden, Poland and Romania
- All compounds = Epoetin, Filgrastim, mAbs
- BS = biosimilar
- Market entry: immediate at IP expiry or 2 years later

Biosimilar Infliximab approval also expected to improve the benefit to cost equation

Infliximab approved by EMA for Psoriasis[1]:

- Remicade is indicated for treatment of **moderate to severe** plaque psoriasis in adult patients…

Yet, National Institute for Health and Care Excellence (NICE) Technology Assessement (TA134; issued January 2008)[2]:

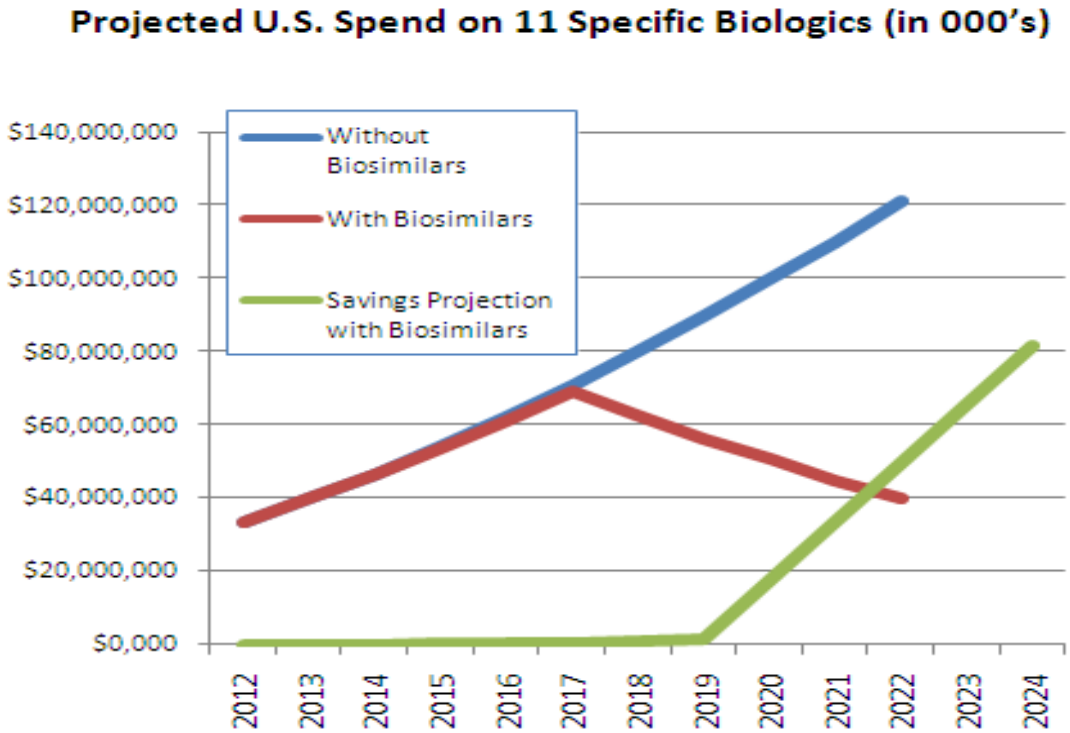
- Remicade is recommended as a possible treatment for adults with plaque psoriasis only if their condition is **very severe**

Biosimilar Infliximab (INFLECTRA™) Approved

NICE TA will need reassessment given reduced cost of biosimilars…thereby improving patient access

1. Remicade EPAR (http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000240/WC500050888.pdf);
2. NICE TA134 (http://guidance.nice.org.uk/TA134)

U.S. biosimilars savings projected at $250B in 10 years, thereby improving biosimilar access



Savings based on 11 existing biologics that are most likely candidates for biosimilars in the next 10 years in the US[1]

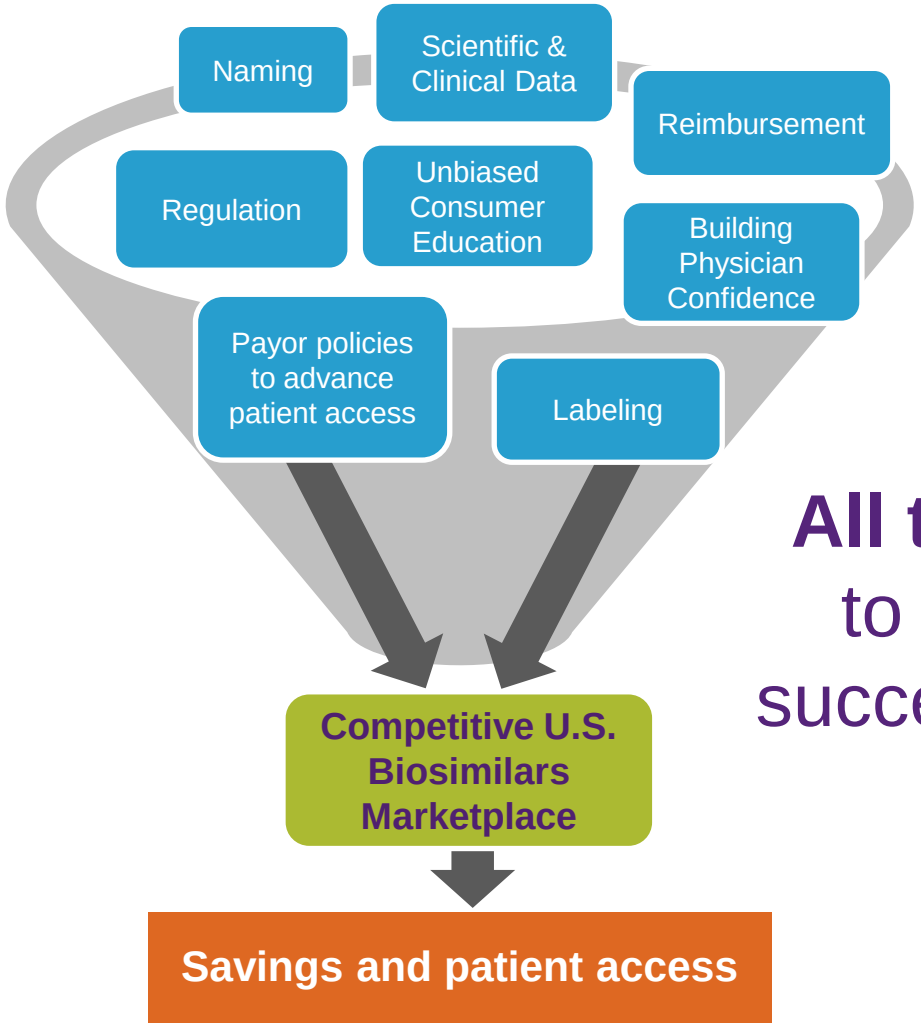
1. http://lab.express-scripts.com/speciality-medications/the-250-billion-potential-of-biosimilars/ Based on the report's analysis: The assumptions were based on conservative estimates of utilization, cost and consumer inflation. By the end of 2024, none of the drugs in this group will be patent protected, unless extensions are granted.. The report also indicated that the savings from a biosimilar pathway is likely to grow significantly greater when an additional set of major biologic drug patents expire between 2026 and 2028. Savings based on 11 existing biologics that are most likely candidates for biosimilars in the next 10 years in the US

Lessons from Europe will lead to U.S. market success

Hospira's key learnings:

- Biosimilar introduction improves patient access to key biologic medicines at more competitive prices
- A high scientific bar leads to trust and greater acceptance of biosimilars among payers and providers
- Shared INN names reduce the chance of healthcare provider confusion and facilitate patient access
- Providers who are educated on biosimilar safety and efficacy become comfortable prescribing biosimilars
- Biosimilar competition thrives in markets where government policies set fair and even playing fields
- Payor rules need to support strong and early market formation, and recognize the difference between biosimilars and small-molecule generics- not to incentivize for higher priced products and not to drive to extremely low prices
- To reduce cost of development and bring better access, extrapolation must be accepted
- Stakeholder information campaigns must provide unbiased biosimilars education

Successful biosimilar market formation requires positive results across a wide range of activities



All these factors need to come together for successful market launch