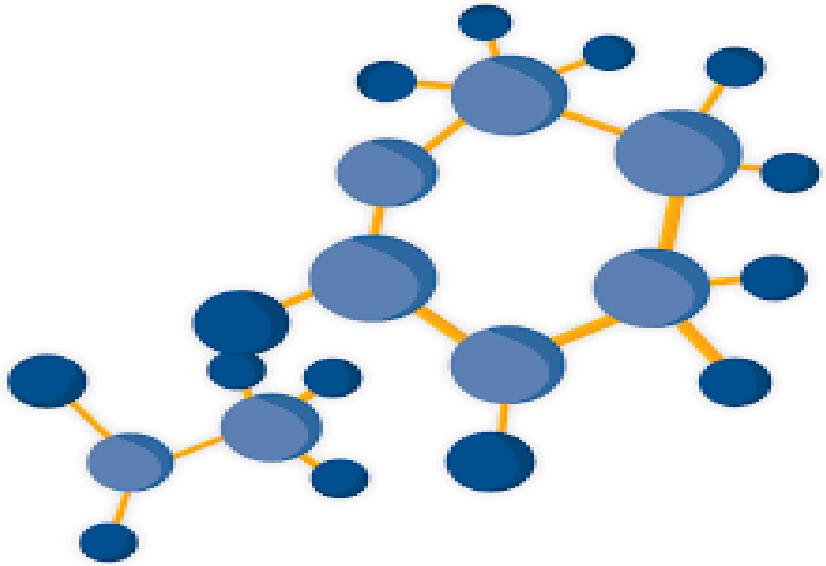
Biologics

A story of regulatory barriers



What are biologicals

BIOLOGICAL drugs (commonly referred to as ‘biologics’ or ‘biopharmaceuticals’) are drugs produced through biological processes. They currently target diseases which, hitherto, had very limited or no available treatment options – including several types of cancers, autoimmune diseases and other non-communicable diseases.

These drugs are different because they are produced in living cells. Biologics are larger in size and more complex than the ‘small molecule drugs’ (SMDs) manufactured using chemical synthesis processes. Biologics have several potential advantages as they can, theoretically, be tailored to hit specific ‘targets’ in the human body.

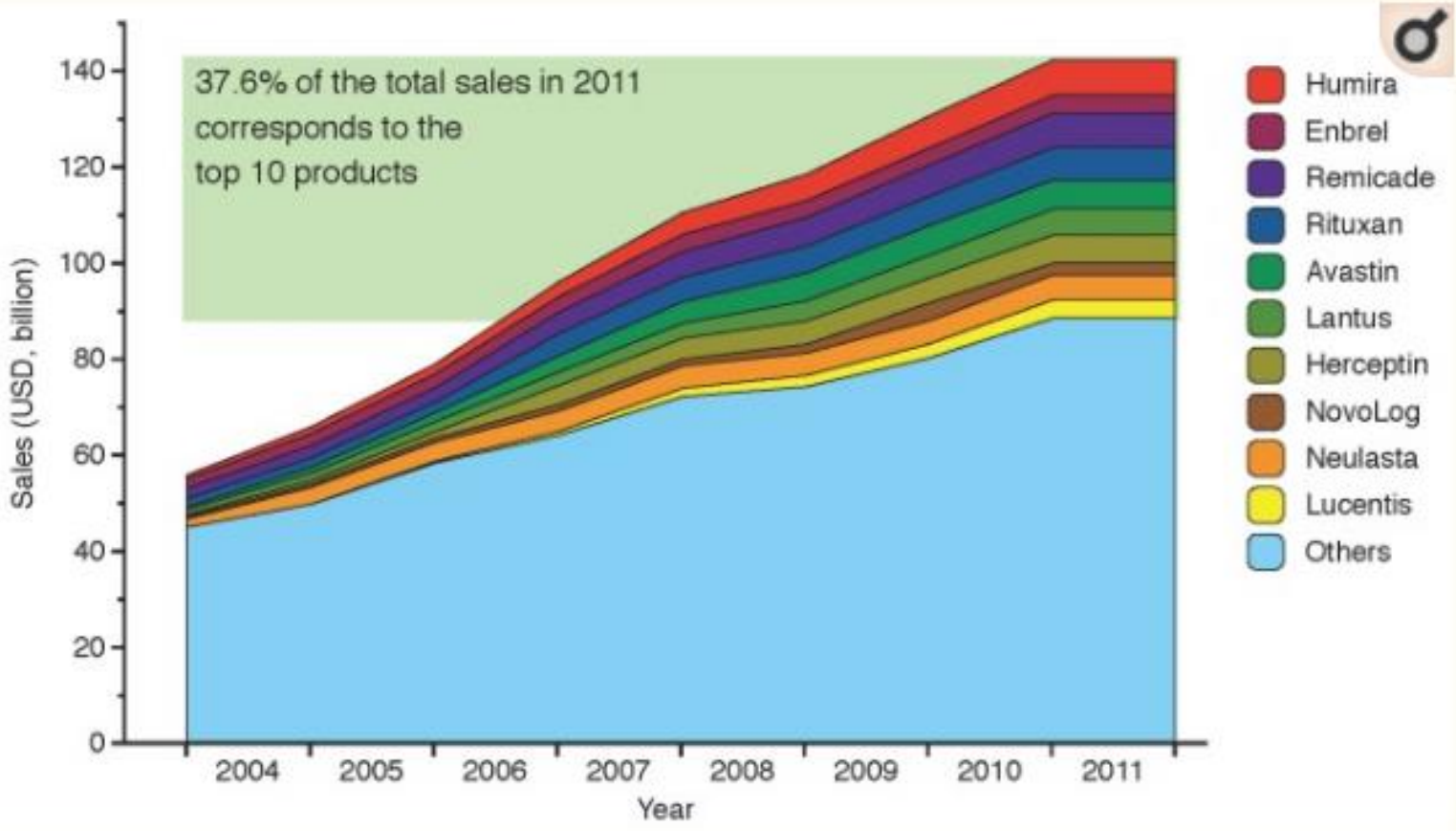
Major kinds of biopharmaceuticals include:

- Blood factors (Factor VIII and Factor IX)
- Thrombolytic agents (tissue plasminogen activator)
- Hormones (insulin, glucagon, growth hormone, gonadotrophins)
- Haematopoietic growth factors (Erythropoietin, colony stimulating factors)
- Interferons (Interferons-α, -β, -γ)
- Interleukin-based products (Interleukin-2)
- Vaccines (Hepatitis B surface antigen)
- Monoclonal antibodies (Various)
- Additional products (tumour necrosis factor, therapeutic enzyme

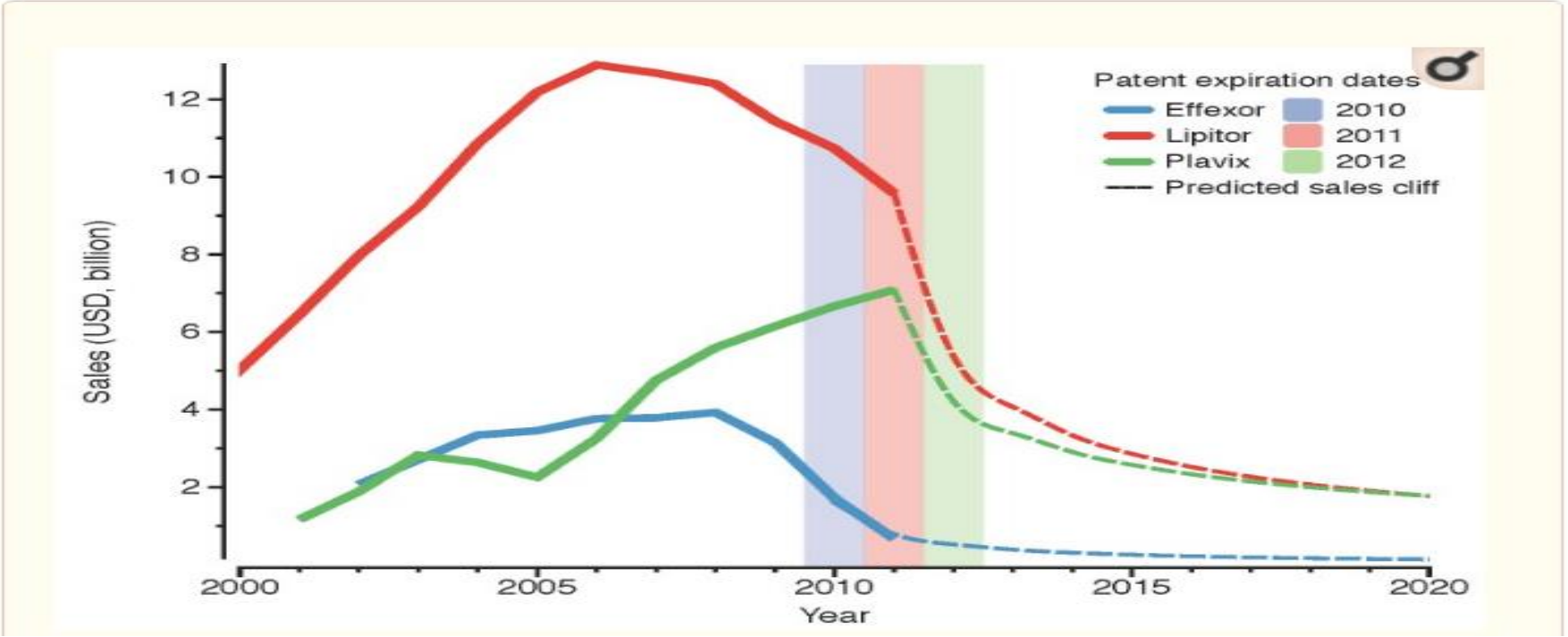
Table 1: Top 10 best-selling drugs in 2015 and the share of biologics[9]

Drug	Company	Ingredient	Indication	Biologic	2015 sales (million US$)
Humira	AbbVie	Adalimumab	Autoimmune disorders	YES	14,012
Harvoni	Gilead	Ledipasvir + sofosbuvir	Hepatitis C	NO	13,864
Rituxan	Roche	Rituximab	Non-Hodgkin's lymphoma	YES	7,327
Lantus	Sanofi	Insulin glargine	Diabetes	YES	7,088
Avastin	Roche	Bevacizumab	Various cancers	YES	6,951
Herceptin	Roche	Trastuzumab	Breast cancer	YES	6,799
Remicade	Johnson & Johnson	Infliximab	Autoimmune disorders	YES	6,561
Prevnar	Pfizer	*Streptococcus pneumoniae* vaccine	Vaccine	YES*	6,245
Januvia/ Janumet	Merck	Sitagliptin	Diabetes	NO	6,014
Revlimid	Celgene	Lenalidomide	Multiple myeloma	NO	5,801

* While vaccine manufacture is through a biological process, it doesn't involve recombinant technology (see below)


37.6% of the total sales in 2011
corresponds to the
top 10 products
Sales (USD, billion)
0
20
40
60
80
100
120
140
2004
2005
2006
2007
2008
2009
2010
2011
Year
Humira
Enbrel
Remicade
Rituxan
Avastin
Lantus
Herceptin
NovoLog
Neulasta
Lucentis
Others

Thankfully, their patents are ending

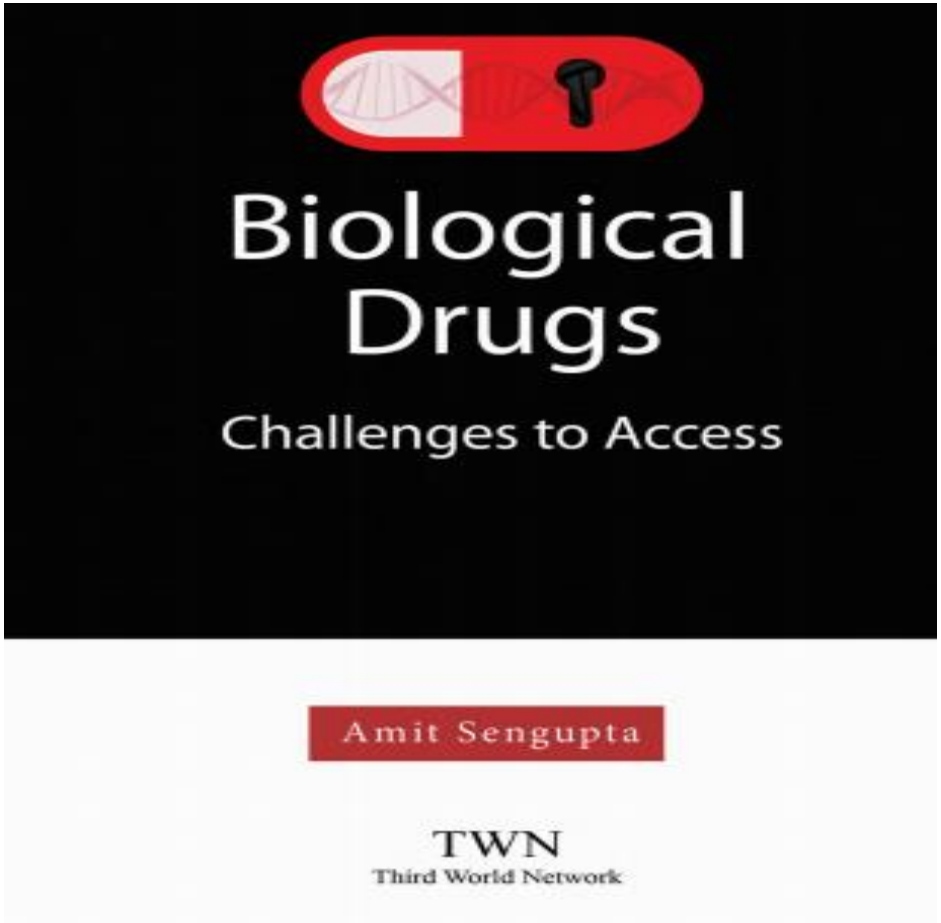


So, the Generics were to take over

- The generic version of the Biologicals have been called as Bio Similars or Similar Biotherapeutic Products.

- Expiration of numerous patents for blockbuster biologics between 2012 and 2019, the interest in biosimilar production, i.e., follow-on biologics, has increased.

- But the Similar Biological Products Guideline approach requires phase III clinical trials for the approval of SBPs. This is very costly as the generic manufacturer will spend a significant amount on the clinical trials and buying the branded biologicals for conducting the tests. This process makes the entry of Biosimilars very difficult and defeats the purpose of access to medicines.



- Many activists had been pointing out that the standards for Bio-similar are unreasonable and too high. And, simple tests such as PK/PD studies were enough.

- In the year 2014, WHO in its 67th World Health Assembly agreed to update of 2009 Guidelines on the Evaluation of Similar Biotherapeutic Products (SBPs).

Submission To The WHO Expert Committee on Biological Standardization for Updating of the 2009 Similar Biotherapeutic Products (SBP) Guidelines (October 2019)

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Demanding a revision of guidelines

We respectfully request the ECBS to start discussing and focus on the entire Part 10 of the 2009 SBPs Guideline, which deals with clinical evaluation of SBPs. We suggest that it be replaced with a language clearly explaining the circumstances that demand in-vitro surrogate efficacy analyses, further comparability analyses for demonstration of non-inferiority and the details of Phase I trial to address safety concerns with an inbuilt PK /PD study.

Thank you