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The long awaited draft 'biosimilar guidelines' of India, though a belated move by the Government, are certainly a step in the right direction

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The Indian biosimilar guidelines factor (in) the Indian context of affordability and accessibility

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A single-window procedure of obtaining marketing approval would have made the process similar to the developed world's approval framework

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The approach to developing and marketing biosimilars is very different and necessitates a new way of thinking

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(It) ... suggests a global biosimilar strategy for both Indian manufacturers and the big multinational players that begins in India

India joined a select but growing club of nations when Dr MK Bhan, Secretary of the Department of Biotechnology (DBT), Government of India, released the draft guidelines for manufacturing and marketing of biosimilar drugs in India this July.

Initially slated to come into effect from this Independence Day, August 15, the regulators postponed the implementation date to September 15, to give stakeholders more time to send their comments and suggestions on the draft guidelines to the DBT.

Will India be able to position itself as a manufacturing hub for biosimilars, in the same way that it has done with generic drugs? Clearly, small-molecule generics are losing their sheen. The wafer thin margins, thanks to low entry barriers, make it a high volume, low margin business. In contrast, the biosimilar opportunity promises to give better margins, even after patent expiry, as the cost and complexity of biosimilar development and manufacturing prevents the entry of too many players. Thus it is no wonder that the share of biologics in the global biopharma market is projected to rise to 28.9 per cent in 2015, from a base of 4.5 per cent in 1990. Similarly, the share of biosimilars among biologics is projected to rise from 0.1 per cent in 2009 to 6.4 per cent in 2017. *(See chart: Growth rate of biologics and biosimilars versus traditional drugs)*.

Remicade (i&i's infliximab) serves a good example of the biosimilar boom around the corner. Reportedly the top selling biologic and monoclonal branded antibody with $8.5 billion in sales in 2011, analysts predict that the brand could well turn out to be the top selling branded drug in 2012. It would be fair to say that many biosimilar manufacturers are waiting for Remicade to fall off the patent cliff in 2013.

And Remicade is not alone on this path. In fact, various reports predict that biologic patent expiries worth more than $40 billion are expected by 2016. *(See table: The allure of biologics: Patent expiries from 2012 - 2019)*

The allure of biologics: Patent expiries from 2012 - 2019

($billion)	Ingredient	Originator	Therapeutic indications	Global market size	Patent expiry (in the US)
Enbrel	Etanercept	Amgen	Rheumatoid arthritis treatment	6.6	2012
Epogen	Epoetin-alpha	Amgen	Anaemia treatment	5.0	2013
Remicade	Infliximab	i&i	Rheumatoid arthritis treatment	5.9	2013
Avonex	Interferon beta-1a	Biogen Idec	Multiple sclerosis	2.3	2013
Rebif	Interferon beta-1a	Serono	Multiple sclerosis	2.1	2013
Humalog	Insulin lispro	Eil Lily	Diabetes treatment	2.0	2013
Neupogen	Filgrastim	Amgen	Neutropenia	1.3	2013
Cerezyme	Imiglucerase	Genzyme	Gaucher disease	0.8	2013
Rituxan	Rituximab	Genentech	Non-Hodgkin's lymphoma, etc.	5.7	2015
Neulasta	Pegfilgrastim	Amgen	Stimulates white blood cell production	3.4	2015
Lantus	Insulin glargin	Sanofi-Aventis	Diabetes treatment	4.2	2015
Erbitux	Cetuximab	BMS/Merk	Colorectal cancer, etc.	1.6	2015
Humira	Adalimumab	Abbott & Eisai	Rheumatoid arthritis treatment	5.5	2016
Herceptin	Trastuzumab	Genentech	Breast cancer	4.9	2019
Avastin	Bevacizumab	Genentech	Colorectal cancer, etc.	5.8	2019
Lucentis	Ranibizumab	Novartis	Wet AMD	2.3	2019

Source: Quintiles, Hyundai Securities

WILLIAM LEE
Head of Regulatory Strategy
Quintiles Asia

The Indian guidelines make no mention of data exclusivity but that does not mean that there is no protection of intellectual property

Going by the (rule) book

With such a huge market opportunity opening up, it is no wonder that regulation for biosimilars across the world is keeping pace. *(See box: History of biosimilar guidelines)*

Upto now, the regulatory process for biosimilars in India was on a case by case basis, using an abbreviated version of the pathway followed for small molecule drugs, involving the Drug Controller General (India)'s office under the Central Drugs Standard Control Organization (CDSCO) and DBT. While the CDSCO evaluated the safety, efficacy and quality aspect, the DBT through the Review Committee on Genetic Manipulation (RCGM) was responsible for overseeing the development and preclinical evaluation of recombinant biologics.

This system, seen as an *ad hoc* approach, was fraught with flaws. Tapan Ray, Director General, Organisation of Pharmaceutical Producers of India (OPPI) says that there have been instances of so called 'biosimilar drugs' being approved for marketing, reportedly with sub-optimal testing and dossiers, thereby putting into question product quality, comparability and patient safety. Thus he is firmly of the opinion that the long awaited draft 'biosimilar guidelines' of India, demonstrating an overall similarity in the philosophy and approach with the those in the US and Europe, though a belated move by the Government, are certainly a step in the right direction.

The *ad hoc* process also meant inherent delays, points out Shoibal Mukherjee, Chief Medical Officer, Quintiles India & Head, Asia Medical Sciences Group. According to him, India's new draft guidelines have made the pathway much clearer which he believes will lead to a reduction in approval timelines, but he adds an important caveat: "provided the Government infrastructure is in place to support the requisite approval processes."

The *ad hoc* process may have had its flaws, but it got the job done: more than 20 biologics have been approved in India by this process. But now with more biologics going off patent, the Indian regulators clearly felt the need for a more formalised approach, in line with global norms.

Priyank Gupta and Aditi Gehlot, patent attorneys, Legasis Services point out that most of these biologics and the process to make them, were invented between 1990-2005 and were never patented in India. They opine that the draft guidelines thus open prospects to bring more biosimilar brands in the market at perhaps the lowest costs on this planet.

Similar but not same

Going by initial reactions to India's biosimilar guidelines, they seem to be along expected lines, given that industry representatives were part of the Task Force which drafted the guidelines.

KV Subramaniam, President and CEO, Reliance Life Sciences, one of the representatives from industry on this task force, believes that the Indian biosimilar guidelines factor (in) the "Indian context of affordability and accessibility". While ensuring product safety, quality and efficacy, he points out that "extremely onerous clinical trials are obviated, thereby enabling biosimilars to be launched in a faster time frame at competitive costs in relation to other country context."

Dr Ajay Kumar Sharma, Practice Head - Pharma, Healthcare Practice, Frost & Sullivan, South Asia & Middle East too opines that while they seem to be based on current global guidances like that of the European Union, they are tailored to the needs of the local Indian market and the players in the Indian market.

Attempting to read the Indian regulator's philosophy, William Lee, Head of Regulatory Strategy, Quintiles Asia opines that it is very clear that the Government is creating a level playing field for Indian biosimilar players to compete globally. These draft guidelines "define an approach and provide a framework" for the development of biosimilars. Once implemented, he believes they will evolve further with feedback from the industry. The guidelines already seem to be evolving.