The Latin American biosimilar landscape

Cost containment and safety concerns mean an ongoing tussle between payors and regulators, with the latter gaining the upper hand

Latin America as a region is experiencing an unprecedented period of economic growth and development which is having a direct impact on healthcare in two ways. Firstly, it has allowed the substantial growth of a middle class now capable of accessing private healthcare services. Secondly, as the majority of governments benefit from deeper pockets, people are demanding greater access to healthcare products and services. This is having an effect and governments' healthcare spending is generally increasing. Expenditure in the region more than doubled in the last 10 years, reaching over $350bn in 2012, according to the WHO.

But with cost containment now prioritised in every payor's agenda, pharmaceutical expenditure presents the least politically sensitive target for savings - with biologics at particular risk, accounting for a small portion of prescriptions yet a very high proportion of expenditure. For instance, in Brazil, biotherapeutics account for less than 3 per cent of prescription, but for over 40 per cent of the government's drug budget. Coupled with the impending patent expiry of several branded biologics this makes the biosimilar landscape a very attractive one.

Biosimilars cannot provide comparative saving to generics, mainly due to much higher development, regulatory, manufacturing and promotional costs, but they are priced on average 35 per cent lower than their originators - surely enough for payors, often governments, to ease their entrance onto the market.

To expedite biosimilar market entry, payors want regulators to accelerate the registration process, but there are only a handful of clear pathways in place due to safety and efficacy concerns. The pressure exerted to date has so far achieved heterogeneous outcomes, highlighting the variability within the different Latin American regulatory landscapes and markets. As momentum builds in favor of stricter regulation, the quality of biosimilar clinical evidence will make or break the opportunity in the region.

Gravitating towards an increased quality bar

With an increased expectation of pharmaceutical product safety and efficacy standards, the Latin American regulatory agencies have evolved significantly in the last decade. However, due to the poorly defined regulatory pathways for biosimilars, few companies have managed to gain marketing approval in some markets, and not without residual concerns of the quality and safety of their products from the medical community.

In recent years, several of these authorities, particularly those in the most potentially lucrative markets, such as ANVISA in Brazil, COFEPRIS in Mexico or ANMAT in Argentina, have developed their own biosimilar regulatory abbreviated pathways, by merging WHO and EMA guidelines for biosimilars with their own political, economic and historic context.

Aside from these trailblazers of biosimilar regulation, Latin America remains a heterogeneous reality and one in which most countries are still in the process of establishing their own regulatory pathways. Countries like Colombia, although it is on the cusp of publishing its guidelines, Venezuela, Peru or Ecuador have yet to reach a similar development status, while some smaller countries have yet to start making a first step in this process.

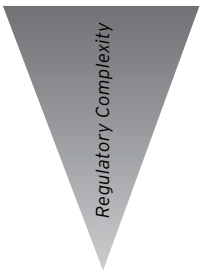
Openness towards biosimilars

The regulatory landscape is not the only difference across different Latin American countries. An example of the complexities and peculiarities of the Latin American markets is the spectrum of openness there is to allowing access to biosimilars and the frameworks developed to allow this to happen.

In Mexico, despite the institution of a biosimilar registration pathway by the regulatory agency, some signals also suggest that a regulatory environment which makes space for loosening the safety and efficacy requirements barriers to entry, in order to ensure broader access, may also be possible in this country. The regional biologics director of a multinational company in Mexico said: "There are political and economic pressures to ease up the regulatory approval process ... clearly the aim is to allow a wider less costly access to key treatments ..."

An example of this is the early access by Probiomed with their rituximab biosimilar Kikuzubam, which came just before this regulation was in place. By contrast, successful entry and establishment of biosimilars in the Argentine market is more heavily influenced by trade-related complexities. A foreign biosimilar manufacturer with an affiliate based in Argentina must export a proportional amount to make up for the importation of biosimilars into that market – i.e. the trade balance cannot be in favour of imports, thus creating a more favourable environment for local players.

Regulatory Landscape



Big Markets *(Brazil Mexico, Argentina)*	• Leaders in biosimilar regulatory pathways • However, strong supporters of the development of local champions
Medium Markets *(Columbia, Venezuela, Chile)*	• Cautious regulatory agencies • Early entrants have failed to enter
Smaller Markets *(Peru, Paraguay, Pueta Rico)*	• More flexible regulatory agency looking for quick savings • Easiest target for early entrants with limited clinical evidence

The LatAm biosimilar players

Despite the shifting hurdles in gaining market approval described, the LatAm biologics market presents a potentially substantial opportunity for those biosimilar players that are able to develop a lean, effective strategy in the coming years. This is evident in the level of interest shown by global, regional and local players that are already responding to this opportunity, yielding an increasingly crowded pipeline of biosimilar monoclonal antibodies (mAbs).

Large multinationals like Sandoz, Pfizer and MSD, are stepping into the LatAm biosimilar landscape by deploying robust clinical development programmes. Equipped with financial capabilities and a deep technical and commercial expertise, these companies are conducting multiple clinical trials across all phases of development globally in countries like Brazil, Mexico, Argentina, Colombia, Chile and Peru.

Closely followed in commitment, but not necessarily in experience, Latin America is witnessing the entrance of international biosimilar players possessing a diverse range of clinical evidence propositions. While there are companies like Dr. Reddy's or Shanghai CP Goujian whose biosimilar products (Reditux and Etanar) have already been approved with limited supportive clinical data in poorly regulated markets, there are also companies like Celltrion whose clinical development programmes are already well advanced in the region and abroad.

Most importantly, local biosimilar developers and/or manufacturers are also pursuing a stake in the market and in some cases are supported to become "local champions" in their respective countries, as is the case of Probiomed in Mexico, Bionovis and Orygen in Brazil, and Grupo Insud in Argentina. These companies have a clear regional commercial target and follow hetereogeneous clinical development strategies of varying degrees of clinical robustness to pursue this objective. Smaller local players are also expected to leverage their national market expertise to enter into commercial partnership agreements with foreign biosimilar manufacturers.

Despite this increasingly crowded competitive landscape, it isn't all necessarily bad news for the established branded players. Increasingly stringent regulations are delaying entry to these markets. For example, as of February 2013 there were only three second-generation protein therapeutics approved in the major Latin American markets. In terms of speed to market, local biosimilar players will most likely gain first mover advantage in their domestic markets. Their clinical development is aimed at navigating regional standards which may provide a moderate advantage when contrasted with big pharma's global pathway. Additionally, they will have the urge to capitalise on their early entry momentum to compensate for levels of investment of development they are only now experiencing. Early followers are likely to be the Asian biosimilar companies and last in the market big pharma, undoubtedly armed with the strongest dossiers.

What does the future look like?

It is very likely we will continue to see partnering activities both on a global and local level as companies try to leverage their existing competencies and capabilities to achieve market entry and commercial success. Core areas of interest for partnerships are: clinical trials and regulatory processes, market access, efficient biologic manufacturing and sales and marketing. For instance, the advent of the announced partnerships between Dr. Reddy's and Merck Serono, and between Samsung Bioepis and MSD may point to a potential new business model in which established big pharma offer their clinical development expertise to biosimilar developers who offer their better knowledge of the emerging markets. Similarly, the existent relationships between Celltrion and OliMed, and Shanghai CP Goujian and LaFrancol or EMS suggest a trend in the establishment of symbiotic relationships between Latin American companies in need of biosimilar products developed abroad and foreign companies in the need of local expertise.

Biosimilars are on the verge of creating a new type market with its own dynamics and complexities. Innovator biopharmaceutical companies are very active in developing strategies to shape, where possible, but in most cases to adapt to, the upcoming landscape. Many have decided to enter in this market, others are trying to develop brand and pricing strategies to directly compete with biosimilars, other will focus on developing 'biobetters' and probably most will pursue a combination of these.

Different developing scenarios call for different tactical responses; a detailed understanding of the market is fundamental to monitor and interpret market events as they unfold, especially in light of such a fast moving, dynamic and still unknown landscape.

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Biosimilar mAbs in Latin America

For a combrehensive list of the current state of development and marketing of biosimliar monoclonal antibodies (mAbs) in Latin America visit **pmlive.com/intelligence**