Generics and biogenerics in Brazil

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As technology evolves to meet the challenges facing humanity, one constant is the fight against diseases affecting large parts of society. The development of new technologies for health products and medicines is thus a key priority.

Today, with quality of life an increasingly hot topic, drugs aimed at preventing diseases and increasing longevity are regarded as the best discoveries of a generation. Among such technologies gaining prominence on the global marketplace are biopharmaceuticals: drugs that use live organisms instead of a chemical substance as their active base, produced through genetic engineering and DNA recombination techniques.

Biotechnology, as defined by the Convention of Biological Diversity, means any technological application that uses biological systems, living organisms or derivatives thereof to make or modify products or processes for specific use. In Brazil, biotechnology is ruled by Law 11.105, dated 24th March 2005. This law defines genetic engineering as the manipulation of DNA/RNA recombinant molecules.

Although there is no specific regulation of biopharmaceuticals resulting from genetic engineering techniques, all such products must be approved by the National Biosafety Technical Commission (*Comissão Técnica Nacional de Biossegurança*, which provides technical support to the federal government to establish safety technical norms for the authorisation of research activities and the commercial use of genetically modified organisms and their by-products), based on zoo-phytosanitary, health and environmental considerations.

Biopharmaceuticals are usually proven to be more efficient than traditional medicines and usually present no side effects in clinical tests. However, the costs of biopharmaceuticals are high, since the relevant industries invest at least 15% of their sales budget in research and development (R&D) for new medicines. They must therefore rely on special protection to ensure them a safe return on these high-risk activities – such as compensation through the patent system.

A patent is granted by the government and allows its owner to commercially exploit a given technology on an exclusive basis for a limited period. Accordingly, the patent system works as a protection instrument which contributes to scientific research.

Up until the 1990s, several countries did not recognise patent protection for pharmaceutical products and consequently allowed local companies to copy patented drug products. However, in response to pressure from developed countries, by the late 1990s most of these countries, including Brazil, had joined the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs), an international treaty which established minimum grounds of protection for intellectual property.

In the wake of signing up to TRIPs, Brazil approved a new Industrial Property Law in 1996 which governs the rights and obligations relating to industrial property. The new law had a significant impact on the pharmaceutical industry: patents for new medicines were recognised and copies of products protected by valid patents were prohibited. From that point on, generic medicines were restricted to copies of unpatented products, most of them with an extinguished patent protection term.

A patent in Brazil is usually valid for 20 years, starting from the date of filing at the governmental agency responsible for its approval. The administrative procedure for a pharmaceutical patent application generally begins in the first stages of the pre-clinical tests and continues for many years during

clinical tests until final approval and registration. In fact, when pharmaceutical companies consider patenting any substance, they are usually in the first stages of their research and the lengthy duration of proceedings thus reduces the drug protection term while the product is on the market, leading to further competition with generic products.

As defined by Brazilian law, generic medicines are products commercialised without trademarks and identical to the patent-protected medicines known in the sector as "brand products" or "*medicamentos de referência*" ("reference medicines"). As they are absolutely identical in composition and formulae, generic products and brand products are interchangeable. The precondition for being officially considered interchangeable is the compulsory performance of generic products in bioequivalence tests conducted by official entities certified by the federal agency responsible for sanitary vigilance.

In Brazil, the health policies of recent administrations have focused on the free distribution of pharmaceutical products to the poorer classes of the population. As part of this policy, the Brazilian government has negotiated with leading pharmaceutical companies on cost reductions for certain drugs. As a result of this strategy, access to these drugs has been widened and the Brazilian government has been able to acquire new drugs and distribute them to the population. The Brazilian government has also created the "people's pharmacy" ("*farmácia do povo*"), comprised of drugstores that must sell certain specified drugs at pre-determined prices. Hypertension and diabetes medicines are among the most popular of these drugs.

Further, Brazilian health surveillance was greatly expanded in 1999 with the creation of the National Agency for Sanitary Surveillance (ANVISA) and the establishment of a National System for Health Surveillance. Since then, ANVISA has assumed the duties of the former Secretariat of Sanitary Compliance and is now in charge of monitoring and inspecting companies and products considered to be of interest to public health.

This notwithstanding, the enactment of regulations on generic pharmaceuticals in 1999 is still considered one of the most relevant initiatives of the Brazilian government within the health sector.

Today, generic medicines are widely used throughout the Brazilian population and are increasingly prescribed by physicians. However, the barriers preventing biogenerics (also known as biosimilars or follow-on protein products) from entering the market are much higher than for small molecule generics, as companies face higher development costs due to clinical testing requirements, longer development times and uncertainties over the approval of patent procedures.

As a consequence, biogeneric companies need to work harder than typical generic companies. Specific skills are required in biotechnology, manufacturing, clinical trials, regulatory compliance, pharmacovigilance testing and marketing. Moreover, one of the most pressing issues regarding biogenerics is the proof of essential similarity and how to demonstrate equivalence. Arguments between the branded and generic industries have focused on the question of equivalence: if a protein cannot be absolutely characterised, can it be regarded as equivalent to the originator's product and approved without full clinical trials?

In Brazil, this issue also centres on the legislation that may be applicable to such drugs.

The Brazilian Industrial Property Law establishes restrictions for the protection of living beings by establishing that the following are not patentable: "all or part of natural living beings and biological materials found in nature, or isolated therefrom, including the genome or germ plasma of any natural living being and the natural biological processes."

Several bills on generic drugs are currently before the National Congress. One sets out the National Policy of Research and Technological Development for the Pharmaceutical Sector (*Política Nacional de Pesquisa e Desenvolvimento Tecnológico do Setor Farmacêutico*), which pays special attention to generic drugs. The other bills propose to regulate the following:

- The promotion of generic drugs already on the market.
- The mandatory prescription of generic drugs.
- The compulsory distribution and commercialisation of generic drugs.

The National Policy aims to promote the research, technological development and production of pharmaceutical semi-products, in order to boost the industry's innovation capacity for the benefit and wellbeing of Brazilian society.

As regards the generic drugs sector, the National Policy specifies as one of its objectives the pursuit of technological solutions and the production of strategic raw materials and drugs, even potentially through

the compulsory licence of patents. The National Policy also plans to foster the R&D of generic and other alternative drugs, resulting in either technological improvements or reduced costs, and to enhance the quality and security of the registration of generic drugs.

Under the National Policy, the effects of legal patent protection in Brazil will also be monitored, with special attention paid to the progress of R&D investments and access to drugs used for the treatment and prevention of prevalent diseases.

This bill is still awaiting analysis by both the House of Representatives and the Federal Senate. Its approval may have a significant impact on the production and commercialisation of drugs in Brazil, with specific implications for the patent protection of brand drugs deemed important to public health programmes. To this end, the proposed legislation would compel pharmaceutical companies to provide information about the existence of generic drugs alongside their advertisements for brand products. Another proposal would oblige drugstores to display a sign listing all generic drugs available.

The National Congress is also considering whether physicians, clinics and hospitals should adopt in their prescriptions the Brazilian Common Denomination of Drugs (*Denominação Comum de Medicamentos Brasileira*), used to identify generic drugs. Exceptionally, the prescription of brand drugs would be accepted, but only where the Common Denomination was indicated alongside the brand.

A bill including this proposal has already been approved by the House of Representatives and is under analysis before the Senate. If approved, it will force pharmaceutical companies to review their marketing strategies, which currently focus on physicians, clinics and hospitals, as in future consumers will be able to compare and choose from among different brands and generic drugs.

In order to ensure access to generic drugs available in Brazil, several bills would require drugstores to list in their inventories the generic drugs included in the National List of Essential Drugs (*Relação Nacional de Medicamentos Essenciais*). Furthermore, distributors of drugs within the national territory would be required to supply drugstores with these drugs.

If approved, these measures may help to boost the consumption of generic drugs, thus significantly increasing their market share in Brazil.

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