

# *Life Sciences* 2020

*Key issues for senior  
life sciences executives*

**Biologics and biosimilars in Brazil – the strategic questions**

Kasznar Leonardos

Anderson Ribeiro, Priscila Kashiwabara and Aline Ferreira



## KASZNAR LEONARDOS: THE BEST STRATEGY FOR MANAGING INTELLECTUAL PROPERTY RIGHTS AND REGULATORY MATTERS IN BRAZIL

Our team balances its renowned IP practice with a multidisciplinary approach to deal with regulatory and transactional issues linked to life sciences industries, such as biodiversity, biotechnology, pharmaceutical, foods, cosmetics, household products, pesticides and medical devices.

We manage all aspects of the IP life cycle, help clients through each step of entering the Brazilian market and handle an array of commercial issues.

If your brand, patent or product is present or heading to Brazil, count on Kasznar Leonardos.

---

**[www.kasznarleonardos.com](http://www.kasznarleonardos.com)**

Rio de Janeiro +55 21 2113.1919 - [mail@kasznarleonardos.com](mailto:mail@kasznarleonardos.com)

São Paulo +55 11 2122.6600 - [mailsp@kasznarleonardos.com](mailto:mailsp@kasznarleonardos.com)

**Kasznar** 1919  
**Leonardos**

# Biologics and biosimilars in Brazil – the strategic questions

By Anderson Ribeiro, Priscila Kashiwabara and Aline Ferreira

---

Biologics are typically very large, complex molecules produced by genetically modified living systems (eg, bacteria, yeast, animal and plant cells) through biotechnological processes. Different from small molecule drugs, biologics are not well-defined structures and are extremely difficult to definitively characterise. Biosimilars are products that are highly similar to a previously approved biological product (ie, reference product), notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences in terms of safety, purity and potency. Due to their inherent structural complexity and intrinsic heterogeneity due to post-translational modifications, biosimilars are subject to specific regulations.

Biosimilars are expected to have a significant impact on the pharmaceutical market, due to the loss of patent exclusivity of several biological pharmaceuticals in upcoming years. They are expected to lower prices in their product category and occupy a relevant part of the market share.

To date, the majority of biosimilars in Brazil have monoclonal antibodies as reference products. Monoclonal antibodies comprise a significant part of the worldwide biopharmaceutical market. It is vital to review and comprehend the Brazilian definitions and regulations in this field, as the Brazilian pharmaceutical market promises a bright future for this drug category, particularly considering the epidemiological transition of Brazil's population from infectious diseases to chronic conditions and age-related illnesses.

This chapter highlights the strategic questions surrounding patent prosecution, patent litigation

and the regulation of biologics and biosimilars on the Brazilian market.

## Patent prosecution

Brazil has some particular practices that should be brought to the attention of companies interested in exploring the Brazilian market.

First, regarding patentability, there is no definition of 'invention' in Brazilian legislation. In order to qualify as a patentable invention, the subject matter must meet the patentability requirements and cannot be included in the statutory bars provided in the law.

For biologics specifically, certain patentability bars should be kept in mind.

According to Article 10, IX of Law 9,279/96, natural living beings, in whole or in part, and biological material, including the genome or germplasm of any natural living being, when found in nature or isolated therefrom, and natural biological processes are not considered as inventions. This provision is known as the 'product of nature bar'.

The exclusion of biological material isolated or purified from nature is one of the most controversial and debated provisions of Brazilian Law 9,279/96. The isolation and purification processes are allegedly insufficient for the product to be considered new and different from the one existing in nature. In addition, biological material produced by means of a technical process is not eligible for patent protection in case it has a natural equivalent and from which it cannot be distinguished.

Even in those cases where a particular portion of a larger naturally occurring sequence cannot



be found in nature, patent protection for the smaller fragment is not granted. In fact, only those sequences that do not exist in nature may be patented, provided that they meet the patentability requirements.

In view of this, the Brazilian Patent and Trademark Office (BPTO) analyses antibodies as proteins which are not entitled to patent protection if the polypeptide sequence is found in nature or isolated therefrom. In line with this understanding, polyclonal antibodies are excluded from patentability. However, monoclonal antibodies, obtained from hybridoma or genetic engineering techniques are eligible for patent protection. The antibody must be defined through the deposit of biological material or by its specific sequence.

Monoclonal antibodies obtained by genetic engineering techniques (eg, chimeric, humanised and fully human antibodies) must be characterised by the sequence of the variable portion of the antibody and, when applicable, the definition of other elements as the fragment crystallisable portion. It is also possible to specifically define the complementary determinant regions (CDR) of both heavy and light chains. Modifications in antibody fragments, such as in the case of single chain variable fragments, may also be the subject of patent protection.

There have been rapid and significant developments in the biotechnology field, specifically antibodies, meaning that it is difficult for patent offices to follow and update their biotechnology guidelines quickly. In 2019 the BPTO launched a public consultation on the biotechnology guidelines, which is still under discussion. It is a great time to discuss the guidelines regarding the protection of antibodies, which are so restrictive in Brazil, since the protection of an antibody by the deposit of biological material, by its variable sequences or by the CDRs, is often unfair in view of the in-depth analyses and insights concerning the mechanisms of interaction between the claimed antibody and its target.

Besides the facts around the patentability bars, it is of utmost importance to be aware of the practice concerning voluntary amendments, in that the applicant can amend the set of claims up to the filing of the examination request. However, once the examination has been requested, the applicant can only introduce restrictive amendments. In addition to the new independent claims, change and enlargement of the claim scope in relation

to the set of claims for which examination was requested are promptly rejected.

For those companies interested in entering the Brazilian biosimilar market, it is vital to conduct a thoughtful and conscientious due diligence process beforehand. The BPTO has been struggling with a huge patent backlog, which has resulted in patents remaining valid in Brazil when they have already expired in other countries. If a relevant patent or patent application is unveiled, it is advisable to present post-grant (nullity request) or pre-grant third-party observation (known as ‘subsides’), respectively, grounded on a careful patentability assessment (for pending applications) or validity evaluation (for granted patents), in view of Brazil’s unique patent



### **Anderson Ribeiro**

**Partner**

**[anderson.ribeiro@kasznarleonardos.com](mailto:anderson.ribeiro@kasznarleonardos.com)**

Anderson Ribeiro is a partner at Kasznar Leonardos. He heads the team for transactional and regulatory matters affecting the life sciences industries and provides advice on strategic IP issues. Mr Ribeiro is experienced in dealing with leading cases discussing patents and strategies for sensitive sectors of the pharmaceutical industry, including rare diseases and government sales. His wide expertise embraces multifaceted challenges involving clinical trials, compliance, pharmacovigilance, economic regulation, technology transfer (relating to the Productive Development Policy), health technology appraisals and government procurements.

Mr Ribeiro has an LLM in competition law and regulation from the University of Lisbon and an LLM in intellectual property from Queen Mary, University of London.

practices. Moreover, a granted patent may be challenged both before the BPTO within a six-month term counted from the grant decision, or before the Brazilian Federal Courts at any time during the life of the patent.

It is also important to assess whether it would be cost-effective to license the patent instead of engaging in a patent infringement dispute, or whether it would be worth designing around a process or product that does not infringe the already granted patent.

### Patent litigation

Before addressing the particularities of biologics and biosimilar patent litigation, it is vital to highlight some aspects of litigation in Brazil:

- Proceedings are mostly conducted in written form and hearings happen infrequently.
- Preliminary injunctions are available and may be decided only a few days after the filing of the complaint.
- Nullity lawsuits are prosecuted before federal courts, while infringement and non-infringement lawsuits are prosecuted before state courts. This means that defendants of an infringement lawsuit may only seek the nullity of a patent by filing a new lawsuit before federal courts.
- Specialised courts are only available in Rio de Janeiro, São Paulo and Rio Grande do Sul. The judges have no technical background.
- There is a significant difference between



### Priscila Kashiwabara

Partner

[priscila.kashiwabara@kasznarleonardos.com](mailto:priscila.kashiwabara@kasznarleonardos.com)

Priscila Kashiwabara graduated in biology and has a master's in biotechnology from the University of São Paulo. She is a registered industrial property agent and works in the Kasznar Leonardos life sciences division, specialising in patents, biodiversity and plant varieties. Ms Kashiwabara is co-coordinator of the Plant Variety Study Committee at the Brazilian Association of Intellectual Property.



### Aline Ferreira

Partner

[aline.ferreira@kasznarleonardos.com](mailto:aline.ferreira@kasznarleonardos.com)

Aline Ferreira de Carvalho da Silva is an expert in litigation, legal counselling on patents, licence agreements, plant varieties and genetic resources. She is currently handling lawsuits concerning monoclonal antibodies and has advised companies on plant variety agreements.

She is a coordinator of the International Law of Intellectual Property Study Committee at the Brazilian Association of Intellectual Property.

Ms Ferreira de Carvalho da Silva graduated in law from the State University of Rio de Janeiro, has a master's in IP law from the University of Cambridge and was a postgraduate in IP law at the Pontifical Catholic University of Rio de Janeiro.

*“Where the court-appointed expert must be familiar with biochemistry of proteins and recombinant DNA techniques, it is important to highlight to the court that the court-appointed expert must have such skills in order to avoid the risk of having a neophyte in charge of conducting a key aspect of the litigation”*

---

the average time for a decision between the jurisdictions, meaning that the place where the lawsuit is filed should be considered carefully.

- Precedents are generally not binding, although there are a few situations where lower courts must follow case law from the Superior Court of Justice and the Supreme Court.
- Judges are generally uncomfortable with rendering decisions on the merits without the production of technical evidence. In line with Brazilian law, this is conducted by a court-appointed expert, who is chosen by the judge using a database of professionals registered within the court.

Although parties may agree to jointly appoint an expert, and may even hire private experts and produce their own opinions, the opinion delivered by the court-appointed expert is highly valued by the judges. This is because court-appointed experts are deemed to be neutral, since they offer their opinions after hearing both parties and having access to evidence.

In such a scenario, parties must correctly identify who is the person skilled in the art in order to enable the judge to appoint an expert who meets this qualification – otherwise, the judge may choose someone who is not particularly familiar with a technology that requires a specific skill, especially considering that degrees and CVs may be misleading to laypersons.

For example, although chemical engineers study bioprocesses while at university, it does not mean that they are necessarily familiar with the biotechnology used in the pharma industry. Likewise, pharmacists may have little knowledge on how to develop a monoclonal antibody because their career has focused on small molecules. Therefore, in a case where the court-appointed expert must be familiar with biochemistry of proteins and recombinant DNA techniques, it is important to highlight to the court that the court-

appointed expert must have such skills in order to avoid the risk of having a neophyte in charge of conducting a key aspect of the litigation.

In case the court appoints an expert that does not have the necessary skills to conduct the production of evidence, parties may lodge an appeal to have a new expert appointed.

Another relevant topic for parties to consider is the effect of the BPTO backlog. Since patentees only have title and may assert patents only once they are issued by the BPTO, parties may have their ability to prevent the entrance of newcomers hampered by the delay in having applications examined.

Article 44 of the Brazilian Industrial Property Act allows patentees to recoup damages since the publication date of the application once the patent is issued. However, since the issuance of the patent is required to be able file a lawsuit and newcomers drug prices tend to be lower than the price of the innovative drug, the patentee may lose a relevant share of the market in view of the inability to get an injunction to prevent the market entrance of a biosimilar.

A way to mitigate this is to send a cease and desist letter to the infringer, giving notice of the infringement and warning that measures will be taken as soon as the patent is issued. This cease and desist letter has three purposes:

- to inform the newcomers about potential patent rights;
- to allow the patentee to request fast-track examination before the BPTO; and
- to suspend the five-year statute of limitation for damages.

Biosimilars may also suffer as a consequence of the backlog, since biologic products generally have a broader patent portfolio than small-molecule drugs. For this reason, some of the relevant patents may still be at examination stage when the active ingredient falls into the public domain.

A way to mitigate the risk and clear the way for the biosimilar is to:

- properly map the patent landscape;
- identify pending applications that may pose a high risk to the biosimilar and check whether they may be circumvented; and
- if that is the case, file non-infringement lawsuits before launching the product.

### Biologics and biosimilars: regulatory overview

The marketing approval of biologics and biosimilars in Brazil is regulated by Resolution 55 (16 December 2010) – an ordinance issued by ANVISA (the Brazilian federal agency in charge of food and drug administration). For new biological products, the usual pathway, based on a full dossier submitted by the applicant, is required. For similar biological products, the following two regulatory pathways have been introduced:

- Individual development pathway – a reduced dossier can be submitted. The applicant must submit full data regarding quality issues, but this does not have to be comparative. The number of non-clinical and clinical studies submitted can be reduced, depending on how much data is available on the pharmacological properties, safety and efficacy of the originator product. At least one comparative Phase III study (ie, equivalence, superiority or non-inferiority) with the originator biological product is mandatory (except for haemoderivatives, vaccines and biological products for oncological use). When available, the results of Phase IV studies should be submitted.
- Comparative pathway – a comparator product must be elected. The applicant must use comparability in terms of quality, safety and efficacy between the comparator biological product and the biological product.

However, the regulation does not address the matter of interchangeability. Interchangeability

is the ability to replace a biologic drug with its biosimilar. This matter was the subject of Explanatory Note 00303/2017/GPBIO/GGMED in 2017, in which ANVISA stated that it is not up to the agency to declare if the biosimilar is interchangeable with the innovator, as interchangeability studies are not mandatory in Brazil. In view of the continued controversy regarding this matter, the note was reviewed in October 2018 and its interpretation of ‘interchangeability’ and ‘substitution’ was clarified by reinforcing that the issue concerns medical practice, which is not considered during the registration procedure.

Investing in Brazil means access to a vast consumer market; however, due to the particularities and complexities of Brazilian patent and regulation environment, biological and biosimilar companies should seek an experienced and knowledgeable firm that can knit together the necessary expertise in patent prosecution, litigation and regulation to develop a strategy tailored to their needs.

*Marisa Momoli, biologist and patent specialist, assisted in the preparation of this chapter. iam*

# Kasznar Leonardos

1919

## Kasznar Leonardos

Teófilo Otoni st 63

5th to 7th floors

Rio de Janeiro RJ 20090-070

Brazil

**Tel** +55 21 2113 1919

**Web** [www.kasznarleonardos.com](http://www.kasznarleonardos.com)



