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PATENT PROTECTION FOR BIOTECH COMPANIES IN BRAZIL

In this paper, we will delve deeper into these specific aspects of our legal framework, shedding light on some opportunities for patenting innovations in this area.

A must know guide created by Murta Goyanes' patent team

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Introduction

Modern Biotechnology has revolutionized science in the last few decades, and its applications in the fields of agriculture, medicine and pharmacy have attended to several needs of society and brought solutions for many unsolved problems of humanity.

Although many techniques have emerged from the modern Biotechnology, such as cloning, transgenesis, gene therapy, among many others, which look like something steaming from a Sci-fi movie, today Biotechnology is in our day-by-day, bringing countless improvements to our lives.

As a matter of fact, Biotechnology can be defined, under simple terms, as the use of the potentialities of the living beings in something useful for society. Conceptually, Biotechnology is not something new, as human beings have been employing it along millenniums, such as for brewing wine, bread and beer; however, it is undeniable that more recently we are witnessing a tremendous evolution in this technological area, which is giving raise to the so-called “Forth Industrial Revolution”.

Biotechnology is highly intensive sector in Research and Development (R&D). Therefore, Intellectual Property (IP) protection is of utmost importance for Biotech companies due to the unique and complex nature of their research. Biotech firms invest substantial resources in R&D, and without robust IP protection mechanisms - such as patents, copyrights, and trade secrets, these companies would be vulnerable to unauthorized appropriation of its intellectual property and unfair competition. This vulnerability could deter investment and hinder the incentive for further innovation, as Biotech companies would have little assurance that they can reap the rewards of their pioneering discoveries.

Nevertheless, since this science directly deals with technologies involving the use of living beings and their genetic codes, discussions regarding the threshold for “patenting life” always emerge, crossing the borders of ethics, moral and public health. Accordingly, many countries have set forth specific rules for regulating the patentability of biotechnological inventions.

In Brazil, securing patent protection for biotechnological innovations is indeed feasible. Similar to the most jurisdictions around the world, in case the subject-matter claimed in a patent application meets the patentability requirements, i.e., presents novelty, inventive step and industrial applicability (as well as the clarity, precision and support conditions), once the invention patent is granted, the owner has the right to exclude others from making, using and selling its invention in Brazil for a period of twenty years counted as from the application's filing date. This is particularly important in the biotechnology area in which the industry and big-pharma companies belong to a very competitive market, as patents provide protection over their inventions, contribute and encourage the development of new products and processes of high importance for the society. In the following sections, we will delve deeper into the specific aspects of our legal framework, shedding light on the opportunities for patenting innovations in this area.

Biological material found in nature

It is undeniable that nature is a source of a variety of valuable substances and products from which humanity can benefit. Drugs can be obtained or developed from substances produced by and isolated from microorganisms, plants and animals. In fact, the scientific community clearly recognizes that the biodiversity is a synonym of chemical diversity, in the broadest sense. For instance, many drugs in the market are from natural origin or inspired in molecules of natural occurrence. Still nowadays, the screening and testing of extracts against a variety of pharmacological targets in order to benefit from the immense natural chemical diversity is a concern in many laboratories worldwide[1].

A study carried out by Newman and Cragg reported that out of the 1,328 new chemical entities approved as drugs between 1981 and 2014, only 359 were purely of synthetic origin. From the remaining ones, 326 were "biological" entities (peptides of more than 50 residues, including therapeutic antibodies), and 94 were vaccines.

A little less than half of those new drugs (549, exactly) were from natural origin or derived inspired from natural compounds [2].

Keeping the above in mind and given the pivotal role of intellectual property in safeguarding the rights of innovations within the pharmaceutical and biotechnological sectors, the debate surrounding patent eligibility of naturally-occurring materials remains an ongoing subject marked by ethical and legal complexities.

The Brazilian Industrial Property Law (BIPL) No. 9,279/96 sets forth in its Article 10 (IX) that (i) natural living beings, in whole or in part, and biological material, including the genome or germ plasm of any natural living being, when found in nature or isolated therefrom, and (ii) natural biological processes, are not regarded as inventions. This means that, for instance, natural extracts, isolated molecules, proteins and nucleic acids which encounter counterparts in nature, even of obtained synthetic or recombinant techniques, are not eligible to patent protection in our country.

Nonetheless, it would still be possible to protect innovations in this area, such as for example:

- Enriched extracts, which can be differentiated from its natural counterpart for being enriched in any of its components, when they present in its composition characteristics not normally attained by the species and that do derive from the direct human interference;
- Compositions containing a natural biological product, provided that (i) it is not a mere dilution of the material, and (ii) other components are present in such composition, being necessary to clearly define parameters and features capable to determine, with no doubt, that the claimed composition is an actual composition, like a ready-to-use composition, with a defined functionality;
- Microbiological processes that use, apply to and result in microorganisms;

- Biological and enzymatic processes for the obtainment of chemical compounds, which present a technical step necessary for the final result;
- The use of natural products for the preparation of medicaments or compositions[1];
- Proteins and peptides having modifications in their amino acid sequences, which differentiate them from the naturally occurring sequences, for instance:
    - insertions, substitutions, deletions of natural amino acids provided that the resulting sequence do not find a natural counterpart;
    - insertions of non-naturally occurring amino acids in the sequence;
    - addition of chemical groups in the carboxy- or amino-terminus (e.g., Fmoc, t-boc, lipids, carbohydrates, prosthetic groups, iron, calcium, heme etc); or
    - fusion proteins, which do not find a natural counterpart;
- Nucleic acids having modifications in their nucleotide sequences, which differentiate them from natural correspondents;
    - insertions, substitutions, deletions of unmodified nucleotides provided that the resulting sequence do not find a natural counterpart;
    - insertion of non-naturally occurring nucleotides and protecting groups;
    - degenerated oligonucleotides that do not find natural correspondents;
- Expression cassettes and vectors;
- cDNAs produced from genes that contain introns (to allow the distinction of the same from the template DNA originating the same.

[1] According to the Patent Examination Guidelines currently in force, use claims are considered to be process claims.

Accordingly, despite the restrictions regarding the patentability of biological materials found in nature, as set forth by our IP Law, there are many possibilities of obtaining protection for inventions in this area. Care should be taken with respect to the patentability requirements and conditions, including novelty, inventive step, industrial applicability, sufficiency of disclosure and clarity. For instance, pursuant to the Patent Examination Guidelines in force, in the case of proteins/peptides and nucleic acids, the sequences must be clearly defined by their SEQ IDs.

Genetically Modified Organisms

The World Health Organization (WHO) defines genetically modified organisms (GMO) as organisms (i.e., plants, animals or microorganisms) in which the genetic material (DNA) has been altered in a way that does not occur naturally by mating and/or natural recombination. The technology is often called "modern biotechnology" or "gene technology", sometimes also "recombinant DNA technology" or "genetic engineering". It allows selected individual genes to be transferred from one organism into another, also between nonrelated species. [3] Nowadays, the GMOs are increasingly present in our everyday lives. For instance, genetically modified cells are capable of producing insulin, hormones, and antibodies for therapeutic use; and plants having improved traits such as tolerance to agrochemicals, resistance to agricultural pests, drought resistance or improved nutritional features are a reality in many crops around the world.

In terms of IP protection, in light of the provisions of Article 18(III) of the BIPL, living beings, in whole or in part, are not patentable in our country, except for transgenic microorganisms. The sole paragraph from Article 18 further establishes that "transgenic microorganisms are organisms, except the whole or part of plants or animals, that exhibit, due to direct human intervention in their genetic composition, a characteristic that cannot normally be attained by the species under natural conditions".

In view of the above, despite the fact that the common sense definition of the term “microorganisms” may encompass plant and animal cells in culture, in view of the Guidelines for Examination of Patent Applications in the Field of Biotechnology, the definition of transgenic microorganism does not extend to transgenic plant and animal cells (which are regarded as parts of plants or animals in the sense of sole paragraph of Article 18 of the BIPL), being only possible to obtain protection for transgenic archaea, bacteria, protozoa, fungus and unicellular algae (not classified as plants).

Under the same rationale, transgenic plants and animals are not eligible to patent protection in our country, however, it is possible to patent the methods of producing them[2], as well as accessory inventions related to the same, such as genetic constructs used for transformation and methods for identifying them.

Still, in 2022 the Brazilian Patent and Trademark Office (BPTO) published Technical Note No. 01/2022, which provides specific guidance on the patentability requirements and conditions for accessory inventions related to elite events. According to said technical note, an elite event is defined as “a transformation event of a plant (1) through the insertion of a transgene (2) using a genetic construct (3) in a stable manner, where this insertion occurred at a specific location in the plant's genome (4) and imparts to the plant a superior technical effect compared to other transformation events (5)”. This note reinforces that transgenic plants originated from the elite event are not patentable in light of the above-discussed Article 18 of the BIPL. Nevertheless, considering that the transgenic plant is at the center of potentially patentable inventions involving the elite events, such as for example, the hybrid DNA molecule used to transform the plant and methods for detecting the same, it was made necessary to draft examination guidelines for directing the evaluation of the novelty, inventive step, sufficiency of disclosure and clarity of inventions related to the so defined elite events, considering the characteristics of the obtained plant.

Moreover, it must be emphasized that Brazil opted for a sui generis system for the protection of new plant varieties, which is regulated by a separate IP system administered by the Ministry of Agriculture and Livestock.

[2] In the case of animals, it should be observed that processes involving them, which cause suffering without any substantial medical benefit for the human being are not patentable for being contrary to morals, good customs and public security, based on Article 18 (I) of the BIPL.

In fact, the protection of plant varieties and National Plant Varieties Registry were created in Brazil through Law No. 9,456 of April 25, 1997. Such Law created within the Ministry of Agriculture a department in charge of conducting, supervising and coordinating the applications, allowances and granting of certificates concerning plant varieties.

Such certificates are considered to be commodities for all legal purposes and the sole form of protection for plant varieties, establishing provisions regarding the use of plants and of reproduction or vegetative multiplication parts thereof in the country.

Still worth to mention is the fact that Brazil is a member of the Union for the Protection of New Varieties of Plants (UPOV), and ratified the Convention as revised in 1978. Law No. 9,546/97 is currently being revised so as to be adapted to the UPOV's Act as revised in 1991. However, it is not possible to predict when said new alterations will come into force.

Antibodies, fragments and binding moieties

Antibodies can be broadly defined as plasmatic proteins secreted by lymphocytes, which are capable of binding to a specific antigen, helping the organism to fight against viruses, bacteria, fungus, cancer cells, etc. Monoclonal antibodies (mAbs) are produced by B cells and specifically target antigens. The hybridoma technique introduced by Köhler and Milstein in 1975 has made possible to obtain pure mAbs in large amounts, greatly enhancing the basic research and potential for their clinical use. Other scientific and technological advances have also enabled the successful translation of mAbs to the clinic. Around the world, a study carried out in 2020 indicated that at least 570 therapeutic mAbs have been studied in clinical trials by pharmaceutical companies, and 79 therapeutic mAbs have been approved by the United States Food and Drug Administration (US FDA) and are currently on the market, including 30 mAbs for the treatment of cancer.[4] The use of mAbs for the diagnosis of many diseases is also remarkable in the medical area.

In Brazil, it is possible to pursue protection for molecules that would not be normally attained without the direct human intervention. For this reason, it is possible to pursue protection for mAbs and to those antibodies obtained by genetic engineering, such as chimeric and humanized antibodies. Further, bispecific and PEGylated antibodies, nanobodies, antibodies with particular glycosylation patterns, antibodies fused to pharmaceuticals or to other proteins, among others are also eligible to receive patent protection in our country.

On the other hand, polyclonal antibodies cannot be patented in view of Article 10 (IX) of the BIPL, discussed above, for being considered as biological materials isolated from nature. Moreover, since we are dealing with an indetermined mixture of antibodies, they would fail to meet clarity and precision requirements. Accordingly, this type of subject matter cannot be patented in our country.

In what concerns the most appropriate manner for defining antibody-related inventions, it is important to highlight that the antibodies should be defined either by its amino acid sequence (at least the sequence of their Complementary Determining Regions- CDRs) or by the hybridoma secreting the same. At this point, the hybridoma should be duly defined by its Accession Number in a Depository Authority for complying with the sufficiency of disclosure requirement, according to our rules. Moreover, the hybridoma itself is also eligible to patent protection for consisting of the fusion of an antibody producing cell with a tumoral cell, having characteristics which are not achievable under natural conditions without the human direct intervention. However, isolated transgenic animal cells that produce antibodies, such as some mammalian cell lines, cannot be patented, even if genetically transformed, for the reasons explained above with respect to the provisions of Article 18 of the BIPL, which restricts the patentability to transgenic microorganisms.

Stem Cells

Stem cells are unspecialized cells of the human body. They are able to differentiate into any cell of an organism and have the ability of self-renewal. Stem cells exist both in

embryos and adults. In recent years, stem cell therapy has become a very promising and advanced scientific research topic. The development of treatment methods using such technology has evoked great expectations.[5]

For being obtained directly from human or animal body, the stem cells themselves are not patentable in Brazil, even if genetically modified, for falling within the

patentability limitations imposed by Articles 10 (IX) and 18 (III) of the BIPL, as explained in the sections above. In addition, therapeutic methods involving the stem cells would not be entitled to patent protection in light of the provision of Article 10 (VIII) from the BIPL, which establishes that therapeutic, surgical and diagnostic methods, applied to human or animal body are not considered to be inventions.

In spite of the above, it would still be possible to seek protection in Brazil for inventions related to stem cells, as the methods for culturing and transforming them, carried out in vitro, as well as compositions containing the same and their obtainment methods are not excluded from patentability.

For instance, the protection of the following products and processes involving stem cells is foreseen by the Guidelines for Examination of Patent Applications in the Field of Biotechnology (BPTO Normative Instruction No. 118/2020):

- Compositions containing stem cells and other ingredients (assorted implants containing cells, cell and matrix formulations, growth factors and cells, etc.);
- Compositions containing mixtures of different types of stem cells;
- Purification, preparation, conditioning, differentiation and dedifferentiation methods, or any stem cells processing, provided that they are performed in vitro;
- Uses of stem cells for preparing medicaments to treat disease X;
- Uses of stem cells for preparing implants to treat disease X;
- Uses of stem cells for preparing compositions to diagnose disease X;

- Diagnostic methods that include steps employing stem cells or synthetic tissues, provided that they are performed in vitro;
- Drug tests that include steps using stem cells or synthetic tissues, provided that they are performed in vitro;
- Stem cells growth methods; and
- Conditioned culture media obtained during stem cell growth.

As it can be seen above, there are several manners for seeking patent protection for stem cell-related inventions in Brazil.

Genetic use restriction technologies (GURTs)

Genetic use restriction technologies (GURTs), also known as terminator technologies, were developed with the aim to restrict the access to genetic materials and their phenotypic traits. There are two major classes of GURT: V-GURT (variety-based GURT) and T-GURT (trait-based GURT). The V-GURT restricts the use of the variety through blocking the plant reproduction via production of non-viable seeds. Conversely, the T-GURT regulates the expression of certain genes that confer desirable agronomic traits, such as stress tolerance, pest resistance (against insects and diseases) and herbicide resistance. Plants carrying T-GURT produce viable seeds, but the offspring does not express the transgene of interest. Ultimately, the GURTs were developed to preserve the intellectual property of genetically modified (GM) crops and ensure the return of investments made by industry to obtain technology delivered through seeds.[6]

[6]With respect to GURTs, our Biosafety Law No. 11,105/2005 establishes the following in its article 6 (VII) and its sole paragraph:

> *"Article 6 – The following shall be prohibited: (...)*
>
> *VII – the use, commercialization, registration,* ***patenting*** *and or licensing of genetic use restriction technologies.*
>
> *Sole paragraph - For the purposes of this Law, genetic use restriction technologies shall be deemed to be any process of human intervention for*

generation or multiplication of genetically modified plants for the production of reproductively sterile structures, as well as any form of genetic manipulation which aims to activate or deactivate genes related to fertility of plants via external chemical inducers." (Our emphasis)

Accordingly, in view of the limitations imposed by our Biosafety Law, no Brazilian patents can be granted for this type of technology. Hence, claim constructions such as the following would more than likely be objected during their substantive examination, grounded on Article 6 (VII) of the Biosafety Law:

- Method for producing a variety capable of bearing fruit without seeds, characterized by the fact that a male sterility variety having a parthenocarpic feature is backcrossed with a plant of a fixed lineage.
- Method for producing a hybrid plant characterized by fusing protoplasts from a sterile male plant with protoplasts from a second variety, to confer the characteristic of sterility to the second variety.

On the other hand, intermediate products, such as vectors and constructs can be patented if they meet the regular patentability requirements and conditions established by our Law. In addition, methods for restoring the fertility can be also entitled to patent protection.

Lastly, with regard to the manipulation of fertility, care should be taken with the draft of the claims so that they do not cover methods that produce both fertile and infertile structures, as in this case the restriction only to methods that produce fertile structures will be permitted by the Examiner.

Conclusion

In this paper, we have explored some types of inventions within the field of Biotechnology that may be eligible for patent protection according to Brazilian laws. Additionally, we have given an overview on the best practices for claiming these types of inventions.

Nevertheless, it should be emphasized that the scenario discussed above is based on the current regulatory and legal frameworks in Brazil that govern the patenting of biotechnological inventions. It is important to take into consideration that, in light of the constant, rapid, and crucial technological advancements in this area, the BPTO has been making efforts to periodically update its examination guidelines for patent applications in this sector. This is essential for enhancing the legal certainty for patent applicants within these arts.

With these general guidelines in hands, we hope to have provided a concise roadmap for initiating the process of seeking Intellectual Property protection for biotechnological innovations in our country.

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