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On the assignment of biopharmaceutical patents

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ABSTRACT

This study focuses on the patent assignments for six selected biopharmaceuticals: filgrastim, infliximab, somatropin, imiglucerase, betainterferon and factor VIII. These very expensive proteins are not currently produced in Brazil, and their production would enhance Brazilian technological capacity. Accordingly, we characterized the current profiles of the patent holders for these proteins. *Data mining* techniques were used to simplify the screening and analysis of thousands of patent entries retrieved from data banks worldwide, using the International Patent Classification (IPC) codes A61K, A61P and C12N as a guide. A critical assessment of the historical evolution of biopharmaceutical patents and a geographic distribution analysis of their depositors conclude that individual depositors have a strong, growing influence on the overall patent assignment profile. Individual depositors file patents primarily in collaboration with companies, research centers or universities. We also concluded that, in the next few years, emerging or *spin-offs* companies will constitute an increasing share of the competitors of consolidated technology holders (Big Pharma companies, research centers and universities). This information may prove interesting for entrepreneurs involved in public, private or joint ventures regarding the fabrication of strategic biopharmaceuticals.

1. Introduction

The biotechnology industry is considered the most important source of new drug development—in addition to its role as a strategic social and economic sector. Because innovation is the foundation of progress in the health sector, the pharmaceutical industry invests millions of dollars each year in research to develop new products, including biomolecules. The development of biopharmaceuticals may yield new treatment options for complex diseases with high incidences in the population, including multiple sclerosis, Alzheimer's disease, brain tumors, chronic lymphocytic leukemia, cancer and many other diseases.

In Brazil, the acquisition of specialized medicines is part of the role of the Unified Health System (Sistema Único de Saúde—SUS), which provides specialized medicines to the population. This role is dictated by the policy of the Ministry of Health (Ministério da Saúde—MS) according to decree GM/MS nº 2.981/2009 [1]; according to this decree, some biopharmaceuticals are included in the category of specialized medicines. Specialized medicines are those used to treat patients with rare or chronic diseases or diseases that require special management, including Gaucher's disease, rheumatoid arthritis and multiple sclerosis. Specialized medications are classified into three groups according to their characteristics, forms and which organization is responsible for providing them (federal, state and/or municipal government). These groups of medicines are of the great economic significance in Brazil because the federal

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government is responsible for their distribution for the treatment of complex diseases and they are composed of expensive products and because of the drug development activities undertaken by the Industrial Health Complex (Complexo Industrial da Saúde—CIS).

Because of sectorial policies formulated by the state through the SUS, the Brazilian population's access to healthcare has been extended to drugs; this has had a major financial impact both in terms of the monetary amounts involved and in terms of the MS budget. Spending associated with purchasing specialized medicines increases each year; in 2011, 31% of the funds allocated to all drugs (strategic, basic biopharmaceuticals, oncology and others) were directed to the specialized class of medications [2].

The CIS is intended to boost industry, including the national pharmaceutical industry and the healthcare equipment industry, to reduce Brazil's dependence on imported products. One of its goals is the reduction of the trade deficit by US$ 4.4 billion through the development of technology to locally produce 20 strategic products for the SUS by 2013. However, the import deficit must not be confused with the technology deficit; there may be technologies in the country that are not economically feasible to produce and must be imported. In 2008, the healthcare supply chain represented between 7% and 8% of Brazil's gross domestic product (Produto Interno Bruto—PIB) and mobilized approximately R$ 160 billion into the national economy [3]. With respect to social impact, approximately 10% of the population is actively employed within the industry, and the national pharmaceutical market mobilizes R$ 22.1 billion and grows at a high annual rate. In 2010, it was ranked the seventh largest pharmaceutical market worldwide and surpassed even that of the United Kingdom [4]. These numbers may increase further in the future under the Productive Development Policy, guided by the Ministry of Industry and Trade and Development (Ministério da Indústria e Comércio e Desenvolvimento—MDIC), which includes the CIS as one of its branches [5].

In cooperation with the development of the CIS, the decree GM/MS nº 1.284/2010 [6] defines the list of strategic products under the SUS and identifies the key players involved, i.e., public and private producers and regulatory agencies, to promote the CIS strategy. The decree lists the products that should be targeted with specific initiatives to increase local production and innovation and technology transfer and to update regulatory mechanisms. The list of strategic products is split into two sections. In Section 1, includes four groups; Group 4 contains products obtained by biological routes. This ordinance also allocates more than R$ 10 million for product purchases and is featured in the decree GM/MS nº 2.981/2009 [1].

When the Brazilian market was opened to foreign companies in the 1990s, the Brazilian healthcare industry was weakened; the accumulated trade deficit grew from US$ 700 million at the end of the 1980s to US$ 7.13 billion by 2008. Brazil has become extremely dependent on imported knowledge- and technology-dense products. For example, in 2008 alone, Brazil imported US$ 1.4 billion in vaccines, serums and other blood products and exported only US$ 37 million worth of products with low added value. Changing this imbalance requires investment, an increase in the number of higher-quality competitive products, an improved industrial infrastructure and the formation of public–private partnerships (PPPs). In return, the economic and social benefits will include an increased industrial presence in the pharmaceutical market, a broadening of the spectrum of drug treatments and the specialization of human resources in this area of technology, with the resulting creation of more domestic jobs [5].

The aim of this paper was to select the most interesting Brazilian biopharmaceuticals and identify the types of patent depositors in this field. However, it is important to note that the market is not only limited to innovative molecules but also includes biosimilars which can be manufactured after the expiration of the patent for the first commercial product [7,8], as shown in worldwide studies of the biopharmaceutical industry [7,9–11] and studies concerning the technologies used for the production of biopharmaceuticals [12–15].

2. Materials and methods

2.1. Selection of the biopharmaceuticals

Biopharmaceuticals were selected using three criteria. The first criterion was the inclusion of the biopharmaceutical in the Group 4 list of strategic products, which is composed of 23 products obtained via biological routes (Decree GM/MS nº 1.284/2010) [6]. The second criterion was the inclusion of the biopharmaceutical from a list of the 20 drugs with the highest values approved by the MS in 2007 [16]. A drug meeting either of the first two criteria was selected subject to the final criterion that it must be centrally procured by the MS and not produced in Brazil (Decree GM/MS nº 2.981/2009) [1].

2.2. Main technical and market information

Information concerning the selected biopharmaceuticals was gathered from dependable sources, including the scientific literature (scientific articles, MSc dissertations and PhD theses) and technology production materials (patents entered in the global databases). We evaluated the information available from the websites of the Ministry of Health of Brazil, national research centers worldwide, the World Health Organization (WHO), and the biopharmaceutical manufacturers as well as from selected documents from the National and International Regulatory Agency and current Brazilian legislation. The sources of information used in this work will be reported as the data are presented in the "Results and discussion" section.

2.3. Evaluation of the patent applications

We quantified the number of biopharmaceutical patents within two-databases—maintained by the Brazilian and American patent offices: the National Institute of Industrial Property (Instituto Nacional de Propriedade Intelectual—INPI) and the United