

PHARMACEUTICAL MARKET AND OPPORTUNITY IN THE 21ST CENTURY FOR GENERIC DRUGS: A BRAZILIAN CASE STUDY OF OLANZAPINE

Jorge Lima de Magalhães

Aix-Marseille Université, France
Oswaldo Cruz Foundation/FIOCRUZ, RJ, Brazil
E-mail: jorgemagalhaes@far.fiocruz.br

Luc Quoniam

University du Sud Toulon-Var, Toulon, France
E-mail: mail@quoniam.info

Núbia Boechat

Oswaldo Cruz Foundation/FIOCRUZ, RJ, Brazil
E-mail: boechat@far.fiocruz.br

Abstract

This paper aimed to identify and analyse the evolution of the generic pharmaceutical market in Brazil, specifically olanzapine drugs. For this purpose, it has been demonstrated trends through access free tools. By bibliographical survey in indexed databases as well as official data in Brazil for generic drugs and public policy, it was analyzed and performed a case study. In 2012, global pharmaceutical industry surpassed US\$ 950 billion in sales with trend to reach US\$ 1,2 trillion by 2016. In Brazil market has grown in its global ranking, jumped from 10th place to 7th place in five years and projection it'll stay Top five by 2015. Brazil has significant presence in pharmerging markets by increasing US\$ 10 billion/year. Generics segment accounts approximately to 20% of the total market. 2003-2011 registered a growth of 42.3%. Patents expiration in the neuroleptics area becomes more promising like a market of olanzapine in the last eight years is around US\$ 120 million. After the end of the olanzapine patent (2011) sales increased 270% which demonstrate potential Brazilian market in this new century. Management problems for developing nations and undeveloped such as network management and patents analysis for health care might reveal great opportunities for investors, e.g., creation of the Big Brazilian biotechnology pharmaceutical industry.

Key words: *competitive intelligence, pharmaceutical trends, technological and innovation management.*

Introduction

According to IMS Health (2012) shows the growth of the sales in the pharmaceutical market with expectation about 3% annually. Already in 2011 probably reach US\$ 1 trillion. With sales of US\$ 26 billion, Brazil holds the 7th position in the world ranking with forecast to overcome countries as UK, India, Spain, Italy and the Russia and will occupy the 5th place in the global ranking. Among the reasons that drive the expectation of Research, Development and Innovation (R,D&I) in this area are the entry of generic drugs, targeted therapies, new mechanisms of actions and approval of biosimilars and Pharmerging¹ market. This market consists of 17 emerging countries, leading among them China, Brazil, Russia and India (BRIC) which

accounts for more than two-thirds of the increase those sales (IMS Institute for Healthcare Informatics, 2012).

The worldwide market for generic medicines grows approximately 17% per year and moves approximately US\$ 80 billion, with growth predicted for 2012 at around US\$ 120 billion. Projections indicate that by 2015 Brazil will become the third largest generics market in the world behind the United States and China. Currently, the industry moves around 21.3% of total medicines and 17% in value, or US\$ 3,2 billion. This market is the largest amount of income for the pharmaceutical industry in Latin America and is the third in all America; back only from EUA and Canada (IMS Institute for Healthcare Informatics, 2012).

The participation of multinationals in the generics market has tripled since 2009. This fact is confirmed by the change in this scenario with the entry of the French Sanofi-Aventis to buy domestic Medley in 2009 and Pfizer, which acquired 40% of Teuto domestic laboratory, in 2010. The Swiss Novartis already operates in generic by Sandoz (PróGenéricos, 2012).

The Brazilian pharmaceutical market contains relevant companies of national capital (Quental, Abreu, Bomtempo, & Gadelha, 2008), as the EMS group, Achè, Eurofarma, Cristalia and Hypermarcas. These companies have been shown to innovative with launch of generic medicines and similars² not only, as well as reference. This due to the efforts of R,D&I. Another example in the pharmaceutical market is the formation of a “super pharmaceutical company” through a joint venture. In March 2012, four Brazilian companies created the BioNovis, promising to put Brazil in the future market of biological products. The project brings together national laboratories EMS, Aché, União Química and Hypermarcas. According to executives with access to the negotiations the new company must have capital of approximately US\$ 400 million. They had the National Bank of Economic and Social Development (BNDES – Brazilian term) in the business. Another company that was created is the Orygen Biotecnologia (Partnership companies: Eurofarma, Cristália, Biolab and Libbs). According to director of Syndicate of pharmaceutical industries in the State of Sao Paulo (Sindusfarma – Brazilian term) the idea is create an industry of biosimilars.

It is noteworthy that the Brazilian pharmaceutical market has a health public market (government purchases for hospitals) that is not accounted for in direct sales to pharmacies (Magalhães, Antunes, & Boechat, 2011). This market represents approximately US\$ 6 billion in annual sales, therefore increasing the total market at around US\$ 32 billion in 2012.

According to the Brazilian Institute of Geography and Statistics (IBGE – Brazilian term) Brazil has more than 192 million inhabitants, an area of over 8.5 million square km and still has about 9% of people living on the poverty line (IBGE, 2011). However, the social policies (Gadelha & Costa, 2012) implemented by the Brazilian government in the last decade have contributed to the increase in consumption in the country.

From 2003 to 2009, 48.8 million Brazilians had the rise of social class (A, B and C) and therefore decreasing the class E - less favored. By comparing with the other members of the BRICS countries (a group of countries formed by Brazil, Russia, India, China and South Africa) in the 2000s, Brazil has the second highest annual growth rate of per capita household income between the poorest 20% of the population (Fundação Getúlio Vargas, 2011).

According to World Resource Institute, the large potential market opportunity is located in emerging countries. Looking at the BRICS, Brazil is second behind China promising (World Resource Institute, 2007). However, a major problem in the health care is still that half the population does not have full access to essential medicines. Thus, entry of generic drugs with lower prices assist to improve this problem since the population has increased their purchasing power.

Public policy should ensure the population access to essential medicines (Quick, 2003). In this sense, after the government’s actions that encouraged public and private investments, the country has established itself as emergent in the global scenario. Thus, the pressure for quality and differentiation in the products has been increasingly demanded, opening the need for innovation. In the pharmaceutical area, there’s no difference. So, the main purpose is to highlight

trends in the Brazilian pharmaceutical market growth and investment opportunities in the field of generic drugs, as an example, neuroleptics area. Nevertheless, it can provide better access to the population.

On the other hand, identify and analyze the amount of scientific information and state of the art with respective correlations has become hard work. The world's technological per-capita capacity to store information has roughly doubled every 40 months since the 1980s. As of 2012, every day 2.5 quintillion (2.5×10^{18}) bytes of data were created (Lynch, 2008). So, the challenge for Science and enterprises is managing big data for scientific visualization and decision making.

Therefore, researchers depict the relationship international networks connection and examine the trajectory of Brazilian pharmaceutical market with regard to the generics, especially olanzapine, at the same time demonstrating the advancement of science and opportunities also highlights issues for big data management in the new century.

Methodology of Research

General Background of Research

This study involves data mining. The data were taken from IMS Health, Association of Brazilian generic drug industry (Pró Genéricos) and National Health Surveillance Agency (AN-VISA), a governmental science and technological research agency. Bibliographical references were also consulted on indexed scientific databases such as Scielo, Medline and Lilacs. In addition to get the massive information in the world and demonstrate synthetically a technological pharmaceutical network connection with Brazil.

Instruments

The big data were treated using data mining in a cluster engineering Lingo3G carrot2 – version 3.6.2. Regarding the data gathered was treated using Excel software spreadsheets (Microsoft Office 2010). After, the results were analysed and conclusions drawn as set forth in the following sections.

Data Analysis

Principal analysis was in generic drugs and public policy in this area as well as a case study of olanzapine drugs analyzed in 8 years (available time in the database).

Results of Research

It was identified 554,000 documents linking Brazil with the world in regard to generic drugs. With the total amount of data and data mining by Lingo3G there was obtained 203 documents. These results allowed correlations to be found to spot business trends, research technologies and give subsidies so establishment of public health policies. Figure 1 shows the clustering of map information. The Brazilian generic drugs are intimately tied to various actions and partnerships both nationally and internationally. Exemplified by 25 Brazilian generic, 16 generic AIDS, 13 Country, 12 pharmaceutical markets, 10 India and so on.

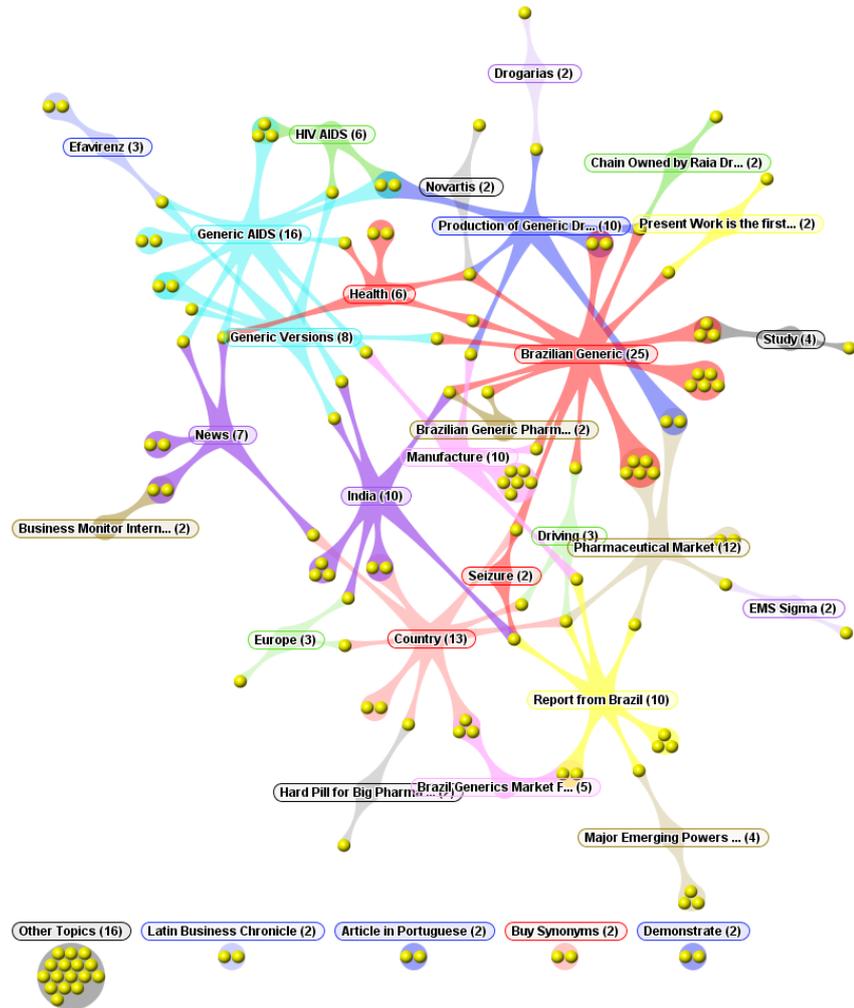


Figure 1: Cluster map of generic drugs in the Brazil.

Source: Created by the authors.

Brazilian market can be seen in Figure 2. In a decade revenues in dollar grew up over 500%.

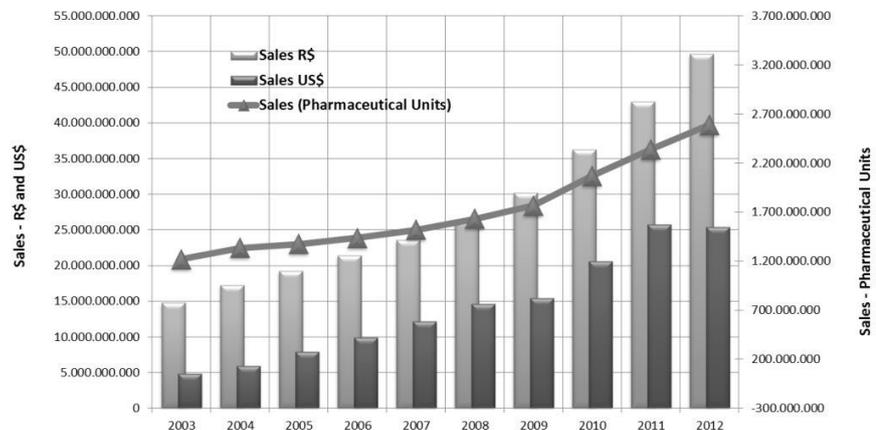


Figure 2: Pharmaceutical market in Brazil – period: 2003-2011.

Source: Created by the authors with data from IMS Health.

In Table 1, shows the Brazilian scenario of seven manufacturer's olanzapine. Note the entry in 2010 of the first generic medicine.

Table 1: Producers of olanzapine (before/after patent expiration).

Manufacturers of olanzapine	Medicine registration	Year	Quantity of presentation
GLAXOSMITHKLINE	Similar	2011	2
EMS PHARMA	Generic	2010	3
GERMED PHARMA	Generic	2011	3
MEDLEY	Generic	2011	9
LEGRAND	Similar	2011	3
EMS PHARMA	Similar	2011	3
LILLY	Reference	1997	7
LILLY	Reference (new presentation)	2005	4

Source: Created by the authors.

Figure 3 can be noted the market evolution of olanzapine drugs with the consistent trend over the last three years. The same year that the patent expired and the entry of only 01 generic drug consumption increased more than 37%.



Figure 3: Brazilian market of Olanzapine medicines

Source: Created by the authors.

The data confirm the influence of “big-data” and growth trends in generic drugs in emerging countries, mainly Brazil. Nonetheless, the urgent need for treatment of information to aid in the science management and decision makers to improve the health care of their populations.

Discussion

Somehow access to medicines to the population has been provided through public policy as the generics strong presence of the pharmaceutical industry and in consequence the need to seek ways to deal with the massive information management in the new century (Cameron, Ewen, Rossdegnan, Ball, & Laing, 2009). IMS Health (2012) points to a growth in global pharmaceutical sales about 3% annually. These countries representing for more than two-thirds of the increase or about US\$ 151 billion, namely will also represent 30% of the total sales in 2016, up from 20% of the total in 2011.

On the other hand, pharmaceutical sales in the U.S. will grow by a little more than 1%

annually during the same period (from US\$ 322 billion to US\$ 350 billion) accounting for 30% of the total in 2016 roughly the same as the pharmerging countries compared to 34% of the total in 2011. Meanwhile, in Europe are expected to drop by about 1% annually from US\$ 159 billion to US\$ 135 billion, reducing the European contribution from about 17% of the total in 2011 to about 12% in 2016, where developed markets will account for 57% of total pharmaceutical sales in 2016, a steep decline from 73% in 2006.

Accordingly, pharmaceuticals sales rises $\frac{3}{4}$ in pharmerging while the markets of developed countries have stagnated. BRICS countries are responsible by 73%. Together with 21 far-flung nations ranging from Venezuela to Vietnam, Chile to the Czech Republic etc. In summary, pharmerging sector accounts for more than 3 billion people or 45% of the planet. While much is made of their exploding middle-class population as well as its potential buying power (Fundação Getúlio Vargas, 2011).

Progress of the Brazilian market (see figure 2) includes generic medicines that is linked to the regulation law in 1999; investments of both national and multinational companies and the expiration of patents on several medicines. Addition of a new market in general provides a reduction in approximately 50% of product price and after eight years an increase consumption about 300% occurs (PróGenéricos, 2012). In 2010 sales grew by 32% with revenues of US\$ 3,5 billion. Already in 2012, reached US\$ 5,3 billion with increase 48.5% (Sindicato da Indústria de Produtos Farmacêuticos no Estado de São Paulo, 2012). In part, this progress can be explained when throughout of the year 2011 it reached the market some generic medicines with expired patents. Under Brazilian law, generic must be at least 35% cheaper. In practice, there is a reduction beyond that percentage due to competition. Some medicines that have expired patents include Viagra, Lipitor, Crestor, Dilvan and other brands. More than 12 medicines had patent expiration in 2012, among them Xeloda (Capecitabine) from Roche for the treatment of breast cancer and colorectal cancer, Gleevec (Imatinib) Novartis' leukaemia and Pfizer's Geodon, for psychological disorders. These drugs have very high price providing new opportunities for generic market.

Trust and quality of generic medicines can be measured by ANVISA's guidelines over the past 10 years. For example, tests of bioavailability and pharmaceutical equivalence. So, the formula: trust of the population allied to expand purchasing power makes the choice of the generic drug grow up. Pró Genéricos research (2011) show that when the consumers replace a brand medicine by a generic their expenses are reduced by more than US\$ 13 billion (ANVISA, 2012; PróGenéricos, 2012).

The Brazilian pharmaceutical market has achieved a higher level of technology. It can be noted that companies are indeed seeking opportunities in domestic and international markets. In 2011, among Top 10 pharmaceutical companies operating in Brazil there are four domestic companies while eight years ago there was only one company. These companies represent 25% of the national private sector. They are EMS Group, Hypermarcas Group, Aché and Eurofarma.

Among several programs of the Brazilian government to improve people's access to medicines, there is the "Popular Pharmacy" (Farmácia Popular – Brazilian term) where generics account for 65% of the total volume of products distributed free to the needy population used in the control of hypertension and diabetes (Magalhaes, JL, Antunes, AMS, & Boechat, N, 2012).

In this sense, we can deduce that investments in generic medicines are a good business. There are trends to build public-private partnerships (PPP) in research and/or technological development through government incentives, patents expiration and the knowledge in universities and companies (Gadelha, Costa, & Maldonado, 2012).

Nevertheless, one area that is beginning to be explored within this segment is neuroleptic generic such as Zyprexa® medicine (olanzapine active ingredient) that had its patent expired in 2010. After one year, ANVISA has received several requests for authorizations in news olanzapine medicines. As can be seen in Table 1, they were granted 15 generics and 8 similars

generating 23 records. In 2011, 76,7% of all olanzapine medicines are not reference (brand). It is worth noting that in early 2012 ANVISA has granted license for more 6 pharmaceutical companies (4 private companies and 2 public³ institutes). They are Sanofi-Aventis, Novaquímica, Sandoz, Sigma Pharma (a division of EMS), LIFAL (Laboratory Industrial Pharmaceutical of Alagoas) and NUPLAN (Center for Research in Food and Drug Administration, Federal University of Rio Grande do Norte). These last two, are public.

The sales potential of olanzapine can be also demonstrated by the quantity of dosage form registered by manufacturers. In addition to the owner of the brand (Eli Lilly) has 11 presentations. Other laboratories have 3 generics with 15 different presentations and 3 similars with 8 presentations. With these new authorizations market will contain with nine private olanzapine manufacturers being strong presence of foreign capital and only two domestic enterprises. This scenario represents about 78% of this product in transnational companies.

Figure 3 shows the growth in the pharmacy sales for olanzapine in the period 2004 to 2011. Until 2010, represents only the market restrained by Zyprexa®. In 2011, growth represents also the sale of the generic drug olanzapine. Despite the decline in the number of pharmaceutical units from 2007 to 2009 note this fact it was not significantly reflected in dollars but in Real (Brazilian currency). There was a much bigger drop only in 2008 which perhaps can be explained due to global crisis. However, market grew 23,1% from 2009 to 2010 with revenues US\$ 16 million in 2009

Notwithstanding, with the expiration of the Zyprexa® patent, sales of olanzapine in 2011 grew 37.2% over the previous year that was only 4.5%. Sales growth in dollars of 2009-2010 and 2010-2011 were 23.1% and 29% respectively. In the same period but in Real were 10% and 22.6% respectively.

Final Considerations

Big data is difficult to work with using most relational database management system, howsoever becomes great ally to determine public policies that promote intensity in science research and contribute significantly to innovation and technological development of the countries. Cluster engineering proves the effective assistance in this area of knowledge

Brazilian government efforts and incentives have placed the country as an important emerging nation. Thus, in the pharmaceutical area is not different. Evolution investments represented by the internal staff of companies demonstrate a trend for change in the strategic orientation of these domestic pharmaceutical groups.

The largest domestic enterprises in the Brazilian pharmaceutical industry have shown signs of capabilities to change strategy and innovation. Biggest domestic pharmaceutical EMS group pioneered the launch of the first generic olanzapine. In the same year that the patent of the reference product expired the company managed to meet all legal requirements to register at ANVISA the generic product which somehow drove the access in 23.1% already in the same year of 2010.

Considering that after eight years to launch a generic product consumption increases 300%, it can be stated that the olanzapine volume in 2018 will reach 18,7 million of pharmaceutical units, with a turnover of US\$ 102 million.

Therefore, from a trajectory perspective since 1999, it is possible to infer that the Brazilian market of generics is undergoing a process of acquiring the empowerment for consolidation in the area. It is clear that, domestic pharmaceutical is not presented as a big pharma in the international market. However, their competence and growth in the area of generic medicines and similars has awakened “looks” of large international players such as French Sanofi (acquired national Medley) and the American Pfizer (acquired part of the national Teuto).

Acknowledgements

Appreciate the CAPES grant and support infrastructure of the Aix-Marseille Université as well as the data provided by PróGenéricos.

References

- ANVISA (2012). Agência Nacional de Vigilância Sanitária. *Lista de Estatísticas*. Recuperado 18 de fevereiro de 2013, de http://portal.anvisa.gov.br/wps/portal/anvisa/anvisa/home/medicamentos!/ut/p/c4/04_SB8K8xLLM9MSSzPy8xBz9CP0os3hnd0cPE3MfAwMDMydnA093Uz8z00B_A_cgQ_2CbEdFADghJT0!/?1dmy&urile=wcm%3Apath%3A/anvisa+portal/anvisa/inicio/medicamentos/publicacao+medicamentos/lista+de+estatisticas+-+genericos.
- Cameron, A., Ewen, M., Rossdegnan, D., Ball, D., & Laing, R. (2009). Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *The Lancet*, 373 (9659), 240–249. doi:10.1016/S0140-6736(08)61762-6.
- Fundação Getúlio Vargas. (2011). Os Emergentes dos Emergentes: Reflexões Globais e Ações Locais para a Nova Classe Média Brasileira | CPS/FGV. FGV Editora. Recuperado de <http://cps.fgv.br/brics>.
- Gadelha, C. A. G., & Costa, L. S. (2012). Saúde e desenvolvimento no Brasil: avanços e desafios. *Revista de Saúde Pública*, (ahead), 0–0. doi:10.1590/S0034-89102012005000062.
- Gadelha, C. A. G., Costa, L. S., & Maldonado, J. (2012). O Complexo Econômico-Industrial da Saúde e a dimensão social e econômica do desenvolvimento. *Revista de Saúde Pública*, (ahead), 0–0. doi:10.1590/S0034-89102012005000065.
- IBGE. (2011). *IBGE :: Instituto Brasileiro de Geografia e Estatística* (6 No. Tábua completa de mortalidade - 2010). Brazil: IBGE. Recuperado de <http://www.ibge.gov.br/home/estatistica/populacao/tabuadevida/2010/>.
- IMS Institute for Healthcare Informatics. (2012). *The Global Use of Medicines: outlook through 2016* (p. 36). Recuperado de www.imshealth.com.
- Lynch, C. (2008). Big data: How do your data grow? *Nature*, 455 (7209), 28–29. doi:10.1038/455028a.
- Magalhães, J. L. de, Antunes, A. M. de S., & Boechat, N. (2011). Laboratórios farmacêuticos oficiais e sua relevância para saúde pública do Brasil. *RECIIS*, 5 (1). doi:10.3395/reciis.v5i1.367pt.
- Magalhaes, J.L., Antunes, AMS, & Boechat, N. (2012). *Technological Trends in the Pharmaceutical Industry: the matter of neglected tropical diseases – An overview of the Research, Development & Innovation in Brazil*. Synergia Editora. Recuperado de <http://www.livrariasynergia.com.br/livros/M39700/9788561325732/tendencias-tecnologicas-no-setor-farmaceutico-a-questao-das-doencas-tropicais-negligenciadas-edicao-bilingue.html>.
- PróGenéricos (2012). Associação Brasileira das Indústrias de Medicamentos Genéricos. *Brazilian Association of Industries of Generics*. Recuperado 15 de fevereiro de 2013, de <http://www.progenericos.org.br/index.php/mercado>.
- Quental, C., Abreu, J. C. de, Bomtempo, J. V., & Gadelha, C. A. G. (2008). Medicamentos genéricos no Brasil: impactos das políticas públicas sobre a indústria nacional. *Ciência & Saúde Coletiva*, 13, 619–628. doi:10.1590/S1413-81232008000700011.
- Quick, J. D. (2003). Ensuring access to essential medicines in the developing countries: A framework for action*. *Clinical Pharmacology & Therapeutics*, 73 (4), 279–283. doi:10.1016/S0009-9236(03)00002-X.
- Sindicato da Indústria de Produtos Farmacêuticos no Estado de São Paulo. (2012). Sindusfarma. *Syndicate of pharmaceutical industries in the State of Sao Paulo*. Recuperado 15 de fevereiro de 2013, de <http://www.sindusfarmacomunica.org.br/indicadores-economicos/>.
- World Resource Institute (2007). The Next 4 Billion: Market Size and Business Strategy at the Base of the Pyramid. Recuperado 21 de fevereiro de 2013, de <http://www.wri.org/publication/the-next-4-billion>.

(Endnotes)

- 1 Term created by IMS Health to define emerging markets with high growth potential in pharmaceuticals, in the period from 2009 to 2013.
- 2 In Brazil, there is this drugs class. They are medicines that have the same active

ingredient and quality, but differ in the form of presentation (dose, concentration). Just like generics, are granted only after the expiry of patent.

3 Brazil has public pharmaceutical laboratories, which are linked to the Ministry of Health or state governments. They do not sell to private initiative. Produce only to meet the specific demands of the Government of medicines whose patent has already been expired. They supply a small part of the demand of the Brazilian Health System, as medicines for malaria, Chagas disease, tuberculosis etc.

Advised by Naglis Švickus, SMC "Scientia Educologica", Lithuania

Received: *February 05, 2013*

Accepted: *February 14, 2013*

Jorge Lima de Magalhães	DSc, Post-doctoral in Aix-Marseille Université Laboratoire IRSIC (EA462) France. Researcher in Public Health in Oswaldo Cruz Foundation/FIOCRUZ, Capes Fellow 12.298, Brazil. E-mail: jorgemagalhaes@far.fiocruz.br Website: http://lattes.cnpq.br/9829199474735249
Luc Quoniam	DSc, PhD, Professor, University du Sud Toulon-Var – France, Avenue de L Université 83957 La Garde, France. E-mail: mail@quoniam.info Website: http://quoniam.info
Núbia Boechat	DSc, Researcher in Public Health in Oswaldo Cruz Foundation/FIOCRUZ, Head of Organic Synthesis in Farmanguinhos, Brazil. E-mail: boechat@far.fiocruz.br Website: http://lattes.cnpq.br/9152983185617827