ISSN 1613-9615

Journal of Business Chemistry

Vol. 2, Iss. 3
Special Issue
September 2005

www.businesschemistry.org

Streptomyces *as a host for secretion of heterologous proteins for the production of biopharmaceuticals*

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Published on Behalf of the Institute of Business Administration at the Department of Chemistry and Pharmacy, Westphalian Wilhelms-University Muenster, Germany

SUBSCRIPTION

The Journal of Business Chemistry (Print ISSN 1613-9615, Online ISSN 1613-9623) is published every four months by the Institute of Business Administration at the Department of Chemistry and Pharmacy, University of Münster.

Online-Subscription is possible at subscription@businesschemistry.org.
Free download is available at www.businesschemistry.org.

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PUBLISHER

The Journal of Business Chemistry (ISSN 1613-9615) is published by the Institute of Business Administration at the Department of Chemistry and Pharmacy, Westfälische Wilhelms-University, Leonardo-Campus 1, 48149 Münster, Germany.

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 ISSN 1613-9615

Letter from the Editors

Trends in Biotechnology

Opportunities and Threats for Developing Countries!?

Abstract: Biotechnology is one of the “hot spots” in research and development in this century. Great chances and opportunities lie ahead, but also tremendous threats. While technology and knowledge is easily available all over the world, it can be quite difficult to access markets and to commercialize biotechnological products. What are the main obstacles? What are the newest scientific insights? How can developing countries bring biotechnology successfully to the market?

Biotechnology, regardless of red, green or white biotechnology, promises high profits. However, the field is also complex, fast moving and costly. Especially in the field of medical applications there are many risks associated with biotechnology. One example is a drug developed against multiple sclerosis, which had possible profits of 3$ billion. After two patients developing a rare brain disease in clinical trials the profits vaporized and the stock market were in an uproar. Nevertheless does the United Nations Development Program see “biotechnology innovation and globalization as a means of helping the poor of the world live fuller, richer and more secure lives”. Only through commercialization this promise will come true.

Commercialization is converting or moving technology into a profit making position [1]. What are the major problems? How to commercialize biotechnology best? And as most research in this area focuses on either the US or Europe: What are the specific problems companies and institutes in developing countries face?

In our opinion the most important point is to bridge the gap between technology and markets. The matching of technological challenge and market challenge is difficult and many tools have been developed to address this problem [2]. Why does this problem still exist?

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First of all there is always a difference in doing business and doing science. And second, taking into account the enormous amounts of publications in the field of biotechnology each year, it is obvious that it is very difficult to keep up with the fast moving technology on the one hand and the market developments on the other. In an extreme case, e.g. nutraceuticals, you have both the fast moving biotechnology and the fast moving food market.

In this Special Issue of the "Journal of Business Chemistry" we address the problems of biotechnology, especially in Latin American countries like Cuba or Brazil.

The 14th International Scientific Congress CNIC 2005 in Cuba – with many sessions devoted to biotechnology and the commercialization of it – gave a good overview of the developments in this field. This Congress was organized by the Cuban National Center for Scientific Research (CNIC), which was founded in 1965. Currently it is devoted to scientific research in important fields like natural, biomedical and technological sciences.

This Congress (from June 27th to 30th) had as a slogan "40 Years at the Service of Science and Technology" and was an ideal space for meeting foreign (250 delegates) and national (600 delegates) specialists in different fields of scientific research. Many research topics were discussed, to mention just a few: Natural Products from Plants and Phytotherapeutical Products, II Symposium on Infectious Diseases: Vaccines and Adjuvants, Diagnosis, Immunology, Molecular Biology and Proteomics, Systems for Fast Diagnosis in Microbiology and the First International Symposium on Scientific-Technological Prospects.

From this International Conference very few papers were selected and then again reviewed by the "Journal of Business Chemistry".

Although there were many good works, we could not take all articles. We tried to get a very varied overview of the topic from a scientific, commercial and social point of view and thank all authors for their great contributions.

This Special Issue (Vol. 2, Issue 3) on Biotechnology of the "Journal of Business Chemistry" will give some new insights into protein expression and its possible use in disease treatment, as well as an example of a political initiative in Brazil to foster nano- and biotechnology. We also present articles with some interesting patent analysis and others, which give a theoretical social and techno-economic point of view.

For the first time, we also have a commentary section in the "Journal of Business Chemistry" where people can discuss their opinion in certain fields connected to the articles presented.

For us it seems clear that one can only be successful in "bringing biotechnology to the market" by cooperating with others. This might be true especially for small companies and companies in developing countries. First, firms should develop a sense of what they can do best and what their strategy is. Second, they should find the right partner for fulfilling the aims. Thus biotechnology might yield high profits for all!

[1] Siegel, R.A., Hansen, S., Pellas, L.H. (1995) Accelerating the commercialization of technology: Commercialization through co-operation; *Industrial Management & Data Systems*, Vol. 95 (1), pp. 18-26

[2] Maine, E., Probert, D., Ashby, M. (2005) Investing in new materials : a tool for technology managers, *Technovation*, Vol. 25, pp. 15-23

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Stefan Picker and Beatriz Garcia

Commentary

Different Rhythms of Health Biotechnology Development in Brazil and Cuba

Halla Thorsteinsdóttir[*#], Tirso W. Sáenz[**], Peter A. Singer[*], Abdallah S. Daar[*]

* Canadian Program on Genomics and Global Health, Joint Centre for Bioethics, University of Toronto, 88 College Street, Toronto, Ontario, Canada, M4G 1L4

** Centro de Desenvolvimento Sustentable, University of Brasilia, SHIN QL 11, Conjunto 4, Casa 11 Lago Norte, Brasilia DF CEP: 71 515 745, Brazil

\# Correspondence to: halla.thorsteinsdottir@utoronto.ca

Abstract: Biotechnology is typically associated with the centres of learning and firms in industrialised countries but usually not with institutions in developing countries. Developing nations are however, becoming active in this field and are increasingly using recombinant methods to produce new and innovative health products for their populations. Here we will examine health biotechnology development in two developing countries, Brazil and Cuba. We will compare the major characteristics of their health biotechnology sectors and highlight factors that have shaped their development in order to understand better what main factors and conditions can promote health biotechnology innovation in developing countries.

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Introduction

Even though the biotechnology sector is dominated by some of the richest countries in the world, developing countries are increasingly making their mark on the field. Biotechnology can be used to address various health problems of people in developing countries and contribute towards better global health [1-3]. Furthermore, developing countries themselves have been shown to be active in this field; they are engaged in health biotechnology research and are increasingly using recombinant methods to develop new and innovative products for their populations [4]. There is increasing recognition that instead of importing solutions for their health problems, developing countries can innovate and find solutions locally [5]. Our previous research on health biotechnology innovation has supported this observation [6]. We examined health biotechnology development in seven developing countries that have demonstrated successes in this field. Amongst them were Brazil and Cuba [7,8]. Here we will compare the development in these two countries and discuss the major factors that have shaped the characteristics of their health biotechnology sectors. We chose Brazil and Cuba as they are amongst the most advanced countries in the Latin American and the Caribbean region in terms of health biotechnology. They share important characteristics that can influence activities in this field but have at the same time followed quite different routes in their developments.

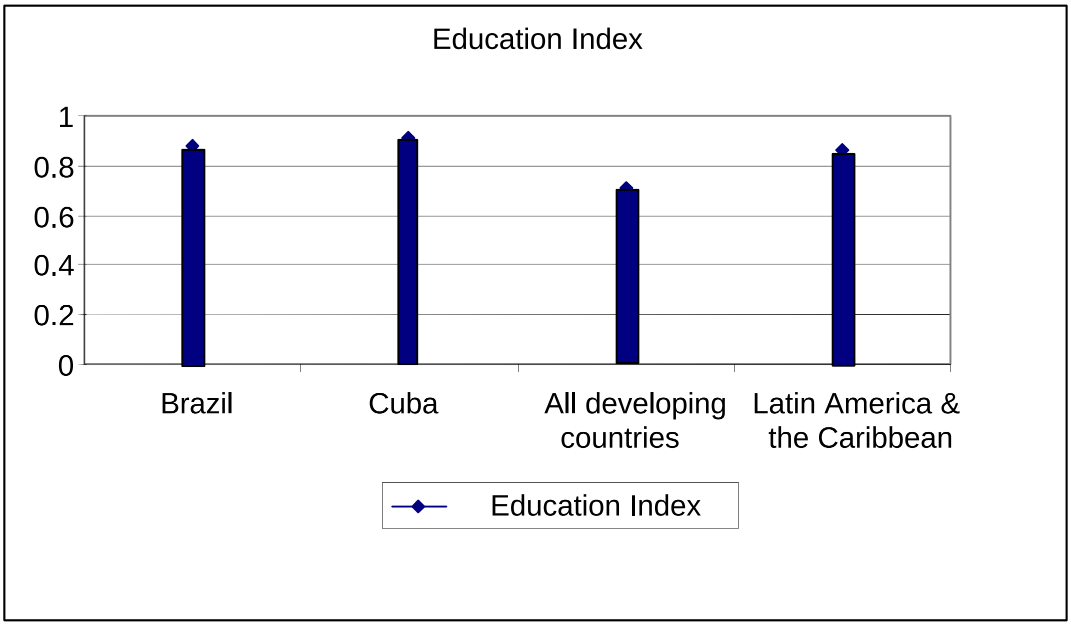
What Brazil and Cuba share

Both Brazil and Cuba are developing countries that fit the World Bank's lower middle income category [9]. The GDP/Capita is US$7770 for Brazil (ranked 63 of 177 countries) and US$5259 for Cuba (ranked 91 of 177 countries) and their ranks in the human development index are 52nd for Cuba and 72nd for Brazil [10]. On the other hand Cuba and Brazil share the characteristic that they have a relatively high educational level. Figure 1 demonstrates that both Cuba and Brazil have populations with relatively high education levels with education indices well beyond the averages for developing countries. Life expectancies are also relatively high in both countries, especially in Cuba where it has reached developed countries' levels.

In addition, Brazil and Cuba share the characteristic that their governments emphasised health biotechnology development relatively early on as biotechnology was taking off in the 1970s and 1980s. In Brazil two programmes that featured biotechnology development were launched in the 1970s by Brazil's National Research Council (CNPq), the Integrated Programme on Genetics (PID) and the Integrated Programme on Tropical Diseases (PIDE). In 1981, the government set up the National Biotechnology Programme (PRONAB) to integrate activities in the different types of biotechnology. Since then further programmes have been set up to promote biotechnology development and despite frequent turnover, the governments have continued to support biotechnology [7,11].

The Cuban government also singled out biotechnology as a promising field in the early 1980s and gave strategic importance to its development [8,12]. They promoted education in the field and set up various institutions to engage in biotechnology. They also created an interdisciplinary forum for biotechnology development the so called Biological Front, in 1981 which had the task to explore the potentials of biological sciences for Cuba. The support of the Cuban government for biotechnology development did not waiver during the hardship of the so called ´Special Period´, in the early 1990s after the disintegration of the Soviet Union and Cuba's major Eastern European markets.

An additional characteristic that Cuba and Brazil share that can influence health biotechnology development is that they are members of the World Trade Organisation (WTO). Both countries have been members of the WTO since 1995 and are signatories of the Trade-Related Aspects of Intellectual Property (TRIPS) agreement. They started to implement TRIPS in 2005, which will make it difficult for them to export products without licensing if those are already patented by others. Both countries have



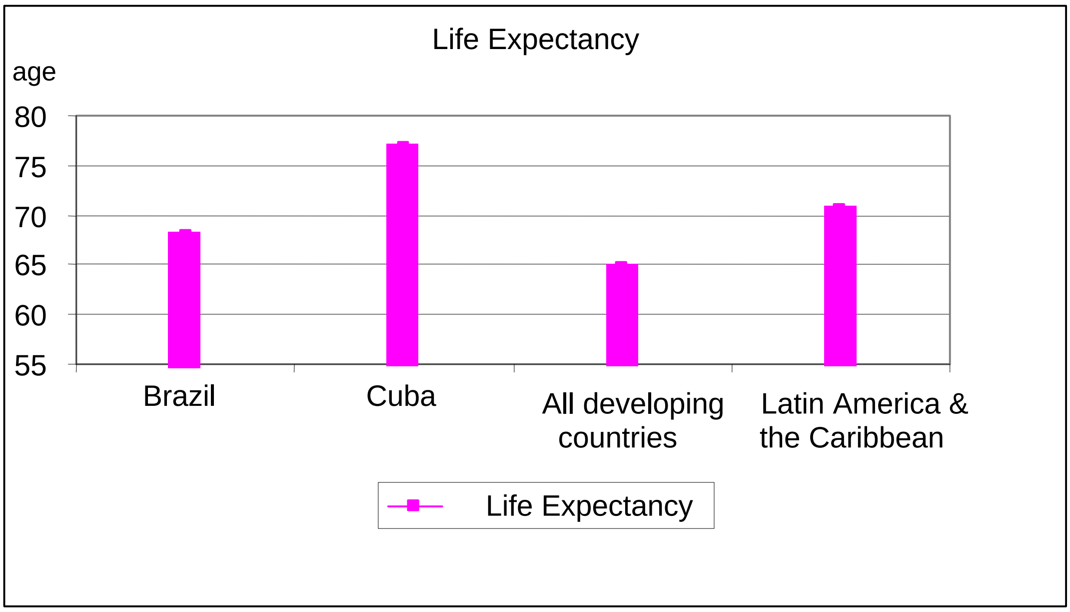


Figure 1: Education and Life Expectancies in Brazil and Cuba Compared to Other Developing Countries (Source: UNDP, Human Development Report 2004)

been driven to revise their intellectual property systems and set up more stringent patent regulations than they previously had. Their health biotechnology sectors therefore are gearing up to become innovative in order to sustain and surpass their current activity levels.

How Brazil and Cuba differ

With regards to the health biotechnology sector the major difference between Brazil and Cuba are the types of activities they emphasise. In Brazil the focus has been stronger on more fundamental research and publishing in high impact journals whereas in Cuba the emphasis has been more on developing new and innovative health biotechnology products. This does not mean that Cuba does not have its share of scientific publications or that Brazil has not developed an innovative health biotechnology product but rather the bulk of activities seem to be focused on these different types of activities, respectively. In Figure 2 we show the number of papers published in health biotechnology in the international peer reviewed literature by authors in the two countries over the period from 1991 to 2002. As can be seen the level of publishing is substantially higher in Brazil than in Cuba. This can partly be explained by a much larger population size and much larger scientific community in Brazil than in Cuba. The citation rate of Brazilian papers is also higher than Cuban papers, or 0.63 average relative citation level (1991-2002) for Brazil versus 0.45 for Cuba [13]. Brazil also has significant strengths in agricultural biotechnology. For example, it was the first country to sequence the genome of a plant pathogen, Xyllella fastidosa, which is a bacterium that attacks citrus fruits [21].

When comparing the product portfolios in health biotechnology of Cuba and Brazil, the latter displays a more modest success. A recombinant human insulin product developed in the 1990s by the Federal University of Minas Gerais and the Brazilian biopharmaceutical firm Biobrás was identified by Brazilian experts to be one of the best examples of Brazilian innovation in this field [7]. Brazil also has a strong diagnostic sector and has for example developed a recombinant antigen test for Chagas disease [14]. In general Brazil has had difficulties capitalising on its strong publication record in biotechnology, as the Minister of Science and Technology, Eduardo Campos stated ‘Brazilians get lost between basic research and its transformation into technology, between academic life and the manufacturing system [15].

Cuban health biotechnology has, however, a very applied focus with an impressive product portfolio. One of the early examples of Cuban innovation in this field is the world’s first meningitis B vaccine developed in the late 1980s. Cuban innovation has continued and includes, for example, humanized anti epidermal growth factor receptors monoclonal antibodies against head and neck tumours as well as the world’s first human vaccine with a synthetic antigen against pneumonia and meningitis introduced in 2004 [16,17]. James Larrick, a biotechnology expert and entrepreneur in Palo Alto, California says for example, the following about Cuban biotechnology: “Their pipeline is very, very deep now …. It’s gone into an adolescence and it’s looking pretty good” [18].

Cubans have been active in licensing and setting up strategic alliances and joint ventures based on Cuban biotechnology with companies around the world. They have, for example, made an agreement with GlaxoSmithKline to produce and distribute the meningitis B vaccine in Europe and North America; a joint venture with the Canadian firm YMBiosciences to develop and market cancer therapeutics; an agreement with the US firm CancerVax to undertake joint development and licensing of Cuban cancer vaccines; a strategic alliance with the Indian firm Panacea Biotec to manufacture hepatitis B vaccine in India; and joint ventures with the Chinese firms Beijing Jingyitaixiang Technology Development, Shanxi Xinyutong Material Commerce and China International Science Centre for cancer research. Despite a relatively small population size and limited economic resources Cuba has been able to build up an enviable track record in biotechnology products.

ISSN 1613 – 9615

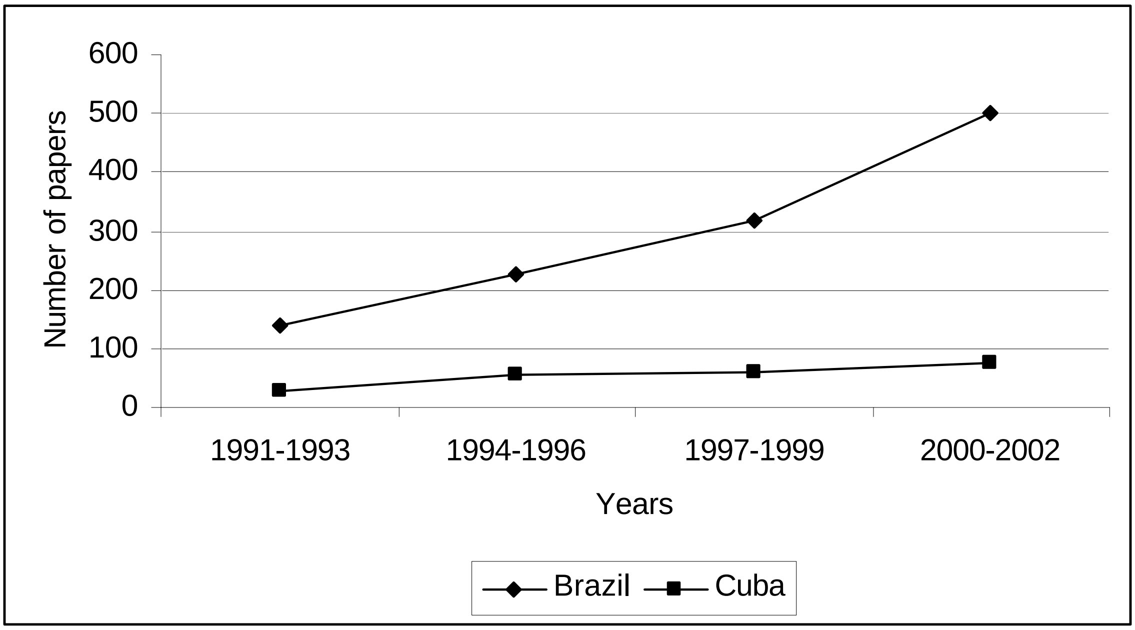


Figure 2: Number of papers in health biotechnology in Brazil and Cuba, 1991-2002
Source: Science-Metrix (data from Science Citation Index Expanded, ©Thomson ISI)

What explains the differences in health biotechnology between Brazil and Cuba

Innovation is a complex process so a multitude of factors and conditions can explain the differences in health biotechnology development between Brazil and Cuba. Here we will briefly highlight a few factors we believe to have played a strong role in shaping the development but a more complete discussion of those factors is beyond the scope of this paper.

1. Governmental involvement.

In Brazil promoting health biotechnology has been the mandate of the Ministry of Science and Technology whereas in Cuba the development of the sector has been under the auspice of the Council of State, the highest decision making power in the country and championed by its President Fidel Castro. As a result the successes in Brazil have been confined to the science and technology sector and not well aligned with industrial and commercialisation development.

In Cuba the biotechnology sector has had a high national priority and its development has been tightly connected to industrial and foreign affairs policies. An emphasis on health biotechnology fits especially well with the Cuban strategy of promoting health, education and sciences.

2. Domestic linkages.

In Cuba the public research institutes, such as the Centre of Genetic Engineering and Biotechnology (CIGB, Havana), the Finlay Institute (Havana) and the Center of Molecular Immunology (CIM, Havana) are the main actors in health biotechnology. They, for example, published over 97% of health biotechnology papers covered in the international peer reviewed journals from 1991 to 2002 [13]. The institutes cover a breath of activities including research, development, manufacturing, quality control and commercialisation. The fact that all these activities are under the same leadership is likely to make the knowledge flow and integration between these activities easier.

In Brazil, universities, together with such public research institutions as the Oswaldo Cruz Foundation (FIOCRUZ, Rio de Janeiro) and the Institute Butantan (Sao Paulo), are the main actors in the health biotechnology sector. Universities published 80% of the Brazilian health biotechnology papers in the international peer reviewed journals in 1991-2002, whereas the public research institutes published 31% [13]. Both of the main public research institutes in Brazil share with the Cuban institutes the characteristic of being involved in a variety of activities in health biotechnology which include, for example, manufacturing. Knowledge flow to and from Brazilian universities and public research institutes is, however, limited as they are not well connected to enterprises [7,19]. University professors are often sceptical about close associations with companies and until recently there was a decree prohibiting university professors to be employed by industry. A recent Innovation Law altered this and makes it possible for university professors to work for a limited time for the private sector. As a result knowledge may flow more easily between universities and the private sector in Brazil and the formation of university spin-off companies can be stimulated.

3. Connection with the health system.

The connections between the main actors of the health biotechnology sector and the health system are much better aligned in Cuba than in Brazil. In Brazil, public procurement policies demand that the lowest cost products are purchased by the public health system. This requirement may constitute a responsible public policy but can squeeze out local biotechnology endeavours especially when large multinational companies temporarily underbid local suppliers. The public procurement policy led the health system in Brazil to choose recombinant insulin from Novo Nordisk (Bagsværd, Denmark) over a locally developed product produced by the Brazilian biotechnology company Biobrás. The price difference between these products was small but the decision to purchase led to the downfall of the Brazilian biotechnology company and ultimately it was acquired by Novo Nordisk [7,20].

Cuba's health biotechnology sector is closely aligned with the health system. Cuban products are preferred to be imported ones in order to save foreign currency. The government has also harnessed the expertise in the health biotechnology sector to address domestic health problems. That was, for example, the case when the meningitis B vaccine was developed. A special research group was formed to come up with a vaccine candidate to address a meningitis outbreak in the country. In general the knowledge flow between the health system and the health biotechnology sector is active and the information from health practitioners has been said to spur innovative ideas [8].

It is evident that Cuba and Brazil have different strengths and weaknesses in the health biotechnology field. There is tremendous scope for them to learn from each other's experience. So far there has been limited collaboration between these two countries in the health biotechnology field. The presidents of Brazil and Cuba have however singled biotechnology out as a field where they intend to promote closer co-operation [22]. From our analysis it will certainly be a mutual advantage for these two countries to collaborate. To combine the scientific strengths of Brazil with the product development expertise of Cuba will be for the benefit of both countries.

Conclusion

In general, the bulk of health innovation in the world is focused on the lucrative markets of the industrialized countries. Limited efforts are aimed at developing countries' health needs. With rampant health problems in developing nations and massive health inequities in the world, it should ultimately be the goal of health biotechnology sectors in developing countries to develop new and innovative health products for their own populations rather than to focus solely on the markets in richer countries. It is encouraging when we observe successes in this respect and see developing countries that have built up impressive capacity to address health needs in this field as is the case of Brazil and Cuba. Still, health biotechnology is a risky field and it is difficult to predict how these countries will fare in the future. They will face stiff competition from industrialized countries that have actively promoted the biotechnology field for many years. They will also face competition from other developing countries active in this field such as India. It remains to be seen what approach is going to be successful in the long run to follow product led or science led development. In any event these two countries have much to learn from each other and to teach other countries in the region and around the world. Stronger south to south collaboration between countries such as Brazil and Cuba is a promising strategy that can strengthen the rhythm of biotechnology created for and by developing countries.

Acknowledgements

Grant support: The Canadian Program on Genomics and Global Health is primarily supported by Genome Canada through the Ontario Genomics Institute, and the Ontario Research and Development Challenge Fund. Matching partners are listed at www.geneticsethics.net. ASD is supported by the McLaughlin Centre for Molecular Medicine. PAS is supported by a Canadian Institutes of Health Research Distinguished Investigator award.

References

[1] WHO, *Genomics and World Health. A Report of the Advisory Committee on Health Research*. 2002, World Health Organization.: Geneva.

[2] Daar A.S., et al., *Top 10 biotechnologies for improving health in developing countries.* Nature Genetics, 2002. 32: p. 229-232.

[3] Juma, C. and Y.-C. Lee, *Innovation: Applying Knolwdge in Development*. 2005, UN Millennium Project: Task Force on Science, Technology and Innovation: London, Sterling Va. p. 1-220.

[4] Thorsteinsdóttir H., et al., Introduction: Promoting global health through biotechnology. *Nature Biotechnology*, 2004. 22(Supplement): p. DC3-DC7.

[5] Morel, C.M., et al., Health Innovation Networks to Help Developing Countries Address Neglected Diseases. *Science*, 2005. 309(5733): p. 401-404.

[6] Thorsteinsdóttir, H., et al., Conclusions: Promoting biotechnology innovation in developing countries. *Nature Biotechnology*, 2004.

[7] Ferrer M., et al., The scientific muscle of Brazil's health bitechnology. *Nature Biotechnology*, 2004. **22**(Supplement): p. DC8-DC12.

[8] Thorsteinsdóttir H., Sáenz T.W. et al., Cuba - innovation through synergy. *Nature Biotechnology*, 2004. **22**(Supplement): p. DC19-DC24.

[9] The World Bank., *World Development Indicators*. 2005, The World Bank http://www.worldbank.org/data/wdi2005/index.html

[10] UNDP, *Human Development Report 2004: Cultural Liberty in Today's Diverse World*. 2004, United Nations Development Program: New York.

[11] Oda L.M., Correa Soares B.E., and V.-I. M.C., in *Biotechnology in Developing World and Countries in Economic Transition*, Tzotzos G.T. and S. K.G., Editors. 2000, CAB International: Wallingford, UK.

[12] López-Saura, P., *Cuba*, in *Biotechnology in the Developing World and Countries in Economic Transition*, T. GT and S. KG, Editors. 2000, CABI Publishing: Wallingford.

[13] Science-Metrix, *Benchmarking of Genomics and Health Biotechnology in Seven Developing Countries, 1991-2004*. 2004, Report prepared for University of Toronto, Joint Centre for Bioethics: Montreal. p. 1-67.

[14] International Buisness Strategies, *The Biotechnology Market in Brazil*. 2003, International Buisness Strategies: Los Gatos, California, USA.

[15] Cruvinel T.A., *lei da inovacao.* Panorama Político O Globo, 2004.

[16] Thorsteinsdóttir, H., et al., Cuba - innovation through synergy. *Nature Biotechnology*, 2004. **22**(Supplement): p. DC19-DC24.

[17] Verez-Bencomo, V., et al., A Synthetic Conjugate Polysaccharide Vaccine Against Haemophilus influenzae Type b. *Science*, 2004. 305(5683): p. 522-525.

[18] Kaiser, J., Glycobiology: Synthetic Vaccine Is a Sweet Victory for Cuban Science. *Science*, 2004. 305(5683): p. 460

[19] Dantas E., The 'system of innovation' approach, and its relevance to developing countries. *SciDev Net*, Policy Briefs, 2005.

[20] Sutz J. *Strong life sciences in innovative weak contexts: A "developmental" approach to tantalizing mismatch.* A presentation at the Bringing Science to Life. conference 2005. Toronto.

[21] Simpson, A.J.G. et al, The genome sequence of the plant pathogen Xylella fastidiosa, *Nature*, 2000 (406), pp. 151

[22] Carribean Net News, 2003; http://www.caribbeannetnews.com/2003/09/28/cuba.htm

Research Paper

Streptomyces as a host for the secretion of heterologous proteins for the production of biopharmaceuticals

Carlos Vallin[*#], Elsa Pimienta[*], Astrid Ramos[*], Caridad Rodriguez[*], Lieve Van Mellaert[**] and Jozef Anné[**]

* Department of Biomedical Research , Center of Pharmaceutical Chemistry, Atabey, Playa, Havana , Cuba PO Box 6990, Tel. (537) 2085236 ext.276; Fax (537) 2736471
** Laboratory of Bacteriology, Rega Institute, K.U.Leuven, Leuven, Belgium
\# Correspondence to: val@infomed.sld.cu

Abstract: The commercial production of therapeutic or diagnostic proteins in recombinant micro-organisms is of considerable interest. Several microbial protein production systems have been developed. So far, *Escherichia coli* have been the commonly employed host. However, proteins expressed in this host remain intracellular and often precipitate as inclusion bodies, which may seriously complicate downstream-processing. Faced with this problem, several genera of Gram-positive bacteria are being tested as host for the production of heterologous proteins due to their ability to efficiently secrete proteins in the culture medium. Among them is the genus *Streptomyces* since several of its species are known to secrete high amounts of proteins. Due to the absence of an extensive restriction-modification system, limited protease activity and the availability of suitable vector systems, *Streptomyces lividans* is the host of choice for the secretory production of heterologous proteins. The presented results show, that *S. lividans* can act as an interesting host to produce a number of proteins useful in several disease areas important in the worldwide pharmaceutical sales: i.e. oncology, immunology, cardiovascular diseases and infectious diseases.

  ISSN 1613-9615

Introduction

Streptomyces

Streptomycetes are Gram-positive soil microorganisms that produce a wide variety of secondary metabolites, many of which have potent biological activities. They produce more than half of the known biologically active microbial products, including many commercially important antibiotics, immunosuppressive compounds, animal health products, and agrochemicals [1,2,3]. They also produce various enzymes that are commercially and academically valuable as extracellular enzymes capable of degrading lignocellulosics [4,5]. This vast reservoir of diverse products makes *Streptomyces* one of the most important industrial microbial genera and consequently, a battery of tools for genetic manipulation of this germs is available [6]. *Streptomyces coelicolor* A(3)2 is genetically the best characterised *Streptomyces* strain. However, over the past years, *Streptomyces lividans* 66 or its derivatives were evaluated as potential host for heterologous protein production [7,8,9]. Secretory production of heterologous proteins by-passes the problem of inclusion body formation in the cytoplasm a problem encountered in the commonly used *E. coli* system. Additional advantages of *S. lividans* include very efficient secretion directly into the growth medium, the absence of lipopolysaccharides and simple genetic manipulation, and low-protease activity. *Streptomyces lividans* has been used for the heterologous secretion of several polypeptides of bacterial and eukaryotic origin. In most cases, heterologous genes are fused to signal sequences from highly expressed/secreted proteins [10].

Recombinants proteins production

The production of recombinant proteins by microbial fermentation is a main research topic in many bio-industries [11,12]. The Production of therapeutic proteins will increase 15% annually the next 5 years Examples: The worldwide sales for therapeutics IFN α (+PEGylated) will be aprox. $2700 million as Antitumor/Anti-HIV [13].

For a variety of biological and technical reasons, proteins of therapeutic or commercial interest are synthesized in either eukaryotic or prokaryotic systems. The most extensively used prokaryotic system *Escherichia coli*, offers several advantages including growth on inexpensive carbon sources, rapid biomass accumulation, amenability to high cell-density fermentations and simple process scale-up. But problems with inclusion body formation, rapid heterologous protein degradation and the need to purify the protein of interest free of endogenous protein often makes downstream-processing very labor-intensive and thus expensive. These drawbacks drive to search for alternative production systems. As a consequence, a variety of expression platforms has been described ranging from Gram-negative and Gram-positive prokaryotes, over several yeasts and filamentous fungi to mammalian cells [14,15,16,17].

In this study we investigated showed the feasibility of *Streptomyces lividans* as a host for the expression/secretion of the therapeutic proteins, human interferon alpha 2b (HuIFNα-2b). Hui*fna2b* cDNA was fused to signal sequences of well-expressed native genes. Under appropriate fermentation conditions, significant amounts of mature biologically active HuIFNα-2b could be recovered from the spent growth media.

Materials and Methods

For expression studies, *S. lividans* derivatives were cultured in a suitable liquid medium (10% sucrose, 1% yeast extract, 1% glucose, 0.5% NaCl, 0.5% soya fluor, 1.7% triptone, 0.25% K_2HPO_4) at 27°C and 300 rpm.

HuIFNα-2b from culture supernatants of *S. lividans* transformed with pAΔXS, pUCIAS, pOVsiIFN or pOW15 was detected by immunoblot and ELISA according to Sánchez et al. (1998) [18].

Results and Discussion

Secretion of human interferon alpha 2b (HuIFNα–2b) by *Streptomyces lividans*

The interferons are a multigene family with a broad range of biological properties, including potent antiviral, antiproliferative and immunomodulatory activities.

The cloning the *huifna2b* cDNA was achieved through recombinant DNA technology [17]. The large-scale production of this protein for therapeutic purposes using *E. coli* was achieved several years ago but the overexpression of HuIFNα-2b in *E. coli* leaded to the formation of inclusion bodies. In this study, *S. lividans* was used as an alternative host for the obtainment of HuIFNα-2b. Therefore the cDNA was placed under control of the regulatory sequences i.e. promoter, Shine-Dalgarno and signal sequence of *Streptomyces venezuelae* subtilisin inhibitor (vsi) gene or *Streptomyces exfoliatus* M11 Lipase A (lipA) gene. The results of the immunoblot analysis of secreted HuIFN α-2b are shown in the fig.1. The ELISA results and obtained antiviral titers of HuIFNα-2b secreted by recombinant strains of *S. lividans* are shown in table 1.

Plasmid pAΔXS encodes a fusion protein L*ipA*-sp/HuIFNα–2b maintaining nine additional amino acid residues of mature LipA between the LipA signal peptide and HuIFNα–2b. [pUCIAS] encodes a fusion protein L*ipA*-sp/HuIFNα–2b with three additional amino acid residues of mature LipA at the border of the fusion pOVsiIFN encodes a fusion protein *Vsi*-sp/huIFNα–2b containing two amino acid residues of mature *Vsi* between the *Vsi* signal peptide and HuIFNα–2b.

The protein HuIFNα–2b was thus expressed in *S. lividans* and subsequently secreted into the medium. The yield obtained for this protein and their biology activity results demonstrated the potential of *S. lividans* as an alternative host for E.coli aiming the production of HuIFNα-2b.

Sample	mg/L	IU/L
S. lividans TK24 [pAΔXS]	0.58197	9.4 x 107
S. lividans TK24 [pUCIAS]	0.22566	1.8 x 107
S. lividans TK24 [pOVsiIFN]	0.23590	0.9 x107

Table 1: ELISA results and Antiviral titers of *S. lividans* TK 24 recombinants (Interferon-induced antiviral activity was determined by the inhibition of the cytopathic effect of mengovirus on Hep-2 cells)

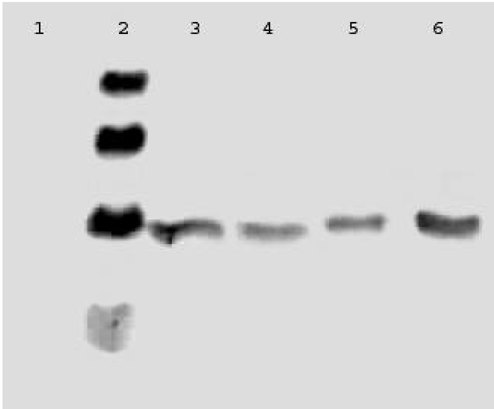


Figure 1: Immunoblot analysis of secreted HuIFN α-2b. Lanes:

1 20µl *S. lividans* TK24 [pOW15] culture supernatant

2 Prestained SDS-PAGE standard, Bio-Rad, Carbonic anhydrase 38.289 kDa, Soybean trypsin inhibitor 29.678 kDa, Lysozyme 20.669 kDa, Aprotinin 6.969 kDa

3 20µl *S. lividans* TK24 [pAΔXS] culture supernatant

4 20µl *S. lividans* TK24 [pUCIAS] culture supernatant

5 20µl *S. lividans* TK24 [pOVsiIFN] culture supernatant

6 25 ng of reference HuIFN α

Conclusions

The presented results show, that *S. lividans* can act as an interesting host to produce a number of proteins useful in several disease areas important in the worldwide pharmaceutical sales: i.e. oncology, immunology, cardiovascular diseases and infectious diseases through a cost effective production systems. Although proteins of prokaryotic origin are in general more efficiently produced than eukaryotic proteins in *Streptomyces lividan*. Yields can be optimized using strong promoters and efficient translation signals of well-expressed native genes. Furthermore translocation signals can be modified in order to improve heterologous protein production [14]. As such for each biopharmaceutical protein a tailor-made secretion strain can be constructed.

Future developments of the fermentation processes will be investigated in order to evaluate the industrial applicability of the engineered strains and downstream processing will be optimized allowing the most efficient recovery of the secreted proteins from the culture broth.

References

[1] Goodfellow, M., and Williams, S., (1983), Ecology of Actinomycetes, *Ann. Rev. Microbiol*., 37, pp 189-216.

[2] Morosoli, R., Shareck, F., and Kluepfel, D., (1997), Protein secretion in streptomycetes, *FEMS Microbiol. Lett.*, 146, pp 167–174.

[3] Connell, ND. (2001), Expression systems for use in actinomycetes and related organisms, *Curr Opin Biotechnol*, 12, pp 446-449.

[4] Diaz, M., Adham, S.A., Ramon, D., Gil, J.A., Santamaria, R.I.,(2004), Streptomyces lividans and Brevibacterium lactofermentum as heterologous hosts for the production of X22 xylanase from Aspergillus nidulans, *Appl. Microbiol. Biotechnol.*, 65, pp 401-406.

[5] Morosoli, R., Shareck, F., and Kluepfel, D., (1997), Protein secretion in strepto-mycetes. *FEMS Microbiol Lett.*, 146, pp 167–174.

[6] Hopwood, D.A., Bibb, M.J., Chater, K.F., Kieser, T., Bruton, C.J., Kieser, H.M., Lydiate, D.J., Smith, C.P., Ward, J.M., and Schrempf, H., (1985), Genetic manipulation of *Streptomyces:* A laboratory manual. Norwich, C.T: John Innes Foundation.

[7] Anne, J., and Mellaert, L.V., (1993), *Streptomyces lividans* as host for heterologous protein production, *FEMS Microbiol. Lett.*, 114 pp 121–128.

[8] Binnie, C., Cossar, J.D., and Stewart, D.I.H. (1997), Heterologous biopharmaceutical protein expression in Streptomyces. *Trends Biotechnol.*, 15, pp 315-320.

[9] Gilbert, M., Morosoli, R., Shareck, F., and Kluepfel, D., (1995), Production and secretion of proteins by streptomycetes, *Crit. Rev. Biotechnol.*, 15 pp 13–39.

[10] Lammertyn, E., Van Mellaert, L., Schacht, S., Dillen, C, Sablon, E., Van Broekhoven, A., and J. Anné (1997) Evaluation of a novel subtilisin inhibitor gene and mutant derivatives for the expression and secretion of mouse tumor necrosis factor alpha by *Streptomyces lividans*, *Appl. Environ. Microbiol.*, 63, 1808-1813.

[11] Noack, D., Geuther, R., Tonew, M., Breitling, R., and Behnke, D., (1988), Expression and secretion of interferon-alpha 1 by *Streptomyces lividans:* Use of staphylokinase signals and amplification of a neo gene, *Gene*, 68, pp 53–62.

[12] Binnie, C., Jenish, D., Cossar, D., Szabo, A., Trudeau, D., Krygsman, P., Malek, L.T,, and Stewart, D.I., (1997b), Expression and characterization of soluble human erythropoietin receptor made in *Streptomyces lividans* 66, *Protein Expr. Purif.*, 11, pp 271–278.

[13] Das, R.C., (2003), Progress and prospects of protein therapeutics (application note), *American Biotechnology Laboratory*, October 2003, pp 8-12.

[14] Lammertyn, E., and Anne, J., (1998), Modifications of *Streptomyces* signal peptides and their effects on protein production and secretion, *FEMS Microbiol. Lett.*, 160, pp 1–10.

[15] Bender, E., Koller, K.P., and Engels, J.W., (1990), Secretory synthesis of human interleukin-2 by *Streptomyces lividan*, *Gene*, 86, pp 227–232.

[16] Harth, G., Lee, B.-Y., and Horwitz, M.A. (1997), High-level heterologous expression and secretion in rapidly growing nonpathogenic mycobacteria of four major *Mycobacterium tuberculosis* extracellular proteins considered to be leading vaccine candidates and drug targets, *Infect. Immun.*, 65, pp 2321–2328.

[17] Silva, A., Menendez, A., Ubieta, R., Montero, M., Torrens, I., Morales, J., Santos, A., Gonzalez, M., Jimenez, V., De la Fuente, J., Santizo, C. and Herrera, L., (1991), Expresión de Interferones Humanos en *E. coli*, *Biotecnol. Apl.*, 8, 400–405.

[18] Sánchez JC, Padrón G, Santana H, Herrera L (1998) Elimination of an HuIFN a2b readthrough species, produced in *Escherichia coli*, by replacing its natural translational stop signal, *Journal of Biotechnology.*, 63, 179–186.

Research Paper

Science and Society in Cuba in the Context of Techno-economic Globalization

Aqueil Ahmad[*#]

* The Department of Sociology, University of North Carolina, Greensboro, NC 27402, U.S.A.
# Correspondence to: a_ahmad@uncg.edu

Abstract: This paper is in continuation of the author's earlier work on Cuba. It builds upon a similar presentation at the 14th International Scientific Congress held in Havana, Cuba in late June-early July 2005. The eclectic theoretical background for this analysis is provided by the general Modernization Theory and the World System Theory. The focus is on the problems and prospects for the development of science and society in Cuba within the context of interdependent economic and technology relations in global society. It is argued that the recent experiences of some of the other newly industrializing non-western societies may be highly instructive for Cuban development planning in the 21st century.

ISSN 1613 – 9615

Introduction

Globalization is opening up new opportunities for techno-economic development in the newly industrializing countries. The notion of techno-economic development in the context of globalization implies an interdependent relationship between technological and economic development in that one dovetails the other. It also implies that economic and technological activities in both the developed and the developing countries are now increasingly interconnected, shared, and traded through multilateral arrangements, such as international patents, licenses, royalties, joint ventures, outsourcing, and a variety of other human and financial capital transfers [1,2]. Participation in these activities requires major shifts in public and international policies of nations to align their developmental priorities with the realities of a globally interdependent world [3,4]. For the developing countries, participation in this global techno-economic system is no longer a matter of choice. It is a necessity for their survival and growth. But it is a necessity that involves both costs and benefits. These must be weighed in terms of short and long term social, economic, political, and environmental consequences that such participation entails [5,6]. This paper will highlight recent shifts and alignments that are now occurring globally and discuss some of their implications for the development of science, technology, and society in Cuba in view of its current strengths and weaknesses.

There is paucity of information in the international literary sources about science, technology, and society relations in Cuba. The following analysis is duly informed by my two visits to Cuba – in June 2000 and June-July 2005. During these visits, I participated in a number of meetings, seminars, and symposia and interviewed numerous Cuban scientists, scholars, and educators. Following the first visit, a detailed study on the implications of globalization for Cuban society was published in the fall of 2001 [7]. The implications were examined through the opposite perspectives of general Modernization Theory and the World System or the Dependency Theory [8,9,10]. The conceptual framework for this analysis also resides in the critical dimensions of the very same perspectives. Informed by these perspectives, it is assumed that the correct path for overall development of the less developed societies at this historical juncture lies somewhere between independence and dependence, between autarky and subservience.

It is argued in this paper that globalization of technology has made it possible for a developing country with Cuba's knowledge base to buy or borrow from abroad appropriate technologies for local needs, as well as to undertake collaborative R&D (research and development) with international partners. Cuba should also be able to transfer locally developed products and processes from areas of particular strength (e.g. biotechnology) to other developing countries according to their own specific needs. Such multidirectional transfers are now occurring in almost all the major scientific fields [11]. But if not planned and executed properly, they may pose serious threats to local cultures, economies, and environments [12, 13].

Globalization of Technology: Opportunities and Threats for Cuba

Some of Cuba's scientific and technological strengths and weaknesses are shared by almost all the developing countries. These include abundance of natural and human resources while their full utilization is often marred by shortages of capital, advanced technologies, and other internal and external pressures. This is not to deny the special problems and inventiveness to resolve them that may be unique to particular societies. The Cuban experience too is indeed unique in many ways. Pre-revolutionary Cuba was a corrupt and bankrupt society. In 1958, it experienced one of the most significant social revolutions of the 20th century, only to face massive problems of redistribution of national resources for the common good, while threatened and embargoed by its powerful neighbor next door. This turmoil notwithstanding, Cuba's resolve to build an effective science, technology, and education infrastructure for societal development has remained unshaken for the past half a century.

ISSN 1613 – 9615

> "Today, Cuba is a society where some consumer goods are not available. But not a single school has been closed, nor a single hospital, nor are there children that sleep in the street for lack of shelter, nor the sick left abandoned for their survival. In spite of the present day difficulties, the average Cuban today retains a strong safety net that his or her counterparts lacked in the pre-revolutionary era" [14].

Cuba, and the rest of the world, are now faced with a new reality – the reality of a global society where a lot can be gained but a lot can also be lost. Globalization can lead to fast techno-economic and societal development in nonwestern societies, as it has already done in Japan, South Korea, Taiwan, and Hong Kong, and is now doing in China, India, and a host of other Asian and Latin countries. The hallmark of this experience is opening up to the rest of the world. But as suggested above, that could also be risky. Nascent local industries may suffer through international competition. Indigenous R&D efforts may be pushed to the back seats. Environmental pollution may set in otherwise unpolluted environments. Either wrong choices or missed opportunities to collaborate, buy or borrow in the global techno-economic market could cause serious developmental disabilities. Two cautionary notes are in order to help avoid these two types of errors. First, globalization of technology may neither be an unqualified boon nor an unmitigated bane for national development. Second, globalization, and its twin process of modernization, should not be rejected as a neo-colonial westernization of nonwestern societies; for none of these processes is entirely western or entirely new [15].

Cross-cultural fertilization of ideas and transfer of knowledge, goods, and services has been going on for centuries, although not always with positive intentions or results [16]. In the contemporary world system, serious techno-economic, and consequently political, power shifts are now occurring globally as countervailing forces to hegemonic power of few nations over the many [17,18]. The old dichotomies between East and West, Third World and First World, the core and the periphery are no longer entirely valid [19,20,21]. These shifts can work for the benefit of developing countries. For example, there are powerful competing vendors of modern technologies around the globe. If one of them refuses to supply or sell these to a buyer for whatever reasons, there may be others willing to do so on competitive terms, as Cuba has learned to its enormous advantage in building its tourist, transport, and energy industries [22]. Such options and opportunities need to be carefully assessed and exploited by every developing country in need of advanced scientific and technical knowledge.

Cuba has a long history of planned development of science, technology, industry, and agriculture to serve human needs. It also has a long history of regional and international collaboration in these areas, first with the Soviet Block, and now with many European, Asian, and Latin countries. Cuba is an effective member of the North, Central, and South American community of nations, except the United States, which continues to ignore and blockade it. Canada, Mexico, Venezuela, Chile, and Brazil, for example, have established good economic and industrial relations with Cuba. Its abundant natural and human resources are effectively utilized in an increasingly diversified economy through such bilateral arrangements [23].

Biotechnology in Cuba

Like China and India, Cuba has shown the wisdom of combining its vast reservoir of ancient and modern knowledge to serve human needs. This intermixing is clearly seen in Cuba's biotechnology research, inventions and innovations, among the strongest in the developing countries. Biotechnology has received the greatest attention in the Cuban national science and technology policy. This policy began to take shape as early as 1964 with the inception of the parent research outfit called the National Center for Scientific Research (CNIC). CNIC spawned a number of other research institutions over the years, among them the most notable and prestigious Center for Genetic Engineering and Biotechnology (CIGB) in 1986. A network of four or five other centers is now affiliated with CGIB, specializing in such fields as immunology and development and production of vaccines for human and animal diseases [24].

> "Some of CIGB's 160 products available in over 50 countries are a hepatitis B vaccine, human alpha interferon, certain enzymes, diagnostic kits including one for HIV, and a cattle tick vaccine" [25].

The list of CIGB accomplishments is endless. Currently it is pushing the development of HIV/AIDS and hepatitis C vaccines. Biotechnology may be the single-most important area in which Cuba can contribute to, as well as learn a great deal from other advanced players in this emerging scientific frontier. Further dissemination of these technologies globally would indeed require for Cuba to acquire international patents for its innovations and market them aggressively. This strategy was strongly recommended by several authors at the 14th International Scientific Congress in Havana during June 27-July 1, 2005, which I also attended along with approximately 1000 Cuban and international scientists [26, 27].

A small indication of Cuba's contribution and potential in the field of biotechnology was clearly visible at the 14th International. A significant portion of the Congress's agenda was devoted to the treatment of human, animal, and plant diseases through the eclectic approach of mixing folk knowledge with modern science. The symposium on biotechnology had 20 separate sessions simultaneously held in the large and modern convention center. Over 200 papers were presented in these sessions, mostly by Cuban scientists. There is urgent need for affordable treatment to improve human, plant, and animal health around the developing world. Cuban biotechnology research can indeed help fill this gap effectively and humanely.

Careful Considerations for the Future

Despite these accomplishments in biotechnology and other areas, gaps remain in several other areas. For example, Cuba's manufacturing and service infrastructures for consumer and electronics goods, automobile and aircraft industries, computer engineering and information sciences in general have a long way to go before reaching world standards. Advanced technology vendors in these and other deficient areas should be encouraged to enter the country at this stage in Cuba's march to modernity. But a well-endowed nation like Cuba need not be too dependent on the global technology system, and consequently on the global economy. A healthy balance between independence, dependence, and interdependence should be worked out. These options may not be available to lesser developed countries with meager natural, human, and scientific resources.

As mentioned above, unchecked and deregulated entry of foreign capital and technology in a less developed country involves many risks. At the same time, too many restrictions on external inputs can quickly set back a developing country by decades, for such is the fast pace of global scientific and technological change. These types of experiences are not uncommon in the recent history of newly industrializing nations. The cases of both India and China may be highly instructive for the Cuban technology transfer strategy at this time in terms of costs and benefits of closing and opening up to the world techno-economic system as well as the costs and benefits of centralized control versus decentralized initiative and enterprise [28, 29].

I raise the following questions for further consideration of the Cuban science, technology, and development policy makers at the highest levels.

1. What does it mean to be self-reliant in the context of globalization? It certainly does not mean delinking from the global techno-economic system, for it is virtually impossible to do so and be able to survive. No country, not even the United States or any other major world economy is or can be totally self-reliant any more. The motto, long proposed by various organs of UNESCO (United Nations Educational, Scientific, and Cultural Organization) ought to be: "Make some, borrow some, and buy some."

2. What should be the role of national science, technology, industry, and education in a rapidly globalizing, interdependent world? This is a vital question for a country like Cuba with substantial

local strengths in all these areas. Cuba, like other similarly situated countries, will have to find its own specific formulas in light of the above motto. Systematic demarcation of local strengths and weaknesses in each area will have to be done with one goal in mind - social, cultural, and economic development. It is through such demarcations that Cuba can participate in the process of globalization as an equal partner and fully benefit from it.

3. How to share Cuba's unique experience of pressing science, technology, industry, and education to serve human needs with other developing countries? International agencies, like the UNESCO and UNDP (United Nations Development Program), may take an active role in bringing the Cuban experience to the attention of others through conferences, joint research programs, scientific exchange, and transfer of technologies.

4. How to balance the acts between global information processing and participating in the global research, development, and manufacturing networks? Some developing countries – India, the Philippines, and the new members of the European Union are prime examples - are diverting their valuable technical expertise to information processing and customer service for giant multinational corporations. While this aspect of globalization may be mutually beneficial in the short run, such outsourcing may not prove beneficial either to the 'source' or the 'outsourced' in the long run. Cuba may tread on this false 'technology transfer' path with great caution.

5. How to further enhance the development and utilization of the national human capital? Cuba has made substantial investments in science and engineering education at all levels. But a significant number of its workforce is employed in the non-technical tourist industry. In order to fully participate in the global techno-economic system, the future generations of Cubans in both rural and urban areas need to be technically trained through distance education using advanced information technologies, with assistance from outside vendors.

6. How to build stronger scientific communities at the national level? Cuba may consider: (a) Making bigger investments in science and engineering education at all levels by providing more scholarships, upgrading research laboratories, and modernizing instructional technologies in colleges and universities. (b) Building closer connections and exchange between Cuban and international scientific communities.

Endnote

Cuba is a small island nation with a large potential for scientific and technological modernization for social and economic development. It has overcome many hurdles in achieving these goals through a combination of local efforts and international collaboration and assistance. Its policy of planned but cautious approach to mobilize natural and human resources to build an effective developmental strategy and infrastructure seems to fall within a mixed rubric of Modernization and World System theories. This approach has helped Cuba achieve a measure of success without becoming an appendage of the global capitalism which runs through the global techno-economic system. But it has also slowed down the pace of modernization of science, technology, and society in Cuba. The dizzying pace of economic growth in the newly industrializing countries suggests that the massive sweep of globalization is insensitive to ideological, national, racial, or cultural differences. The winning strategy in this sweep is to remain focused on enlightened self-interest and to use one's own competitive advantage to exploit the explosion of opportunities in the wider world. In this context, greater participation in the global techno-economic system through international collaboration seems highly desirable at this time for Cuba in its continuing march to modernity and a rightful place for it in the community of nations – embargo or no embargo.

References

[1] Wayne Ellwood, *The No-Nonsense Guide to Globalization*. New York, U.S.A.: St. Martin's Press, 2000.

[2] Aqueil Ahmad, "*Globalization of Technology: A New Paradigm in International Development.*" Paper presented at the Annual Meeting of the American Sociological Association -

Section on Science, Knowledge, and Technology, Atlanta, GA, U.S.A., August 24-28, 1988.

[3] Robert B. Reich, *The Work of Nations.* New York, U.S.A: Alfred A. Knopf, 1991.

[4] A. Goskin Samli, *In search of Equitable, Sustainable Globalization.* Westport. CT, U.S.A.: Quorum Books, 2002.

[5] John Tomlinson, Cultural Imperialism: *A critical Introduction.* London, U.K: Continuum International Publishing, 1991.

[6] Wolfgang Sachs, Planet Dialectics: *Explorations in Environment and Development*. London, U.K.: Zeda Books, 1999.

[7] Aqueil Ahmad, "*Globalization and the Developing Countries, with Especial Reference to Cuba*." Globalization, 1, 1, fall 2001, pps. 27. (www.globalization.icaap.org/content/v1.1/aqueilahmad.html)

[8] Stephen K. Sanderson & Arthur S. Alderson, "*Economic Development and Under-development,*" Chapter 9 in Sanderson & Alderson, World Societies. New York, U.S.A.: Pearson Education, 2005, pp. 183-218.

[9] Immanuel Wallerstein, *The Modern World System*. New York, U.S.A.: Academic Press, 1974.

[10] Samir Amin, *Unequal Development: An Essay on Social Formation of Peripheral Capitalism.* New York, U.S.A.: Monthly Review Press, 1976.

[11] *Global Knowledge Flows and Economic Development.* Organization for Economic Cooperation and Development (OECD), Paris, France, 2004.

[12] Joseph E. Stiglitz, *Globalization and its Discontents.* New York, U.S.A.: W. W. Norton, 2000.

[13] *The Sienna Declaration on the Crisis of Economic Globalization.* www.twnside.org.sg/title/sienna-cn.htm

[14] Jose Bell Laura, "*Preface,*" in Cuba in the 1990s. Instituto Cubano del Libro, Havana, Cuba, 1999, p. 8.

[15] Amartya Sen, "*How to Judge Globalism.*" The American Prospect, 13, 1, January 2002, pp.1-14.

[16] Aqueil Ahmad, "*Globalization: Boon or Bane.*" Share the World's Resources (STWR), London, U.K., 2004. pps. 7. (www.stwr.net/articles2/articlesIIahmad.htm)

[17] Jessica T. Mathews, "*Power Shift.*" Foreign Affairs, 76, 1, January/February, 1997

[18] Susan Strange, *The Retreat of the State: The Diffusion of Power in the World Economy.* Cambridge, MA, U.S.A.: Cambridge University Press, 1996.

[19] Kenichi Ohmae, *The End of the Nation State: The Rise of Regional Economies.* Glencoe, IL, U.S.A.: The Free Press, 1995.

[20] Robert O. Keohane & Joseph S. Nye, "*Realism and Complex Interdependence*", in Keohane & Nye, Power and Interdependence, New York, U.S.A.: Longman, 2001, pp.3-7.

[21] "*China and the World Economy.*" Special Report, The Economist, July 30th-August 5th, 2005, pp.61-63.

[22] Aqueil Ahmad, "*Globalization and the Developing Countries, with Especial Reference to Cuba*" op.cit.

[23] "*Cuba's Economy: With Help from Oil and Friends.*" The Economist, January 15th-21st, 2005, p. 35.

[24] Harold Ramkissoon, "*Science and Technology in Cuba Today.*" (http://www.cariscience.org/casarticle01.htm)

[25] Ramkissoon, Ibid, p. 3.

[26] Lionel Scott, "*Opportunities in Life Science Exploitation.*" Paper presented at the 14th International Scientific Congress, Havana, Cuba, June 27-July 1, 2005.

[27] Stefan Picker, "*Prospects and Innovation in Biotechnology: Bringing New Technology to the Market.*" Paper presented at the 14th International Scientific Congress, Havana, Cuba, June 27-July 1, 2005.

[28] Aqueil Ahmad, *"China's Quest for Advanced Technologies: Nagging Questions,"* in D. Vajpayei & R. Natarajan, (eds.), Technology and Development: Public Policy and Managerial Issues. Jaipur, India: Rawat Publications, 1991, pp. 219-251

[29] Aqueil Ahmad, *"India's Quest for Technological Self-Reliance"*, in Y. Malik & A. Kapur, (eds.), India - Fifty Years of Democracy and Development. New Delhi, India: APH Publication Corp., 1998, pp. 213-253.

Research Paper

Propolis: Patents and technology trends for health applications

Dámarys Suárez*, Daniel Zayas*, Frenkel Guisado**

* Center of Beekeeping Research. El Cano. Arroyo Arenas. La Lisa, Postal Code 19190, Havana City, Cuba.
** National Center for Scientific Research, Cuba.
\# Correspondence to: damarys@eeapi.cu

Abstract: In this paper are shown the main trends for the use of propolis based on the patent or invention documents. Information is given on the owners, innovators, international patent classification, subject groups and priority countries. The obtained results show that propolis is a natural product of interest for the current technological and scientific world, since the innovation capability has been kept in the subjects studied in this work. There is remarkable work on the application of propolis for treatment and care of skin. Japan is known to be the leading country in the use of propolis in health care.

  ISSN 1613 – 9615

Introduction

Propolis is manufactured by bees from the sap of trees and flower blossoms. Propolis protects the beehive from penetration of harmful insects and aids in insulating the beehive, and maintaining a sterile environment.

Many studies have proven propolis' effectiveness in fighting viruses, bacteria and fungi, and as an anti-inflammatory agent. Propolis is known as Nature's Antibiotic, capable of fighting pathogenic (disease causing) bacteria, as opposed to conventional antibiotics which destroy all the body's natural flora. In addition, bacteria do not become resistant because many natural factors (the sap source, climate and geographical region) all indiscernibly yet significantly continually alter the natural composition.

Propolis strengthens the body's resistance to winter's ailments: infections, flu and colds. Propolis can be used externally to heal cuts, torn tissues and burns (up to second degree) and for surgical scars. Propolis has been found to be effective in the treatment of gum and mouth infections. It has been used for centuries as a folk remedy and has only in recent years been "re-discovered" by science resulting in comprehensive research regarding the active ingredients of propolis and its antibacterial properties [1].

The many functions of propolis include: nourishes face, postpones senility, softens blood vessels, purifies the blood, promotes reproduction of tissue, accelerates healing of injuries, refreshes vital energy, improves function of stomach and intestines, overcomes constipation, decreases blood fat and blood sugar, kills bacteria, fungus, and virus, improves capillary circulation, eliminates toxins [2].

Propolis helps regulate hormones and is an antibiotic substance that stimulates the natural resistance of the body. Propolis may be used by everyone, sick or healthy, as a means of protection against micro-organisms. Propolis is also efficient against conditions caused by bacteria, viruses of different fungi. It cures many diseases because it is a special natural substance with strong effect. The whole research program had a single purpose, namely, to investigate this substance against the great number of diseases mentioned, the numerous healings are relevant by themselves and the number of people using propolis is ever increasing.

In another paper by N. Popovici and N. Oita they set out to investigate the effects of propolis on Mitosis. Mitosis is a term for cell division, the procedure by which cells replicate themselves. In cancer, malignant cells divide by multiplying rapidly. Clearly a substance which might affect cell division is important in the management of cancer. It is not unusual for the body to harbour malignant cells [3].

From the information in patent documents regarding propolis, the research “Introduction to the analysis of trends of the propolis’ patents in project management and marketing” [4], was carried out. It provided interesting conclusions, such as the ascending trend in the development of inventions on the health-linked propolis application that were the basis for the performance of this study.

In this research, we perform an analysis of the invention documents related to the use of propolis in health, expressed as drugs, cosmetics or nutritional supplements. The processed patent documents contain highly valuable legal, economic and technical information, hence the results obtained from their processing, make it possible to obtain highly valuable information to reach conclusions useful as key elements for the design of R&D, technological survaillance, market studies, marketing strategies, etc.

The objectives of this paper are:

- To carry out a valuation on the current trends of the use of propolis in drugs, cosmetics or nutritional supplement in health care, from the analysis of the inventions recovered.
- To create a Database on Patents of Propolis in health applications. This will be a valuable source of information for the people involved in research, manufacturing and marketing of this product.
- To specify technology trends such as: the source countries, the technologies structure, etc.

Materials and Methods

Database of Patent Documents: The searches for information were performed on free-access databases in Internet:

- Delphion Patents Database [5]
- Esp@cenet Database [6]
- DEPATISNET Database [7]
- Canadian Intellectual Property Office (CIPO) Internet Database [8]
- United States Patents And Trademarks Office (USPTO) Internet Database [9]
- Cuban Industrial Property Office (OCPI) Digital Database [10]
- Japan Patents Office (JPO) Internet Database [11]
- INPADOC Database [12]

Automated System for Patents Surveillance (SiVigPat®) Version 3.1: The SiVigPat®, designed in the National Center for Scientific Research (CNIC), makes possible to process the patent information retrieved from some free-access Databases in Internet and to obtain the results as graphics and tables [13].

Scientific and Commercial Documentation in Internet on propolis, its applications and the trends of the international market.

The used methods were centered in the strategy of traced search that had as premise the definition of:

- Object of Search: Propolis (linked to the branch of the health)
- Objective of the Search: to determine aspects related with the introduction of the propolis in the health and their linking with market elements.

Strategy 1: Preliminary search of patents by key words:

To carry out the search of information was used the key word “propolis”, taking as universe the recoveries of the documents of Patents, for a better precision in the number of obtained patents.

All documents were processed by SiVigPat®, creating a general database. The documents were processed to determine the main owners, inventors and the international classifications of patents (IPC) of more incidences.

Strategy 2: Search of patents by inventors and owners:

To carry out the search were selected the names of the owners and inventors with more incidence from the results obtained in the database of patents processed from the search carried out according to the Strategy 1.

Strategy 3: Search of patents by international classification (IPC):

Later to the analysis of the results according to the international classification of patents (IPC) was carried out a complete search of the sub classifications of more incidences: A23L 1/076 that it is also specific for beehive products. And were eliminated the patents that didn't refer to the propolis (related with some other product of the beehive: like royal jelly, pollen, etc.).

Results

We performed a choice that allowed obtaining a database containing only the patents related to the fields of interest: drugs, cosmetics or nutritional supplements genuinely for health. The database is formed by 270 inventions selected from the criterion to clearly define their health-linked use or possible use, though it is not the objective claimed in the invention.

In Figure 1, the number of requests of patent documents (absolute value) filed per years is shown. In the period of 1972-1981, there was an average of 1.3 inventions per year; in the period of 1982-1990 there was an increase in the average number of patent documents to 7.3 inventions per year. This rate was increased even further in the 90ies (1991-2000) to an average of 19.4 inventions a year. Most patents, 138 inventions, were filed in the period of 1995-2000 (51.11 % of the 270 inventions included in the Database).

That rate could increase even more, since, the inventions corresponding to the 1997-2000 years can still increase, because some of the offices surveyed began to publish the patents filed from March, 2001, so there can be records of inventions corresponding to the last year still unpublished.

The studied subject is very important and the innovation capability persists in this field (drugs and cosmetics or nutritional supplements, whose aim is only their use for health care) since 1995.

Regarding the International Patents Classification (IPC), the higher number of inventions corresponds to the IPC: A61K (Preparations with medical, stomatological or cleaning purposes) and A23L (Food, nutritional supplements or soft drinks). The A61K classification also represents 53.6 % from the 138 documents processed in the period of 1995-2000.

By using the database created, we perform customized classifications or groups, completely independent of the IPC that make possible to adjust the trend results to the concrete purposes of the given analysis, corresponding in this case to 14 classifications. Figure 2 cumulatively shows the behavior of the inventive activity in the different groups for the 1972-2000 period, when a higher incidence in those products with medicinal, nutraceutical properties and with dermatological applications are obvious. We call “Medical Properties” those patent documents where the medical applications are diverse or do not have one particularly specified.

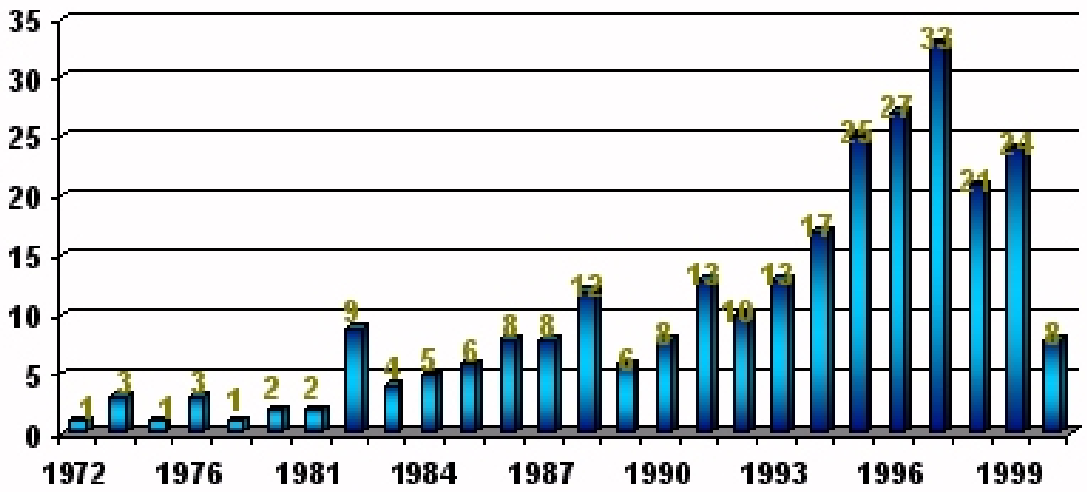


Figure 1: Number of filings (absolute value)

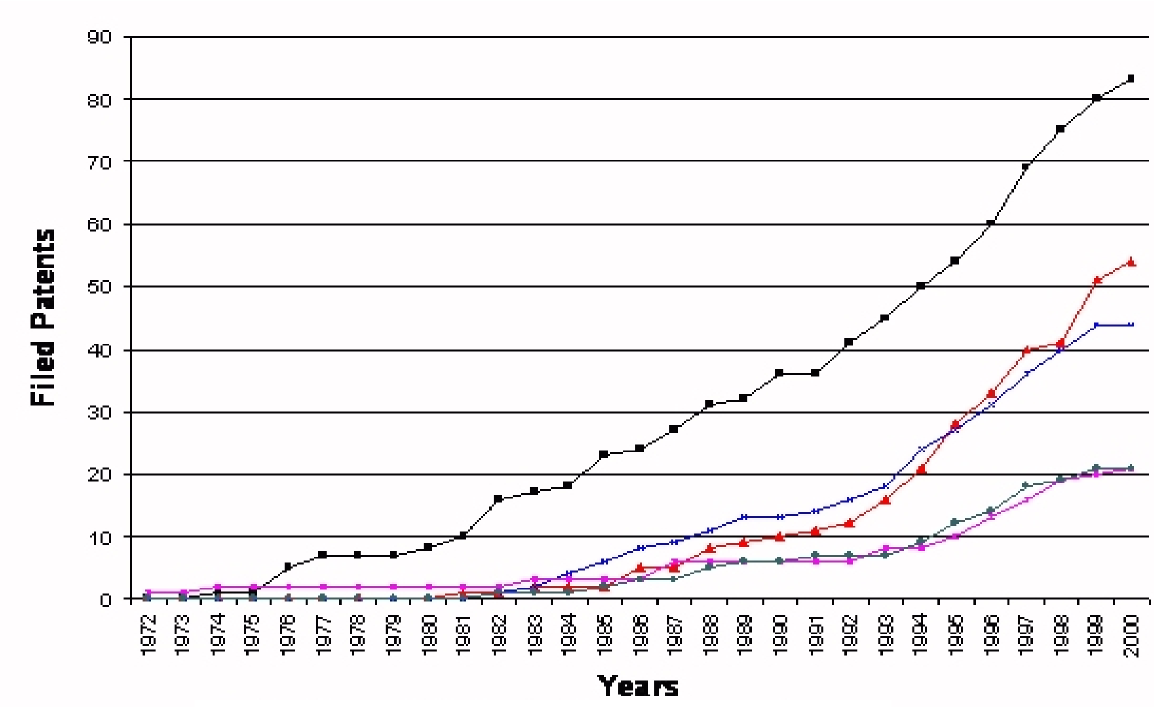


Figure 2: Trend of the patent filings according to group; other medical applications (filled square), nutritional (filled triangle), dermatology (double line), stomatology (small square), antimicrobic (circle)

Until 1993, the inventions referred to methods for preparing propolis and to formulations containing that product (Figure 3). But since then, the trend in this field is to protect the products (formulations) more than the extraction methods.

By analyzing the inventions processed according to their priority country (the country where the product is first filed), Figure 4 shows that the highest number of filings corresponds to Japan with 131 (48 %), followed by the United States with 28 (10 %), Germany and Hungary with 15 and 12 filings, respectively. As for the documents with Japanese priority, the most of them correspond to Japanese people.

There are 132 inventions filed by Japanese natives, this means that Japan is the country with the highest innovation activity with regards to the use of propolis for the studied groups. Japan imports almost all the propolis used in the country: 80% comes from Brazil, 10% from China and other countries [14]; this is shown in their inventions, since in the analysis carried out to the content of the Japanese inventions we can see that the Brazilian propolis is a target of invention [15].

From the analysis of the results obtained in this work, we observe that since 1972, the first invention linked to the use of propolis for therapeutic purposes was from German Democratic Republic (DD1972072165709: “Composition for treating periodontopathy”) [5]. All the filed patents linked to the use of propolis for therapeutic purposes in the 70s corresponded to European countries. In the 80s, the United States of America joined the European countries, with four patents filed. Since the Nagoya Conference, held in 1985, the efficacy of propolis started to be very much known in Japan and then new filings of invention started to be made in Japan.

Currently, Japan is the country that has filed the most patent requests in this field.

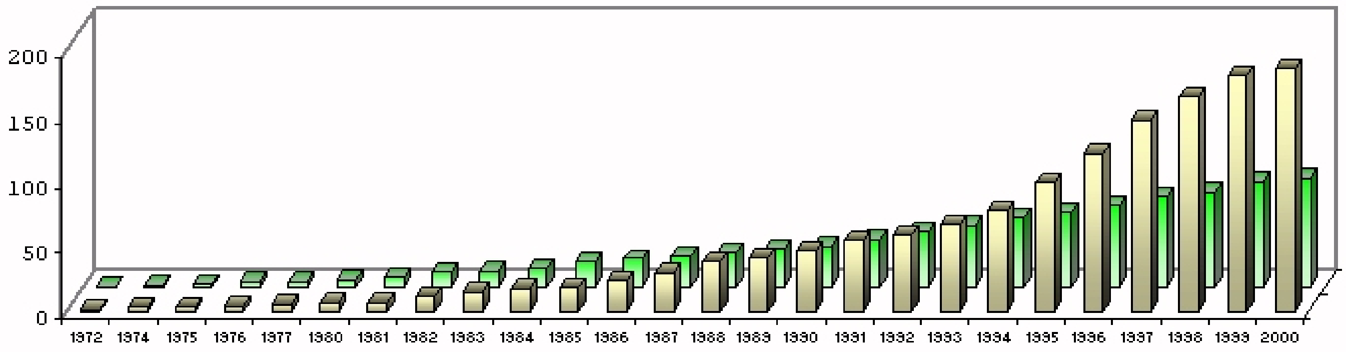


Figure 3: Trend to the patent filings (accumulated) according to the invention's features; in front: formulations, in the back: preparation methods (green)

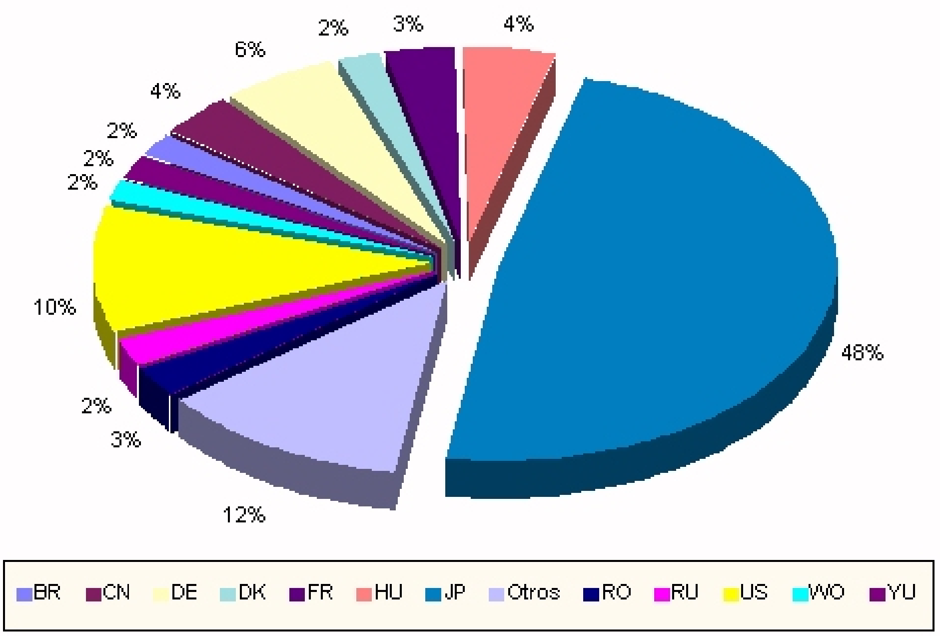


Figure 4: Total Percent of Patents by Priority Countries; US: United States of America, Otros: Others; JP: Japan; HU: Hungary; DE: Germany

Conclusions

- The use of propolis for the 1972-2000 period has been dedicated to the development of new products, especially in those products related to their medicinal and nutraceutical properties and with dermatological applications.
- The growing number of filings for the 1995-2000 period shows that propolis is a natural product of interest for the scientific and technological world at the present time, since the innovation capability shows an ascending trend in the fields that are the subject of this study (drugs, cosmetics or nutritional supplements).
- Japan and the United States appear in the first and second place as Source and Destination Country, so both countries are innovators and tributary of the inventions. Japan appears as the country with the most innovative strength in the field of propolis in the studied fields.

References

[1] *Propolis Health Products* www.propolishealth.com. 2000.

[2] *Propolis one of the oldest and successful medicines of the World.* www.natureproducts.net/Products/Propolis 2002.

[3] *Properties of Propolis* - a Description. www.apitherapy.biz/propolis/medicinal-properties-2 2002.

[4] Zayas, D. et al. : *Study of the Development of the Patents Concerning Propolis*. Memories from XXXVIII Internacional Beekeeping Congress of Apimondia, p. 256 – 257. 2003.

[5] *Delphion Patents Database* www.delphion.com.

[6] *Esp@cenet Database.* www.ec.espacenet.com.

[7] *DEPATISNET Database.* www.depatisnet.de.

[8] *Canadian Intellectual Property Office (CIPO)* patents1.ic.gc.ca/intro-e.html.

[9] *US Patents and Trademarks Office* (USPTO) www.uspto.gov/patft/index.html.

[10] *Cuban Industrial Property Office (OCPI)* Digital Database.

[11] *Japan Patents Office (JPO)* www.jpo.go.jp.

[12] *INPADOC Database* pk2id.delhi.nic.in.htm.

[13] García, B., Zayas, D.: *Manual de Usuarios del Sistema Automatizado de Vigilancia de Patentes*, SiVigPat®, v. 3.0. CNIC. 2002.

[14] *Miel y Propóleos*. Informe de la Embajada Argentina en Japón. www.embargentina.or.jp 1999.

[15] Dos Santos, A. et al. Propolis: *100 anos de pesquisa e suas perspectivas futuras*. Quim. Nova, Vol 25, No. 2, 321-326. 2002.

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Journal of Business Chemistry Vol. 2, Issue 3 September 2005
www.businesschemistry.org

Research Paper

Future Studies in Brazil

CGEE Approach for Bio- and Nanotechnology

Lelio Fellows Filho[*#], Dalci Maria dos Santos[*], Gilda Massari Coelho[*], Márcio de Miranda Santos[*]

* Center for Strategic Management and Studies – CGEE, Ed. Corporate Financial Center, sala 1002/3, 70712-900 – Brasília - BRAZIL

\# Correspondance to: lelio@cgee.org.br

Abstract: Companies and governments are increasingly using “Future Studies“ for the design of their strategic planning. Techniques and methodologies are in a very accelerated development all over the world. So it is necessary to establish the right set of tools and best way to use it in order to have results that you could compare and reproduce if you have in mind to generate inputs for either companies or countries policy definition. This article describes the methodological approach adopted by a Brazilian Institution – Centre for Strategic Management and Studies – CGEE, mainly devoted to future analyses, and uses the recent examples of the Biotechnology and Nanotechnology foresight exercises in Brazil to show the real use of their results in the process for definition of national strategies.

  ISSN 1613 – 9615

Introduction

Considering the increasing complexity of the decision making process, the speed of the technological changes and its economic and social impacts, the markets interdependence and the need of support for information coming from formal and informal sources internal and external to the organization, it is obvious that an organization, nowadays, depends more and more on an efficient system of knowledge management.

Considering the high levels of uncertainty with which the society is confronted, the area of strategic planning is being shifted from the traditional approach to a more dynamic one that considers the changes of current times. The studies developed under the denomination of foresight fill the space where there is an intersection between the fields of strategic planning, future studies and policy analysis.

Thus, future studies, foresight and technological forecast are important for strategic planning and for supporting the decision making process and public policies formulation, since they allow the anticipation of technological breakthroughs, trends and discontinuities, new perspectives and opportunities that are presented for a society from the identification of its challenges and potentialities.

Concerning different possible interpretations, the words in Portuguese “prospecção”, “prospectiva”, “exercícios prospectivos” or “estudos do futuro”, as well as its English versions, forecast, foresight, future studies, have become generic denominations - not free of controversies - for the diverse methodologies and approaches that try to answer questions presented by the challenges of the future, either for technologies and its impacts, or for important social issues.

In fact, trying to understand the potential risks and threats, analyzing the future and glimpsing new ways and opportunities that allow the choice of reasonable futures is not a trivial challenge and involves complex questions that must take into account many factors of social and technical nature and different realities and situations.

It is important to emphasize that foresight, forecasting and future studies are fields in constant evolution and that countries and organizations are in search of models, tools, methodologies and concepts that can face the challenges of the future.

This paper presents not only the conceptual and theoretical model elaborated by the Centre of Management and Strategic Studies - CGEE to guide its foresight activities but also some examples of the use of this model, and represent some results already obtained by the Centre.

Science, Technology and Innovation and the role of the Centre of Management and Strategic Studies – CGEE

Brazil and the world are experiencing a significant movement represented by a new look at the importance of science, technology and innovation as transforming agents of the society. The search for solutions on emergent social problems, the formulation of future strategies, as well as the exercise of democratization, that can make possible the participation of the society in the construction of a desired future, points out the necessity to diversify the economic tissue, to rescue cultural values and the process of planning and management of public goods and the environmental questions, preserving the national identity.

Despite its recognition for the exploitation of the economic and regional national potentialities, the Brazilian historical path in the last decades lacks the strengthening in relation to the construction of a nation with a modern economy, integrated to the global markets, with internationally competitive industries, high investments in science and technology, strong ecological conscience and with an operating structure in the concretion of citizens social rights and in the development of the social tissue in more democratic basis.

Initiatives towards structuring a broad spectrum policy of science, technology and innovation, capable of facing some of the emergent questions in the scientific and technological fields, have been part of the national agenda in 2002. This happened, among other factors, as a result of the Brazilian Conference on Science, Technology and Innovation (ST&I) and the publication of the

Green and the White Books on ST&I, representing a new movement that stimulated the country to insert the technological innovation as one of the main objectives of the national efforts of science and technology.

In this context, CGEE was created as an institution which aims at promoting and accomplishing future studies and foresight in the field of science, technology and innovation, as well as the activities of evaluation of strategies and economic and social impacts of scientific and technological policies, programs and projects. Moreover, CGEE acts on the dissemination of information, experiences and projects to the society. One of its main features is its capacity of communication and interaction with the science, technology and productive sectors.

CGEE's strategy was based upon the perception that decision making emerges of a negotiation between multiple actors. This perception was the key point of the methodology known as foresight, which can be defined as a process that leads to a more complete understanding of the forces that shape the future and that must be considered in the formulation of policies, planning and decision making [1]. It means that this approach aims to link the present actions to a strategic perspective, coping with the possibilities of the future for the construction of commitments and coordination concerning the national priorities of research and innovation.

Based upon some of the concepts developed by the European Union, CGEE considers foresight as an activity that connects three different dimensions on the same process: thinking, debating and shaping the future [2].

Moreover, the structuring of communication channels and the process of coordination in different levels points out to the importance of the governance process that must guarantee the validation of technological opportunities identified during the process by the different stakeholders and be transformed into concrete actions by decision makers. Thus, CGEE has a pro-active attitude regarding the future, stimulating the search for an institutional culture of foresight, with a global vision of science, technology and innovation, which estimates complexes mechanisms of interaction, exchange of information, experience and feedback among different involved actors [3].

CGEE's prospective approach

There is an extensive list of studies related to exploring the future. In a simple examination of literature it is possible to find different denominations for "families" or conceptual structures, such as technological forecasting, technological foresight, social foresight, inclusive foresight, technology assessment, monitoring (environmental scanning, technology watch), prospective networks, roadmapping, scenarios studies, multicriteria decision analysis, etc [4]. This has generated some problems in the terminology. Therefore, the elaboration of simple and direct models and the establishment of different levels of scope and use of such methods, techniques, methodologies and tools becomes rather complex.

As a result, it is common to find techniques developed for specific objectives being used to answer questions of broad and complex nature. This, in certain cases, contributes to discredit this field. This also confirms how difficult it is to face the uncertainties about the future. The reflection on the different approaches is necessary as a way to improve the activity and its results.

Nowadays, the approach called foresight is the most used methodology to assist the establishment of research and development priorities and to promote the alignment of R&D and Innovation policies to the economic and social needs of the countries.

Foresight includes qualitative and quantitative ways to monitor indicators of development trends, and is better and more useful when directly linked to the analysis of policies and its implications. It prepares people for future opportunities.

In the government, foresight does not define policies, but it can help them to be more appropriate, more flexible and more robust in its implementation, in changing times and conditions.

The theoretical model organized to guide foresight in CGEE is presented in figure 1. This model was created taking into account the methodological structure proposed by Horton[5] and improved by the ideas of Conway and Voros

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[6], as well as the orientations of the Handbook of Knowledge Society Foresight [7] and Godet [8].

CGEE's approach also considers that many forms of analyzing future technology and its consequences coexist, for example, technology intelligence, forecasting, roadmapping, assessment, and foresight. All of these techniques fit into a field called technology futures analysis (TFA) by Porter et al. [4]. New methods need to be explored to take advantage of information resources and new approaches to complex systems. Examination of the processes sheds light on ways to improve the usefulness of TFA to a variety of potential users, from corporate managers to national policy makers. CGEE methodology tries to have an open mind about the several TFA forms and to introduce new approaches from other fields incorporating new methods and processes to better inform technology management as well as science and research policy.

Understanding the Process

Foresight studies constitute powerful assistants in planning and managing uncertainty levels. However, they must be placed in a planned context, that is, to be based upon pre-established policies and needs. Its effectiveness is intrinsically linked to an adequate methodological proposal and planning, which include: a correct delimitation of the questions to be answered; the type of desired replies; the spatial orientation; the scope of the issue; the strategic focus; the time horizon; the institutional and experts mobilization; the choice of the methodology; the target audience, its extent frequency and reach; the establishment of partnerships; the relationship with ongoing initiatives; the dissemination strategies; the available infrastructure, duration and cost. A very important step is the constitution of a network of stakeholders, able to articulate and reach the necessary consensus and commitments aiming to the implementation of the identified plan of action. (Figure 1)

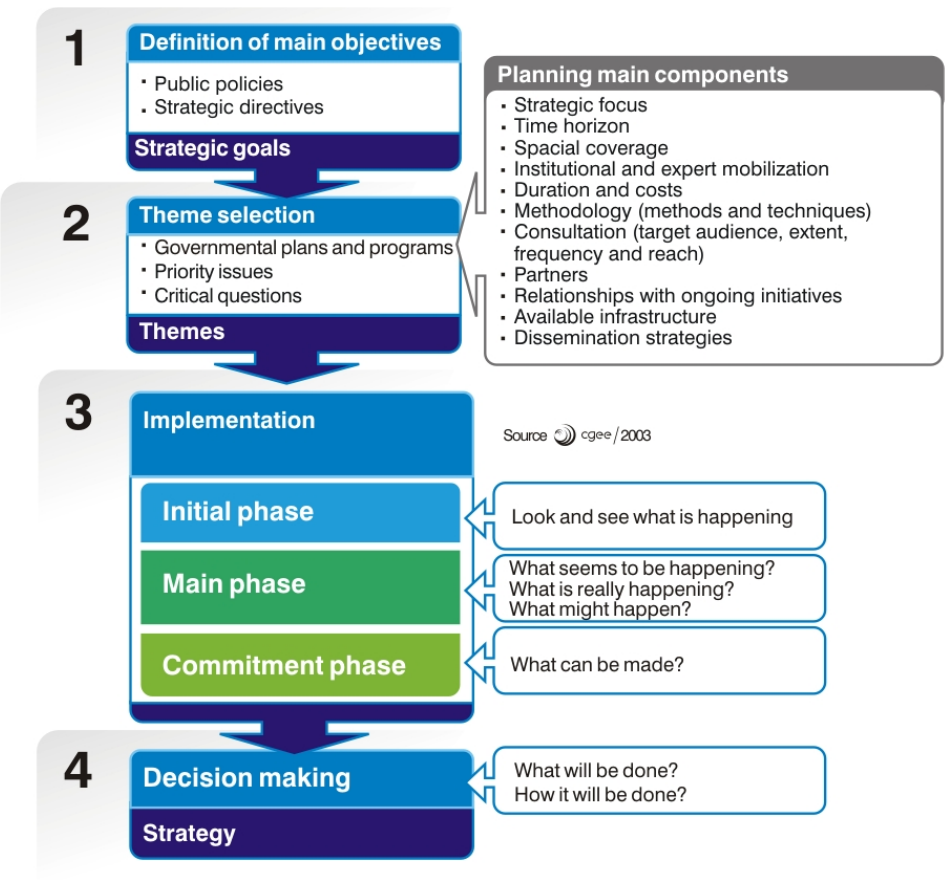

Figure 1: CGEE methodological foresight approach

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The management of foresight exercises in CGEE tries to follow the theoretical model, considering four great sets for its implementation: definition of objectives, theme selection, implementation and decision making.

Definition of Objectives

The definition of objectives is established between CGEE and its clients, which are mainly governmental institutions, as the Ministry of Science and Technology and the Nucleus of Strategic Affairs of the Presidency of the Republic. The objectives are related to public policies and strategies of the federal government and consider also the characteristics of the subject or sector that will be studied and the arising needs of the Brazilian society. Many times, the studies are anchored in governmental plans and programs, as the studies developed to subsidize the application of Science and Technology Sector Funds. (Table 1)

Identification of Themes

Once the strategic objectives are defined, the priority themes that answer the critical questions are selected.

For each selected theme, it is made a rigorous planning, that takes into account the strategic focus, the time horizon, the space scope, the institutional and expert mobilization, duration and costs, the choice of the methods and techniques that will compose the methodology. It also considers the target public of the research, considering its extension, frequency and reach, possible partners of the initiative, the available infrastructure, the relationship with the initiatives in progress and the strategy of dissemination. After all this information is obtained, the exercise can effectively begin. (Table 2)

Examples of objectives defined for foresight studies carried out by CGEE to attend the demands of the federal government, addressing the establishment of public policies and priority areas of investment in R&D:

Biotechnology

Mapping challenges and opportunities for biotechnology in Brazil, with particular focus on research, development, production, distribution and commercialization of genetically modified organisms (GMOs), as well as aspects related to public perception and the current Brazilian legal framework aiming at the enrichment of the democratic process and an improvement in the quality of policy-making relating to science and technology.

Nanotechnology

Mapping the current situation and future trends of nanotechnology in the country and worldwide, contemplating the identification of better investment choices in competitive niches for the Brazilian market.

Table 2: CGEE's experience: definition of objectives

Implementation of the Foresight Exercise

This step, in general, is divided in three phases. Each phase adds value in relation to the previous one creating a chain that turns information into knowledge and knowledge into strategy. Each phase has a higher level of complexity, diminishing the uncertainty level and increasing the potential of contribution of the results to the decision making process.

Initial phase

The question here is: *What is happening?*

This phase corresponds to the identification of the current situation, and involves the collection, organization and summary of the available information on the theme or subject under analysis, using for this purpose studies, diagnosis, organization and summary of the available information on the theme or subject under analysis, using for this purpose studies, diagnosis, analyses and intelligence systems in order to have a better understanding of the problem. **It means the collection and analysis of the explicit knowledge available.** Explicit knowledge means: formal models, processes, rules and procedures which can be communicated externally [10].

The themes, object of the prospective studies lead by CGEE, can be essentially scientific and technological or involve aspects related to the impacts of technology, environmental, economic or social questions and can be configured as sub-themes to answer to specific objectives.

Biotechnology

The choice of the themes of study on biotechnology presented peculiar characteristics. The challenges on the establishment of the legal framework and public perception in relation to the possible impacts of the technology have oriented this study to focus the boundary questions more than the scientific aspects properly said, approaching: economic impacts; evolution and consequences of the legal framework; applied metrology for biological products and processes; public perception about the commercial use of GMOs; technological and commercial strategies (long term perspective); financing mechanisms; impacts of the adoption of RR soybean; national competencies and skills in biotechnology; and intellectual property rights.

Nanotechnology

The strategies adopted worldwide in different institutional programs, the analysis of the investments by the private sector, the mapping of international scientific and technological research, the existing capabilities in Brazil (main groups of research, laboratorial infrastructure and international interactions of the research groups) have been the main constraints of the theme.

Table 2: CGEE's experience: identification of themes

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In this phase, to obtain a panorama of the current situation, CGEE uses different techniques and methods in its studies. The choice of the method or technique is made in accordance with the subject and the objectives of the study. In general, more than one technique or method is used, to obtain different or complementary visions on the same subject.

Biotechnology

Mapping of national capabilities, by searching on the Lattes databases, Directory of Groups of Research, etc; (www.cnpq.br)

Technological monitoring using text mining techniques (software Vantage Point) to get relevant information and trends from databases of scientific publications and patents, presenting a techno-scientific panorama of the subject.

Interviews with experts looking for primary and original information;

Trend analysis of the international legal framework on biosecurity in the following countries: European Union, United States, Argentina, Mexico, Colombia, Brazil, Australia, Japan, India, Indonesia, China and South Africa;

Trend analysis in Brazil of adoption of RR soybean identifying current impacts and future perspectives;

Evaluation of public perception in relation to new technologies, based upon synthesis of secondary material (state of the art, position papers, etc.);

Nanotechnology

Technological monitoring using text mining techniques (software Vantage Point) to get relevant information and trends from databases of scientific publications and patents, presenting a techno-scientific panorama of the subject.

Benchmarking, using the results of nanotechnologies technological monitoring. This has allowed a better understanding of the process of scientific and technological development in benchmark countries (United States, Germany, Spain, France, United Kingdom, Sweden, Ireland, Israel, Japan, Korea) and those that are in comparable levels to Brazil (China, Taiwan, India, Australia, South Africa, Malaysia and Thailand).

Among the important information obtained by the study is the indication that innovative countries have nanotechnology programs, with increasing budgets of the same level as biotechnology, information and communication technologies and environment. All the programs are anchored with national strategies for economic development and competitiveness. Although they have their own characteristics, they always engage the biggest possible number of participants and have defined economic targets.

Table 3: CGEE's experience: initial phase

Elements that can potentially impact the theme/subject under study are identified and delimited as opportunities and threats, forces and weaknesses, and cultural, social, technological, economic, political and environmental factors.

In a complementary way, the experts and other stakeholders are identified and mobilized (Table 3).

Main Phase

In this phase, the questions are: *What seems to be happening? What is really happening? What should be happening?*

During the main phase, processes of translation and interpretation concerning the current trends and the future possibilities occur, using forecast and foresight techniques, as Delphi, expert panels, scenarios, etc. It is emphasized, in this phase, the broad participation of experts, groups of interest and decision makers, strengthening networks and collective learning.

The expected result is to empower the existing knowledge with a better understanding of the involved conditionings and the possibilities presented for the future. It represents the integration of tacit knowledge into foresight studies. (Table 4) Tacit knowledge can be defined as a knowledge which is personal, specific to a given context and difficult to articulate in a formal language.[10]

Phase of commitments

In this phase, the question is: *What can be done?*

Here, it is crucial to disseminate the results and to strengthen the commitment of stakeholders that participated on the previous stages with the decisions based upon the results of the study, with procedures of validation, dissemination and assimilation for a broader public. The expected result is the establishment of consensus and commitments and the transformation of the accumulated knowledge in strategies and proposals that can be taken by the decision makers, searching the expansion of the perception of strategic options. (Table 5)

In this phase, CGEE identifies future trends, drivers, opportunities and threats. It is a stage of intense participation of experts, making feasible a more qualitative vision of the question. It is also an opportunity to capture tacit knowledge in many ways.

Biotechnology

Experts panels: It involved discussions on the economic impacts of GMOs; on the evolution and consequences of the national and international legal framework; on the access of genetic resources and traditional knowledge; on the impact on the training of human resources for the plant improvement programs in Brazil, and finally on the intellectual property rights issues in biotechnology.

Nanotechnology

Delphi: Carried through Internet, the enquire involved about 1800 participants, with 582 respondents in the first round. It covered the following subjects: nanotechnology for sensors; nanotechnology for processing, storage and transmission of information; nanobiotechnology; nanotechnology for structured applications; tools and equipments for N&N; nanotechnology for electrochemical processes; energy; agribusiness; water resources and environment; social impacts of nanotechnology; long range researches. A second round is currently happening.

Table 4: CGEE's experience: main phase

Decision making

Here, the main questions are: *What will be done? How will it be done?*

The strategic options which seem to be more adequate amongst the identified ones are selected, through interaction with the main decision makers. The expected results involve the definition of mechanisms and tools for implementation of the selected options, as well as the identification of other themes for future analysis.

The commitment of the decision makers during the whole process is essential since it is their responsibility to define what and how things will be done, that is, the final decision belongs to them and prospective studies are only finished when recommendations are put into action.

CGEE's foresight expanded model

Figure 2 presents the expanded model of the methodology in use by CGEE. The central idea of this approach is to provide flexibility to planning, considering the high level of uncertainty associated with complex and hyper-competitive environments of current times.

The final goal of a foresight exercise is always setting priorities to guide decision-making process. However, as pointed out by Skumanich & Silbernagel[9] "forecasting activities cause impacts to organizations (or society) in a variety of ways most of which are extremely difficult to measure. As a result, foresight activities tend to rely on high-level buy-in and public legitimization as sigh of their effectiveness". (Table 6)

CGEE's model incorporates different views, methods and techniques, using tacit and explicit knowledge in order to obtain a shared view of the future. It gives consistency to the results of the studies and amplifies the possibilities of its acceptance and usage by the decision makers.

Conclusions: Key Points and Lessons Learned

The creation of visions of the future to anticipate emergent opportunities, potential threats and to indicate trends and priorities is vital for the success of the innovation process and requires permanent monitoring and sharpened perception to catch the indications that allow this anticipation. In relation to the construction of future strategies, the efficient use of the different techniques and existing methods stands out as a basic aspect, in order to comply with the specificities of the problem, as well as the emphasis on participatory approaches, communication networks and horizontal and vertical communication channels.

One of the main tasks in future studies and foresight exercises is the careful and disciplined exploration of representative landscapes of future situations. The information, the knowledge and the perceptions obtained as a result of these activities are used by people and organizations to make decisions, to elaborate strategies and, above all, to get a better view of the future.

The global leadership in any field depends, more and more, upon a change that includes the effective and innovative use of technological management. The key for leadership is in process management of creative ideas, the generation of new technologies, the development and commercialization of new products in existing and new markets. The innovation management tries to congregate mechanisms and tools, methodologies and forms of organization that guarantee the organizations innovative capacity and, as a result, its competitiveness.

Strategic and multidisciplinary themes with a high degree of complexity that involve different and contradictory interests and mobilize the public opinion, require adequate methodological approaches to make possible the decision making based on information of quality, obtained by shared, participatory and articulated means within the academy, government and enterprises with the involvement of representatives of the civil society.

In this phase, the main recommendations and results of the studies are submitted to decision makers and to society through seminaries, workshops, publications and Internet.

Biotechnology

The biotech study is underway; however, some partial observations from the panels can be drawn:

- There will be economic impacts with the adoption of GMOs, especially regarding to national seed industry. The cost of segregation and rastreability could compromise the competitiveness of the Brazilian products;
- Following implementation of the biosafety law there could be impacts on the research, production and commercialization of grains and seeds, especially for GMOs;
- The large transnational companies ("post-geographic") are creating 'legal marketing' offices responsible for following the discussions on legal framework on a worldwide basis;
- The biotechnology legal framework has been lead by key countries such as the USA, Japan, China, Brazil, European Union and South Korea, known as 'legal decision block'. Countries that had built their legal framework did it based on the Cartagena Protocol;
- In relation to intellectual property rights it is clear that there is a need for investment on the training on human resources capabilities able to deal with the subject of patents on the international basis;
- The majority of the genomic research in the country is on the basic science. At the same time, in the developed world, the GMOs products are being generated based on the genomic knowledge pointing out that there is a gap in Brazilian development in this area;
- There will be possible consequences of the actual legal structure related to access of genetic resources in Brazil. In that scenario, the competitiveness on R&D activities and innovation related to biodiversity use and genetic resources will be threatened.
- The changes on the knowledge basis, going from traditional knowledge to molecular biology, are impacting now and will impact even more in the future on the capabilities and skills in plant improvement programs. To face this challenge is crucial to be able to select possible new fields for investment leading to opening new market opportunities.

Nanotechnology

The nanotechnology study is in progress; however, some partial comments can be highlighted:

- All innovator countries have nanotechnology programs, with strong investments in ICT, biotechnology and environment;
- The amount of resources dedicated to nanotechnology are increasing and have the same order of magnitude of other relevant technological areas;
- The programs are drawn to engage the biggest possible number of participants, either of companies, either of academics and/or research institutions;
- Each national program has very clear proper characteristics, reflecting the peculiarities of the financial S,T&I system of each country, either in traditional aspects either in recent trends;
- The programs are tied with the national strategies of competitiveness and economic development reflecting clearly the effects of some factors: the profile of the economic activity of the country, its human resources and the recent history of the technological development;
- The programs have targets of short, medium and long term that are associated to the perspectives of economic exploitation of the results, in each country;
- Many programs have elements of attraction of researchers of other countries, either through offer of jobs, either of excellent conditions for research.

Table 5: CGEE's experience: phase of commitments

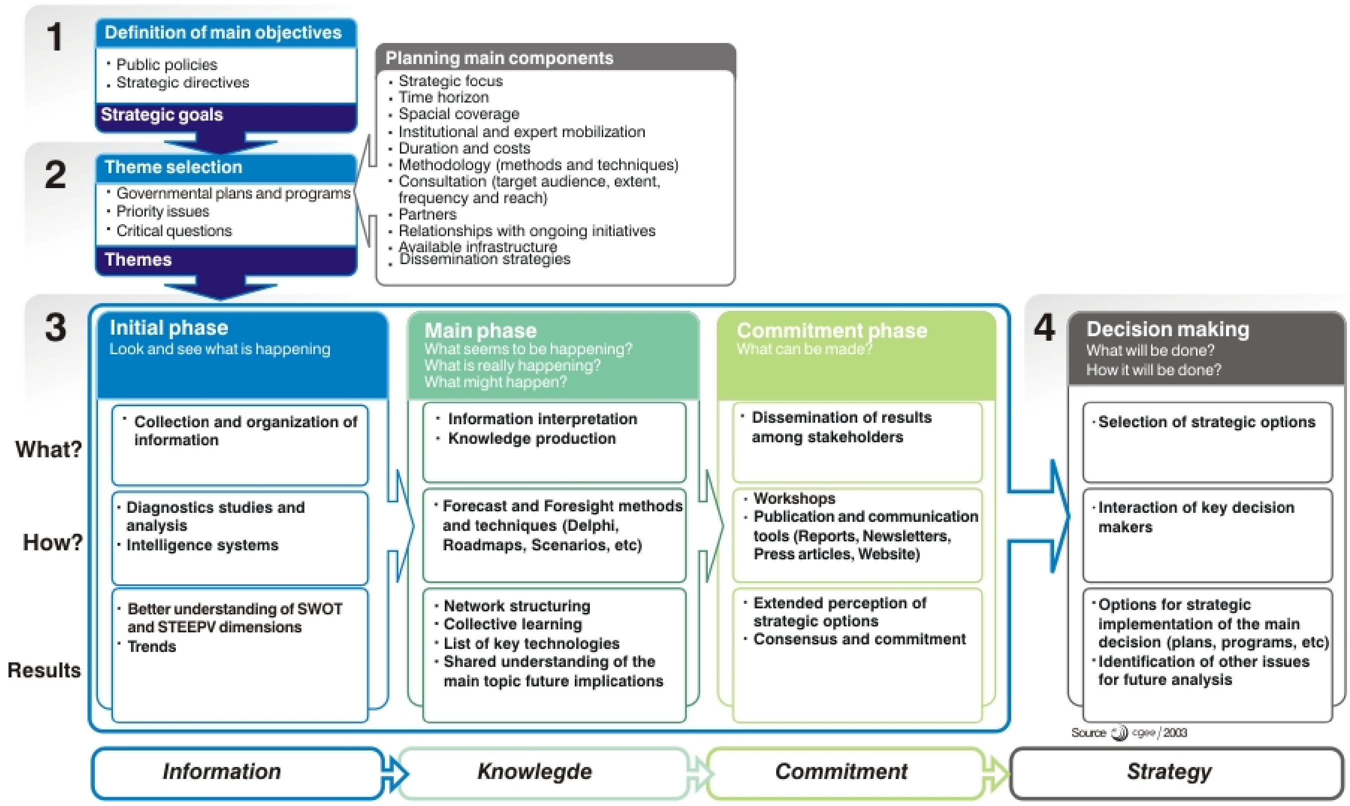

Figure 2: Expanded model

The studies carried out through CGEE had been used to inform the decision making process, in different spheres of the government, as for example, the decision of R&D investments in Sector Funds for Science and Technology.

Biotechnology

The study is still in progress. However, partial reports have already been supplied to the government, standing out the needs of new mechanisms and tools as strategic projects, emphasizing the culture of the work in nets, fortifying activities of patenting, training human resources in ICTs looking towards biotechnology and researchers with enterprise vision;

Nanotechnology7

The study it is still not concluded, but its results will be used to define the policies of investments of the Science and Technology Ministry in the area. However, part of this work has supported the decision making process in order to formulate the national laboratory/program of nanotechnology.

Table 6: CGEE's experience: Decision making

In the particular cases of the studies on bio and nanotechnology conducted by CGEE for NAE (Nucleus of Strategic Issues of Presidency of the Republic of Brazil) the conclusions were used as the main base for the proposition of specific laws and programs of development adopted by the Brazilian Congress and Government as well.

Another important point is related to the need of creation of new tools and approaches that can deal with the increasing trend towards multidisciplinarity and flexibility, necessary to understand the complexity of the current reality, when the models in use seem to be insufficient.

Through the communication and cooperation between researchers, users and financiers, the methodology in use by CGEE looks forward to articulating the search for "visions of the future". Privileging the knowledge of the environment and the factors that determine the context of the problem, a more effective communication occurs among the stakeholders, which influence the development of science and technology, leading to the strengthening of the technical-economic networks that they participate. Additionally, the activities of foresight developed by CGEE look forward to leverage the process of technological innovation in the country, adding value to the existing information and transforming it into useful knowledge ready to be used.

References

[1] Cuhls, K.; Grupp, H. *Alemanha: abordagens prospectivas nacionais*. Parcerias Tecnológicas, n.10, mar.2001.

[2] Santos, D. M., Santos, M. M. A *atividade de foresight e a União Européia (EU).* Parcerias Estratégicas, n. 17, 2003.

[3] Santos, M.M. et al. *Prospecção em Ciência, Tecnologia e Inovação: a abordagem conceitual e metodológica do Centro de Gestão e Estudos Estratégicos e sua aplicação para os setores de recursos hídricos e energia.* Parcerias Estratégicas, n. 18, 2004.

[4] Porter, Alan L. et al., *Technology futures analysis: towards integration of the field and new methods.* Technological Forecasting and Social Change, n. 49, 2004.

[5] Horton, A., *A simple guide to successful foresight*. Foresight - The journal of future studies, strategic thinking and policy, v.1, n.1, Feb. 1999.

[6] Conway, M.; Voros, J., *Implementing organizational foresight: a case study in learning from the future.* In: Probing the future: developing organisational foresight in the knowledge economy, July 2002.

[7] Miles, I.; Keenan, M. & Kaivo-Oja, J. *Handbook of knowledge society foresight.* Manchester: Prest, 2002.

[8] Godet, M., *Creating Futures – Scenario Planning as a Strategic Management Tool.* 269 p. Econômica Ltd., 2001

[9] Skumanich; Silbernagel (1997), *Foresighting around the world.* Battelle Northwest Lab. Apud Gordon, T.J.; Glenn, J.C. (1999) Factors required for successful implementation of futures research in decision making. Atlanta, Army Environmental Policy Institute, p. iii.

[10] Nonaka, I; Takeuchi, H (1991). *The knowledge-creating company.* Oxford University Press, 1995.

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