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Ipen's Social Role in Scientific and Technological Development of Radioisotope and Radiopharmaceutical Production – (1950 – 1980)

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ABSTRACT

Some facts and figures are present in the existent interaction between the Instituto de Pesquisas Energéticas e Nucleares (IPEN) and the medical community. Among other characteristics, the IPEN has a permanent seat in the Biology and Nuclear Medicine Society and, the present Radiopharmacy Center, has had the continuous concern, since the Instituto de Energia Atômica (IEA) creation until today (2009), to perform an excellent approach with the medical faculty. In the past, some physicians would complete their courses in Europe and in the United States of America, and there noticed the importance of radioisotopes applications in medicine, mainly, in the beginning of these activities, with the I-131. Returning to Brazil, they requested that the former IEA, today IPEN researchers used the research reactor IEA-R1, installed in São Paulo, at Universidade São Paulo (USP) campus, for radioisotopes production. Then, in the late 1959, the first production line from the I-131 took place. The IPEN starts to accomplish what was planned as one of its targets, at the act of its official creation on August 31, 1956. From 1961 on, there was a continuous flux of I-131 and other radiopharmaceuticals production. The recovery and analysis of these happenings, in the Brazilian society cultural historic context, were partially published in different previous works. Nevertheless, history is dynamic and gains new interpretations, in the present research, from the reading of novel research sources, both primary and secondary, not explores so far – reports, interviews with IPEN researchers and papers published or divulged in meetings, either scientific or bureaucratic. This research is part of project supported by the Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP), with the aim, among others, of contributing for the analysis of the transformations occurred in all of the IPEN research lines, plus the social role of this institution for science and technology development. The question proposed to be answered in this work is, to what extent the present Radiopharmacy Center may be considered as an innovative producer, within the so-called Neo-Schumpterian concept of innovation.

I. INTRODUCTION
(Brazil's Insertion in the society of knowledge)

> The past is, thus, a permanent dimension of human consciousness, a inevitable component of institutions, values and other standards of human society. The problem for historians is to analyze the nature of this past feeling in society and seek its changes and transformations.
>
> Eric Hobsbawm[1]

From the second half of the 20th century, technology has become an object of desire for companies. Research institutions and universities around the country have initially, a strategic-political role to play in policy formation for development. Technology not only offers the state-of-the-art and innovative processes and products but offers those with the best possibilities of being accepted by consumer demand. The concept that investing in technology transforms the cost/benefit relationship into advantages to those who invest in innovation is discussed by policy makers. However, Brazilian businessmen have done little in the way of adopting this practice. Although it is well known that the market in the capitalistic market promotes the quest for the development of new technologies, there also is a preoccupation among companies of losing money and time which in the end could mean less profit. Even so, there is evidence of an emerging society and economy based on knowledge and learning. These days it is easier to analyze that intangible resource such as formal and tacit knowledge, information, individual competencies and learning, innovative and cooperative capacity, together, play an important role in society since they widen dynamics, competition and sustainable survival of countries, regions, organizations and individuals.

In the Brazilian academic world, this becomes more apparent during de 1990s. However, the role of research institutions and universities takes a secondary role to production. In the nuclear area, during the same decade**,** placed apart by the new Brazilian government guidance, the innovation inducer role is inexistent.

Even so, there is a sector motivated by the necessity of survival of institutes of the nuclear sector for the production of radioisotopes and radiopharmaceuticals that react due to its specific nature. Driven the interest of the medical field and import difficulties, among other reasons, this sector receives a wave of technological innovation as a new paradigm in those institutions involved with nuclear technology development. How this took place openly in front of a good part of the scientific community and another part unaware of what was happening will be analyzed in this study.

Along with these observations, it must be noted that during the 20th century in Brazil, the government exerted great influence in the development of the country. Governmental policy during this period and the beginning of the 21st century ended up supporting industrialization, independent of its type. Universities and research institutions, however, had no central role for support in most industrialized areas of the country, relegating this role to state-owned companies which were the key for this support. Yet, other considerations of the role of universities and research institutions

[1] Translation into English was made by the author from the original: "O passado é, portanto, uma dimensão, permanente da consciência humana, um componente inevitável das instituições, (...) da sociedade humana. O problema para os historiadores é analisar a natureza desse "sentido do passado" na sociedade e localizar suas mudanças e transformações."

should not be ignored, especially in certain fields of expertise. One of these is that neither private nor public industry exerted production activities of radioisotopes and radiopharmaceuticals. Also noteworthy is a partial if not detailed explanation of the reasons which allowed, in this case, nuclear research institutions to lead the way and supply clinics and hospitals that worked with radio diagnoses and therapy. The analysis will also address the suppression of the capitalistic society's need for promoting competition and profit by way of technological innovation. Thus the analysis must be explicit on what exactly is understood when discussing innovation. This will be done further on along with the dynamic analysis of the innovation that occurred at Instituto Pesquisas Energéticas e Nucleares (IPEN) with the implementation of the production of radioisotopes and radiopharmaceuticals in Brazil. Finally, how the country adopted the first traces of neoliberalism at the end of the 1980s which promoted a gradual reduction of government influence on society, managed to maintain government monopoly of the production of radioisotopes and radiopharmaceuticals. It should be noted that in general terms, the consequences of the change in economic policy as of 1990, penalized the development of science and technology, without directly affecting the radioisotope and radiopharmaceutical production sector.

It is well known that when the country entered the 1990s, it redirected its priorities and there was a wave of privatizations of state-owned companies. This implied in a selective restructuring of the scientific-technological base. Investment is diverse areas of research were reduced. One of the sectors that suffered a drastic reduction of government incentives was the nuclear sector. Nuclear researchers had to turn to other financial institutions for scientific development and were successful after two or three years of insisting, although practically no projects were in the nuclear area, at least not directly. A general overview of what was taking place throughout the world, what models were being adopted for the science and technology development in the developing world, in which stage of this development was Brazil and how IPEN adapted to the economic and science and technology policies adopted by the Brazilian government will be commented. This will serve as a background for the more specific analysis to be undertaken, i. e., whether or there is not a great amount of academic literature on the subject [Cassiolato & Martins, 2005].

The basic argument of the analysis of this study stems from the general idea the science and technology development affects industrialization and increases the nation's Gross Domestic Product (GDP) and is intimately related with innovation, both the process as well as the product and thus turns the economy. Innovative companies can grow although the number of jobless may or may not decrease. In the analysis of Kondratiev/Schumpeter, the latter affirms that capitalism is the one system that is inherently unstable to permanent change, although not continuous, promoted by innovation. But in this case the economist speaks of changes in paradigms and that self-induced transformations of a capitalistic economy occur in waves. This study adopts only partially Schumpeter's concept as radical creations are not the only ones to be considered as innovative. Expanding further, is it possible to identify local innovative processes of social and economic development based on the knowledge produced by Brazilian universities and research institutions, given the specificity of each case? This study will attempt to show that IPEN since its foundation under the name Instituto de Energia Atômica (IEA) in 1956, in the radiopharmaceutical production area, promoted a process of innovation and management which added to the country social improvement, in spite of not always having the comprehension of a part of its researchers which was in fact, innovating. Furthermore, the decrease of some imported products generated a savings in foreign currency which was felt directly in the Brazilian trade balance.

What took place in the country, in view of the science and technology models adopted throughout the world and which had a role in introducing the innovation of products and processes for the diagnoses and treatment of diseases with the use of radioisotopes and radiopharmaceuticals answers the first questions of this study. An account of how the institution acted in the area under study will be given, as well as, a discussion of how from the adopted concept of innovation within IPEN's framework, the acquisition of new capacities that lead to final products that transformed the acquired learning of the process into a competitive edge, at least within the institute. With the perspective of introducing a concentrated effort of society for development, an idea emerged that the integration between university/institute and industry should be encouraged. This discussion started in the 60a and was fortified itself during the 70s and 80s. Basically it is this idea that dominates Brazilian society. It was also the leading hand that led the military governments to invest in science and technology, specifically the Geisel government.

> "(...) innovation was seen as occurring in successive stages and independently of basic and applied research, development, production and diffusion (a linear view of innovation)".[Cassiolato& Martins, 2005][2]

The linear model that in practice was used by the country up until 1990, above all in state institutions and universities, was pioneer in influencing the creation of the first science, technology and innovation indicators. It was in this perspective that nuclear institutions were encouraged to develop. This was especially true for the fuel technology sector in Brazil [Gordon, 2004]. This would have consequences for research in the production of radioisotopes and radiopharmaceuticals at IPEN.

II. THE FUNDAMENTAL CONCEPT OF DEVELOPMENT ADOPTED BY IPEN AFTER THE 70s

Returning to the Brazil of the 1970s, know-how is singled out as one of the main pillars of dynamic economic, social and cultural development. In this sense, the analysis of the results obtained for radioisotope and radiopharmaceutical production during 1960 and 1980 was chosen, although some results before this time can be credited to the work carried out during analyzed interval and reflects the problem of quantifying measurements between knowledge production and implementation in Brazil. Not always does science and technology development enhance transformations in terms of citizenship and the social economic advancement which this study feels is much more important than simply affecting the Gross Domestic Product (GDP) of a region. When society incorporated this knowledge in its activities and daily routine, the advancement of knowledge has fulfilled its primary role. One can affirm that it is possible to identify local innovative processes based on the development of know-how in universities and research institutions of a country that bring a contribution to social and economic development, in spite of the idea of having most of the academics on the subject. There is no doubt that this is not the rule but an anomaly within the capitalistic system where profit is responsible for the supply of new products, whereas universities and state research institutions do not seek profit. This, of course, in regarding only to state universities and research institutions.

Some considerations will be made in order to understand the basic conceptual analysis of the study. The linear model concept of innovation incorporated the idea that in order for knowledge to return to society it should be of good quality. Thus any investment should be allocated by the scientific community itself. It is for that reason that at the end of the 1960s there is a restructuring

[2] Translation into English was made by the author from the original : "(...) a inovação era vista como ocorrendo em estágios sucessivos e independentes de pesquisa básica, pesquisa aplicada, desenvolvimento, produção e difusão (visão linear da inovação).

of the universities in Brazil. This restructuring also created distortions since the academic community was unable to decide where the resources that scientific financing institutions had given them should be spent. Thus some areas of knowledge were not contemplated.

Between 1960 and the end of 1980, IPEN followed a line of research in the area of fuel technology pushed by the idealism of the Brazilian military government dream of a Brazilian power. Humanities and social studies, which have a good condition to reflect on social exclusion, violence, and related issues, received, eventually, less incentive and financial support for the projects submitted to foment institutions. In spite of the fact that in the 1960s a vision that proposes that the relationship between university and industry has to be closer, this vision comes up against a new one that starts to appear between 1970 and 1980.

The relationship between university and industry was still being discussed at the end of the 20th century and beginning of the 21st century in Brazil. But the process of innovation obtains greater relevance for the country's economic development and consequently the interaction between the market and technical progress attains greater relevance, as well. New forms of association between companies and between companies and universities and research institutions emerge.

Thus, we have the first idea that the market is the main regulator of the relationship between company and university/research institute and that the academic community will be included, resulting in a social contract between these institutions. At the same time, scholars realize that not always do universities (or institutes) participate in a more effective manner in the economic development of the country. This occurs because it is understood that research in the laboratory, although very important, is not automatically transferred to industry. A process research on the laboratory scale requires a series of adaptations, new studies and experiments before it can become a product to be offered to the market.

In any case, due to a lack of understanding, many researchers end up migrating to those areas of study related to the development of technology. The university/institution is reinvigorated in this process but is not a fundamental agent of the innovative process since in the context of the present society it is industry and its businessmen, as one of its agents, which have the privileged position of innovation which makes sense in a capitalistic system, but which is not everything. Allied to this context, a timid understanding of the role of the implicit character of technological development is difficult to transfer and not within the scope of this study or the sale of a company, machine or equipment as it is acquired through know-how.

What is important in this study is to close the rationale for the nuclear sector. In Brazil, the nuclear field situation acquires an even greater specificity as there was no "nuclear industry" per say, not even at the end of the 20th century. Even after the foundation of the Indústrias Nucleares Brasileiras (1988) one could say that there was still no nuclear industry in Brazil, a fact which has no bearing in this study. Even so, the general idea during the 70s was that the interaction between those institutions involved in the process that resulted in innovation was important, but the business attitude was that it was the conducting wire of the diffusion process of innovation and that the businessman would have to embrace dynamic business.

Before this, other ideas were being incorporated to the theoretical concept and the innovation process could not be summarized only by "totally innovative" creations and the important role of business. Adaptations and less radical innovations can lead to profit for industry which can differentiate it in the nation's GDP, etc since at any given time it can produce something that only it is capable of. The university/institution that in the linear model proposed during the 40s and considered then to the center of the innovative process takes on a different role that some say is more modest. With the passing of time, it was realized that even in industry the percentage of researchers coming from universities that were concerned with research and development was quite high. The university becomes important not because of results but because of the human element. The idea at Instituto de Pesquisas Energéticas e Nucleares (IPEN) is that business is still important; however there is an emerging notion that the transfer of technology from university to business demands university administration for patent registration [Gordon, 2004]. Technological centers and poles have to be located next to large universities. Innovation incubators today are the latest fashion, would be the privileged locations of the innovative process.

Even during the 90s at IPEN, the administration of virtuous trajectories similar to those of the developed countries was important and that institutional mechanisms were created that made the university-industrial relationship more efficient. That is when the figure of the administrator appears in research institutions such as IPEN. The administrator's role according to the discussed concepts was to transfer developed technology to industry promoting social welfare. Institutions start to incorporate "missions" in their objectives. This can be noted when visiting the websites of research institutions and having their institutional mission appearing. This phenomenon reorients research institutions that become much more practical after the 70s. The institutional culture is slowly modified at IPEN [Gordon, 2004]. What follows is a summary of some of the activities in the area of radioisotope and radiopharmaceutical production at IPEN.

III. RADIOISOTOPES AND RADIOPHARMACEUTICAL PRODUCTION BETWEEN 1960 AND 1980

After the creation of the IEA, now IPEN, the production of radioisotopes a primary concern even though at some moments it did not receive as much attention of funding institutions as did fuel technology. Even though there was a constant concern of the present radiopharmaceutical center, from the creation of the IEA to the present date in forging close ties with the medical field. Some vehicles, such as IPEN's permanent chair on the Biology and Nuclear Medicine Society, make themselves felt in the interaction between IPEN and the medical field. During this time IPEN did not loose its focus on the process of the quest for knowledge even if under the form of reverse engineering.

> "Some doctors had been to Europe and the United states and started to work with the I-131. Upon their return to Brazil they asked us if we could prepare the I-131. That in fact, in 1959 the first I-131 was produced at IPEN (...) we started to develop nuclear medicine. It was then that it took off. As of 1961 to date, there was a continued increase of I-131 production as well as other radiopharmaceuticals." [Silva in Gordon, 2004][3].

In 1958, the IEA had laboratories for the study of radioisotope production methods, cells for chemical processing of irradiated material and for measurements and packaging of radioactive materials for medical and agricultural applications. In 1959 a order was filled to produce modest amount of 10 mCi of I-131. In 1960, the total production reached 100 mCi. This same year also saw the production of the radioisotope P-32 for application in agriculture from magnesium sulfate irradiated under of flux of 10^{13} neutrons/cm^2seg for16 hours. In 1963 there was interest of doctors

[3] Translation into English was made by the author from the original: "Alguns médicos tinham estado na Europa, nos E.U.A e começaram a trabalhar com I-131. Voltando para o Brasil nos solicitaram se nós poderíamos preparar o I-131. Assim de fato em fins de 1959 já saía aqui do IPEN à primeira partida de I-131 (...) começamos a desenvolver a medicina nuclear. Foi aí que tomou um grande impulso. A partir de 1961 para cá, foi um crescimento contínuo de produção de I-131 e outros radiofármacos".

to use colloidal Au-98 for the treatment of tumors. In 1964, experiments were undertaken to produce Cr-51 using the Szilard-Chalmer process. In 1968 about 120 mCi of that isotope was produced. As of 1960 the demand for I-131 increased and the institution started to supply 900 to 1,000 mCi of this isotope.

The radioisotope production cells had been installed at the Radiochemical Division under the command of Fausto Walter de Lima from the University of São Paulo. The Radiochemical Division also met the internal demands of the IEA. In 1964, studies started to separate fission products irradiated with uranium oxide. At the end of 1965, processing cells were installed for work with fission products. Researchers had personal interests to develop scientific studies and technologies, after all, they had recently graduated in a country that had only just begun to create its first modern universities. Even so there was a general awareness of the role of research work undertaken to support the country's development under the concept that developing of science and technology was enough and that industrialization of the country would be a direct consequence.

> *"I do not think an exaggeration to repeat once more the words of Waine Meinke in connection with utilization of research reactors in developing countries (...): "Research and development programs in chemistry as well as chemical service to research and development programs in physics, reactor engineering, agriculture etc, make sense only if they contribute something to the overall scientific effort of the developing country! The amount scientific manpower available in such countries is severely limited and cannot be squandered on projects which are of no consequence to the country or the area"". [Lima, 1967].*

This study argues the strategy employed mainly by researchers of what is now IPEN, reinforced and widened the initial objectives of the Brazilian academic community involved in the creation of the institute as a means of participating in the development process of the country. There was a mobilization to obtain knowledge and to use it in a productive capacity, in spite of the university culture of the time still being influence by the positivist's philosophical ideals of the country. Although there was no implicit consciousness of "innovative systems" and possibly in the work produced by the institution, researchers probably had no knowledge of the writings of such economists such as Schumpeter, a mobilization of researchers of the radioisotope and radiopharmaceutical production swung towards the present concept of innovation of the neo-Schumpeterians.

During the 90s when the country started to the debate on innovation and at the institution during the second half of the decade, the concept had not been assimilated institutionally. A few, especially in the administrative area tried to be heard even without being in touch with the implanted industrial and technological policies of the government and much less with the economic policy of the time that favored above all the control of inflation. Past studies [Gordon, 204] showed that the IPEN administration gave much importance to marketing and sales activities and ties with external sources with the institution such as the medical community, hospitals, clinics and transportation that led to over control of documentation required by ISO regulations. It was in this way that during the decade courses were started to supply internal auditors and contracts with external audit companies appeared. In contrast to some other studies, the concern already existed as to the necessity of the users, not only in commercial terms but in terms of social benefits, as well as the formation of networks that could use the exchange of knowledge.

This exchange took place between Brazilian and foreign researchers, researchers and employees of the International Atomic Energy Agency (IAEA), the international financing organ that in many cases subsidized nuclear research in the country. Also participating in this network were foreign companies that produced radioisotopes and national and international medical communities. In the area of specialized labor, several master and doctoral dissertations took place and made use of reverse engineering to obtain knowledge generated abroad. Many researchers were sent overseas to interact with international companies and universities in developed countries. In this way sources of information were constantly used. In this particular case, as one of the objectives of the IEA in the program “Atoms for Peace” had been the social benefit of the peaceful use of nuclear energy or the production of radioisotopes, there had been no bottleneck due to international pressure against the country developing such activities. That being so ever since the start, the production of radioisotopes had the full support of the IAEA and foreign companies since this did not interfere with the highly sensitive fuel area. Those researchers involved in this activity had been present since the second half of the 50s accumulating a great amount of knowledge in the area.

It needs to be added that the planned cooperation of these network participations are influenced by governmental science and technological policies. Either directly or indirectly, Brazil ended up promoting, even through the years in which fuel technology was the priority, the development of radioisotope or radiopharmaceutical production since this production generated internal revenue for the country. There were government administrations, such as that of General Humberto de Alencar Castello Branco (April 15, 1964 to March 3, 1967), in which priority was given to the production of radioisotopes with the argument that the country did not need to introduce an energy grid based on nuclear energy.

Towards the end of the 80s, the institution with its accumulated knowledge and experience started to receive more support for the production of radioisotopes and radiopharmaceuticals with the idea that these activities were important for the country. As such, with the disruption of research in fuel technology, several researchers migrated to these activities. This in turn enabled the production of radioisotopes to receive the complete attention of IPEN’s administration and allowed it great support and the introduction of modern laboratory infra-structure reforms and of radiologic protection. Added to this is the fact that the era of informatics came to speed up not only the production process but the transmission of information along with user service. A new concept and paradigm of what would be a serious idea to explain what took place established itself at the institution that came to alter the relationship between components of the network which was beneficial for the increase in production and for society in the way of the increasing number every year of patients attended. It is understood that the innovative process also incorporated process changes, administration, reverse engineering, etc. – not so radical innovations. Creativity, the interaction between components of the network, organizational innovations, techniques and implicit knowledge take on a much greater importance and productivity comes in the wake of these processes. This also took place in the radioisotope and radiopharmaceutical production. Thus incremental innovations fruit of accumulative processes took place at the institution. In spite of the small number of researchers, there were many times compensations of creativity and adaptations as seen in the following observation:

> *“A method for obtaining free radioactive phosphorous from elemental irradiated phosphorous was presented. The 32P formed by the irradiation is extracted with a agitated heated chloride acid and octonal solution. The solution is then percolated by a catatonic resin so as to eliminate eventual existing impurities of the sulfur. The yield of the extraction is about 85%”.* [4] *[Pagano da Silva & Retter, 1965]*

Until then the adopted method used could be found in the IEA-37 publication. Several methods were either too laborious or required very expensive equipment. This new phosphorous method solved the problem. In 1968, the division irradiated uranium oxide (100 hours) and it takes three years of waiting to separate the ^{137}Cs for the preparation of sources for this radioisotope. A method

[4] Translation into English was made by the author from the original: *“Apresenta-se um método de obtenção de fósforo radioativo livre de carregador, a partir de enxofre elementar irradiado. O P-32 formado na irradiação é extraído com uma solução de ácido clorídrico e octanol, a quente sob agitação. A solução é em seguida percolada por uma resina catiônica a fim de eliminar impurezas eventuais existentes no enxofre. O rendimento da extração é de cerca de 85%.*

had been developed by Lima (1967). Aside from the mentioned radioisotopes, others were on much smaller scales due to demand such as Na-24, S-35, Br-82, and K-42. Some molecules such as hipuran, rosa bengala, albumin serum, oleic acid, triolin, lipiodol and macroaggregates of albumin serum were labeled with I-131 by the Radiobiology Division during this period. Finally, the injectable isotopes were submitted to biological assays under the same requirements established by traditional pharmacopoeia. During this period countries such as Bolivia and Paraguay were also benefited the the IEA's production. At the end of the 1970s [Pagano da Silva, 1968] , the IEA was already producing around 32,000 mCi of I-131, 2,500 mCi of P-32, 3,500 mCi of Au-198, 34 mCi of Na-24, 970 mCi of Cr-51, 75 mCi of S-35, 45 mCi of Br-82 and 160 mCi of K-42.

> "In *1960 we continued production (...) on a small scale and Professor Damy along with Professor Fausto invited me for an internship in Saclay at the "Centre d'Etudes Nucleaires" in order to familiarize myself with the production of radioisotopes. I remained there for 6 months and when I returned we started on the new installations at the old building (...) we constructed some cells for the preparations of I-131, P32, coloidal Au that were in use at the time. (...) After that in 1970, I defended my master's thesis while producing I-131 under the orientation of Dr. Fausto W. de Lima. Around 1972, Professor Pieroni who had a great vision of the future of nuclear medicine in the country, built a building for the production of radioisotopes. In 1975, the building which still stands today was ready. Nuclear medicine services expand and new radioisotopes appear (...)"*[Pagano da Silva in Gordon, 2004].[5]

The production of radioisotopes has great significance for society and the insertion of this field of research and production in new research orientations in the nuclear segment from 1990 on, for countries like Brazil. Even with precarious funding, the institute invested in a new cyclotron and within its projects it was a correct decision. The new cyclotron 30 was acquired from Belgium. The production of fluorine that took place at the CV28 (cyclotron) was transferred to the new accelerator with new cells for the dismantling of the irradiated targets and a new environmental monitoring system[6]. After the implementation of the production of fluorine, there was an effort on the part of the three centers at IPEN to develop an irradiation device using 100% national technology of xenon gas to produce I-123. This made possible a savings of revenue and the development of technology that would benefit the country. The system had a sophisticated automation technology for its time. It proved to be dependable and the Belgium company that sold the new cyclotron was interested in marketing the irradiator on its Ion Beam Applications product list.

During the period that includes the liberation of nuclear energy for peaceful purposes until the oil crisis in 1973 two big projects were developed at the institute: the production of radioisotopes and the cycle of nuclear fuel. But the purpose of this paper is to study the production of radioisotopes and radiopharmaceuticals. This is an area that feels the need to improve and develop processes due to its interaction with other communities besides IPEN. The word change does not cause any discomfort as there is an almost natural need motivated by the existing relationship between researchers and the medical community to rationalize material, improve production, reduce employee exposition to ionic ionization, flexible work hours, concerns with radioactive waste, radioactive material storage and liquid and gaseous effluent monitoring to ensure less risk to the installations, the environment and the working professionals. The work team has grown substantially due in part to new work shifts which change old habits. According to Mengatti:

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[5] Translation into English was made by the author from the original: "*Em 1960 continuamos com a produção (...) o professor Damy junto com o professor Fausto me convidaram para fazer um estágio em Saclay, no "Centre d'Etudes Nucleaires" para me familiarizar com a produção de radioisótopos. Fiquei 6 meses (...) voltei começamos a fazer (...) as instalações no prédio antigo (...). montamos algumas células para do I-131, P-32, Au coloidal que eram muito utilizados na época. (...) 1970, fiz a minha dissertação de mestrado juntamente na produção de I-131 tendo como orientador o Doutor Fausto W. de Lima. Por volta de 1972, o professor Pieroni que tinha uma visão muito grande sobre a medicina nuclear no país, construiu um prédio para a produção de radioisótopos. Em 1975 estava pronto o prédio atual de produção de radioisótopos. (...) Cresce atendendo a medicina nuclear, surgiram outros radioisótopos*

[6] Projected by: Gordon, Ana Maria Pinho Leite and Romero, Christovan Romero.

> "You have greater proximity with customers if you know their necessities, know your customers evaluations of your products and services and if all this culminates in a constant process of improvement of the Radiopharmaceutical Center (RC). This also allows you to project the future with new work to permit the CR and IPEN to compete with the best institutions of its kind in the world in terms of the number of products produced, as well as the search for new processes and products to meet the ever growing demand of the country's nuclear medicine."[7][Mengatti in Gordon, 2004].

The year 1981 marks the beginning of the production of generators of technetium with technology developed at the institution and molybdenum imported from Canada. Imoto (1979) developed a study (master's dissertation) where the separation of the molybdenum/ technetium pair in aluminum oxide. The generator consists of a column containing material as a support over which the Mo-99 is absorbed. This radionuclide decays with a half-life of 66 hours to Tc-99. Technetium decays by way of isometric transition emitting photons of energy of 140 keV that are detected and can be used in imagery studies. Sodium pertecnate Tc-99m is used as a scintilographic agent to visualize brain images, salivary gland, thyroid, etc. It can also be added to organic substances to obtain bone, liver, lung, kidney and other organ images. Technetium's affinity to aluminum is small, thus it can be eluded with a sterile physiological solution stored in hermetically sealed flasks. Between 1995 and 2001 the number of generators grew from 5,657 to 11,300 and the number of patients treated by all the radiopharmaceuticals produced and distributed by IPEN were on the order of 1,870 10^3 whereas in 1995 this number was only 80,010^3. What is important in this case is the increase of 134% which reflects a modification in the 90s in view of the institution's effort through scientific and technological research supported by a new administrative model that could offer the medical community an increase in the supply of radioactive products to be used in the field of nuclear medicine. This ended up reflected in the following years. In 2006, the number of patients attended with radioisotopes produced and distributed by IPEN reached the number of 3 10^6 patients. This included diagnosis, treatment of different diseases and mainly in the area of oncology, cardiology and neurology. Among the products produced by IPEN, the FDG-18 radiopharmaco, used in PET (Positron Emission Tomography) image diagnosis presented an enormous growth rate over the last years. This technique allows early diagnosis of several types of cancer in their initial stages helping in the choice of the most efficient strategy for treatment. The studies with the Tc generators at IPEN continued [Gasiglia & Enoshita,1980; Mengatti, 1983; Acar, 1987]. In 1987, IPEN was able to supply Ga-67 and in 1992 the I-123, both produced in the cyclotron. The Ga-67 had to wait until 2001 for the IPEN certification for its cyclotron production. This posture of the institute led to the result that in the 90s IPEN had become the institute that in 1997 initiated the production of F-18 for nuclear medicine diagnosis. It became one of the main research institutes to supply the country with radioisotopes and radiopharmaceuticals. The F-18 radioisotope is produced in the cyclotron particle accelerator. The diagnosis uses fluorine in the form of deoxiglucose and is important to measure the consumption of glucose by the brain and heart as well as other applications. During this period the institution was responsible for the medical community service of 10^6 patient per year, diagnosis and therapy included

IV. PARTIAL CONCLUSIONS

[7]Translation into English was made by the author from the original: "Você tem uma maior aproximação com os clientes a partir de levantamentos das necessidades dos clientes, questionários onde os clientes avaliam os nossos produtos, avaliam o atendimento e que culminou com o processo de melhoria contínua do Centro de Radiofarmácia (CR). Isto também nos permite projetar para um futuro alguns novos trabalhos permitindo colocar o CR e o IPEN concorrendo com as melhores instituições congêneres no mundo no que tange a quantidade de produtos produzidos, qualidade assim como a busca de novos processos e produtos para atender esse crescimento contínuo da medicina nuclear no país".

IPEN did not always internalize the concept of innovative systems and even when it did, it was only partially. Even so, due the particularities of the country, of the implanted science & technological and industrialization policies and the state monopoly of the nuclear sector in the country it was relevant so that the area of radioisotope and radiopharmaceutical production. There was an advance when included in the analysis along with the research itself, the production of services and goods if not as durable as radioisotopes, followed the new forms of production. The importance of the acquisition of developed technology from the developed countries was emphasized especially due to the implicit knowledge obtained since the institute's creation. This knowledge was possible because this sector although strategic was not included in nuclear energy for military purposes. Thus it was possible to internalize and adapt imported technology. Much experience, knowledge, strategic market vision and technological interpretive capacity is required. To work with radioactive material is not in any way simple and nor is working with research reactors, cyclotrons, radioisotope distribution cells, biomolecular labels, etc. It is observed that, in spite of the commercial interest by industrialized countries in selling radioisotopes to Brazil, in some cases this was practically, impossible, since there was the inconvenience of the isotopes short half-life. Nevertheless, there was still the positive aspect of selling equipment and primary products. In the case of fluoride 18 production, for example, the country imported oxygen 28, cyclotron, and others. This approach was evidenced in the historical context presented in the production of radioisotopes and radiopharmaceuticals at the institution and by the neo-Schumpeterian conceptual notion of innovation that implies in a series of changes in the practices of institutions and in their productive processes. It should also be emphasized that in spite of the fact that IPEN is a research institute and is not part of any state company, it does exercise the functions of a company since by way of Brazilian law prohibits private companies to produce and commercialize radioisotopes with a half life of more than two hours. The institute's activities also fomented other sectors of the economy such as the radioactive transportation sector, the production of led shields, the production of containers for Tc-Mo generator containers, special plastic packaging for radiopharmaceutical distribution, etc. Not to mention the formation of capacitated hospital personnel to work with radiological protection and radiopharmaceuticals that will be used in patient diagnosis and treatment. More specific analysed in a future study with the production of radioisotopes and radiopharmaceuticals after 1980 until de beginning of the 21st century.

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