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Development, organization and management of techno-economic networks: the Cuban biotech sector and vaccine industry

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Abstract

This paper, the second out of two about the Cuban biotech sector and vaccine industry, gives an account of the creation, organization, and management mechanisms of the techno-economic networks of the Cuban biotech sector and vaccine industry, by applying the concept of techno-economic evaluations developed by Michel Callon. It also seeks to explain the apparent paradox about shifting the emphasis of the biotech sector from that of targeting a 'modern' disease pattern to that of a' traditional' one that was identified in the first paper. Centralized and participatory decision making processes seem to facilitate close coordination and cooperation between the different research and development centers. The paper also inquires into the relation between the biotech sector and the national System for Science and Technological Innovation.

Keywords: Innovation systems, techno-economic networks, Cuba, vaccines, biotechnology.

Introduction

The first paper about the Cuban vaccine industry (Plahte 2010) discussed how the interests of public health and commercialism were articulated in the biotech sector, and the issue was approached by looking at strategic evaluations undertaken in the process of developing the sector. In the present paper the main issue is how the Cuban biotech sector – of which the vaccine industry is an integral part – was established, and how it is organized and managed within its national political and administrative framework. The application of the techno-economic network approach developed by Michel Callon (Callon 1991; Callon 1992; Callon, et al. 1992) as the conceptual framework for the analysis will cast light on several questions that arise in relation to that main issue.

While strategic evaluations are related to the selection of desired products of a particular intervention, techno-economic evaluations revolve around questions of which actors and organizations that have to be enrolled or created, and how to order them and whichever other heterogeneous resources that should become involved. This paper is an attempt at identifying or inferring some of the most important techno-economic evaluations that have been carried out in the Cuban biotech sector.

An additional objective of this paper is to explain the apparent paradox that was identified in the first paper, namely that despite the fact that a main rationale for creating the biotech sector was to confront the morbidity and mortality transition towards a modern, or 'Northern', disease pattern dominated by cancer, cardiovascular and congenital conditions, a strong vaccine industry was created, whose products target mainly a traditional, 'Southern', disease pattern dominated by infectious diseases.

The techno-economic network is thought of as consisting of three main sub-networks – the scientific (S), the technological (T), and the market (M) sub-networks – and the two intermediate border zone sub-networks between them: the S-T sub-network that transfers the results of the scientific sub-network (S) into the technological and productive (T) sub-network, and the T-M commercializing sub-network, which brings the products to the end-users and consumers in the market (M) sub-network, see Figure 1 on page 7. The government may intervene in a techno-economic network by acting on any of these sub-networks. This paper analyses the Cuban biotech sector and vaccine industry in terms of these main conceptual elements. This analysis is structured around the following research questions.

- which elements of biomedical techno-economic networks existed in Cuba prior to the creation of the biotech sector, and what kinds of actions and interventions were decided upon in relation to the initial techno-economic evaluations?
- how did the techno-economic networks of the Cuban biotech sector emerge, and what is the ordering principle for the division of labor between the different biotech centers?
- how are the main techno-economic sub-networks S, T and M connected, and what are the consequences for the R&D activities in the S sub-network of that connection?
- why did a vaccine industry targeting 'traditional' infectious diseases evolve, when the main rationale for creating the biotech sector was to confront the emerging pattern of 'modern' diseases related to cancer and cardiovascular and congenital disorders?
- to what extent do the Cuban biotech centers collaborate across organizational boundaries?
- how are the techno-economic networks of the Cuban biotech sector managed and coordinated?
- what are the relations between the techno-economic networks of the Cuban biotech sector and the general domestic scientific, technological and productive systems in Cuba?

The accumulated responses to these questions will result in a comprehensive narrative about the Cuban biotech sector in general and the vaccine industry in particular. As stated in the first paper, the vaccine industry is an integral part of the biotech sector, to the extent that in Cuban and international literature and discourse it is not common to regard the vaccine related activities of the sector as an industry proper. The present analysis will demonstrate this integration. Nevertheless, it makes sense to analyze the vaccine related activities as a separate, but by no means isolated, phenomenon.

This paper starts with a brief introduction to the concept of the techno-economic network, with an emphasis on techno-economic evaluations and the options for interventions that are available. Then follows an account of the status of Cuban biosciences at the time of the initial techno-economic evaluation in the late 1970s. The paper proceeds with a description of the main biotech centers, their specialization and the way the different sub-networks (S, T and M, as well as the intermediate sub-networks S-T, T-M, and M-S) are ordered and organized by application of the concept of the 'complete cycle'. The next section is a detailed account of how the Finlay Institute was created in the process of combating the meningococcal epidemic in the 1980s, which in turn partly explains the apparent paradox related to the morbidity transition.

The next section describes how one of the production lines of the vaccine industry centers is integrated. Then follows an analysis of the management model that has been applied in the Cuban biotech sector: a centralized decision making process, which is facilitating, and to some extent mitigated by, formal and informal horizontal collaborative mechanisms. The final section before the conclusion is about the (weak) relation between the Cuban biotech sector and the remaining part of the Cuban national innovation system.

Techno-economic networks

Before presenting the empirical material some additional concepts of Callon's model should be introduced. A techno-economic network is *incomplete* whenever one or several of the sub-networks (S, S-T, T, T-M, M [and M-S]) are almost absent or severely underdeveloped. If, on the other hand, the sub-networks are in place, the techno-economic network is *chained*.

In a *convergent* network the links are strong and well developed to the extent that the various actors may mobilize resources from another sub-network at low costs in terms of efforts, translations and reordering. Conversely, in a *dispersed* network the links are weak in the sense that the translation of phenomena from one sub-network to another is cumbersome and problematic. For instance, in a convergent network a salesperson (T-M) may have a direct link with a scientist (S), while in a dispersed network even the interaction between designers (S-T) and production engineers (T) may be weak.

The notion of *short* and *long* networks is similar to that of incomplete and chained networks. Long networks comprise the entire chain from S to M, while a short network may not include S, only T and M, for instance. The difference, then, between a short and an incomplete network is that a short network would not be improved by adding the 'missing' sub-network, because the missing part is considered redundant for meeting the strategic goals in the first place.

Based on these distinctions it is possible to identify two main types of interventions: *breakthrough* action is to create new sub-networks in a discontinuous way, primarily whenever an incomplete network is present. Similarly, a dispersed network calls for *continuity* actions that aim at stimulating, extending or strengthening existing (weak) relations between the different sub-networks.

According to Callon, interaction between the main actors is mediated by *intermediaries,* like artifacts (products, prototypes, models, cargo transporting vehicles and vessels), texts (journal papers, R&D proposals, tender announcements, contracts), hybrid objects like money and its derivatives, and skills incorporated in humans. Having now (re)introduced the conceptual framework, we may move to the empirical sections of this paper.

The initial techno-economic evaluations

This section seeks to answer the first of the six research questions of this paper, namely what was the status of the biomedical techno-economic networks in Cuba by the late 1970s, and how did the Castro government go about in creating the Cuban biotech sector. In other words, which main considerations were influential in the initial techno-economic evaluations that resulted in the main design of the biotech sector?

The first paper touched briefly on a decisive event in the history of the Cuban public health system, namely the morbidity and mortality transition emerging in the late 1970s that subsequently became an important motivation for creating a domestic biotech sector. The following paragraphs assess the status of the Cuban biomedical scientific and technological capabilities

at that time, and on that basis we will try to infer the core ideas of the techno-economic evaluations that initiated the creation of the Cuban biotech sector.

This section describes the historical preconditions to the Cuban biotech sector, of which early interventions in medical sciences on part of the revolutionary government are important. It also points at the creation of the Biological Front and the interferon pilot project as two important stepping stones for what was later to come.

The history of Cuban biomedical science

The dedication to science by the Castro government is not to say that Cuban science started from scratch in 1959. Cuba's tradition of science and intellectual life dates back to the 18th century – one of the first universities in the New World was founded in the city of Havana in 1728 (García and Sáenz 1989).

Cuban science boasts a few but quite spectacular accomplishments, in particular in medicine. In 1901 the Cuban scientist Carlos J. Finlay (1833-1915) in cooperation with Walter Reed of the USA established that the mechanism of transmission of yellow fever was by way of the mosquito species *Culex* (García and Sáenz 1989). In 1951 a foundation for cardiovascular disease research was founded by Agustín Castellanos, who was subsequently nominated for the Nobel Prize in medicine. The institute was however closed in 1960, when its founder left the island (Anon. 2004) along with almost half of the share of the Cuban population that had a higher education of some sorts. Achievements like these two selected examples seem to have been results of individual excellence rather than organizational strength, since the research organizations appear to have been small and poorly funded.

With such a fragmented scientific infrastructure as a point of departure during the 1960s and early 1970s the revolutionary government established some 100 research centers at the universities, at the ministries, and at the Academy of Sciences (Fernández 1999). Of these there are some important research centers in medicine and related disciplines that would be of great importance in the later development of the biotechnology sector.

In 1962 the Institute of Basic and Preclinical Medical Sciences 'Victoria de Girón'[1] in Havana was created as a medical school and an organization for education of cohorts of medical professors, who in turn were deployed as teachers as new medical schools were founded in other cities (Figueras and Pérez 1998). While 'Victoria de Girón' educated medical professors, the National Center for Scientific Research (CNIC),[2] established in 1965, served a similar purpose in disciplines related to biomedicine, with research activities and training of scientists in physics, chemistry, biochemistry, biophysics, microbiology, mathematics and computer science (Bravo 1998).[3]

The same year 10 centers dedicated to research into the most important medical disciplines were established. Some of these were based on former hospital departments. The mandates were threefold: research, tertiary medical service, and education in medical specialties (Anon. 2004; Figueras and Pérez 1998).[4] By the late 1970s these centers, along with the university sector, constituted the main components of the Cuban S sub-network in biomedicine.

[1] Instituto Superior de Ciencias Básicas y Preclínicas 'Victoria de Girón'.
[2] CNIC: Centro Nacional de Investigaciones Científicas.
[3] Personal communication with Emilio García Capote, President of the Agency for Science and Technology, 3 July 2001.
[4] Personal communication with Emilio García Capote, President of the Agency for Science and Technology, 3 July 2001.

The T sub-network was less developed, however. In 1959 the Cuban chemical pharmaceutical industry consisted of some 110 private nationally owned laboratories and about 10 branch plants of US multinationals (Lilly, Pfizer, Lederle, etc.). The US laboratories were nationalized in 1960, and in 1966 they were transferred from three different ministries to become a state pharmaceutical industry under the Ministry of Public Health. During the 1970 the activities were concentrated to a total of 14 laboratories, in which investments were made for increased productivity and expanded product range with the main aim of generics manufacturing for import substitution (Figueras and Pérez 1998; Ratanawijitrasin and Wondemagegnehu 2002).[5] In other words, the chemical pharmaceutical industry was a *short* techno-economic network, comprising T, T-M, and M, but not S, since any S sub-network seems not to have been regarded as a desired or missing element. However, this techno-economic network had hardly any T capabilities in biopharmaceuticals.

Thus, this industry was no firm foundation for a science based and innovative biotech sector. Cuban sources agree that the biomedical sector developed largely independently of the pharmaceutical industry (Bravo 1998; Figueras and Pérez 1998). The main reason is that the chemical technologies that are used in traditional pharmaceutical production constitute a very different knowledge domain from that of biotechnological technologies. The only direct link that has been identified is the fact that by the 1970s the Biological Products Company 'Carlos J. Finlay' (not to be confused with the Finlay Institute) produced tetanus, diphtheria, smallpox, BCG, and rabies vaccines, as well as culture and diagnostics media. Nevertheless, a prominent example of this limited technological basis is the pharmacist and member of the Cuban Politburo Dr. Concepción Campa, who worked at the 'Carlos J. Finlay' factory prior to heading the group that invented the Cuban meningococcal vaccine.[6] More indirectly, it is possible that the pharmaceutical industry represented a pool of labor trained in pharmaceutical production.

As stated in the first paper, by the late 1970s Cuba had developed a highly integrated system of public health, biomedical science and higher education. Simultaneously, it was becoming widely acknowledged that genetic engineering could be a promising technology for health interventions, in particular for addressing the diseases of developed economies that were emerging as primary health problems on the island.

The initial techno-economic evaluations

However, the strategic question of how to proceed forward on this basis could not be resolved by the existing political and administrative bodies, so one of the first techno-economic evaluations that were performed in relation to the biotech initiative resulted in Fidel Castro's personal decision to create a high-profile interdisciplinary scientific consultative body in 1981, called The Biological Front,[7] headed by the president of the Academy of Sciences and former Director of CNIC. No such thing as a white paper or any other documents issued by the Biological Front is publicly available, but all sources agree that it had a profound impact in shaping the basic principles for the would-be Cuban biotech sector (Bravo 1998; Feinsilver 1993; Reid-Henry 2008; Thorsteinsdóttir, et al. 2004).[8] That is, as part of a techno-economic evaluation it was decided to set up the Biological Front, which in turn participated in later

[5] Personal communication with Celeste Sánchez, Senior Consultant at CECMED, 29 May 2001.
[6] Personal communication with Franklín Sotolongo, Finlay Institute, 4 September 2002; and with Celeste Sánchez, Senior Consultant at CECMED, 29 May 2001.
[7] The Biological Front: El Frente Biológico.
[8] Personal communication with Emilio García Capote, President of the Agency for Science and Technology, 3 July 2001.

decision making, both in strategic and techno-economic evaluations. Since the mandate of the Biological Front was to advice on how existing national resources in the S sub-network could be used in creating the T sub-network, it makes sense to think of the creation of the Front as a breakthrough action intended at constructing an S-T sub-network.

In terms of techno-economic networks then, what was present in Cuba by the late 1970s? Let us start by sketching out the techno-economic network of the public health system. The public health system may be thought of as a *chained* and *convergent* techno-economic network, since all the elements were present, and there were well developed links between them. The ten research centers in the most important medical disciplines represented the science (S) sub-network, but also the S-T sub-network since they comprised tertiary medical services. The primary and secondary health institutions produced *health services*, that is, the T sub-network. The universal and free access to the health services constituted the T-M sub-network linking the public health system (T) to the entire Cuban population (M).

If we now change the perspective from that of medicine and the public health system to that of medical biotechnology, the situation in the late 1970s was somewhat different. As in medicine the science (S) sub-network existed in the capacity of the same ten centers, as well as the multi-disciplinary CNIC, and again the Cuban population represented a potential market (M), but with the public health system now representing part of an as yet underdeveloped T-M sub-network. Note that in this sense one and the same actor-network – the public health system – fulfills the T functions in one techno-economic network, and the T-M functions in another.

In other words, the S and M sub-networks existed, and part of the T-M sub-network was also present, so by the late 1970s the Cuban biomedical techno-economic network was *incomplete*, with the T sub-network almost entirely non-existent. The situation that faced the Castro government at that time was that almost the entire productive capability would have to be created from scratch in order to create a chained techno-economic network. President Castro, supported by the Biological Front, decided to start with a small pilot project.

The interferon pilot project

In early 1981 Kari Cantell of the at the Finnish Serum Institute in Helsinki was surprised by a request made to him by the Cuban embassy in Finland, asking whether his Interferon Laboratory would kindly receive a delegation of Cuban scientists for training in production and purification of human leukocyte interferon. At that time interferon was hailed as a potential 'magic bullet' against both cancers and viral diseases, and Cantell's lab had earned a reputation as a world leader on interferon research. After a few moments of initial doubt Cantell conceded, and six Cuban scientists stayed at the lab for a few weeks. Back in Havana the group produced interferon in its own laboratory just a few months later (Cantell 1998), and two years later the group performed recombinant interferon production in clinical trial quality and quantities. Subsequently, the interferon pilot project was converted into a permanent research center, the Centre for Biological Research (CIB),[9] which still exists.

The success of the interferon pioneers was taken as a proof that the Cuban S sub-network was in possession of the required capabilities for appropriating advanced bioengineering techniques and executing targeted product developing projects. As a result of techno-economic evaluations in 1982-3 the major *breakthrough action* was decided upon. An entire and comprehensive biotechnological T sub-network was to be established, almost from scratch.

[9] CIB: Centro de Investigaciones Biológicas.

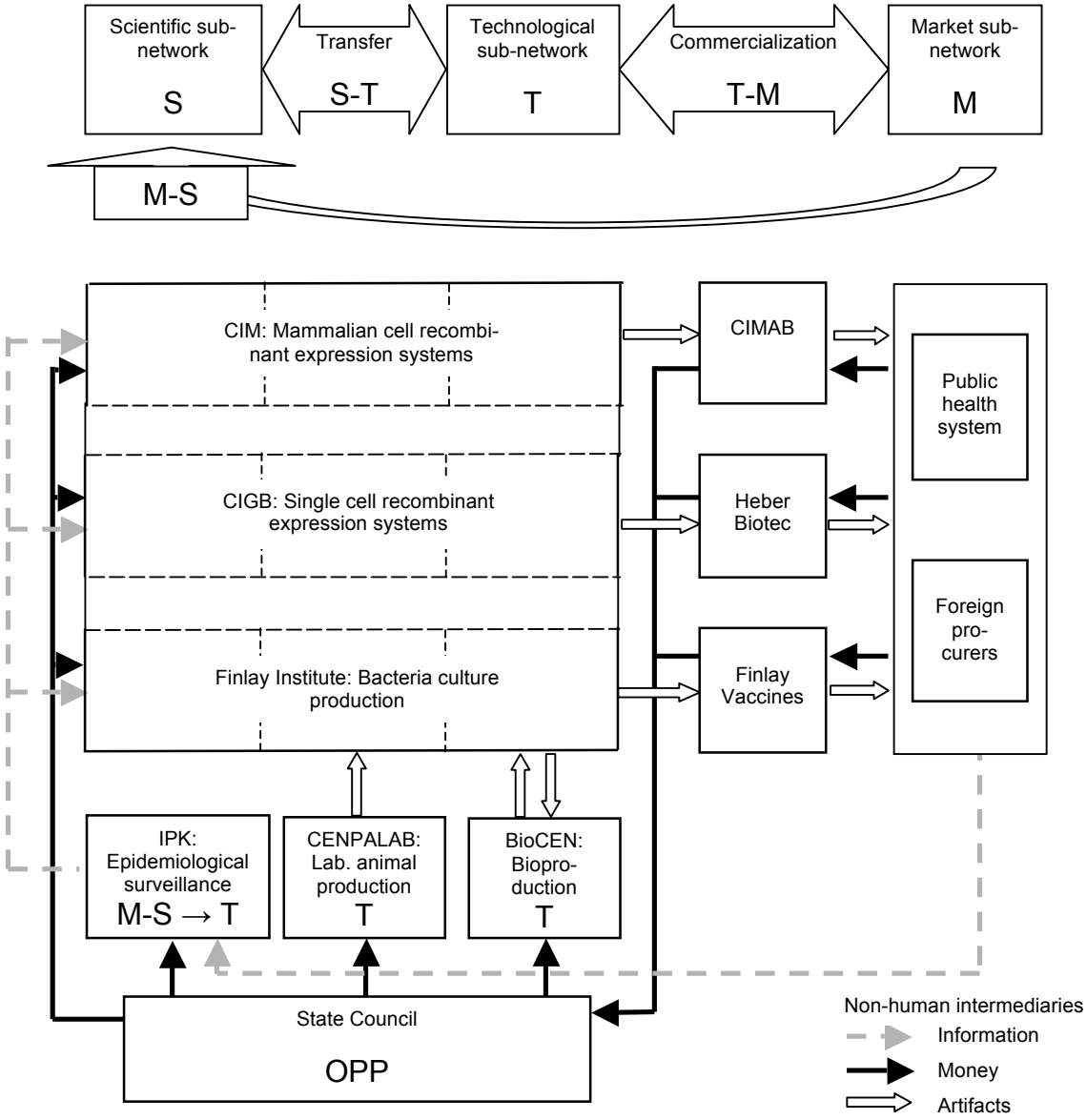

Figure 1. The Cuban vaccine industry as a techno-economic network. Adapted from Callon et al. (1992).

In 1986 President Castro proudly announced the inauguration of the flagship organization of Cuban biotechnology, the Centre for Genetic Engineering and Biotechnology (CIGB),[10] with a main focus on recombinant technologies in medical, industrial and agricultural biotechnology. Several other centers – among them Finlay Institute[11] and the Centre for Immunoassays (CIE)[12] – were also under construction or being planned for. A national *chained* and *convergent* techno-economic network in biotechnology was emerging.

[10] CIGB: Centro de Ingeniería Genética y Biotecnología.
[11] 'Instituto Finlay'
[12] CIE: Centro de Inmunoensayo.

The emerging techno-economic networks of the Cuban biotech sector

This section turns to the second of the main research questions of this paper, namely how the techno-economic networks of the Cuban biotech sector emerged, and what is the ordering principle for the division of labor between the different biotech centers. The section starts with an overview of the biotech centers that may be said to constitute the Cuban vaccine industry, framed by the techno-economic network concept. The division of labor and functions between the centers is described, and it will be demonstrated that the division of labor between the main centers is based on technology platforms, and that a few auxiliary centers are functionally specialized.

The Cuban vaccine industry as techno-economic networks

Figure 1 depicts the Cuban vaccine industry as a set of techno-economic networks, adapted to Callon's original model. In the capacity of their technological specialization, each of the centers could be said to constitute a techno-economic network in its own right, since most of them operate according to the concept of 'complete cycle'. The 'complete cycle' implies that each center is responsible for the entire value chain, from research through development, manufacturing, marketing and sales. In other words, for each of the technology platforms the S, T and S-T sub-networks are placed under the same roof and management. There is one dedicated T-M sub-network for each centre. The reason for them being separate legal and organizational entities will be explained below.

The main vaccine industry centers

Let us now turn to the most important research and production centers in the Cuban biotech sector. It is fair to say that four organizations also make up the core of the Cuban vaccine industry:

- Center for Genetic Engineering and Biotechnology (CIGB)
- the Finlay Institute
- Center for Molecular Immunology (CIM)[13]
- Center for Biomolecular Chemistry (CQB)[14]

The CIGB, inaugurated in 1986, is the flagship of the Cuban biotech sector, being as it is by far the biggest organizations. Its main focus is on recombinant technologies based on single cell organisms, and the main products are vaccines as well as in other medical, industrial and agricultural biotechnology products. The main income of the CIGB is derived from sales of their recombinant hepatitis B vaccine and recombinant streptokinase.

The CIM – inaugurated in 1994 – has its main focus on cancer, and its primary technology platform is recombinant mammalian cell cultures, that is, production of biological substances by inserting genes coding for that substance into a cell line taken from mammals. For instance, their erythropoietin[15] is produced in the Chinese Hamster Ovarian Cells (CHOC) expression system.[16] The product portfolio of CIM is dominated by therapeutic cancer vaccines and monoclonal antibodies.

The product portfolio of the Finlay Institute is dominated by vaccines based mainly on 'traditional' bacterial fermentation technologies. The institute has several processing lines for bac-

[13] CIM: Centro de Inmunología Molecular.
[14] CQB: Centro de Química Biomolecular.
[15] The hormone erythropoietin stimulates the production of red blood cells.
[16] Personal communication with Rolando Pérez, Director of R&D at CIM, 5 May 2009.

terial vaccines, and heads the National Program for Science and Technology in Human and Veterinary Vaccines. The Finlay Institute is almost entirely dedicated to vaccine products.

The last of the core centers to be mentioned is also the latest to be created. It was founded in 2008 by fusing the Center for Pharmaceutical Chemistry with the Center for Synthetic Antigens at the University of Havana into the new entity Center for Biomolecular Chemistry (CQB). The Center for Synthetic Antigens developed a method for industrial production of synthetic haemophilus B (HiB) polysaccharide to be used as the active ingredient (antigen) in the HiB vaccine, which protects against meningitis and sepsis. CQB specializes in development of methods for producing biological molecules (like antigens for vaccines) by way of chemical synthesis.

The reason for omitting the CQB in the figure is that it is so recently established that there was not sufficient data available to locate it accurately in the scheme. The perforated boundaries of the three other core centers illustrate the close horizontal collaboration that is facilitated by the Scientific Pole, whose functions will be explained in more detail below. Since the three auxiliary centers near the bottom of the drawing are also part of the Scientific Pole, applying dotted lines on their boundaries would have been easily justifiable. However, it was preferred to underscore their status as functionally specialized organizations by placing them apart from the rest, and rather connect them by the arrows indicating the main flow of non-human intermediaries between them. The State Council has established itself as an obligatory passage point in the actor-network of the Cuban biotech sector by siphoning off and controlling the export revenues generated by the commercializing branches of each of the centers.

Most of these biotech centers were created around research groups in existing laboratories and research centers. One group at the 'Victoria Girón' Institute working on hepatitis B immunology was subsequently transferred to the CIGB to develop the hepatitis B vaccine (Bravo 1998; Pentón, et al. 1994). A group of researchers at CNIC originally working on detection of alpha-fetoproteins for prenatal diagnosis neural tube malformations became the germ seed for the CIE, which later on developed the mass screening equipment MicroSUMA (Bravo 1998).[17] As will be spelt out in more detail below, the National Reference Laboratory for Meningococci at the Institute for Hygiene, Epidemiology and Microbiology, making the first steps in developing a Cuban meningococcal vaccine, later evolved into the Finlay Institute (Valcarcel, et al. 1991). Finally, somewhat later a group at the National Center for Oncology and Radiobiology (INOR)[18] – one of the ten medical research centers created during the 1960s that were mentioned above – working on monoclonal antibodies was 'spun off' to found the Centre for Molecular Immunology (CIM), which was inaugurated in 1994 (Bravo 1998).

Auxiliary centers

In addition, there are three entities that serve important auxiliary purposes:

- National Center for Bioproduction (BioCEN)[19]
- the tropical medicine institute 'Pedro Kourí' (IPK)[20]
- National Center for Production of Laboratory Animals (CENPALAB)[21]

[17] Personal communication with Roberto Guilarte, Sales Manager at TecnoSuma International S.A., 23 May 2001.
[18] INOR: Instituto de Oncología y Radiobiología.
[19] BioCEN: Centro Nacional de Biopreparados.
[20] IPK: Instituto de Medicina Tropical 'Pedro Kourí'.
[21] CENPALAB: Centro Nacional para la Producción de Animales de Laboratorio.

Contrary to the 'complete cycle' centers, BioCEN is a pure production facility without any in-house R&D activities aimed at therapeutic, preventive or diagnostic product development to speak of. In addition to several complete bioproduction lines BioCEN has facilities for finalization of vaccine products, i.e. formulation, filling and lyophilization, that are produced at the other centers. Moreover, the center has a product portfolio of culture media and other intermediary biological products (BioCEN 2006). In other words, BioCEN is a specialized T functions center.

The tropical medicine institute 'Pedro Kourí' (IPK) is the hub of the epidemiological surveillance systems in Cuba. It also houses hospital facilities, which are used in early clinical trials of vaccines, and it has a dengue fever vaccine development project underway. The immediate rationale for creating a dedicated tropical medicine organization was increasing contact with African countries – both military and civilian – throughout the 1980s.[22]

The IPK may be said to constitute an M-S sub-network, a category not included in Callon's original model. As a 'center of calculation' for the Cuban epidemiological surveillance systems, it translates knowledge generated by the public health system about the national market M – *i.e.* the Cuban population – into scientific information about the incidence, prevalence and disease burden of different illnesses, as well as the impacts of the products – effectiveness data and adverse events – that are distributed. This scientific information is then fed into the science sub-network S. Note that this additional knowledge flow is not channeled through the T-M and S-T sub-networks that are in operation, but by way of a separate sub-network.

Note that in vaccines also the T, T-M and M sub-networks use the information generated by the M-S sub-network. The T sub-network uses information about strain specific incidence rates in deciding culture strains for antigen production, the T-M sub-network uses disease burden data in its marketing activities, and similarly, the procuring organizations in the M sub-network also use disease burden data in calculating vaccine needs prior to issuing their purchase tenders. IPK also houses some S and T activities like the dengue fever vaccine development project, and the clinical trials services that are provided to the other centers could be said to be a T-M function.

Lastly, the CENPALAB, which was created as early as in the mid 1980s, produces a diverse range of laboratory animals to the biotech centers, to the extent that Cuba is practically self-sufficient on this product line. The auxiliary centers do have some in-house R&D activities, but these are mainly aiming at perfecting and improving on their production methods.[23] Like BioCEN, CENPALAB is specialized in T functions, but while BioCEN does end-of-pipeline processing, CENPALAB provides input to both the S and the T sub-networks.

We may now respond to the second main research question of the paper. In techno-economic evaluations in the early 1980s the Cuban government decided to found a number of different biotech centers. While the main biotech centers have specialized according to their technology platform, the auxiliary centers are specialized according to *function*.

We may now move to the third main question of this paper, namely that of how the S, T and M sub-networks connect to each other in the Cuban biotech sector. The following section presents the fundamental principle for securing the convergence of the techno-economic networks in the biotech sector – 'the complete cycle' – and it is becoming evident that each of

[22] Personal communication with Emilio García Capote, President, the Agency for Science and Technology, 3 July 2001.
[23] Personal communication with Emilio García Capote, President, the Agency for Science and Technology, 3 July 2001.

the main biotech centers constitute separate techno-economic networks covering the entire chain from S through to T-M on their respective assigned technology platforms.

The concept of the complete cycle

A fundamental principle for the organization and division of labor in the Cuban biotech sector is the concept of 'complete cycle' innovation, which means that each center is responsible for the entire innovation process, from 'directed basic science', applied science, development, industrial scale-up, IP management, clinical testing, registration, marketing and sales (Lage 2006). The complete cycle not only connects T and M, but also serves to create the S-T sub-network securing the reciprocal transfer of knowledge and other intermediaries between the scientific (S) and technological (T) sub-networks.

Connecting S and T by the complete cycle

What kinds of knowledge producing activities take place when the scientific sub-networks are divided according to technology platforms, and placed under the management of a highly market-oriented organization? Or in other words, what happens to the S sub-network when it is connected to the T sub-network by organizational and physical co-location?

As early as in 1993 Feinsilver (1993), referencing international biotechnology experts, expressed concerns that applied science was prioritized at the cost of basic science, which could jeopardize the performance of Cuban biotech in the long term. De la Fuente (2001) followed up by criticizing what he sees as a priority for short term profit making products instead of long term technology development, following the crisis in the 1990s.

Bravo's (1998) compilation of interviews with prominent Cuban bioscientists also discusses this issue, and although different opinions on the matter were expressed, several of the interviewees agreed that publishing was a low priority and that most research was carried out with a concrete medical application in mind. It is also my impression that in Cuba it is difficult to get funding for a research project that has scientific publication as its sole objective.

Thorsteinsdóttir et al. (2006) conducted a comparative scientometric study of the performance of seven emerging or developing countries in the field of health biotechnology from 1991 to 2002, among them Cuba. Cuba is number 40 in the world when ranking countries according to number of papers in absolute terms, but the figures are so disparate that the graph featured is on a logarithmic scale: while the USA – unsurprisingly topping the list – had 59,865 papers that time period, Cuba had 216, which places her close to the world average of number of papers per capita. CIGB, Finlay Institute and CIM accounted for 97 percent of the Cuban papers (Thorsteinsdóttir, et al. 2005), which may be indicative of the extent to which the S activities in Cuban biotech are concentrated to these centers, possibly at the cost of the university sector. One of the conclusions of Thorsteinsdóttir et al. (2006) is that further research should discuss whether developing countries ought to structure their public sector health biotechnology research around universities or research institutes. At any rate, it is a fact that the Cuban biotechnology S sub-network is capable of producing internationally publishable science.

Let us turn to the question of which scientific strategies that are pursued under such conditions. In Reid-Henry's (2008) opinion

> […] the key element in Cuba's 'experimental milieu' [is] the development of basic research within an applied research framework. (Reid-Henry 2008), p 5

Rolando Pérez at CIM expanded on the concept of 'translational research' (Reid-Henry 2008): the first phase of the innovation process would be 'science driven, but patent oriented',

characterized by exploratory, knowledge generating activities. Part of these efforts would be granting resources for so-called 'Question of the year'-research projects, which are proposals submitted by individual scientists to put a designated amount of work into preliminary but risky research into a specific topic. One step further down the pipeline full blown research projects would have a timeline of 3-4 years, with the aim of generating a 'proof of principle' and a patent application.[24]

I also had the joy of listening to Vicente Vérez at CQB ridiculing what he saw as the 'myth of pure basic science'. In his not much controversial opinion virtually all research activities – wherever in the world – would be funded with some sort of practical or commercial application in mind. Apart from that, he advised against developing countries putting too much of their scarce resources into science without practical objectives. He envisaged instead 'basic directed science' with concrete medium term medical objectives,[25] a concept very similar to Pérez' notion 'translational research'.

The centers seem to be at liberty to organize their research activities according to their own preferences. My interview with Gustavo Sierra at the Finlay Institute left the impression that their R&D project portfolio was more influenced by requests and assignments made by the State Council than what was the case with CIM for instance.[26] This might be explained by the fact that while the technology platform of the Finlay Institute is based on traditional bacteria culture techniques, CIM's therapeutic cancer vaccines, based on proprietary antigens and adjuvants,[27] are cutting-edge science.

In relative terms the Cuban S-T sub-networks display a superior performance in Quach et al.'s (2006) comparative analysis of biotechnology patenting in seven selected developing or emerging economies,[28] with a ratio of health biotechnology papers to health biotechnology patents of 9:1. South Korea's 12:1 was second, while Brazil and Egypt were forming the base with 70:1 and 80:1 respectively. In other words, in Cuba a comparatively high proportion of the scientific results is translated into patentable technology.

We may conclude that the Cuban biotech sector is capable of producing scientific information of international standards, and that its co-location of the S and T sub-networks does not represent any direct obstacle to scientific knowledge production. Rather the contrary: although the scientific knowledge production is guided by demands for practical application, the Cubans are willing and able to conduct research into basic scientific matters whenever circumstances so demand. The relatively low paper to patent ratio suggests that there is strong convergence between the S and T sub-networks.

It seems like the Cuban biotech sector is organized more like a commercial pharmaceutical conglomerate than as a traditional public sector institute. For instance, in Brazil it is the Ministry of Science and Technology that has had the responsibility for promoting health biotechnology, and the links with the industrial sector have been somewhat poorly developed

[24] Personal communication with Rolando Pérez, Director of R&D at CIM, 5 May 2009.
[25] Personal communication with Vicente Vérez, Director of CQB, 4 February 2009.
[26] Personal communication with Gustavo Sierra, Vice President, Finlay Institute, 3 February 2009.
[27] The antigen is the substance that is intended to induce a *specific* immune response, i.e. a response directed at the specific microbe that the vaccine is suppose to protect against. The adjuvant is the component of the vaccine that produces a *general* immune stimulation, without which the specific stimulation of the antigen would not be sufficiently strong to elicit protection against the (specific) microbe – or in this case the malign cells – in question.
[28] Quach et al. (Quach, et al. 2006) is a result of the same research project as Thorsteinsdóttir (2006; 2005). The group comparatively studied the biotechnology sectors of Brazil, China, Cuba, Egypt, India, South Africa, and South Korea.

(Thorsteinsdóttir, et al. 2005). In contrast, the Cuban biotech sector could be seen as an example of applying private sector organizational principles in a publicly operated industry.

Connecting T and M with the complete cycle

In Figure 1 on page 7 the commercializing arms of each biotech center appear as separate boxes below the T-M double arrow. Heber Biotec is the commercializing division of CIGB, Finlay Vaccine markets the vaccine products of the Finlay Institute, and CIMAB takes CIM's products to the markets. In other words, the T-M sub-network connecting the development and production sub-network T to the market sub-network M in the Cuban biotech sector was established by creating one marketing division for each techno-economic network.

There are some exceptions, though. CQB's HiB vaccine is marketed by CIGB's Heber Biotec, and the 'Pedro Kourí' tropical medicine institute heads a dengue fever vaccine project without having manufacturing or marketing capabilities in-house, so the complete cycle concept is not dogmatically applied to all centers.

At any rate, such anomalies do not explain why the T-M sub-networks have been legally separated. In practice the managing directors of the main centers seem to be responsible for the activities of the respective commercializing companies, so there seems to be a high degree of convergence across this organizational boundary. The reason for the separation is in fact drawn into the figure: the cash flow is diverted out of each techno-economic network and transferred to the State Council.

However, before spelling out the full rationale for this way of ordering the techno-economic networks this paper presents a more detailed account of the process of developing the meningococcal group B and C vaccine and of creating the Finlay Institute. In this way a more profound understanding of the techno-economic evaluations that underlay the creation of the biotech sector is provided, and we also respond to the fourth main question of the paper by explaining the apparent paradox that was identified in the first paper: Why was it decided to create a vaccine industry targeting 'traditional' infectious diseases, given the fact that the main initial strategic evaluation resulted in a decision to confront the emerging patterns of 'modern' diseases like cancer, and cardiovascular and congenital conditions?

The history of the meningococcal vaccine and the Finlay Institute

This case study illustrates the point made in the other paper that strategic and techno-economic evaluations do not proceed in a linear fashion in which the latter succeeds the former. Quite on the contrary, although in this case a techno-economic sub-network based on bacteria fermentation vaccine production technologies – the Finlay Institute – evolved as a result of the strategic decision of developing a meningococcal vaccine, that very sub-network constituted an irreversibility that influenced later strategic evaluations in the direction of expanding the vaccine innovation capabilities of the biotech sector.

Meningococcal meningitis and septicemia are frightening diseases. Apparently healthy children and adolescents may succumb in a matter of days. Meningitis manifests itself when the meningococcal bacteria invade the membranes of the brain, and neurological sequelae like deafness and mental retardation are common in survivors. Septicemia, or blood poisoning, occurs when the bacteria invade the blood stream, obstructing circulation with the potential of causing multiple organ failures. Survivors risk amputations and disfiguration due to disrupted blood supply to limbs and skin tissues (Cartwright 1995; Dull and Rosenstein 2001).

The Cuban health authorities reported slightly increasing incidence rates of meningococcal disease in 1976. In 1978 it was clear that a national meningococcal epidemic was developing,

and the Ministry of Public Health founded a National Reference Laboratory for Meningococci at the National Institute for Hygiene, Epidemiology and Microbiology, with three employees (Valcarcel, et al. 1991).

In 1979 the Cuban health authorities purchased 3.2 million doses of a bivalent meningococcal group A and C vaccine from Institute Mérieux of France, which were distributed at a coverage rate of 78 percent of the total population up to 19 years of age. At that time 34 percent of the cases were of group B of the *Neisseria meningitidis*, and 50 percent were of group C. As a result of the campaign, the incidence rate of group C infection plummeted, but only to be replaced by a corresponding increase in group B infection. And the total incidence rate continued to rise.

The problem was that no vaccine against group B meningococci was available. The capsular polysaccharides of group A, C, W-135, and Y meningococci are immunogenic and safe vaccine antigens, but the group B polysaccharide is poorly immunogenic, and to make things worse, in 1983 it also appeared some evidence of a theoretical risk that using it as an antigen could cause autoimmune reactions against human brain tissue (Finne, et al. 1983). In other words, some experimental vaccines based on alternative antigens would have to be explored. This strategy entailed using the National Reference Laboratory as part of a T-M sub-network, in an effort at connecting to existing overseas T sub-networks (in turn backward connected to their respective national S and S-T sub-networks) to create a convergent international techno-economic network for a meningococcal group B vaccine.

The Cubans first contacted the Metchnikov Research Institute in Moscow in the Soviet Union, which worked on a trivalent group A, B and C meningococcal vaccine. In 1981 that vaccine was tested in Cuba on some 48 000 children between 6 months and 15 years of age, but it turned out tragically that both morbidity and mortality were higher in the vaccine group than in the unvaccinated control group (Valcarcel, et al. 1991).[29]

Then the Canadian Institute 'Armand Frappier' was contacted with the aim of testing their trivalent group A, B and Y vaccine in Cuba. However, the Phase I trial involving 11 children demonstrated only short lasting protection. The reason was that as it turned out the group B component of the Frappier vaccine was a different serotype from the group B strain causing the Cuban epidemic, and did not elicit protection against that strain (Valcarcel, et al. 1991).

The strategy of building on existing prototype vaccines was abandoned, or perhaps put better, was becoming depleted of viable options. As a result of a strategic evaluation in 1983 it was decided to start developing a vaccine in Cuba. In other words, instead of connecting to overseas T sub-networks, a techno-economic evaluation resulted in a decision to create a T sub-network in Cuba, based in part on the scientific capabilities (S) that had accumulated at the National Reference Laboratory.

The National Reference Laboratory for Meningococci was relocated from its downtown Havana location at the Institute for Hygiene, Epidemiology and Microbiology, and its new premises were completed in March 1984, on the same site where the Finlay Institute is located today, in a western suburb of Havana. While the formal affiliation of the laboratory was with the BioCEN, after the relocation the State Council and Fidel Castro became its real sponsors. A research group consisting of 15 persons was created, under the leadership of Dr. Concepción Campa, the pharmacist who had been working at the Biological Products

[29] At that time almost 500,000 doses of that vaccine had been distributed in an immunization campaign targeting 80 percent of children over 5 years of age in 7 provinces, the effect of which is not documented.

Company 'Carlos J. Finlay' (not to be confused with the Finlay Institute) of the pharmaceutical industry.[30]

Combating the epidemic had received high priority from the Ministry of Public Health all the way, but now the direct sponsorship shifted upwards to the top national political level. The research group could now count on extensive support from and cooperation with other research and production centers, like the Institute for Tropical Medicine 'Pedro Kourí' (IPK), whose epidemiological surveillance system improved significantly through the experiences made during the epidemic, the National Center for Scientific Research (CNIC), the Center for Biological Research (CIB), the Biological and Pharmaceutical Laboratory (LABIOFAM), the Center for Laboratory Animals (CENPALAB), all of which would later become parts of the Polo Científico. In addition, the group still collaborated closely with the Vice ministry of Hygiene and Epidemiology and the National Institute.[31]

The group had direct and regular contact with Fidel Castro, who personally sanctioned requests for investment in equipment and materials, and several sources testify that he even personally inspected that their food and lodging conditions were satisfactory (Bravo 1998; Valdés, et al. 1999). In other words, a convergent – but still incomplete – domestic techno-economic network comprising the sub-networks from S through to T was in operation.

The next major step was to contact Dr. Carl Frasch at the Food and Drug Administration (FDA) in the USA. His laboratory at the Biologics Division at the National Institutes of Health (NIH) campus outside Washington DC had developed a meningococcal group B vaccine based on outer membrane protein complexes instead of capsular polysaccharide, and a Phase III trial in South Africa (Frasch, et al. 1983) had been prematurely terminated because his South African partners had run out of money. Hence, he was eager to test his principle in Cuba, and by traveling as a consultant for the Pan American Health Organization (PAHO) he was able to evade the US embargo legislation.[32] The objective was to develop a meningococcal group B outer membrane protein vaccine based on Dr. Frasch's production method, but using the Cuban bacterial strain instead of the South African strain used in his original prototype.

Over the next few years Frasch visited Cuba four or five times, with travel grants from PAHO. He taught the Cubans the principles for producing a vaccine based on protein complexes of the outer membrane of meningococci. Also Dr. Claire Broome of the Centers for Disease Control and Prevention (CDC), whose first visit to Cuba was in 1979, assisted in designing the clinical trials. After preclinical testing and a number of Phase I and II trials, the Cuban vaccine was tested in a Phase III double blind trial starting in early 1987 that involved about 106,000 volunteering children and adolescents. The protective efficacy rate was estimated at 83 percent, which proved that the vaccine would be feasible for implementation in immunization campaigns and programs.

Such activities started in 1990, and the entire population in the age group 0 – 20 on the island was immunized by April 1991. Incidence rates, which were already on the decline when the campaign was initiated, quickly returned to their low pre-epidemic endemic level (Frasch 1983; Sierra, et al. 1991; Valcarcel, et al. 1991).[33] Eventually, by mobilizing and enrolling the

[30] Personal communication with Franklín Sotolongo, Finlay Institute, 4 September 2002.
[31] Personal communication with Franklín Sotolongo, Noel González and Arturo Talavera, Finlay Institute, 28 June 2001.
[32] Personal communication with Carl Frasch, Chief, Laboratory for Bacterial Polysaccharides, Center for Biologics Evaluation and Research, Food and Drug Administration, 5 February 2002.
[33] Personal communication with Carl Frasch, Chief, Laboratory for Bacterial Polysaccharides, Center for Biologics Evaluation and Research, Food and Drug Administration, 5 February 2002.

T-M distribution capabilities of the public health system a chained and convergent techno-economic network – comprising all the elements from S through to M – came into operation.

Commercial exports to Brazil commenced in 1989, and the vaccine was used in immunization campaigns in eight states in that country. In epidemiological terms the results were mixed, probably due to the fact that the Brazilian epidemic was caused by several group B serotypes in addition to the one that was used to produce the vaccine (Noronha, et al. 1995). By this act the M sub-network extended itself from the national public health system to overseas markets.

Feinsilver (1993) estimates that up to 1991 at least 30 million doses had been exported to Brazil, at an average price in the area of US$ 5 – 7, and a total value of at least US$ 180 million. An agreement for transferring the production technology to Brazil was signed in 1992, but was later that year suspended because of the low efficacy of the vaccine in Brazil (Feinsilver 1993). To date, the VA-MENGOC-BC® has been manufactured in a total of 55 million doses and exported to 15 countries (Sotolongo, et al. 2007).

In 1999 the US Treasury Department granted SmithKline Beecham (later merged into GlaxoSmithKline) an approval to enter an agreement with the Finlay Institute. The agreement covers testing, clinical trials and marketing of the VA-MENGOC-BC® vaccine, and entails a notable exemption from the otherwise extremely tight (and unlawful) US embargo legislation. However, although the agreement held the potential for up to US$ 20 million worth of revenues for the Institute (SmithKline Beecham 1999; TEC 2004), little has materialized from this deal.

The meningococcal vaccine and irreversibility

There are two momentous events in this story. The first is the 1983 decision to initiate a domestic vaccine development project. That decision has a techno-economic evaluation component in creating a new actor by relocating the National Reference Laboratory both physically and organizationally, and it also has a strategic evaluation component in identifying a new target product for the techno-economic network. As a strategic evaluation it deviated from the initial interest of targeting 'modern' health problems, but still served the overarching political goal of reducing both overall and child morbidity and mortality.

The second event is the commercialization of the vaccine by exporting it to Brazil, starting in 1989. A product that was intended exclusively as a solution to a serious domestic health problem turned out to have a commercial potential, and it is possible that this made the Cuban leadership aware of the fact that 'traditional' disease patterns might open windows of opportunity for generation of export revenues.

The consequence of this composite strategic and techno-economic evaluation was that the Cuban biotech sector developed strong specific capabilities in vaccine development and manufacturing (T) based on bacteria culture. In a few years – from 1983 to 1987 – the T sub-network in this technology platform came into being, with development capabilities and industrial scale manufacturing facilities complete with fermentation, purification, formulation, final processing, and filling equipment, as well as the human resources to operate it. The biotech sector as such also developed more general capabilities in vaccine development and clinical testing of vaccines, for instance by improving the epidemiological surveillance systems and drug regulatory institutions. Finally, the Cubans made their first experiences in establishing overseas marketing capabilities (T-M).

This ordered set of heterogeneous resources now punctualized itself into a stabilized techno-economic network that represented what Callon calls an *irreversibility* (Callon 1992). By the

same token it also punctuated itself as a node into other actor-networks – *i.e.* the rest of the emerging Cuban biotech sector.

> In a strongly convergent and irreversibilized network, the actors are perfectly identifiable, and their behavior is known and predictable. (Callon 1992), p 97

Once in place, this irreversibilized techno-economic network in the field of bacteria fermentation based vaccine innovation represented a factor in subsequent strategic evaluations. Or, put slightly differently: these capabilities turned themselves into important premisses for later strategic evaluations. While this techno-economic network was originally created as a tool to solve a specific problem at hand – the meningococcal epidemic – the question of whether there were other problems at hand that could be solved by that tool now arose.

Strategic evaluations and the morbidity transition

We may assume that this techno-economic network lowered the threshold for targeting infectious diseases in the strategic evaluations that were to follow. At any rate, subsequently the leptospirosis and typhoid fever vaccines were developed. Later on, it was also decided to develop the pentavalent DTP-HiB-hepB vaccine, and the DTP components of the old triple vaccine were all based on bacteria culture. The tetanus toxoid – the T component of the DTP – was also needed as the carrier protein in the HiB conjugate vaccine. More recently, the techno-economic network of the Finlay Institute will use bacteria culture technologies to supply the polysaccharide antigens to a polyvalent pneumococcal conjugate vaccine to be developed in collaboration with the newly founded Centre for Biomolecular Chemistry (CQB).[34]

However, it is not only establishment of the irreversibilized techno-economic network in bacteria culture that may explain the apparent paradox of targeting infectious diseases instead of the diseases that were emerging with the morbidity transition. Internationally, the technological frontier in 'vaccinology' was advancing, opening new windows of opportunity. In 1981 the plasma derived hepatitis B vaccine was licensed by Merck, and the recombinant hepatitis B vaccine came on the market in 1986 (Galambos and Sewell 1995). Recombinant protein production in single cell expression systems has later become the core technology platform for the CIGB, and the hepatitis B vaccine project, along with the interferon pilot project, seem to have been essential in creating those capabilities.

Similarly, the conjugation technology that was introduced with the HiB vaccine in the USA in 1988 could be used for other bacterial vaccines, like meningococci and pneumococci. Conjugating the polysaccharide to a 'carrier' protein induces lasting immunity in infants in contrast to the previous 'pure' polysaccharide vaccines. Thus, conjugate vaccines are suitable for childhood immunization programs, and not only immunization campaigns for combating outbreaks or epidemics, like for instance the French meningococcal group A and C non-conjugated polysaccharide vaccine that was used by the Cubans in 1979.

World-wide, the 1990s and 2000s witnessed old polysaccharide vaccines against group A, C, Y, and W-135 meningococci being replaced by or complemented with corresponding conjugates. Similarly, Wyeth's 7-valent pneumococcal conjugate vaccine was released in 2000, and its new 13-valent and GSK's 10-valent vaccines are currently in the process of entering the market. The capabilities in bacterial polysaccharide chemistry now possessed by the CQB will be an indispensable element in developing a Cuban pneumococcal conjugate vaccine, as mentioned above. Consequently, both the Cuban hepatitis B and the HiB vaccine develop-

[34] See also the paper about the pneumococcal vaccine Advance Market Commitment, on page **Error! Bookmark not defined.**.

ment projects – apart from targeting endemic disease in the country – seem to have been strategic moves in order to acquire technology platforms that had been developed abroad.

The above paragraphs illustrate the potential complexity of strategic evaluations. One does not just consider the public health problems and economic opportunities and challenges at hand, but also technological opportunities that may be exploited or appropriated by continuous or breakthrough actions directed at the existing techno-economic networks. Although the 'modern' morbidity pattern was seen as the main public health challenge, the combat against 'traditional' (childhood) infectious diseases was far from won, and there was still a potential of further reductions of the infant mortality rate. Moreover, the techno-economic networks that had developed in the course of the meningococcal epidemic were in a position to exploit novel technological platforms, like recombinant protein expression and chemical conjugation. We must also add the economic considerations that were identified in the other paper.

The creation of the techno-economic networks of Cuban biotech

We may now sum up the responses to the first four questions of this paper. According to Callon a techno-economic network is *incomplete* whenever one or several of the sub-networks (S, S-T, T, T-M, M [and M-S]) are almost absent or severely underdeveloped. If, on the other hand, the sub-networks are in place, the techno-economic network is *chained*. Based on these distinctions it is possible to identify two main types of interventions: *breakthrough* action is to create new sub-networks in a discontinuous way, primarily whenever an incomplete network is present. Similarly, a dispersed network calls for *continuity* actions that aim at stimulating, extending or strengthening existing (weak) relations between the different sub-networks.

The strategic evaluation that resulted in the decision to create a Cuban biotech sector called for massive *breakthrough* interventions. The science sub-networks (S) existed, but were dispersed, and the techno-economic networks were incomplete bordering on non-existence when it came to technological sub-networks (T) that could convert the knowledge from S into products that could be transferred to the markets (M). The national T-M sub-network already existed, represented by a national, universal, comprehensive and free public health system, while the international markets had to be developed by *continuity* actions that are still ongoing.

By applying the concept of the 'complete cycle' chained and convergent techno-economic networks based on selected technology platforms are integrated under one management, from S through to T-M. One organization, the 'Pedro Kourí' institute, constitutes M-S – a direct and separate link between the market (M) and science (S). However, although the organizational boundaries of the techno-economic networks are coinciding with the boundaries of the technological platforms, one of the vaccine products demonstrates that there is close collaboration between several of the centers operating in the vaccine industry.

Horizontal collaboration

So far we have examined the M-S sub-network (at the Pedro Kourí Institute), the technologically specialized S, S-T, and T sub-networks of the complete cycle research and production centers, as well as the T sub-networks of the auxiliary centers. Let us now address the perforated lines separating the three core vaccine centers in Figure 1. To what extent do the centers collaborate in their research and development activities, and to what extent are their production systems horizontally integrated?

Collaborative R&D activities

My sources repeatedly made reference to different collaborative research and development projects, in which typically several organizations in the Scientific Pole were involved. This is supported by Thorsteinsdóttir et al. (2006), who found that in 2000-2 more than 30 percent of internationally published Cuban papers in health biotechnology had authors from more than one domestic organization, a share that had tripled from 1991-3.[35] Thus, the perforated lines in Figure 1 may be empirically justified in terms of R&D collaboration. We now turn the attention to the production capabilities, illustrated by the case of the complex and integrated production line of the pentavalent DTP-hepB-HiB vaccine.

Integration of a production line in the vaccine industry

The case of the pentavalent vaccine illustrates an integrated product line and development process involving four of the centers of the Cuban vaccine industry. This case will demonstrate that although each complete cycle center may be said to constitute a techno-economic network in its own right, together they constitute a meta-network capable of manufacturing a vaccine containing components developed or produced by three of the different techno-economic networks.

The pentavalent vaccine contains antigens against five different childhood diseases: diphtheria, tetanus, whooping cough (pertussis), hepatitis B and haemophilus B, commonly abbreviated as DTP-hepB-HiB. The purpose of such a combination is to reduce the number of injections needed to complete the immunization schedule of national immunization programs, thereby giving rise to savings in terms of both immunization costs and human suffering. Several vaccine manufacturers already have this vaccine on the market, but the Cubans decided to develop and manufacture their own, both as an import substitution measure and as a foreign currency earner. Globally, pentavalent vaccines are used in national immunization programs in both developed and developing countries.

The DTP components of the vaccine is manufactured by the Finlay Institute, and these are for most practical purposes identical to the old triple vaccine, which has been on the market for several decades. The diphtheria and tetanus antigens are modified toxins (toxoids) from the bacteria, and the pertussis antigen is the whole-cell inactivated bacterium. The production processes for these antigens are based on cultivation of the bacteria, and purification and modification of the antigenic substances. The history of CIGB's recombinant hepatitis B vaccine and CQB's synthetic HiB vaccine were accounted for above.

In short, the pentavalent DTP-hepB-HiB vaccine is a combination of a traditional product (the DTP vaccine), a reverse engineered recombinant product (the hepB component), and a truly novel product based on chemical synthesis (the HiB component). The DTP antigens and the tetanus toxoid for the HiB component (the synthetic HiB polysaccharide is conjugated to the tetanus toxoid protein) are manufactured by the Finlay Institute, while the HiB polysaccharide and the hepatitis B antigens are manufactured at GIGB, which also carries out the conjugation of the HiB component. Final processing and filling is done at BioCEN. The Heberpenta® vaccine is marketed by Heber Biotec, CIGB's sales and marketing department. The development process involved constructing a modularized product by close collaboration across organizational boundaries. The production line also demands coordination across organizational boundaries. This is but one expression of the successful inter-organizational collaboration of the Cuban biotech sector.

[35] Cuba also scores high on the international co-authorship figure – also 30 percent.

The boundaries between the techno-economic networks of the three core organizations of the Cuban vaccine industry are porous both in the S sub-networks and the T sub-networks. The question that now arises is how independent organizations working under conditions of extreme scarcity of resources are able to undertake collaborative action undisturbed by turf fights and project ownership struggles. The point of the 'complete cycle' is to place the complete techno-economic network from S to T of each technology platform under one single management, but how is the interaction between personnel of the different biotech centers structured and coordinated? It also remains to explain the somewhat peculiar cash flow of the techno-economic networks, making the State Council the obligatory passage point (OPP) in Figure 1.

In order to answer these questions we will observe two striking characteristics of the Cuban biotech sector: firstly, the centralized decision making structure and the close connection to the top national political leadership; and secondly, the formalized horizontal collaborative mechanism of the 'Scientific Pole'.

Management and coordination of the techno-economic networks

This section aims at responding to the sixth question of this paper, namely how the techno-economic networks of the Cuban biotech sector are managed and coordinated. First the relation between the State Council and the biotech sector will be described in terms of an obligatory passage point. Then I describe how that relation, combined with a horizontal collaboration mechanism called the Scientific Pole, have facilitated the kind of inter-organizational collaboration that was witnessed in the case of the pentavalent vaccine.

As already stated, an important term for conceptualizing power in actor-network theory is the 'obligatory passage point', which is understood as a node in the actor-network that other actors have to pass through in the pursuit of their respective interests (Latour 1987). In the Cuban biotech sector this node is occupied by the State Council, or rather the Pole Office of the State Council, so in this case the obligatory passage point coincides with the summit of a highly hierarchical and formal organizational structure. But in theory, a node in a non-hierarchical actor-network may also become an obligatory passage point.

The State Council

The State Council[36] is at the core of the political leadership in Cuba. Formally, the State Council functions as the working committee of the National Assembly in the five year terms between its sessions. It is headed by the President, in his capacity of Chief of the State,[37] while simultaneously also holding the position of Chief of the Government. In 2008 Raúl Castro succeeded his brother Fidel in these positions. In spite of its formal status as the executive branch of the National Assembly, in my view the State Council rather resembles a personal secretariat for the President. This is the body where major national strategic decisions are prepared for and made.

The State Council is headed by the President, Raúl Castro, and six vice-presidents, among them a former Minister of Health, several members of the Politburo of the Communist Party, several heroes from the insurrection of the 1950s, an army General, a Vice-Minister of Defense, and the secretary of executive committee of the Council of Ministers (Anon. 2008). Among the 25 members of the State Council one finds the Ministers of Health, of Foreign Affairs, and of Communications, the Director of CIGB, Luís Herrera, as well as the President

[36] The State Council: El Consejo de Estado.
[37] Chief of the State: Jefe de Estado

himself, the Vice-President and a secretary of the National Assembly. As stated above, in his dual role the President heads the State Council in his capacity of Chief of the State, and the Government with subordinated ministries as Chief of the Government.

The secretary of the State Council is José Miyar Barrueco, who is also the Director of the office of the State Council that directs the biotech sector, the so-called Scientific Pole Office, or Pole Office. Most of the organizations belonging to the Scientific Pole are subordinated to different sectoral ministries, but the ten most important research and production centers of the biotech sector are managed directly by the Pole Office, among them CIGB, the Finlay Institute, and CIM.

The State Council and the biotech sector

This section explains how political, economic and administrative power is exercised by the State Council by way of its direct link to the biotech sector. The close and privileged affiliation of the primary biotech centers with the State Council is an expression of the priority of health and biotechnology by the revolutionary government. The biotech centers were moved from the ministries to the State Council in the early 1990s in order to protect them from the austerity measures imposed on all other sectors by the declaration of the 'Special Period in Times of Peace',[38] which was precipitated by the collapse of the East Bloc economic CMEA collaboration.

As has already been spelt out, the concept of the 'closed cycle' dictates that each biotech center is a separate legal and organizational entity, with a managing director and sub-directors for the different divisions of the organization. The managing directors of the centers are responsible for initiation of R&D projects, for their execution, for developing the productive capabilities of the center, for managing human resources, for managing regulatory affairs (IP and drug regulations) and quality control, and for marketing and sales.

Nevertheless, the Pole Office at the State Council has full control of the economy of the centers, and that on a highly detailed level. Even international travel activities of individual employees have to be approved of on a case-by-case basis by the Pole Office (De la Fuente 2001),[39] a fact that indicates that economic disbursements of hard currency of the order of magnitude of USD 1,000, and possibly less, are exempted from the personal discretion of the managing directors.

The same applies to the income side, that is, the sales or joint venture contracts with overseas partners have to be approved of by the Pole Office. All exports revenues from the commercializing branches of the biotech centers are collected by the State Council, and subsequently redistributed to the centers to cover operational costs and investments, and the surplus is redistributed to other sectors of the economy, like any other government foreign currency income. By ordering the techno-economic networks of Cuban biotech in this way the State Council becomes an obligatory passage point.

This is but an indication of the level of detailed decision making being undertaken by the Pole Office. All research and development projects to be initiated that may incur foreign currency spending have to be approved of by the Pole Office, and of course the same goes for investment in production equipment. Sometimes even decisions about human resources allocation are taken by the Pole Office, which may happen whenever the unique competence of an employee in one center should be more needed in another.

[38] Personal communication with Agustín Lage, Director of CIM, May 11 2001.
[39] Personal communication with Gustavo Sierra, Vice President, Finlay Institute, 3 February 2009.

Centralized and participatory decision making

We may draw a few corollaries from this. The role of the managing directors of the biotech centers should be described in terms of being administrators, facilitators, and producers of knowledge to be used as input for the decisions of the Pole Office. The managers are responsible for generating economic revenues, but do not control the cash flow. The decisions made by the Pole Office must be orderly executed according to the detailed budgets accompanying them. On the other hand, knowledge generated inside the centers have to be communicated to the Pole Office in order for it to make adequate strategic and tactical judgments.

Consequently, the quality of the decisions made within this managerial model depends upon the degree to which information from lower levels of the organizations is relayed upwards through the bureaucratic hierarchy, which in turn depends on the degree to which individual scientists may express themselves. Obviously, freedom of expression is a relative phenomenon. Former Director of R&D at CIGB José De la Fuente complained about increasing political 'correctness' replacing academic freedom, and removal of protection from 'voluntary work'[40] (for instance in construction work or mosquito eradication campaigns) prior to his defection in 1999, and

> […] a political crusade against scientists occupying prominent positions who defended ideas that diverged from the hard line dictated by the Party. (De la Fuente 2001), p 907

Nevertheless, there is nothing to suggest that Cuban biotech is anywhere in the vicinity of evolving into Stalin-Soviet style 'Lysenkoism', *i.e.* the subordination of science to ideological principles, as described by Roll-Hansen (1989). My general impression from interviews and interaction with Cuban scientists is that the degree of freedom of expression of the Scientific Pole employees in matters relating to their work assignments and to the operation of the organization resembles that of employees in private or public business enterprises in any other country. That is, in technical and scientific matters people may speak *relatively* freely in discussions prior to making decisions, while discussion of more political issues is a task rather left to management.

My sources support the view that there is close and frequent contact between the managing directors and the Pole Office executives. Together the latter and some of the managing directors comprise a 'scientific-technological board', which meets on an almost weekly basis.[41] Perhaps this management model could be described in terms of centralized and participatory decision making.

To sum up, the most important biotech centers are closely connected to the top political leadership – a leadership highly dedicated to using health and science as both tools for development and legitimization of its political power. The biotech sector thus enjoys high priority for investment and other resources. The administrative power of the biotech sector is strongly centralized, and the decision making on part of the Pole Office is on a highly detailed level.

The actor-networks of the techno-economic networks have been ordered so that the Pole Office and the State Council occupy the position of an obligatory passage point. All the circulating intermediaries – funds, research proposals, project progress reports, accounts, managing directors – that are used in the decision making processes that are ordering the techno-economic networks of the biotech sector have to pass through this node.

[40] Personal communication with José de la Fuente, former Director of Research and Development at CIGB, 11 March 2002.
[41] Personal communication with Gustavo Sierra, Vice President, Finlay Institute, 3 February 2009.

In Figure 1 this is illustrated by the monetary flows. The commercial branches of each of the techno-economic networks generate export revenues in overseas markets, and instead of returning these intermediaries back to the techno-economic network that produced the goods that were exchanged, the money is diverted away and transferred to the Pole Office. This is the immediate and material basis for the power of the Pole Office. It is probably also the rationale for establishing the commercializing branches of each techno-economic network as separate legal entities. Apart from that the Pole Office has the discretion of hiring and firing of managers and employees, and so on.

However, it is evident that the Cubans have not regarded this centralized ordering as a sufficient condition for facilitating efficient use of resources in order to exploit the full productive and innovative potential of the biotech sector. In order to promote collaboration across the boundaries of the technologically separated techno-economic networks, a formal organizational body has been created: the Scientific Pole. We have seen that collaboration across the boundaries of each of the techno-economic networks does take place, both in the S sub-networks and the T sub-networks. Is it reasonable to accept the hypothesis that an arena for horizontal coordination is a sufficient condition for successful collaboration to take place?

The Scientific Pole

In the following paragraphs I discuss how successful and efficient horizontal collaboration between the biotech centers is made possible. I also discuss the collaborative culture and consensus based decision making processes that my sources were emphasizing.

Although the Cuban biotech sector is governed by detailed decision making on part of the State Council, there are also horizontal, integrative measures and mechanisms. The most important is the Scientific Pole, made up of more than 60 organizations connected to the biotech sector.

The Scientific Pole of Western Havana[42] was created in 1991, and in 1997 it comprised 38 units, including several research and production centers, a number of research institutions, two faculties of the University of Havana, a consultancy agency, the national drug regulatory agency CECMED, a hospital, the national blood bank, and more. By 2009 the number of participating organizations has increased to more than 60.[43] The Scientific Pole is a cross-sectoral umbrella organization, in that the member institutions belong to eight different ministries as well as the State Council. The responsibility of being the Coordinator seems to rotate among the Directors of the research centers, and the Scientific Pole does not have any separate secretariat or office. The main tasks of the Scientific Pole is coordination, cooperation and strategic planning (CITMA 1997).

The Scientific Pole does have a spatial delimitation of some sorts, and as such it could be understood in terms of a science park or an industrial region (Reid-Henry 2008). To put it briefly, the most of the core biotech centers are located in the suburb Cubanacán, in the western part of the capital, hence the full name The Scientific Pole of Western Havana. Below I will limit myself to a discussion of the organizational aspects of the Scientific Pole.

Firstly, what is the mandate for or purpose of the Scientific Pole? Says Agustín Lage, the Director of CIM:

> It is not an administrative organization, nor an arena for executive decisions or for making business agreements. It is rather a space for strategic discussion. […] The Pole is simply that the

[42] Polo Científico del Oeste de La Habana.
[43] Personal communication with Vicente Vérez, Director of CQB, 4 February 2009.

> managing directors of these institutions meet about once a month for discussions and exchange of information. Present at these meetings are also the Secretary of the Council of the State, and often the ministers of Health, Agriculture, Higher Education and so forth, depending on the agenda. Occasionally, also Fidel Castro attends a meeting. [44]

My impression is that Lage is exaggerating the strategic role of the Scientific Pole. All other sources depicted it as a body for negotiating collaborative use of facilities and equipment, and coordination of joint research projects. One could say that while the Biological Front was a body for strategic and political planning, the Scientific Pole is rather a body for execution of common projects and coordination of tasks.[45]

Collaboration in practice

The above case study of the integrated production line of the pentavalent vaccine is just one indication that successful horizontal collaboration is taking place. Several sources stressed that collaborative research projects were also common. A collaborative mentality was said to manifest itself in informal information sharing between individual researchers, in lending and borrowing of technical equipment, in joint research and development project, and in integrated production lines.

There is no reason to doubt that the Scientific Pole really is an important arena for inter-organizational coordination. Yet, it remains to explain why such collaboration is possible. Over time the individual biotech centers have become increasingly responsible for being self-financed,[46] and de la Fuente (2001) describes

> […] increasingly fierce competition between groups for resources and paternity rights over promising projects. (De la Fuente 2001), p 906

How are controversies like these resolved? Reid-Henry (2008) has commented on workplace relations in Cuban biotech, and he interprets the motivation as a combined result of notions of social values and individual self-realization.

My informants emphasized the consensual nature of the Scientific Pole meetings, and of the way people are working together inside and between the organizations. They described workplace relations with very little rivalry, and the consensual culture was commonly explained by reference to their common understanding of undertaking a social mission of outmost importance, namely to supply the public health with needed biopharmaceuticals, and thereby serving the entire nation as such, as well as the revolution. This dedication on part of the employees in the Cuban biotech sector was contrasted with the commercial incentives driving the employees in capitalist biotechnology, with destructive competition as the obvious and inevitable result. The job security enjoyed in Cuba was also sometimes mentioned as a contributing factor to collegiality and collaboration.

There should be no reason to doubt the dedication, motivation, and morale of the biotech workers. The concept of *consagración* – painstaking and total dedication to work (Bravo 1998) – is the prerogative for the workplace relations in the biotech sector, and implies long work days and abstention from the private foreign currency earning activities that cause widespread absenteeism in almost all other sectors of the Cuban economy.

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[44] Personal communication with Agustín Lage, CIM, 11 May 2001.
[45] Personal communication with Emilio García Capote, President, the Agency for Science and Technology, 3 July 2001.
[46] Personal communication with Gustavo Sierra, Vice President, Finlay Institute, 3 February 2009.

Several informants also stressed the 'fluid' and informal nature of the decision making processes. I was repeatedly advised against putting too much emphasis on formal positions and organizational structures, since people often would counsel and discuss with each other in relaxed disregard of organizational boundaries and hierarchical levels. Maybe Luís Herrera's double assignment as Managing Director of CIGB and Member of the State Council – which manages the CIGB – is but one illustration of this fluidity.

To a certain extent it is imaginable that in discussions while undertaking collaborative work appeals based on references to the higher social end of supplying the nation with pharmaceuticals may have an impact in resolving controversies. However, in my view it is questionable to conclude that attitudes and values alone would be sufficient to achieve consensus in a forum representing tens of heterogeneous organizations and several thousand employees, in an economic environment characterized by extreme scarcity of resources. Moreover, explaining the consensual collaboration by reference to the absence of commercial incentives is to a certain extent undermined by the fact that many of the biopharmaceuticals in Cuban biotech product portfolio are in fact strongly commercially motivated.

I would rather propose, somewhat speculatively, that it is the centralized management of the State Council that facilitates horizontal collaboration between the Cuban biotech centers. Horizontal and relatively informal cooperation – organized mainly by the Scientific Pole of Western Havana – is possible because there exists a body – the Pole Office at the State Council – that has both the competence and the administrative power to cut through and resolve any conflicts that may arise between the (directors of) the different biotech centers. Note the presence of even the Secretary of the State Council (where the Pole Office is located) at the Scientific Pole meetings.

Given the level of detail of the decisions made by the Pole Office at the State Council, the workers in the biotech sector may assume that just about any controversy that may arise could potentially be subject to referral to that higher authority for ruling or advice. And to the extent that the rulings of the Pole Office are predictable, one should expect such predictions to have a structuring effect on the negotiations and horizontal decision making processes within the Scientific Pole. Even the more 'fluid' collaborative processes could be facilitated the by centralized and detailed decision making capabilities of the State Council.

Most writings about diverging interests in the actor-network theory literature describe the resolution of controversies in terms of *translation* of interests, by enrolling other actors, by working to make them shift their goals, by persuading them to make certain detours that nevertheless helps them reach their goals by other means, and so on (Latour 1987). In the case of the Cuban biotech sector, however, the actor occupying the obligatory passage point simply has the power to shift the goals of the other actors, *regardless of their interests*, and to order the techno-economic networks in exactly the way it sees fit.

It must be mentioned, however, that when confronted with this interpretation, Dr. Agustín Lage, Director of the CIM, rebutted it, stating that the decisions made at the State Council only concerned strategic, and not operational, issues.[47] On the other hand, as already stated, several of my other sources confirmed the detailed management mode of the State Council.

Summary: management and coordination of techno-economic networks

We may now sum up the somewhat long and elaborate response to the fifth question about the management and coordination of the Cuban biotech sector. The Pole Office at the State Council functions as an obligatory passage point for the entire sector, by commanding all the

[47] Personal communication with Agustín Lage, CIM, 11 May 2001.

intermediaries like money, project proposals and managers to pass through it. Nevertheless, the close and frequent contact with the managers of the biotech centers and the relative freedom of speech inside the techno-economic networks justify the term *centralized and participatory decision making* as descriptive of the way of exercising power in the Cuban biotech sector.

In order to ensure full utilization of scientific and productive infrastructure, and in order to unleash the full innovative capacity of the techno-economic networks the horizontal collaborative mechanism of the Scientific Pole was created. However, it may be speculated that – contrary to the claims put forward by my sources – it is not any specific 'socialist' collaborative and consensual culture that facilitates the successful collaborative activities, but rather the existence of a centralized power – the Pole Office at the State Council – with the competence and discretion to resolve any controversies appearing in the horizontal interaction.

Despite its porous internal borders and fluid decision making processes, in Figure 1 the Cuban biotech sector and vaccine industry appears as an isolated system. The rest of the economy is represented by the public health system and the State Council only. The next section explores whether this is a justifiable image, or if the biotech sector is part of a comprehensive, overarching national system for support and promotion of science, technology and innovation.

Techno-economic networks and the national innovation system of Cuba

This final section of the paper explores the seventh question: what are the relations between the techno-economic networks of the Cuban biotech sector and the general domestic scientific, technological and productive systems in Cuba? The following paragraphs describe the officially implemented System for Science and Technological Innovation (SCIT)[48] in Cuba, and analyze to what extent the Cuban biotech sector is integrated with the general national institutional framework for science and technology governance. It will be demonstrated that the biotech sector enjoys a highly privileged status in terms of funding and political support compared to other sectors. I will look at the influence of the officially implemented System for Science and Technological Innovation, the National Programs for Science and Technology, and the Ministry for Science, Technology and Environmental Issues on the biotech sector.

Cuba has explicitly adopted the national innovation system as a governing concept in its technology policies – the System for Science and Technological Innovation of the Republic of Cuba (SCIT). The background for its implementation is a critique of lack of links between investigative and productive forces that was put forward in the early 1990s. Richard Nelson's book about national innovation systems (Nelson 1993) was extensively studied in Cuba, and the Ministry for Science, Technology and Environmental Issues (CITMA)[49] came into operation in 1994. The SCIT was formally established in 1994.[50] This system comprises 1) the Government with its ministries, and the agencies of CITMA, 2) research organizations, 3) integrative entities, like the scientific poles, the Academy of Sciences, the Union of Workers of Science, and so on, and 4) national, sectoral and territorial research programs (Brundenius and Monreal 2004).

In 2000 there were in total 15 National Programs for Science and Technology, of which three were of direct importance to the biotech sector: 'Agricultural biotechnology', 'Biotechnol-

[48] SCIT: Sistema de Ciencia e Innovación Tecnológica.
[49] CITMA: Ministerio de Ciencia, Tecnología y el Medio Ambiente.
[50] Personal communication with Emilio García Capote, President, the Agency for Science and Technology, July 3 2001.

ogy', and 'Human and veterinary vaccines' (Brundenius and Monreal 2004). The preceding year the 15 programs were supporting a total of 572 research projects, and 155 projects had been concluded (Faloh, et al. 2000). By 2004 17 programs were in operation, with a total portfolio of 786 active and 537 concluded projects (GEPROP 2004).

Judged by the official documents, at first glance the Cuban research programs resemble those of any other country in the North: for instance the evaluation criteria for peer reviews of the project proposals include relevance, novelty, scientific quality, scientific merits, and so on (CITMA 1995). However, there is a certain emphasis on application, since socioeconomic impact is one of the criteria.

Over the ten year period from 1995-2004 a total of 162 million peso have been distributed through these programs. Of these funds the three biotech related programs (Vaccines, Agricultural Biotechnology and Biotechnological Products) have distributed a total of 33.5 million peso, and the Vaccines program 2.5 million. However, even when converted into man-years using the average scientists' extremely modest monthly salary at that time of 440 peso per month (approximately USD 20), the biotech related programs would cover no more than 634 man-years annually. And that is if all funds cover personnel costs only. In 1997 the Cuban biotech sector employed about 12,000 workers, of which 1,440 researchers (CITMA 1997). It is evident that the National Programs account for just a minority share of the total funding of the biotech sector.

Judged by their relative financial contributions the National Programs seem to play a minor role in making priorities for the R&D activities in the biotech sector. Rather, it seems like the expert committees of the National Programs approve of the project proposals that meet the scientific criteria, and then it is up to the State Council to make the real priorities by allocating the real funding. If this is the case then it is possible that all the R&D projects in the R&D project portfolio of each research and production centre would be formally approved of by the National Programs, but only some of them would be truly prioritized by funding by the State Council. It is in particular foreign currency funding that would be granted by the State Council. By and large Gustavo Sierra at the Finlay Institute confirmed this description.[51] The National Programs also fulfills a scientific consultative role in the follow-up of ongoing R&D projects in the biotech centers.

This may be contrasted with the role of research councils in many other countries, whose financial contributions to public research organizations also may appear to be small compared to the basic funding. However, the important difference is that while the funding from such research councils may have a strong indirect influence on the allocation of the basic funding, in the Cuban biotech sector it is the direct funding of the State Council that sets the true priorities.

I would like to add that in some instances the expert committees will, theoretically, have a hard time while exercising even their relatively limited powers of rejecting sub-standard research project proposals. Gustavo Sierra gave me a vivid account of how Fidel Castro one day in 1991 appeared at the recently inaugurated organization with a copy of a news cable reporting the first cases of a cholera outbreak in Peru, determined that Cuba should develop a cholera vaccine.[52] It is doubtful that any expert committee, anywhere in the world, would have the stomachs to turn down a project that was initiated by the president in person.[53]

[51] Personal communication with Gustavo Sierra, Vice-President at Finlay Institute, 3 February 2009.
[52] Personal communication with Gustavo Sierra, Vice-President at Finlay Institute, 3 February 2009.
[53] This point does *not* suggest that the cholera vaccine development project should be in any way scientifically sub-standard.

It is a bit ironic perhaps that the jewel in the crown of Cuban science and technology, the most innovative sector of the Cuban economy – the biotech sector – is not in reality an integrated part of the official System for Science and Technological Innovation, but a privileged sector run directly by the top national political leadership. Even the public health system, by Thorsteinsdóttir et al. (2004) claimed to play a major role in Cuban biotech innovation, seems to be limited to supplying the M-S sub-network with epidemiological information, and to carrying out clinical trials and distributing biomedical products (T-M). Nevertheless, as demonstrated in the first Cuba-paper, the biotech sector has established itself as a major foreign currency earner, which is probably its main contribution to the Cuban society at large.

An update on the management structure Cuban biotech sector

The Cuban biotech sector has been described as a dynamic field, with constant revisions of strategic and techno-economic evaluations. Just a few weeks after completing the fieldwork in 2009 the newspaper Granma featured a series of news reports announcing reorganization of the Government, of the State Council, and of the responsibility for the biotech sector.

On 2 March 2009 it was announced that several ministers and members of the State Council had been reassigned, and two ministers had resigned (Anon. 2009a; Anon. 2009b). The announcements were accompanied by public letters from the two resigning State Council members Carlos Lage[54] and Felipe Pérez Roque declaring their acknowledgement of and responsibility for the errors that precipitated their personal decisions to resign (Lage 2009; Pérez 2009). Also Fidel Castro issued a statement denouncing the allegedly circulating 'popular rumors' that the hiring and firing process was any expression of 'Raúl's men substituting those of Fidel' (Castro 2009).

Moreover, the Secretary of the State Council and Director of the Pole Office, José Miyar Barrueco, was appointed Minister of Science, Technology, and Environmental Issues (CITMA), and the responsibility of the entire biotech industry was transferred from the State Council to that Ministry (Anon. 2009b). It is beyond the scope of this dissertation to analyze the implications of these changes, and the motivations behind them. However, it may be speculated that the transfer of responsibility of the biotech sector from the State Council to CITMA reflects that the national economy has improved sufficiently to start treating the sector somewhat less preferentially than what has been the case up to now. Another interpretation is that the biotech sector has now matured beyond the phase of receiving prioritized investment, and that its main purpose is rather to be a foreign currency revenue earner for the Cuban state.

Concluding remarks

The main objective of this paper was to study how the Cuban biotech sector and its integrated vaccine industry were established, and how they are managed and coordinated in their overall national context. By organizing the analysis around seven specific research questions it has become possible to draw the following conclusions.

First, the Cuban biotech sector was founded on a well developed health system, a highly educated labor force, and a scientific base in biomedicine and related disciplines, like physics, chemistry, biology, mathematics, computation, and medical specialties. The intervention built on an existing S sub-network and a national T-M sub-network (the public health system).

[54] Incidentally, the brother of the managing director of the CIM.

Early techno-economic evaluations – apart from founding the Biological Front – resulted in decisions of creating the missing T components by breakthrough actions from 1981 onwards.

Second, in 1980 Castro initiated a pilot research and development project, which was succeeded by a massive investment for establishing national biotechnological research and production capabilities (T). Each biotech center represents a separate chained and convergent techno-economic network specialized on a specific technology platform.

Third, the S-T and T-M sub-networks were interconnected by applying the concept of the complete cycle, whereby the S, S-T, T, and T-M sub-networks within designated technology platforms were co-located in separate organizations. These organizations are supported by functional centers like CENPALAB (input to T), BioCEN (end of pipeline of T), and the 'Pedro Kourí' institute, which fulfills a role of connecting the public health system network to the science networks by a theoretically novel M-S sub-network.

Fourth, there was a seeming paradox in developing extensive vaccine innovation capabilities, thereby targeting a 'traditional' morbidity pattern, when it was a 'modern' morbidity pattern that induced the Castro government to establish the biotech sector in the first place. This contradiction is to a large degree explained by the irreversibility constituted by the vaccine innovation capabilities that resulted from the meningococcal vaccine project. It also seems like strategic technology platform development projects aiming at appropriating modern technologies like recombinant protein expression and chemical conjugation of polysaccharide antigens represented similar irreversibilities by opening up windows of opportunity for further vaccine innovation activities. It turned out to be possible to identify several health problems that could be solved by the technological capabilities already at hand, and in a way that could be commercially viable.

This point demonstrates that it is not interests alone that determine the strategic evaluations. The capabilities of the evolving techno-economic networks, as well as the appearance of appropriable new technology platforms on the international scene, open up opportunities for developing new products that demand reconsideration of previous strategic evaluations. As Michel Callon emphasizes, strategic and techno-economic evaluations are done in a recursive and reiterative process.

Fifth, both the pentavalent vaccine itself and my sources testify to the widespread horizontal collaboration that takes place between the Cuban biotech centers. This collaboration is most likely facilitated by the centralized and detailed decision making procedures that are imposed by the State Council.

Sixth, the Castro government placed the State Council at an obligatory passage point in order to centralize the economic and administrative power of the actor-network of the Cuban biotech sector. The entire cash flow is channeled through this body, and detailed budgets are imposed on the individual biotech centers. The Biological Front became a consultative body for the State Council, mainly on strategic and political issues. In order to facilitate horizontal collaboration the Scientific Pole was set up as an arena for tactical discussions and coordination of ongoing collaborative projects involving more than one organization.

Seventh, in a twist of irony, despite the implementation of a national innovation system, in Cuba called the System for Science and Technological Innovation (SCIT), the most innovative sector of the Cuban economy – the biotech sector – is managed and administered separately from that system. For almost three decades the Cuban biotech sector has enjoyed a highly privileged position with respect to investments as well as attention from the top political leadership. It is only after the field work for this dissertation was concluded, more specifi-

cally in March 2009, that some reorganization in the Cuban government structure may be putting the sector on slightly more equal terms with the rest of the Cuban economy.

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References

Anon. 2004 'Los institutos de investigaciones en ciencias médicas y el tercer nivel de atención médica en Cuba', *Cuadernos de Historia de la Salud Pública* 2004 (95).

— 2008 'Miembros del Consejo de Estado', Havana: *Juventud Rebelde*. URL: http://www.juventudrebelde.cu/cuba/2008-02-25/miembros-del-consejo-de-estado/: Accessed on 23 January 2009.

— 2009a 'New appointments of ministers', Havana: *Granma International*. URL: http://www.granma.cu/ingles/2009/march/mar3/New-appointments-of-ministers.html: Accessed on 3 March 2009.

— 2009b 'Official note from the Council of State. Agrees on movement of cadres and reorganization of agencies', Havana: *Granma International*. URL: http://www.granma.cu /ingles/2009/march/lun2/10cambio-i.html: Accessed on 18 March 2009.

BioCEN 2006 'Company web-site', Havana: *Centro Nacional de Biopreparados*. URL: http://www.biocen.cu: Accessed on 3 September 2008.

Bravo, E. M. 1998 *Development within underdevelopment? New trends in Cuban medicine*, Havana: Editorial José Martí.

Brundenius, C. and Monreal, P. 2004 'Structural transformation and S&T policies in Cuba after the demise of 'Real existing socialism': Towards a new system of innovation? ' *Globelics Conference 2004*, Beijing.

Callon, M. 1991 'Techno-economic networks and irreversibility', in J. Law (ed) *A sociology of monsters*, London: Routledge.

— 1992 'The dynamics of techno-economic networks', in R. Coombs, P. Saviotti and V. Walsh (eds) *Technological change and company perspectives*, London: Harcourt Brace Jovanovich.

Callon, M., Laredo, P., Rabeharisoa, V., Gonard, T. and Leray, T. 1992 'The management and evaluation of technological programs and the dynamics of techno-economic networks: The case of the AFME', *Research Policy* 21 (3): 215-236.

Cantell, K. 1998 *The story of interferon. The ups and downs in the life of a scientist*, Second Edition, London: World Scientific.

Cartwright, K. (ed) 1995 *Meningococcal disease*, Chichester: John Wiley & Sons.

Castro, F. 2009 'Reflexiones del compañero Fidel. Cambios sanos en el Consejo de Ministros', Havana. URL: http://www.granma.cu/espanol/2009/marzo/mar3/cambios-e.html: Accessed on 3 March 2009.

CITMA 1995 'Sistema de ciencia e innovacion tecnologica (Documentos basicos)', Havana: Ministerio de Cienca, Tecnología y Medio Ambiente.

— 1997 'Polos cientifico-productivos', Havana: Ministerio de Ciencia, Tecnologia y Medio Ambiente, Agencia de Ciencia y Tecnologia.

De la Fuente, J. 2001 'Wine into vinegar – the fall of Cuba's biotechnology', *Nature Biotechnology* 19 (10): 905-907.

Dull, P. and Rosenstein, N. E. 2001 'Meningococcal disease and vaccines', *Pediatric Annals* 30 (6): 358-361.

Faloh, R., García Capote, E., Fernández de Alaíza, M. C. and Montalvo Arriete, L. F. 2000 *La interfase. Un recurso para la innovación y la competitividad de la empresa. Una primera aproximación de la situación de Cuba*, Havana: Editorial Academia.

Feinsilver, J. M. 1993 *Healing the masses. Cuban health politics at home and abroad*, Berkeley: University of California Press.

Fernández, M. L. 1999 'Scientific and technological development in Cuba in the context of economic reforms ', in C. Brundenius, B. Göransson and P. Reddy (eds) *Reconstruction or deconstruction. Science and technology at stake in transition economies*, Hyderabad: Universities Press.

Figueras, M. A. and Pérez, O. E. 1998 *La realidad de lo imposible. La salud pública en Cuba*, Havana: Editorial de Ciencias Sociales.

Finne, J., Leinonen, M. and Mäkelä, H. 1983 'Antigenic similarities between brain components and bacteria causing meningitis', *Lancet*: 355-357.

Frasch, C. E. 1983 'Memorandum. Meningococcal disease in Cuba and control measures', Bethesda: Department of Health & Human Services.

Frasch, C. E., Coetzee, G. and Zahradnik, J. M. 1983 'Development and evaluation of group B serotype 2 protein vaccines: Report of a group B field trial', *Medecine Tropicale* 43 (2): 177-180.

Galambos, L. and Sewell, J. E. 1995 *Networks of innovation. Vaccine development at Merck, Sharp & Dohme, and Mulford, 1895 - 1995.*, New York: Cambridge University Press.

García, E. and Sáenz, T. W. 1989 *Ciencia y tecnología en Cuba*, Havana: Editorial de Ciencias Sociales.

GEPROP 2004 'Los programas nacionales de ciencia y técnica. 10 años de trabajo', Havana: *Centro de Gerencia de Programas y Proyectos Priorizados*: Accessed on July 9 2008.

Lage, A. 2006 'Socialism and the knowledge economy: Cuban biotechnology ', *Monthly Review* 58 (7).

Lage, C. 2009 'Letter from Carlos Lage Dávila', Havana: *Granma International*. URL: http://www.granma.cu/ingles/2009/march/juev5/carta-lage.html: Accessed on 5 March 2009.

Latour, B. 1987 *Science in action*, Milton Keynes: Open University Press.

Nelson, R. (ed) 1993 *National innovation systems. A comparative analysis*, Oxford: Oxford University Press.

Noronha, C. P., Struchiner, C. J. and Halloran, E. 1995 'Assessment of the direct effectiveness of BC meningococcal vaccine in Rio de Janeiro, Brazil: A case-control study', *International Journal of Epidemiology* 24 (5): 1050-1057.

Pentón, E., Muzio, V. and González-Griego, M. 1994 'The Hepatitis B virus (HBV) infection and its prevention by a recombination-DNA viral surface antigen (rec-HBsAg) vaccine', *Biotecnologica Aplicada* 11 (1): 2-11.

Pérez, F. 2009 'Letter from Felipe Pérez Roque', Havana. URL: http://www.granma.cu/ingles/2009/march/juev5/felipe-perez.html: Accessed on 5 March 2009.

Plahte, J. 2010 'Strategic evaluations and techno-economic networks. Vaccine innovation in the Cuban biotech sector: for public health – or for profits?' *Working Papers on Innovation Studies* (20100108).

Quach, U., Thorsteinsdóttir, H., Renihan, J., Bhatt, A., von Aesch, Z. C., Daar, A. S. and Singer, P. A. 2006 'Biotechnology patenting takes off in developing countries', *International Journal of Biotechnology* 8 (1/2): 43-59.

Ratanawijitrasin, S. and Wondemagegnehu, E. 2002 'Effective drug regulation. A multicountry study', Geneve: World Health Organization.

Reid-Henry, S. 2008 'Scientific innovation and non-Western regional economies: Cuban biotechnology's 'experimental milieu'', *Environment and Planning A advance online publication* 40 (8).

Roll-Hansen, N. 1989 'The practice criterion and the rise of Lysenkoism', *Science Studies* 1989 (1): 3-16.

Sierra, G., Campa, C., Varcacel, M., Garcia, L., Izquierdo, L., Sotolongo, F., Casanueva, V., Rodriguez, R. and Terry, H. 1991 'Vaccine Against Group B Neisseria Meningitidis: Protection Trial and Mass Vaccination in Cuba', in K. Bøvre (ed) *NIPH Annals: The meningococcal Serogroup B vaccine protection trial in Norway 1988-1991*, Vol. 14, Oslo: National Institute of Public Health.

SmithKline Beecham 1999 'SmithKline Beecham and the Finlay Institute of Cuba reach agreement on vaccine against bacterial meningitis', Philadelphia: SmithKline Beecham. Press release 29 July.

Sotolongo, F., Campa Huergo, C., Casanueva, V., Fajardo Díaz, E. M., Cuevas Valdespino, I. E. and Gonzáles, N. 2007 'Cuban meningococcal BC vaccine: experiences and contributions from 20 years of application', *MEDICC Review* 9 (1): 16-22.

TEC 2004 '1999 Commercial highlights': *US-Cuba Trade and Economic Council Inc. New York*. URL: http://www.cubatrade.org: Accessed on 24 March 2004.

Thorsteinsdóttir, H., Daar, A. S. and Singer, P. A. 2006 'Health biotechnology publishing takes off in developing countries', *International Journal of Biotechnology* 8 (1/2): 23-42.

Thorsteinsdóttir, H., Sáenz, T. W., Daar, A. S. and Singer, P. A. 2005 'Different rythms of health biotechnology development in Brazil and Cuba', *Journal of Business Chemistry* 2 (3): 99-106.

Thorsteinsdóttir, H., Saenz, T. W., Quach, U., Daar, A. S. and Singer, P. A. 2004 'Cuba - innovation through synergy', *Nature Biotechnology* 22 (Supplement): DC19-DC24.

Valcarcel, M., Rodriguez, R. and Terry, H. 1991 *La enfermedad meningococica en Cuba. Cronología de una epidemia*, 2 Edition, Havana: Editorial Ciencias Médicas.

Valdés, M. Z., Delgado, T. A., Peralta, L. C. R., Lobaina, L. G., Araujo, L. C. S., Fonseca, P. A., González, J. R. G. and Silva, H. R. 1999 *Y sin embargo...ciencia. Hablan 30 investigadores cubanos*, Havana: Casa Editora Abril.