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Targeting the Biotechnology Clusters in North Carolina and Israel: Lessons from Successful and Unsuccessful Policy Making

Gil Avnimelech
Ono Academic College
Faculty of Business Administration
gilavn@gmail.com

Abstract

This paper analyzes the development of biotechnology clusters in North Carolina (NC) and Israel. In both NC and Israel, when the biotechnology was identified as a potential strategic priority, the framework conditions (i.e. the stage of development of the sector globally, and the relative strength and potential of the local sector) were optimal for successful policy-targeting.

NC presents a case of a successful transition from an agricultural and traditional manufacturing economy to a knowledge economy. The most successful part of this transition was a policy-led development of a biotechnology cluster in the Research Triangle.

While Israel also presents a case of a successful transition from a low-tech economy to a knowledge-intensive economy, Israel failed to develop a successful biotechnology cluster. We suggest that this is due to a policy failure (or could have been prevented by timely implementation of a successful policy-targeting).

We argue that the elements, which separate NC?s success from Israel's failure, are: a clear vision and strategic planning; timely response, long-term commitment; strong leadership and formal institution that support the policy process; cooperation between the government, public sector and academia, and an adjustable policy-making process.

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1. Introduction

This paper analyzes the development of the biotechnology clusters in North Carolina (NC) and Israel in the context of evolutionary policy-targeting (Avnimelech and Teubal, 2008a). Evolutionary policy-targeting is the attempt to trigger co-evolutionary processes, which will lead to structural change and cluster emergence. It is a policy approach based on an Extended Life Cycle Model (See Avnimelech and Teubal, 2004, 2006, 2008b). Evolutionary policy-targeting is a combination of market-led processes with government support and leadership (Rosiello et al., 2010; Rosiello et al., 2013).

Our main argument is that the transformation of an economic system through the emergence or transformation of multi-agent structures can lead to rapid economic growth (Cooke et al., 2011; Dutrenit et al., 2011), and that evolutionary policy-targeting can be implemented to support such structural change through incremental dynamics (Rosiello et al., 2013). We illustrate this argument based on the Case of NC. In addition, we attempt to understand the factors that support or impede the success of evolutionary policy-targeting based on comparison between both cases.

NC presents a case of a successful transition from an agricultural and traditional manufacturing economy to a knowledge-intensive economy. The most successful part of this transition is the development of the biotechnology cluster in the Research Triangle. The development of this cluster was supported by a successful evolutionary targeting-policy.

Since the early 1980s, the strategic priority of NC has been to create a leading global biotechnology sector. The implementation of this strategic priority included heavy capital investment, long-term commitment, continuous policy adjustments, and a mix of supporting programs. In order to facilitate the biotechnology cluster development, North Carolina Biotechnology Center (NCBC) utilized cooperation between the government, the private sector and the academia. As a result, NC has created one of the most dynamic and productive biotechnology communities around the world (Hardin, 2008a, 2008b; NCBC, 2008, Research Triangle Regional Partnership, 2012; DeVol et al., 2004).

While Israel also presents a case of a successful transition from low-tech economy to a leading knowledge-intensive economy, most prominently in the ICT sectors (see Avnimelech and Teubal, 2004, 2006), Israel failed to create a successful biotechnology cluster. In the early 1980s, Israel was in a position to establish a leading biotechnology cluster. However, Israel did not present a clear strategy, had only limited commitment to

the process, and had ineffective coordination between different agents involved with the process.

The remainder of this paper is structured as follows. The next two sub sections describe the theoretical framework and the methodology. The next section describes the development of NC's biotechnology cluster. Section 3 describes the development of Israel's biotechnology cluster. Section 4 presents a comparison of the two cases based on the evolutionary policy-targeting guidelines. Finally, general policy implications are given in section 5.

1.1 The Theoretical Framework

This paper is part of the Target project (www.targetproject.net), which is based on the evolutionary policy-targeting/extended industry life cycle (EILC) policy approach (Avnimelech and Teubal, 2008a, 2008b). It started with the examination of the emergence trajectories of five existing and emerging biotechnology innovation systems. The findings of these case studies were tested within the context of four countries/regions (see Rosiello et al., 2013).

The EILC policy approach focuses on supporting the emergence of multi-agent structures. Multi-agent structures include clusters, sectors, markets, industries, and other multi-agent institutions. Frequently, new multi-agent structures result from a process of emergence, which is a cumulative process of positive feedback involving externalities-generating and externalities-benefiting processes (Avnimelech and Teubal, 2008a). The EILC policy approach is based on the following notion: implementation of government policy in crucial transition points of market-led development processes could have a significant influence on the effectiveness of market forces. Evolutionary policy-targeting involves a number of policy actions related to multi-agent structures: (i) promotion of pre-emergence conditions to generate specific policy-targeting candidates; (ii) selection of the multi-agent structures to be targeted; and (iii) identification of system and market failures blocking the emergence of selected multi-agent structures; and (iv) determination of policy objectives, design, and implementation (Avnimelech and Teubal, 2008a).

Target project's central goals are to test the applicability of the evolutionary policy-targeting approach and to define a set of principles to create a new framework for policy action. This paper's objectives are to analyze the development of NC and Israel's

biotechnology clusters based on evolutionary policy-targeting approach and to present a set of principles for such policy based on both cases.

1.2 Methodology

This paper uses appreciative theorizing to analyze cluster development dynamics: describing our theoretical understanding of development processes, matching it up with empirical reality, and then rebuilding our theoretical arguments (Rosiello et al., 2013).

We described and analyzed the development of NC and Israel's biotechnology clusters based on interviews with policy makers and other key agents and based on in-depth review of secondary resources such as policy reports and academic papers. Written sources included: Katzir Committee report (Katzir, 1988), Israel National Committee for Biotechnology report (Katzir and Herzberg, 1992), Haim Aviv's reports (1997, 2007), Monitor report (2001), Ministry of Science report (Meser-Yaron, 2001), Milken Institute report (Glen, 2008), Glenrock report (2007), and other non-formal reports and articles. Moreover, we used multiple data resources such as USPTO database, the NC's TREE database (see Avnimelech and Feldman, 2010), IVC-online, NCBC database, and CBS Israel data.

We structured the data we collected within the three EILC phases according to a few contextual elements (initiative, coordination, focus, policy measures, and progress indicators). *Initiative* describes the background, the trends and the policy that influences the development at the specific phase. *Coordination* describes which agents throughout the region were involved in the process and how these various agents coordinate their activities. *Focus* describes the focus (in terms of sub-sectors, elements of the industry value chain, and institutions) of the policy actions. *Policy measures* present the specific description of policy actions. *Progress indicators* describe the cluster's situation at the end of each phase.

2. The Biotechnology Sector in NC

In the last three decades, a flourishing biotechnology cluster emerged in NC. While market forces played a significant role in the development of this cluster, policy cannot be over-estimated. In 1984, the government decided to target the biotechnology sector. The strategic priority of NC's policy makers was to create a leading biotechnology sector that would promote significant job creation (NC Board of Science and Technology, 1984, 1985; NCBC, 1990). Since 1984, NC State has invested more

than $2 billion in the biotechnology sector, approximately 70% of which went into research facilities (NCBC, 2008; Research Triangle Foundation, 1999).

2.1. The History of RTP

Since the mid-1950s, developing a knowledge-intensive economy was a strategic priority of NC's policy makers. The initiation and support for this mission were characterized by strong cooperation between the business sector, the government and academic institutions (Link, 1995; Link and Scott, 2003). NC, particularly the Research Triangle, has transformed itself from an economy based on low-income agriculture and traditional industries in the 1960s, to a region that attracts advanced industries since the 1980s. A major element within this process was the creation of the Research Triangle Park (RTP). RTP's success was built around its founder's leadership, commitment, and cooperation (Bowditch et al, 2009).

RTP is an advanced, industrial R&D park, which is focused on the ICT and biotechnology fields. RTP is located between three highly regarded educational, medical, and research universities—UNC at Chapel Hill, Duke University, and NC State University. RTP is home to a broad spectrum of companies—from U.S. federal agencies and R&D operations of large multinational companies to university spin-offs and local startups (Research Triangle Regional Partnership, 2012).

RTP was founded in 1959. At 1966, IBM located a research facility in the Park, and the U.S. Department of Health located its new National Environmental Health Science Center there as well. As a result, the Park gained credibility. Until the late 1980s, public research agencies and large companies comprised the majority of the Park's members (Link, 1995). The Park and its surrounding grew significantly during the 1990s, with a growing role of local companies and academic startups (Link and Scott, 2003). As of December 2008, more than 170 companies employing over 52,000 employees were located in RTP (Hardin, 2008a, 2008b).

2.2. Targeting Biotechnology in NC

We claim that NC's government implemented policy-targeting toward biotechnology that corresponded with the principles of evolutionary policy-targeting. We present NC's policy-targeting course of action throughout the first three EILC phases: background, pre-emergence, and emergence (see details in section 1.1). The focus during the background condition phase (1984-1990) was on developing a research

and human resources infrastructures, including R&D facilities and projects, training programs in the academia and community colleges, and adjusting the high school system to the new target. Since the pre-emergence phase (1991-1998), the investment in the business sector has gradually increased, with more focus on enhancing TTOs activities, developing the business sector infrastructure, and direct support to business sector firms. In the emergence phase (1999-), the government adjusted the policy and enhanced the trends identified by the market - contract research organizations (CRO) and contract manufacturing organizations (CMO) segments) - and focused on leveraging specific biotechnology-related sectors, in which the state had a competitive advantage (e.g., Forestry, Agrotech, and Biofuels). Eventually, NC created a leading biotechnology cluster with a comprehensive eco-system and with a bias toward specific sub-sectors and specific elements of the industry value chains.

Within each phase, we will refer to elements such as initiative, coordination, focus, policy measures, and progress indicators (see details in section 1.1).

Table 1: Progress throughout NC's biotechnology cluster development

	1981	**1991**	**1999**	**2004**	**2012**
The beginning of	**Phase 1**	**Phase 2**	**Phase 3a**	**Phase 3b**	
Total life science related firms	~25	~150	~250	~700	2,073
Drug development firms	3	~40	~55	~140	383
Medical device firms	2	~20	~35	~120	312
CRO/CMO Firms	~10	~45	~60	~200	467
Other bio-related firms (inc services)	~10	~45	~100	~220	911
Bio Employees	4,000	14,000	20,000	37,000	59,000
Bio Patents	17	72	264	209	380
Patents: % Bio Patents	2.6%	6.4%	11.3%	8.2%	8.5%
NC Bio Pat: % Global Bio	0.5%	1.5%	2.0%	2.2%	2.3%

Sources: USPTO (2013); directory.ncbiotech.org (2013); NCBC Annual Reports, TREE database.

2.2.1. Background Phase (1981-1990)

Initiative

In the early 1980s, policy makers, and academic and business sector leaders at NC, recognized that the science and applications of biotechnology fit remarkably well with its economic foundations. At this point, RTP has been already successful. NC's foundations for policy-targeting (institutions, experience, and trust and cooperation between the government, academia and business sector) were set. In addition, NC academic institutions were highly positioned in basic research (with a focus on life sciences), and the 18 universities (16 UNC campuses and 2 private universities), and 59 community colleges were capable of training a high-quality work force.

The state leaders announced a long-term commitment for biotechnology innovation and commercialization. The goal was to become a leading global biotechnology cluster.

NC's General Assembly began its biotechnology initiative in 1981. The first step was the establishment of an ad-hock biotechnology study committee that conducted a comprehensive assessment of the state's potential in the biotechnology field. At the same time, the state (led by the Board of Science and Technology) began to invest in the field. The biotechnology study committee assessment revealed four main findings: 1) biotechnology was positioned to be a significant sector worldwide; 2) many countries considered enhancing biotechnology; 3) NC's academic research was well positioned to be a significant global player in biotechnology; and 4) the creation of RTP demonstrated the effectiveness of cooperation between the government, public sector and academia in policy-targeting. The committee suggested implementing policy-targeting toward the local biotechnology sector (NC Board of Science and Technology, 1984, 1985).

Coordination

A basic recommendation was to create the North Carolina Biotechnology Center (NCBC), which is the organization responsible for strategic planning, policy design, and coordination of policy implementation in the biotechnology area. NCBC board included representatives from the government, the academia, and the business sector.

Focus

During the background phase, NCBC focused on strengthening basic research in biotechnology, building an education infrastructure in the field, and gathering systematic data regarding the sector, and attracting multinational biotechnology companies to the state. NCBC also supported new firms' creation, but it wasn't the main focus.

Policy Measures and Progress indicators

The specific biotechnology-related actions taken between 1984 and 1990 were recruited 26 new outstanding faculty members from out of state; creating 25 significant multi-user research facilities, 8 research centers, and 10 exchange programs; awarding 134 research grants; supporting training programs; training high school teachers; and establishing a comprehensive database of all companies, institutions, and personnel

involved in biotechnology in the state. In addition, the NCBC assisted in attracting approximately 10 multinational biotechnology companies to the state, supported the creation of 32 new biotechnology companies, and supported technology transfer from the research institutions. During these years, the state invested approximately $450 million in the biotechnology field (NCBC, 1990).

During this phase, the leading local biotechnology related role models, such as aaiPharma (CMO, 1979) and PPD (CRO, 1985), were created. In addition, some leading non-local companies, such as Glaxo (1983), commenced operations in NC. In 1990, NC biotechnology sector included more than 100 companies that employed approximately 2,000 scientists and an additional 12,000 employees. The academic institutions trained about 1,200 scientists, and the high school system educated close to 70,000 students in fields related to biotechnology (NCBC, 1990).

2.2.2. Pre-Emergence Phase (1991-1998)

Initiative

In the late 1980s, NC was already well-positioned in terms of the quality and scope of academic research and training in biotechnology and had a significant pool of trained human capital. Thus, the new goal NCBC indicated was to strengthen the NC biotechnology business sector. Between 1987 and 1991, the NCBC conducted an assessment of the required skills in the industry, created advisory committees to design policies to enhance the application of biotechnology in agriculture, and commercialized biotechnology research.

Focus

NCBC focus was on strengthening the business sector through commercializing academic research and supporting the creation and development of startup companies. At this stage, NC also enhanced the biotechnology eco-system and specific segments within biotechnology.

Policy Measures and Progress indicators

Between 1991 and 1998, the NCBC supported the recruitment of 12 new outstanding faculty members and the established 20 multi-user facilities and 8 research centers, as well as additional academic activities. In addition, NCBC supported

university TTOs and creation of biotechnology companies. The state invested approximately $450 million in the field during these years.

In 1998, the NC biotechnology sector included about 150 companies that employed close to 2,800 scientists and 20,000 additional employees. The academic institution trained about 2,900 scientists in fields related to biotechnology, and the high school system educated about 650,000 students in biology (Research Triangle Foundation, 1999).

2.2.3. Emergence Phase – First Attempt (1999-2003)

Initiative

Since the mid-1990s, the NC biotechnology sector has grown rapidly. Within this context, the CRO and CMO segments were the most dominant. At this stage, there was already a critical mass of biotechnology firms and startups, an advanced supporting sector and significant VC activity at the state. The revenues of NC's biotechnology sector were $1.8 billion, with more than 25,000 employees in the sector. As a result, in 2000, the NCBC reassessed the key needs and opportunities for the continued growth within NC's biotechnology industry.

Focus

The new vision was to become a world leader in Bioprocess manufacturing (i.e., CMOs) and in the contract-research sector (i.e., CROs). In addition, the state's goal was to leverage the local agriculture and forestry sectors based on the biotechnology sector. Finally, a rising focus was given to enhancing startup companies through direct capital support.

Policy Measures and Progress indicators

The NCBC initiated the following actions: the establishment of the Genetically Engineered Organisms Act, the recruitment of out-of-state commercial Bioprocess-manufacturing companies, the initiation the NC Bioscience Investment Fund, the expansion of loans to startup companies, and the development of the BioVision 2000.

The financial meltdown of the early 2000s hindered the successful implementation of the new biotechnology policy. Between 2001 and 2003, the number of biotechnology firms and employees in NC did not change dramatically. VC

investments within the state decreased significantly. However, NC biotechnology cluster kept its high global position.

2.2.4. Emergence Phase – Second Attempt (2004—

Initiative

In 2004, NC had more than 200 biotechnology firms; at this stage, technology transfer from academia became frequent and significant. The biotechnology eco-systems became well-developed and diversified.

As the market showed the first signs of recovery from the recession, NCBC implemented a new strategic thinking process and decided to initiate a second attempt to trigger emergence. In 2003-2004, two strategic reports aimed to improve the policy toward the development of the Bioprocess manufacturing sector.

Focus

NC's vision was becoming the world leader in Bioprocess manufacturing and in the contract-research sector. In addition, the state's aim was to leverage different local sectors based on the biotechnology sector. High-earning job creation became the main goal of the state.

Policy Measures and Progress indicators

In 2003, a regional biotechnology leverage plan was initiated. In 2004, a plan for enhancing recruitment for leading firms was initiated—the REAP program. Between 2006 and 2008, three programs focusing on three segments (Medical devices, Agrotech, and Biofuels) were initiated. Between 2003 and 2012, the state invested approximately $1 billion in the biotechnology sector.

At 2011, the total economic impact of NC's biotechnology sector was estimated at $64.6 billion, and the direct and indirect employment effect is approximately 226,000 jobs. More than 500 bioscience companies have operations in NC, employing more than 58,000 people with an estimated $4.5 billion payroll (NCBC Website; Research Triangle Regional Partnership, 2012). The Triangle area's biotechnology cluster is a comprehensive eco-system and is home to the world's greatest concentration of CROs, CMOs, and other testing and services companies; it has a large concentration of agricultural chemical companies and contains major vaccine development companies. There are some very successful companies within the cluster, including more than 50

leading multinational biotechnology firms, 13 companies that held an IPO, and more than 50 companies that have been acquired by multinational companies.

3. The Biotechnology sector in Israel

Israel's government recognized the importance and potential of Israel's biotechnology sector during the early 1980s. In 1984, a National Committee for Biotechnology was appointed, chaired by the fourth President of the State of Israel, Professor Ephraim Katzir. However, we suggest that unsuccessful policy prevent utilizing Israel's opportunity to create a globally leading biotechnology sector. While the excellence of Israel's universities and the quality of their research in life sciences provided the foundation for two Nobel Prizes and five novel drugs (which are currently sold for more than $7 billion annually), most Israeli biotechnology firms are small and struggle to commercialize basic research from universities. The challenge of the Israeli biotechnology cluster is to enhance the conversion of university research into commercial products by Israeli startups and the subsequent development of these startups into large firms. However, Israel's biotechnology sector lacks the framework conditions for such successful commercialization. Israel does not have a comprehensive eco-system to support the development of a biotechnology sector, there is a lack of experienced managing and marketing human resources, and there is a significant funding gap between academic applied research and phase III companies. Currently, biotechnology research in Israeli academia is losing its leading position. It seems that without a dramatic government intervention, the potential of creating a leading biotechnology cluster in Israel would vanish.

3.1. The Development of the Israeli Knowledge Intensive Sectors

In the early 1970s, the Israeli defense system established its own R&D units. The scope of R&D in the army enabled the exploitation of economies of scale. Moreover, these hubs of excellence provided the market with talented and experienced personnel. Simultaneously, the Office of the Chief Scientist of the Ministry of Industry and Trade (OCS) was established with the goal to enhance business sector R&D and implementing Israel's R&D policy towards the business sector. The policy measures implemented by the OCS were mainly horizontal, with no priorities to any specific sector, stage of development or type of company. The 1984 R&D Law further consolidated Israel's support to business sector R&D. Since the mid-1980s, a knowledge-intensive cluster

began to emerge in Israel. Since the mid-1990s, Israel became one of the most important ICT clusters in the world. The OCS role in the successful development Israel's high-tech industry cannot be overestimated (see Avnimelech and Teubal, 2006, 2008b).

3.2. Biotechnology Development in Israel

We suggest that Israel's biotechnology cluster present a case of missing the opportunity for successful policy-targeting. We present information that suggests that the Israeli biotechnology sector was in a great position to emerge as one of the global leading clusters. Moreover, the Israeli government identified its importance and potential very early. However, luck of long-term vision and a non-consist, non-committed, and non-sufficient policy toward biotechnology, prevent utilizing this opportunity. We present the process based on the three first EILC phases. Within each phase, we will refer to elements such as initiative, coordination, focus, policy measures, and progress indicators.

3.2.1. Background Phase (1978-1990)

Initiative

During and prior to the background phase, Israel's government invested a great amount in building a strong academic science base. During this period, thousands of new academic positions were created, and large investments in infrastructure were made. During this period, some institutions, such as the Weizmann Institute and the Hebrew University, received world recognition and were highly ranked globally. This was especially true in life sciences. In addition, most of the academic institutions have opened technology transfer offices.

In the early 1980s, Israel had a strong background in advanced agriculture, a very strong academic research background in life sciences, and a few biotechnology developments in the business sector. In 1984, Katzir committee was created by the science ministry (a ministry with insignificant impact) to suggest policy toward biotechnology. Katzir committee recognized the potential of biotechnology for Israel's economic development and suggested targeting the field (Katzir, 1988).

Focus and coordination

There was no clear decision to target the development of biotechnology at this stage. There was a lack of coordination between the government and the business sector

and between different units within the government. If there was any focus in the Israeli government policy toward biotechnology, it was on academic basic research.

Policy Measures and Progress indicators

Most policy measures in this phase were directed toward strengthening the research facilities in the academia. During the 1980s, 286 new academic projects in fields related to biotechnology were conducted in the Israeli academia (Katzir and Herzberg, 1992). Minimal support for the business sector was given based on the regular R&D program with no priority to biotechnology. The first Israeli Biotechnology company, InterPharm, was established in 1978, as a partnership between Serono and Weizmann Institute. In 1980, BTG (Biotechnology General, today Savient) was the second company established based on research from the Weizmnn Institute. In 1982, BTG was the first Israeli company to receive an FDA approval for a therapeutic product. In 1983, it completed an IPO on NASDAQ and in 1994, it became profitable. During the 1980s, 70 life science companies were created in Israel, 20% in core biotechnology sectors, 40% in Medical device and diagnostic sector and 40% in IT life science sectors.

3.2.2. Pre-Emergence – (1991-1998)

Initiative, coordination and focus

Only in 1991, following Katzir committee recommendations, the Israeli government created a national steering committee for biotechnology, which submitted a report regarding the progress in biotechnology during the 1980s and new recommendations. During the years 1993-2000, a leading VC industry and ITC cluster emerged in Israel. These processes encouraged the biotechnology agents in Israel.

The development of the sector was uncoordinated and lacking significant policy-targeting. The government's focus was mainly on academic basic and applied research. The focus of the business sector was mostly on increasing finance though the growing VC industry.

Policy Measures and Progress indicators

During the pre-emergence period, life science received 30% of the OCS total budget and more than 50% of the incubator budget, which is higher than the portion of the life science industry out-of the total industry. In 1991, the Incubator program, which enabled relatively easy access to pre-seed money and an important tool for supporting

applied research, was launched (Kaufmann, et.al, 2003) During the 1990s, three biotechnology-related MAGNET consortiums operated (about 10% of the consortiums). However, government funding targeted only very early stage projects, leaving a huge funding gap.

The Israeli VC industry was created in 1993 through a government initiative known as the Yozma program (see Avnimelech and Teubal, 2004, 2006). Since the mid-1990s, Israel's VC has been among the top 4 VC industries around the world. During the background phase, there was only one dedicated biotechnology VC fund in Israel, Medica, which managed $20 million. Other VC funds often invested less than 15% of their capital in life sciences (mainly medical devices).

In the pre-emergence period, several important drugs, such as Copaxon from TEVA and Rebif from MERK, were created in Israel, hundreds of patents were registered, and many new life science companies were created.

By 1996, there were approximately 90 biotechnology companies in Israel. It appeared that the local VC industry could take the biotechnology companies to the next stage of development, but the market turned hostile to biotechnology, and it became extremely difficult for early/middle stage companies to secure funding. Between 1996 and 1998, drug delivery and medical diagnostic companies struggled to raise the second or third rounds of financing needed to get their products to market, with very little success.

The pre-emergence phase had a relatively positive impact on the medical device sector, as some very successful IPOs and M&As have occurred. However, the failures of some phase III companies had a negative influence on the willingness of investors to further invest in drug development companies. Therefore, most of the VC investments in life sciences were in medical device companies.

Between 1991 and 1998, 300 life science companies were created in Israel, 25% in core biotechnology sectors, 60% in Medical device and diagnostic sector and 15% in IT life science sectors.

Table 2: Progress throughout Israel's biotechnology cluster development

	1978	**1991**	**1999**	**2008**	**2012**
The beginning of	**Phase 1**	**Phase 2**	**Phase 3a**	**Phase 3b**	
Total life science related firms	12	~80	~360	~842	1,089
Drug development firms	2	~15	~60	~160	206
Medical device firms	8	~40	~160	~400	582
Other bio-related firms	2	~25	~140	~280	301
Bio Patents	15	37	164	128	225

Patents: % Bio Patents	12.4%	10.7%	17.7%	8.6%	7.7%
NC Bio Pat: % Global Bio	0.5%	0.7%	1.2%	1.3%	1.3%

Sources: USPTO (2013); ILSA (2013); IVC (2013).

3.2.3. Emergence – First Attempt (1999-2007)

Initiative, coordination and focus

In 1997, Prof. Haim Aviv's report on the biotechnology sector in Israel was published with specific recommendations to improve applied research in the academic institutions, to strengthen technology transfer mechanisms and to create dedicated funds for biotechnology commercialization. In 2000, the government hired the Monitor Group to construct a strategic plan for developing the Israeli biotechnology sector (Monitor, 2001). The OCS and the ministry of science led different activities related to biotechnology with minimal coordination. The focus of the initiatives was on enhancing the creation of private or public-private sources of finance for biotechnology startups.

Policy Measures and Progress indicators

In 1998, BTG's former CEO launched the Clal Biotechnology Fund – a $100 million VC fund dedicated to biotechnology. Subsequently, the holding company, Koor, has set up a $10 million fund—BioMedica. Agan-Makhteshim, a large chemical company, set up a $30 million VC fund. The Ofer family founded BioCom, a $30 million VC fund. Finally, Medica, the first biotechnology VC in Israel, raised $80 million for its second fund in 2000. As a result of these new sources of capital, a renaissance of biotechnology companies began. In 2002, there were approximately 150 biotechnology companies in Israel with 3,400 employees.

In October 2001, the ministry of science adopted the Monitor Group's recommendations (Meser-Yaron, 2001). In December 2001, the government announced biotechnology as a national priority; subsequently, the Ministry of Trade and Industry planned to launch three biotechnology incubators. These political activities led to high expectations in the private sector. However, the monitor report recommendations were not implemented. The policy measures in this phase were minimal and included offering financial priority to biotechnology (a 50% R&D subsidiary instead of 30% in other sectors), creating one biotechnology incubator in 2004—Bioline XR, and creating two (small) specific OCS programs (Magneton and Nofar) oriented to biotechnology.

During 2002-2003, the growth of Israel's biotechnology sector was not positive. Companies that went public in the late 1980s and early 1990s watched their share prices fall and had no opportunity for seasonal offerings. Others gave up on their IPO attempts, while smaller companies struggled to secure initial funding. In December 2004, Serono closed the operation of InterPharm in Israel. In 2005, BTG (Savient) was sold for only $80 million. In 2005, Pharmos failed in phase III after raising more than $150 million since its inception.

Between 1999 and 2007, 1000 life science companies were created in Israel, 25% in core biotechnology sectors, 60% in Medical device and diagnostic sector and 15% in IT life science sectors.

3.2.4. Emergence – Second Attempt (2008—

Initiative, coordination and focus

During 2007-2008, three research reports (GlenRock, 2007, Aviv 2007, and Glen, 2008) were submitted to the Israeli government urging a dramatic intervention within the Israeli biotechnology sector before the potential of creating a successful biotechnology cluster would be lost. In 2009, the government announced its plan to create four private-public VCs dedicated to biotechnology, funded at $100 million each. The private candidates for these funds were announced in April 2010. However, this initiative was not successful.

Policy Measures and Progress indicators

Eventually, no new policy measure was implemented successfully in the last 4 years. During 2006-2008, three new biotechnology VCs were established in Israel: Medica III, with $100 million; IHCV II, with $50 million; and 7 Health Ventures, with $70 million. The number of biotechnology startups is growing continuously. However, their prospect, when successful, is to be sold at a very early stage of development due to non-sufficient framework conditions. At the medical device sector, the situation is much better with rapid growth in startup creation with a prospect to be sold at later stages.

Between 2008 and 2012, 250 life science companies were created in Israel, 20% in core biotechnology sectors, 70% in Medical device and diagnostic sector and 10% in IT life science sectors.

Currently, Israel's biotechnology cluster is "stuck" at the pre-emergence phase with an incomplete eco-system. Clearly, Israel is facing a serious problem with a lack of

large multinational pharmaceutical companies and lack of supporting services such as CROs and CMOs, which could have brought relevant skills and networks and investment in phase III Israeli biotechnology companies (Kaufmann and Schwartz, 2008).

3.3. Targeting Israel Biotechnology – Summary

In summary, while significant attention was given to the development of the Israeli biotechnology sector since the early 1980s and the pre-conditions were supportive, the "targeting" process was not managed well. There was no clear vision, no operational road map and no coordination between the different government agents. Israel's policy toward biotechnology was not coherent, lacked valid commitment, and was slowly adopted and insufficient in terms of capital, resources, and activities.

4. Comparing Biotechnology Policy in NC and Israel

We suggest that NC's biotechnology policy is an example of a successful policy-targeting, while Israel's biotechnology policy is an example of a missed opportunity for successful policy-targeting. Next, we compare the factors we identified as critical for the success in NC with the same factors in Israel.

Strategic vision and planning. NC's government decision to implement policy-targeting toward biotechnology development was based on a national strategic decision and a lengthy planning process. This decision was based both on the vast impact the biotechnology sector was expected to have on the economy and on the supportive pre-conditions in NC. In Israel, while the vast potential impact of biotechnology and the supportive local pre-conditions were identified in the early 1980s, there was a lack of valid strategic decision, long-term planning and commitment in the process.

Timing and fast response. The implementation of the biotechnology strategy in NC was timed correctly on two levels. First, in the early 1980s, the foundations of RTP were sufficient to take a more focused and aggressive strategy, such as targeting the biotechnology cluster (internal condition). Second, the early 1980s were an appropriate time to implement a policy-targeting toward biotechnology development, as the biotechnology sector was in the early phase of development (external condition). Moreover, NC government acted immediately (even before the final biotechnology steering committee report was submitted, they increased significantly the support of biotechnology and after the report was submitted the acted fast). The first Israeli

biotechnology study committee (1984) was established at an appropriate time; however, the recommendations from this committee were implemented slowly and incompletely (only in 1991 a steering committee was established and increased investment in the field, and only in 2001 the government announced biotechnology as a national priority).

Cooperation between the government, the public sector and the academia. In NC, there was a strong cooperation between, the government, the business sector and the higher-education system. This cooperation was implemented both in the planning process and in the policy implementation. The previous success with cooperation between the government, public sector and academia in the creation of RTP assisted in recruiting and motivating them to this mission. In Israel, there was limited cooperation between the government, public sector and academia in the process of supporting the biotechnology cluster development.

Strategic organization. In NC, the creation of NCBC was one of the first actions during the biotechnology cluster development process. We suggest that the NCBC act as a central strategic organization, provided strategic thinking and act as a crucial coordinating agent throughout the development of the biotechnology cluster.

In Israel, it was not clear which government agency was responsible for management of biotechnology policy (the OCS or the Ministry of Science), and there was no separation between the main budget source and the day-today operation (the OCS) and the strategic thinking process.

Long term commitment. In the case of NC's biotechnology sector targeting, the long-term commitment of leadership on all levels was a crucial factor contributing to its success. NCBC recognized that the results from their investment could take decades to be realized. This long-term commitment is expressed through continuous development, adjustment and assessment of the policy and continued growth in the budget throughout the last 25 years. The Israeli government did not make a long-term commitment, which negatively influenced the willingness of foreign companies and investors to enter Israel and affected the motivation of local researchers to create and develop companies.

Flexibility and policy adjustment. Because of the significant uncertainties in new technologies and new sector development, policy-targeting process should remain flexible and continuously adjust alone the same lines of the overall vision and the EILC principles. In NC, the policy for biotechnology development has been successfully adjusted several times over the last three decades. NCBC was crucial in coordinating this complex task. In NC, initially, the focus was on strengthening academic research,

attracting large biotechnology-related corporations to the area, and supporting workforce training through the universities and community colleges. Later, the focus shifted to entrepreneurial education, network creation, enhancement of technology transfer, and eco-system development with a specific focus on the CRO and the CMO segments. Since the mid-2000s, the focus has been job creation through the strengthening of specific related sectors such as Bio-manufacturing and Agrotech. In Israel, policy was slowly adjusted to the developments on the market. The initial focus was mainly on academic basic research. Since the late 1990s, the focus has shifted mainly to create public-private sources of early stage finance.

Creating a diversified eco-system. Creating a sustainable sectoral innovation system requires attention to the entire elements of the sector eco-system. A significant factor for the success of NC's biotechnology clusters is the development of a full and diversified eco-system. NC's biotechnology clusters include large and established biotechnology and pharmaceutical companies, early stage companies, and critical service providers such as CROs and CMOs. This comprehensive eco-system enables the leveraging of successful inventions and encourages startups to form in the state. Israel focused mainly on the high-edge value chain (i.e., drug development research and startups) and neglected the development of a diversified eco-system. In NC, attracting large multinational biotechnology and pharmaceutical companies and attracting outstanding academic researchers from outside the country was a significant part of implementing the policy-targeting in the background and pre-emergence phases. In Israel, there were some attempts to attract large multinational biotechnology and pharmaceutical companies. However, these attempts were not successful. Currently, the situation in Israel is that even startups with excellent product pipeline would be undervalued and subsequently acquired for a small amount during the development phases because of the underdeveloped eco-system.

Investment in basic research. The engine of new sector development is new knowledge and innovation. NC invested heavily both in academic research and in research facilities. Moreover, in order to increase the impact of the academic research, the state invested in academic technology transfer. In Israel, the strongest element was the investment in academic research. In addition, Israel was a pioneer in technology transfer offices within academia.

University research/Medical centers. Every successful biotechnology cluster must include top level research universities and academic medical centers. These institutions

attract significant grant funding, and the essential research talent required for the basic research, invention and innovation that ultimately produces commercialization of biotechnology products. Both NC and Israel are well positioned in this regard. However, since there is very limited CRO activity in Israel, the biotechnology cluster is not leveraging the potential of these top levels academic medical centers.

Education and workforce training. A significant building block in the biotechnology sector development is a large pool of skilled employees. NC government and the NCBC recognized this important element and invested substantial funding and attention to developing the biotechnology workforce. The NCBC gave financial support and operational assistance in developing new programs to the community colleges and the universities. These new programs were tailored to the specific needs of the industry. In Israel, the academic system supplies a large pool of skilled employees for the science and engineering positions. However, there is a lack of skilled employees for managerial positions within the biotechnology sector.

Investment in public infrastructure services. The NCBC has invested a significant amount of its financial resources and efforts toward public infrastructure services for the biotechnology sector. These efforts include creating a public database, investing in conferences, legitimizing biotechnology throughout the state, and providing entrepreneurial education and assistance. In Israel, there were limited investments in similar public infrastructure.

Funding availability. The creation and development of biotechnology companies require capital. Biotechnology clusters often rely on the large and active presence of venture capital, public funding, bank financing, and corporate strategic funding. In NC, while public funding is quite strong, the business sector sources (especially VC) should be improved significantly. The Israeli VC industry is large and active. However, its main focus is the ICT sectors. Moreover, the absence of other early stage sources (e.g., significant government funding) and late-stage sources (e.g., investment by large pharmaceutical companies) hinders VC investment in the field.

Business and regulatory environment. The overall business environment—taxes, regulatory barriers, operating costs, cost of living—is important. NC created a supportive environment for biotechnology development. Israel created a supportive environment for the high-tech industry in general but did not adjust it to the specific needs of the biotechnology industry.

5. *General Policy Implications*

We draw our conclusions from the comparison between the experiences of NC and Israel in implementing policy-targeting toward biotechnology development, and a comparison with other case studies presented at TARGET project (see Rosiello et al., 2013).

Policy-targeting is effective for sectors in the early stages of development globally. Implementing policy-targeting is a complex policy-making process that might require prior experience of the policy makers and a suitable policy institution. Moreover, the success with the process depends on cooperation between the government, the private sector and the academia. Prior trust and experience with such cooperation increase the chances of success. We suggest that in case of limited experience and trust, the policy-making process should start with horizontal policy and a limited scope of targeted programs in which the relevant experience and trust will be developed.

Implementing policy-targeting toward complex innovation systems requires a comprehensive assessment, full support and commitment of the government; an explicit decision to target; and a clear and explicit vision. Timing is also a crucial element in such dynamic innovation systems. Frequent, unsuccessful full-flag emergence is a consequence of 'too little and too late' policy support.

The creation of an independent organization for strategic thinking, policy design, and implementation coordination is essential for success. Separating between the main budget source and day-to-day operation and the strategic thinking process is significant for ensuring comprehensive and unbiased evaluation and policy design.

Policy-targeting requires a critical mass of actions and resources. Thus, we suggest that when a region does not have enough resources, it should consider promoting the development of a niche market rather than promoting the development of a full-flag cluster.

Policy-targeting is an evolutionary policy which takes place in complex, uncertain, and dynamic environments. This means that policy-makers must be constantly capable of redefining the objectives in a coordinated and time-effective manner (Teubal and Zlotnick 2011).

Whenever policy-targeting mix is introduced into an economy, the likelihood that it will meet all the goals and needs in a limited interval tends to be low, particularly if the targeted sector is rapidly changing. However, not meeting the goals and needs soon

does not mean that the vision and the key structure of the policy-targeting mix must be replaced with a better match. Rather, evolutionary policy-targeting approach allows for adjustments based on learning and new evidence as the policy mix is introduced and progresses.

Another dynamic aspect of policy-targeting relates to the fact that during the multi-phase process of multi-agent structures' emergence, often the successful implementation of a policy measure can actually cause this measure to become unnecessary after a while and to reveal new system failures. On the other hand, some non-successful policy measures should only be suspended until some specific system failures are fixed.

Another characteristic of evolutionary targeting processes is the changing role of policy and market in leading the process. In many cases, policy only enhances processes already existing on the market, in order to achieve faster process and leverage initial success.

The successful implementation of policy-targeting toward advanced technology sectors requires the presence of an adequate research and training infrastructure. Without these framework conditions, the scientific infrastructure would need to be strengthened before implementing more advanced elements of the policy (i.e. first phase of the EILC policy). Within the business sector, the creation of a developed, diversified and capable eco-system and a pool of skilled human capital should precede aggressive support to the creation of global born technology startups. For such capable agents and a pool of skilled human capital to develop, often, a region should not only promote internal development but also attract external experts. The emergence phase is a result of a dynamic increasing-returns-to-scale process. Within this stage, the relevant multi-level structure emerges. A major issue is whether countries in pre-emergence will make a transition to emergence. Success in the crucial phase is subject to sufficient pre-condition, supportive external environment, timely and successful policy implementation and luck.

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