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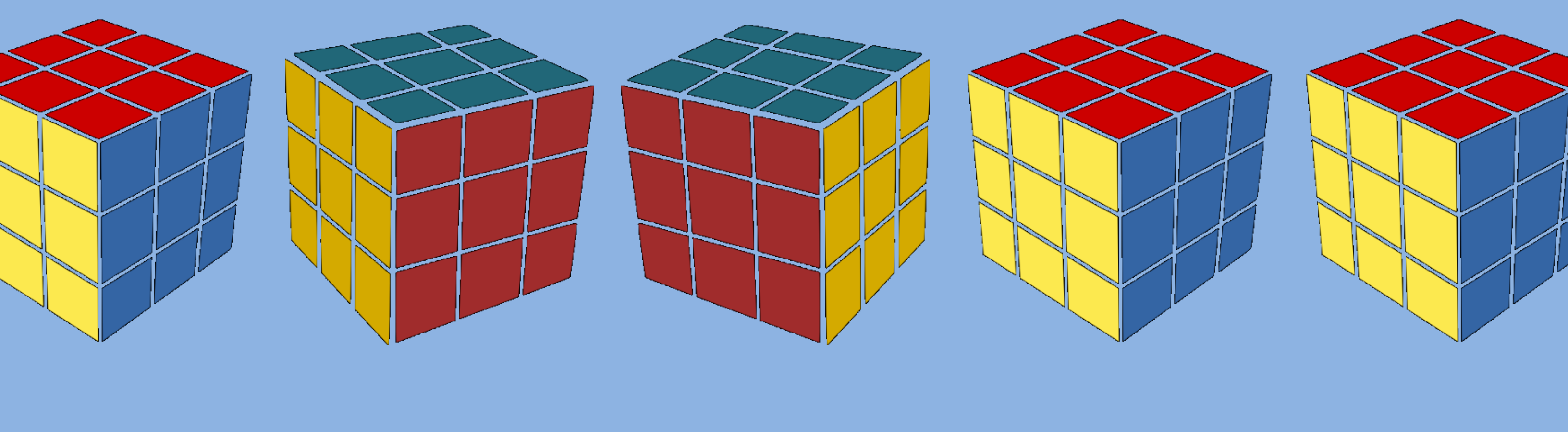
TARGET Policy Report

TARGET

SEVENTH FRAMEWORK PROGRAMME

TARGET Policy Report

Promoting the Biotechnology Sector



 TARGET – Targeted R&D Policy - is a project within the Seventh Programme and is co-funded by the European Union (Grant Agreement 234522). The project duration is July 1, 2009 – September 30, 2011.

Consortium Members:

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Executive Summary

The TARGET project's objective is to design and develop a set of guidelines & recommendations, cumulating in a Toolkit, for creating and executing policies to develop the life science/biomed sector. The TARGET policy Toolkit, presented in chapter II, is based on the Evolutionary Life Cycle approach to innovation, modified to suit the challenges and realities facing life science industries. The Toolkit is also a first step in creating a policy approach applicable to other emerging and innovative sectors. The main challenge of TARGET project was to translate the consortium's insights on life science/biomed innovation into a policy Toolkit that is clear and concise, without being overly simplistic or advocating misleading "cut and paste" approaches to innovation policy.

A consortium consisting of 8 partners from 6 different countries was assembled to carry out TARGET project. The consortium brought together public bodies and research institutes and stimulated a mutual learning process where members combined their knowledge and carried out research which provided a strong and realistic base for decision-making in science and policy.

Over the three past decades, the use of cellular and molecular processes to develop new technologies, products and services has resulted applications in a number of industries. While the structure of these industries is changing, expectations for economic growth remain strong, with major implications for innovation policy. Similar to other areas of the knowledge-based economy, competitiveness in sectors related to life sciences - at both a regional and national level - seems increasingly dependent on the ability to generate new ideas and use them to innovate. This entails the continuous renewal of capability endowments, raising demands for the endorsement of interactive learning, networking, foresighting, and the mobilization of complementary knowledges to respond to new challenges and opportunities.

A similar process is characterized by a remarkable and often unmanageable degree of uncertainty and complexity. Complexity relates to the plurality of techno-scientific knowledges that need to be mobilized as well as the variety of societal, ethical and regulatory factors that must be considered when placing new products and services into markets. Uncertainty relates to the low probability of success that characterizes research and development efforts, the often very long terms of development and the very high investments required to complete it (biological drug development is considered as a classical example of such challenges).

Deployment and transformation over time of dynamic capabilities are the result of an historic and context-dependent process, where context-dependency may be seen through the lenses of regional and/or sectorial systems of innovation. Accordingly, innovation policy is increasingly refraining from linear thinking. Nevertheless, the private sector's reluctance and/or inability to invest in high risk research, and sometimes development, is often described as a classical case of market failure, and prompts public investment in not only basic research but also in the support of industrial applications and entrepreneurial exploitation of bioscience.

Frequently, such investments are explicitly aimed at the emergence of biotech sectoral systems of innovation (BSSIs) or bio-clusters. Understanding the main scientific, technological, economic and institutional drivers of the emergence and growth of such forms of industrial organization is a necessary but insufficient condition to develop appropriate and effective policies. Indeed, mostly because of uncertainty and complexity, assessing the actual/potential impacts of such policies and providing advice to policy-makers becomes extremely difficult.

To begin with, any analytical effort and resulting policy recommendation are intrinsically related to the institutional and structural features of the local system of innovation. From a top-down perspective, it is often assumed that changing the institutional configuration of the system or changing the functioning of some of its components – for instance by providing new types of incentives to certain agents - will solve market/systemic failures. In turn, this will improve the overall performance of the system. Such belief is often reinforced by the study of well-functioning systems, whose routines and structures are seen as replicable across space, time and (less frequently) industrial sectors.

Secondly, while the analysis often concentrates on the setting of relevant players, system components or assets and institutional features, less attention is paid to the roles played by actors (some of whom may not be local) and institutions and the emergent links among them. An initial problem relates to the assessment of national/regional endowments, which can lead to flawed conclusions to the point where almost every region/state/country of the world has great bioscience, unexploited entrepreneurial capacity or the right set of pre-conditions to attract risk capital.

Thirdly, beside the assessment of the key characteristics of the local environment, understanding functions and relationships entails a focus on processes and dynamics. Systems change over time and different policies are often required to support and promote emergence and growth at different points in time. As noted earlier, this process is often sparked by the unpredicted and unpredictable convergence of different types of knowledge and technologies. Finally, it is frequently assumed that any type of policy can be implemented provided that a sound rationale exists. In practice, even policies with sound rationale may not be implementable because of radical uncertainty, political impediments (e.g. lack of long-term commitment) and/or complicated (e.g. multi-layered) governance structures.

Aims and Challenges

Given such difficulties, the TARGET project sets out to design and develop a structured and valorized set of guidelines and recommendations, cumulating into a policy Toolkit, for targeted R&D policies that focus on the biomedical sector to promote the emergence of BSSIs/bio-clusters. In line with the overall OMC-NET objectives,[1] the purpose of the Toolkit is to provide structured guidance and instructions as to how to create, enhance, improve and nurture targeted policies and to enable concrete policy-making decisions.

The proposed Toolkit was developed by identifying key systemic drivers and policy capabilities required in order to formulate and implement successful targeted R&D policies. This includes the ability to define strategic priorities, to evaluate technological gaps in prioritized areas, to identify elements within the national/regional innovation system responsible for achieving the selected priorities (including the missing elements), to identify potential system failures, to formulate effective policy and to ensure coordination between the relevant policymakers and government agencies.

Targeting is seen as an instrument for coping with global competition. The ability to design targeted R&D policies successfully is associated with the ability of policymakers to identify not only basic market failure, which result in the formulation of R&D support schemes, but also coordination failures which may block or impede the growth of the targeted business sector.

The Structure of TARGET Approach

The TARGET Toolkit is meant to provide policymakers with a systemic way of addressing the challenge of supporting the emergence of bio-clusters. Working in a volatile global environment, policymakers are faced with conditions of high uncertainty. Within this context, it becomes very challenging to assess the effect of policy measures on different parts of the innovation system; thus, a systemic way of addressing this issue becomes highly relevant. The focus is on the biomedical sector that presents the highest level of complexity/uncertainty management.

The TARGET approach provides policymakers with a conceptual framework that will be productive for policymaking and policy implementation. By analytically breaking the policy challenge into different elements it becomes easier to understand what has to be addressed and how. The three elements of TARGET Approach are: Industry Life-Cycle; Sector Drivers; and Policy Dimensions.

Element 1: Industry Life-Cycle

The Industry Life-Cycle deals with the development of the biotech sector itself. The TARGET approach recognizes that different industries progress through a cycle of development which is uniquely characteristic to them. In addition, in line with Avnimelech and Teubal (2006) we tested the hypothesis that bio-clusters follow a similar cyclical development, one that is based upon an idiosyncratic set of background conditions. Then, three phases of development have been recognized to date: **Background Phase, Pre-Emergence Phase and Emergence Phase**. Different phases call for different policy measures and its imperative that policymakers identify what phase they are about to interact with. Thus, the very first element of the TARGET approach deals with the identification of the current phase of the sector in terms of the Industry's Life-Cycle. This is done through the Sector

[1] http://ec.europa.eu/invest-in-research/coordination/coordination02_en.htm

Drivers. Once the phase has been recognized, all stakeholders can focus on advancing the sector to the next cycle.

Element 2: Sector Drivers

The Sector Drivers are key functional elements of the sectoral systems of innovation that constitute the real 'engines' which move the sector from one phase of the Life-Cycle to the next one. Studying different case studies around the world, we have identified the following Drivers: **Science, Training, Commercial, Financial, Human Resources and Other Institutions**. For example, at the Background Phase there are no specific capabilities in biotechnology, but there are established capabilities in general purpose R&D. Therefore, the Science Driver will look differently at this phase in comparison to the Pre-Emergence Phase, in which specialization in biotechnology begins. Understanding which of the Drivers is lagging behind helps policymakers determine what the best entry-point is in terms of policy measures.

Element 3: Policy Dimensions

The Policy Dimensions deal with the different decisions that must be taken at any point of the policy process. These dimensions describe how to approach a Driver. Some Policy Dimensions, such as the decisions on the Vision and Assessment, must be present all through the policy process (and will be termed **strategic decisions**), while others change with every policy modification (and are thus termed **tactical decisions**). Supporting a biotechnology sector takes time and the policy process will go through different stages. At each stage there is a need to define the relevant Policy Dimensions and to decide on each one.

The Toolkit's Calibration Process: Case Studies and Policy Dimensions

In this phase, the trajectories of emergence of a number of already emerged bio-clusters were carefully reconstructed and examined. The main objective was to find out whether our approach was fit enough to (1) reconstruct such process of emergence from an historical prospective, (2) reveal cumulative and co-evolutionary processes between any of the abovementioned drivers and/or crucial network dynamics within the local/sectoral system (3) detect policy interventions that stimulated (or hindered) the process of emergence (including an initial setting of strategic priorities).

Scotland

The Scottish pursuit of biotechnology began in the mid-nineties with its strong academic capacity in biomedical research and the belief amongst policymakers that biotechnology would be a future growth-generating industry. The strategy developed and then executed by Scottish Enterprise under the 'Framework for Action' aimed at bringing

Singapore

Singapore's effort at creating a bioscience cluster was completely orchestrated by the government. Following successful government-led economic development campaigns in the 1970s and 1980s, the Singaporean government decided to pursue the emergence of a knowledge-based economy, with bioscience as one of its pillars.

academic work to the market, and starting new firms across various bioscience-related activities

The pre-emergence phase (1999-2003) saw the Framework for Action successfully meeting its numerical targets of job creation and employment numbers. Policy efforts continued through established programs, but as the sector grew and industry became more influential, the strategic emphasis began to change to one of growing existing firms rather than continuing to seed more new firms.

The Scottish system peaked in 2003 in term of its growth, but suffered a setback with the failure of a number of therapeutic firms – these firms had enjoyed success in their IPOs, but suffered failures of their products in trials. The result was a loss of investment from outside Scotland, and a retrenchment of local efforts towards less risky areas of the life sciences such as medical devices and diagnostics.

The official decision to pursue bioscience was made in 1999; however there had been some previous activity in this direction in the 1980s and 1990s. Singapore's capabilities in electronics attracted Big Pharma to establish manufacturing facilities in Singapore. The targeting process began under 'the Science and Technology Plan 2005' and the Biomedical Initiative (BMI), pushing the country from Background Conditions to Pre-Emergence.

Capabilities had to be imported and thus, tremendous incentives were given to star scientists from abroad to relocate to Singapore. New dedicated research institutes were established and international scientists were given managerial positions. The initial goal was to create R&D experience and train local PhDs. Start-ups were founded with public money but were soon privatized. The next strategic phase began after 2005, with an emphasis on translational medicine and the creation of greater network connections between actors in the local cluster.

Israel

The development of the Israeli biotech cluster can be attributed to the very strong science base as well as to high level of entrepreneurship. The latter is partly due to the success of the high tech-sector which was followed by VCs, IP services, links to networks, etc. This progress also signalled to the scientific community that entrepreneurial activity was a possibility for career building.

Medicon Valley

Arguably one of the few European examples of strong fully-fledged biotech cluster, Medicon Valley is located in the cross-border region of Øresund and it can be considered as an example of the joint vision of the Danish and Swedish governments to create Europe's pre-eminent hub for life-sciences R&D and production. An Øresund Committee was created in 1993 as a forum for voluntary

During and prior to the background phase Israel had invested massively in building a strong academic science base, with good results in the life sciences. The pre-emergence phase showed good progress on the medical device sector with some very successful IPOs and M&As.

However, the failures of some phase IIIs had a negative influence on the willingness of VCs to further invest in drug development companies. This phenomenon caused the Government to establish a $400 million public\private VC funds which will be dedicated to biotech. Currently, Israel is "stuck" at the pre-emergence phase with no real support system to take into the next phase.

political cooperation for the region. The Committee decided to focus on biotechnology due to its potential, and to piggyback on the Medicon Valley project, initiated in 1995 by Lund and Copenhagen Universities to stimulate the formation of a cross-border bioregion.

The main elements that allow to identifying a phase of emergence (early 2000) were the high growth of venture capital market, both from the supply and demand side. Moreover, other indicators, such the creation of start-ups, gazelle firms, the drug development pipeline, IPOs or international alliances show a positive and dynamic co-evolution of the elements that form this cluster. Furthermore, new biotech programs have been implemented to strengthening human resources and support entrepreneurship and commercialization.

North-Carolina

Since the mid 1950s developing a knowledge - intensive economy was a strategic priority of NC. Initiating and supporting this mission was characterized by strong collaboration between the business sector, government and academic institutions. In 1959, NC established the research triangle park (RTP). The process was coordinated and involved all major players. In the early 1980s RTP was already a success story; this provided NC the confidence that it could pull-off a coordinated strategic process. The North Carolina Board of Science and Technology (NCBST) was established in 1963 by North Carolina General Assembly to encourage, promote, and support scientific, engineering, and industrial research applications. In the early 1980s the government platform for targeting was already effective and stable.

Since the mid-late 1990, the biotechnology sector started to grow rapidly. Also, because of changing global trends in the bio value-chain, in 2000, NCBST reassessed the key needs and opportunities for continued emergence. In addition, the CRO and CMO sub sectors were growing fast, with the Bioprocess Manufacturing sector as the new focus. The slow-down in the market in the early millennium stalled NC's emergence, but a second attempt was launched, keeping some of the same foci but also including expansion in agro-tech, bio-fuels and medical devices.

The Toolkit's Testing Process: Policy Analysis

At this stage, the framework was tested in the context of four European Partner Countries/Regions **(France, Galicia, Slovenia** and **Lithuania**) as well as in **Israel**. The exercise led to a stimulating learning process, which in some cases resulted in significant and direct changes in policy action. In spite of the heterogeneity of BSSIs (in terms of both emerging and structural features) and systems of governance examined, most policymakers recognized the utility of thinking in terms of cycles and development phases.

With a basic understanding of the Extended Industry Life-Cycle and the Sector Drivers which move the biotechnology sector from one phase to the next and how policy-making was able to support (or hinder) the process of emergence of local bio-clusters, our analysis concentrated on the location of the bio-cluster within a defined phase of development, with a view to understand the current structural and dynamic features of each local system. As noted earlier, this is no easy task as each BSSI presented a much greater degree of complexity than traditionally defined industrial sectors.

This allowed the identification of an initial set of dimensions which are seen as strategic because they establish the call to pursue a BSSI/bio-cluster actively and the broad vision that efforts will work towards achieving. Depending on the stage of development of the local systems, the focus can be on either the assessment of background/pre-emergence conditions or the recognition of key co-evolutionary processes involving the drivers of bio-cluster emergence. Once these high level decisions are made, the specific steps needed to fulfill them will have to be carried out, i.e. the tactical decisions and steps.

Concerning background/pre-emergence conditions, our analysis laid special emphasis on the essential role of the bio-scientific base (more as a source of required skills than as exploitable intellectual property), some key aspects associated with the existence of an entrepreneurial culture (such as acceptance of risk and failure), ability to achieve political consensus, and ability to develop strong leadership (preferably in the form of body of experts able to advise on strategic planning and sufficiently detached from political influences to ensure consistency overtime).

In terms of cumulative dynamics, a series of policy challenges stretching across countries/regions were identified. They concerned not only the need to increase availability of public and private finances and support local start-ups (many development agencies around Europe have devoted significant investments to 'closing financial gaps', with results frequently below expectations), but also: (1) meeting demand for both technical and managerial skills in a timely manner; (2) investing in both soft and physical infrastructure; (3) when feasible, combining local experiences, skills and resources with international partners in order to grow (a number of) local firms into sizable businesses with an international reach; and (4) promoting learning processes that directly involve policy-makers.

The tactical decisions discussed will likely be carried out by policymakers 'on the ground' trying to match their actions to the vision they have been charged with working towards. This tactical level of our analysis is explicitly related to the following dimensions: (a) the identification of key stakeholders and (b) entry-points for policy implementation, (c) effective policy design and (d) efficient policy evaluation. Regarding these dimensions, the testing process allowed for the learning of a number of key lessons.

Important Lessons

While the phases and the drivers within each phase can be generally described, cases' qualities in each phase and their transition through each phase can vary quite widely. However, based on the case studies and discussions with policy experts, some generalized lessons are presented here. These constitute warnings and major guide posts for policymakers following the Target approach.

Timelines and Commitment

(a) The evolutionary development of biotech sector is long. A main lesson to be taken from the various case experiences is that developing a BSSI/bio-cluster requires long timelines of more than 20 years, particularly if starting from a background phase where elements such as an industrial base or commercial experience are missing. This means that the incentives for investors to enter the arena are few, the virtuous cycles of activity become more difficult to create, and most efforts will have to be concentrated on transforming scientific knowledge into commercial use. Without a scientific base, this becomes an even larger challenge with longer timelines. Before pursuing a Targeted policy of biotechnology, a realistic assessment of capabilities and commitment is crucial.

Science and Research

(b) The existence of excellent scientific research is a key precondition for the development of a complete cluster, due to the importance of the scientific knowledge in the development of this sector. Strength in general research and training infrastructure at this stage means that the focus can be on utilizing the knowledge base rather than having to build it up before pushing the strategy's vision. In biotechnology, high quality research is a key success factor; it should be argued that top quality research is a key factor of success. However, it should also be noted that there have been relatively successful biotechnology firms based on less-than-revolutionary science, which highlight the importance of industry applicable science.

(c) Strengthening a science base in pursuit of industry targets is different from targeting a science base for the sake of having the best academic science. In many cases, a strong science basis results in a capable workforce rather than a series of entrepreneurial ventures spurring out of it.

Basic Drivers for Biotechnology

(d) Excellent science in conjunction with financial support for R&D and the availability of VC funds are the basic elements in the development of a biotech sector.

(e) At early stages of a biotechnology sector's development, when excellent science is not well established and there is no biotech industry in place, looking to finance policy and the establishment of start-ups as an entry-point is questionable.

Strategic Leadership

(f) A strong leader can move forward the development of a biotechnology sector by acting as an advocate for the sector and drawing together various interests and stakeholders to cooperate in the pursuit of biotechnology. This leadership of individuals is then normally translated to an organization(s), referred to as **a Body of Knowledge** in the Toolkit (chapter II), which takes these ambitions forward in practical terms. Successful a Bodies of Knowledge are arm's-length, pro-active, forward-looking bodies able to operationalize the strategic vision.

(g) According to focus group comments, without a Body of Knowledge, the success of a Target policy developing a biotechnology sector is highly unlikely. A Body of Knowledge can be a person, an unofficial governance group, or an official body given arm's-length authority to conduct foresight and recommend/implement policy. An important point made, however, was that the a Body of Knowledge had to be able to ask the hard questions and make the difficult decisions which may not necessarily appeal to short term political interests. Without this ability, the difficulty of actively pursuing a biotechnology sector increased.

Political Consensus and Realistic Assessments

(h) The buy in of major players in business, government and academia will help the policy process navigate the complexities of establishing a biotechnology sector. For example, the North Carolina targeting policy benefited from a comprehensive assessment, full-support of the government and an explicit decision to target biotechnology. The creation of the North Carolina a Body of Knowledge resulted in an independent focal-point for strategic thinking, policy design, and implementation coordination. The structure of the Body of Knowledge meant that it was able to offer arm's length, unbiased evaluation and policy design.

(i) Broad political consensus is required to implement an effective biotechnology policy. Failing to reach consensus among the stakeholders and coordinate their action may slow dramatically the development of the cluster. For example, targeting becomes much more complex when a public entity responsible for one aspect of the innovation process is not coordinated with other entities responsible for other parts of the process, a power differential, and a lack of consensus.

The effect of leadership change at the strategic institutional level and at tactical organizational levels can be significant. Changes in leadership may bring about changes in goals, priorities and expectations of a political or ideological nature and may therefore impact the subsequent policy measures and assessment criteria used in building a cluster. While change may be necessary during the long-term implementation of a strategy, changing the strategic vision should be based on regular assessments and evaluations rather than political preferences and short-term reactions.

(j) Many times the "ambition to bio" initially expressed by leaders may be too optimistic or ambitious for the country/region's capacities or resources. This may be because of uninformed expectations, or the desire to emulate "successful" cases. In this case the importance of realistic system assessments becomes apparent. A successful Target strategy does not have to be equivalent to the achievement of a full-fledged, biotechnology cluster that covers a variety of products and services. A Target strategy may aim to achieve success in niche markets, the creation of SMEs, or a more modest participation in the biotechnology value chain; the adequacy of the goals will correspond to what stage of development the region or country finds itself in terms of its scientific and commercial resources and experience.

Acceptance of Failure, Need for Adaptability

(k) As mentioned above, biotechnology is a very risky business; failure must therefore be an accepted part of the process and seen as a source of experience. While the goal is to minimize failure, it should be acknowledged that all of the successful cases of sector development have involved learning through experience, which includes failure. Completely removing support or resources from an industry as a result of a first round of failures may be pre-mature and should be done only after careful systemic analysis.

(l) Decisive policy after a failure during the targeting process may have positive effects in creating momentum and confidence. Lack of success in some areas may also be the catalyst for the discovery of new niches or opportunities in other areas.

Indicators and Metrics

(m) Because of the importance given to system assessment and policy evaluation in the Target Toolkit, qualitative and quantitative indicators must be carefully considered and selected – *and they* must fit the goals of the strategy and policies being implemented. It is dangerous to use indicators as a general check list of progress without understanding why they were selected and how they can feed back into Target efforts.

Changing indicators mid-stream create problems of comparison to previous years, and will likely show a negative performance from policy measures initially planned with different performance milestones in mind. This is not to say that change in indicators should not occur if it is justified, however, it is important to bear in mind potential consequences.

(n) Evaluation of policies demonstrates commitment to achieve results and improve policies. It can also be used as a mechanism of transparency which is attractive to investors and commercial interests.

Sustainable Policy Initiatives and Economic Downturns

(o) Successful measures to increase entrepreneurial activity generally involve lowering the cost of engaging in entrepreneurial activity. However, in some key areas such as drug development and diagnostics, this may not be possible as because of the increasing stringency of the regulatory frameworks (safety/efficacy of new drugs/diagnostic tools).

(p) Economic downturns may have negative effects on otherwise well-functioning sectors by constricting the availability of capital, as well as potentially the demand for products. The strengths of the sector must therefore be recognized through consistent evaluations, and some key policies to help develop the sector should be flexible enough (and effective in lowering the cost of entrepreneurial activity) to deal with this uncertainty (e.g. R&D tax credits). In areas characterized by high capital requirements and uncertainty (drug development) this may require a radical rethink of the strategy's objectives.

I. On Biotechnology, Life Sciences and Biomedicine

Biotechnology, life sciences and biomedicine are close concepts with no clear boundaries. Its conceptualization varies depending on the authors, the context of usage or the specific purpose. **Biotechnology** is a complex and interdisciplinary field experiencing rapid changes in the knowledge base and its applications. Borders between life sciences and biotechnology are moving due the new developments and the cross fertilization among the different areas and techniques. Biotechnology draws on basic biological sciences like genetic, molecular biology, cell biology, microbiology or biochemistry and makes an increasing usage of methods and techniques from other areas like information technology, nanotechnology, robotics or chemical engineering.

These interactions and diffuse borders are clear at the scientific level but particularly notable in the productive sector. There are companies whose activity can be categorised within more than one sector. In fact, the penetration of biotechnology is increasingly widespread and diffuse. This not only shows its potential application to numerous fields, but also the difficulty in delimiting concepts such as biotechnology, biosciences, life sciences, medical technologies, health sciences, medical devices and biopharma.

In order to clarify the main areas and applications included in the broad definition of biotechnology, we refer to the most consensual definition provided by the OECD. Box 1 includes the definition used by the OECD.

Box 1: Definition of Biotechnology

According to the OECD, **Biotechnology is the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.**

This single definition not only covers all modern biotechnology, but also many traditional or borderline activities that have been used for a very long period of time. Modern biotechnology is defined as the use of cellular, molecular and genetic processes in the production of goods and services. It is associated with a different set of technologies including the industrial use of recombinant DNA, cell fusion, tissue engineering and others. Traditional biotechnology refers mainly to fermentation and plant and animal hybridization. The modern and traditional biotechnologies can be used in combination which is considered as modern biotechnology.

Source: OECD, 2005

The OECD displayed an indicative list of biotechnology techniques (see Box 2). This is the list commonly included in EC studies and reports.

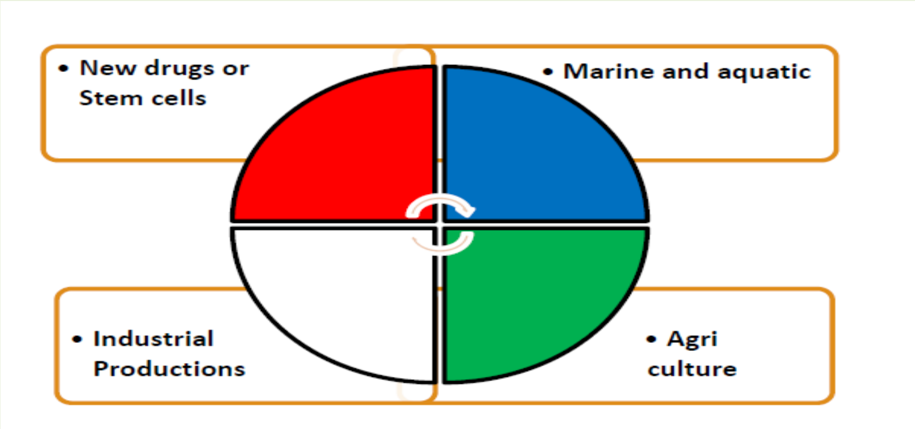
Box 2: List of Biotechnology Techniques

- **DNA/RNA**: Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.
- **Proteins and other molecules**: Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large molecule drugs; proteomics, protein isolation and purification, signaling, identification of cell receptors.
- **Cell and tissue culture and engineering**: Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation.
- **Process biotechnology techniques**: Fermentation using bioreactors, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biofiltration and phytoremediation.
- **Gene and RNA vectors**: Gene therapy and viral vectors.
- **Bioinformatics**: Construction of databases on genomes, protein sequences; modeling complex biological processes, including systems biology.
- **Nanobiotechnology**: Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics etc.

Source: OECD, 2009.

Sometimes biotechnology is classified also according to its applications. The most usual applications are related to health, agriculture, environment, industry and sea. Following this criteria the biotechnology sector is occasionally described as a rainbow (see figure 1), with each subsector having its own color, see figure 1.

Figure 1: The Biotechnology Rainbow



Source: Medicon Valley Alliance

red biotech is focused on health and application to the medical sector; **white biotech** (sometimes known as grey biotech) refers to applications production process of the industrial sector; **green biotech** refers to agricultural, plants and environmental applications of biotechnology; and **blue biotech** refers to the marine-based biotech and marine applications[2].

Life sciences is a broader concept than biotechnology including all scientific areas dealing with biology, medicine, veterinary, biochemistry and pharmacy, making use of all traditional and modern methods and technologies. Thus, biotechnology is a subset of life sciences based on specific techniques. The life sciences sector includes pharmaceutical, biotechnology and medical technology activities. Here are included both the new biomed sciences and the more traditional medical and pharmaceutical fields.

- **Pharma and Biopharma**: drug discovery and development, drug delivery, biotech medical technology, diagnostics and drug production.
- Biotech: Tools and supplies, bio-production, agricultural biotechnology, industrial and environmental biotechnology and food-related biotechnology.
- **Medtech**: Healthcare equipment, active and non-active implantable devices, anaesthetic/respiratory equipment, dental devices, audiologic devices and hearing aids, electromedical and imaging equipment, ophthalmic devices, surgical instruments and supplies for electromedical and imaging applications, medical disposables, contract research organisations (med tech) and IT & training.

Biomedicine can take two different meanings: traditional and modern interpretations. In the traditional sense, biomedicine is a medical science based on the application of biological and other natural-science principles to clinical practice. This "traditional science" includes fields such as medicine, veterinary, odontology and other biosciences (biochemistry, chemistry, biology, histology,

[2] Other colours used are yellow (Food Biotechnology, Nutrition Science); brown (Arid Zone and Desert Biotechnology); purple: Social and legal aspects (Patents, Publications, Inventions, IPRs); gold (Bioinformatics, Nanobiotechnology); grey (Classical Fermentation and Bioprocess Technology) and black (Bioterrorism).

genetics, anatomy, physiology, pathology, biomedical engineering, zoology, botany and microbiology). In the modern sense, biomedicinemakes intensive use of knowledge, methods and techniques developed through biotechnology and is therefore is closely related to red biotech (see box 2 below).

Biotechnology and Life Sciences companies

Biotechnology and life science sectors are clearly science-based activities. However, there are biomed companies which are not science/R&D intensive on a large extent. In addition, even among the scienc-extensive companies, usage of biotech knowledge or biotech techniques is not necessarily part of all these companies' activities. According to the OECD, **a biotechnology firm can be defined as a firm that is engaged in biotechnology by using at least one biotechnology technique to produce goods or services and/or to perform biotechnology R&D.** Some of these firms may be large, with only a small share of total economic activity attributable to biotechnology.

The life science companies include pharmaceutical, biotechnology and medical technology activities (Medtech). The characteristics of companies in the medical technology sector are the development of medical products which are not drugs. On the other hand, the characteristics of companies in the pharmaceutical sector are the development of drugs and various kinds of therapeutic products or methods.

The biotechnology sector is characterised by companies developing applications of science and technology to living organisms as well as parts, products and models and altering living or non-living materials for the production of knowledge, goods and services.

Together, these three sectors (Biotechnology, Pharmaceutical and Medtech) constitute what is known as **the life science industry**. Due to the overlapping nature of the section's definitions, there are companies whose activity can be categorised as belonging to more than one sector. For instance, companies involved in drug discovery could be defined neither as exclusively pharmaceutical nor as exclusively biotechnology companies. Therefore, each company has been classified into one specific business segment, whereas an individual company can be found in more than one sector.

Subsector	Main sector	Main sector	Main sector
Drug discovery/development	Pharma	Biotech	-
Drug delivery	Pharma	Biotech	-
Drug production (not biotech)	Pharma	-	-
In vitro diagnostics	Biotech	Medtech	-
Biotech medical technology	Biotech	Medtech	-
CRO	Pharma	Biotech	Medtech
Bioproduction (healthcare related)	Biotech	Pharma	-
Biotech tools and supplies	Biotech	-	-
Agrobiotechnology	Biotech	-	-
Environmental biotechnology	Biotech	-	-
Food related biotechnology	Biotech	-	-
Industrial biotechnology	Biotech	-	-
Implantable devices (active and non-active)	Medtech	-	-
Anaesthetic/respiratory devices	Medtech	-	-
Electromechanical medical devices	Medtech	-	-
Radiation devices (diagnostic and therapeutic)	Medtech	-	-
Ophthalmic/optical products	Medtech	-	-
Dental devices	Medtech	-	-
Reusable andsingle-use devices	Medtech	-	-
Information and communication tools	Medtech	-	-
Healthcare facility products and adaptations	Medtech	-	-
Assistive products for disabled people	Medtech	-	-

II. A Generalized Toolkit for Policymakers

1. Introduction to TARGET

Policymakers have increasingly taken it upon themselves to introduce policies promoting the economy's ability to host science-based industry. Science-based sectors are emphasised as sources of economic growth and as potential market-arenas for the enhancement of the national or regional economy's competitiveness. Some policies are responses to market failures, plugging gaps in the resources available to firms or the science base while not necessarily seeking to change the systemic structures within which these firms operate. As more research on science-based sectors and innovation has been conducted, and as experience in the business and policy areas has accumulated, arguments for more systemic approaches to policy have increased.

The TARGET approach presented here will help policymakers form a strategic roadmap and determine feasible interventions that lead to a functioning biotechnology system of innovation within a country or region. The goal of the Toolkit is not to present a single recipe of specific policies for success; as will be noted later on, the variety of cases and their development mean that no single path to a functionally biotechnology sector can be realistically described.

The TARGET approach takes the biotechnology system of innovation as the "unit of analysis." By taking such a unit of analysis, the approach can account for the different structures which form a part of the system and affect its actions, as well as take into account external influences, while not losing sight of the sectoral innovation system as the whole unit. Alternatively, what the TARGET approach does offer is a way for policymakers to work through this complexity and come up with a tailored, context specific strategy based on realistic assessments of their country or region's resources and capacities.

The TARGET approach is based on an evolutionary theory of innovation which sees different sectors as going through a life cycle of development. At different stages of a sector's progress, the ground work for development to the next stage is laid and the specifics of this groundwork will influence how the subsequent stage is realized. When describing the different Phases of evolution, Sector Drivers will be discussed which are key to moving the sector through the phases to maturity. The drivers described as necessary to take into consideration for assessment purposes and policy action fall under science, training, commercial capacity/experience, finance and human resources. They also include "other institutions" which would include IP, a working health delivery system and different regulatory systems which can affect the costs of the biotech sector (e.g. drug regulation, tax regime). These categories of drivers will be used when discussing the phases of evolution, however the individual drivers and their values/qualities will change phase by phase; these changes should be reflected in policy interventions implemented to reach policy goals.

2. The Structure of TARGET Approach

The TARGET Toolkit is meant to provide policymakers with a systemic way of addressing the challenge of supporting a biotechnology sector. Working in a volatile global environment, policymakers are faced with conditions of high uncertainty. Within this context, it becomes very challenging to assess the effect of policy measures on different parts of the innovation system; thus, a systemic way of addressing this issue becomes highly relevant. The biotechnology sector is dynamically changing both in terms of the way we understand scientific and technologic developments and in terms of how policymakers are supporting the emergence of the sector.

The main objective of the TARGET approach it to provide policymakers with a conceptual framework that will be productive for policymaking and policy implementation. By analytically breaking the policy challenge into different elements it becomes easier to understand what has to be addressed and how. The three elements of TARGET Approach are: 1) Industry Life-Cycle; 2) Sector Drivers; and 3) Policy Dimensions.

Element 1: The Industry Life-Cycle

The Industry Life-Cycle, presented in Chapter 3, deals with the development of the biotechnology sector itself. Based on an evolutionary perspective, the TARGET approach recognizes that different industries progress through a cycle of development which is uniquely characteristic to them. In the case of biotechnology, three phases of development have been recognized to date: Background Phase, Pre-Emergence Phase and Emergence Phase. Chapter 3 details each phase's properties in terms of the biotechnology sector. Different phases call for different policy measures and its imperative that policymakers identify what phase they are about to interact with. For instance, at the Background Phase there would likely be little specific expertise in biotechnology within public or private R&D, thus the implementation of a grand VC program would not be the best entry-point for policy as there would be few opportunities present in the investment pipeline. **Thus, the very first element of**

The Structure of the Toolkit

Element 1: Industry Life-Cycle

Answers the Question:
Where are we?

Element 2: Sector Drivers

Answers the Question:
What do we need to move forward?

Element 3: Policy Dimensions

Answers the Question:
How to approach what we need?

the TARGET approach deals with the identification of the current phase of the sector in terms of the Industry's Life-Cycle. This is done through the Sector Drivers. Once the phase has been recognize, all stakeholders can focus on advancing the sector to the next cycle.

Element 2: The Sector Drivers

The Sector Drivers, detailed in Chapter 4, are the 'engines' which move the sector from one phase of the Life-Cycle to the next one. Studying different case studies around the world, we have identified the following Drivers: Science, Training, Commercial, Financial, Human Resources and Other Institutions. Chapter 4 details each Driver at length and its features at every phase of the Life-Cycle. Using the example mentioned above, at the Background Phase there are no specific capabilities in biotechnology, but there are established R&D capabilities in general. Therefore, the Science Driver will look differently at this phase in comparison to the Pre-Emergence Phase, in which specialization in biotechnology begins. **Understanding which of the Drivers is lagging behind helps policymakers determine what the best entry-point is in terms of policy measures.** For example, if all Drivers are at the Pre-Emergence Phase, but the Finance Driver is lagging, then starting with financial support may be the appropriated course of action. Thus, assessing how the country/region is doing in terms of each of the drivers allows for policy coordination and clarification of the policy challenge. Once the Drivers have been mapped, the Policy Dimensions will help to address the specific Drivers requiring attention.

Element 3: The Policy Dimensions

The Policy Dimensions, detailed in Chapter 5, deal with the different decisions that must be taken at any point of the policy process. These dimensions describe how to approach a Driver. Some Policy Dimensions, such as the decision on the Vision and Realistic Sectoral Assessment, must be present during the entire policy process (and will be termed *strategic decisions*), while others, such as the decision on Entry-Points, change with every policy modification (and will thus be termed *tactical*

> TARGET offers conceptual tools that make the challenge of supporting a biotechnology sector easier and clearer. Due to the complex nature of the challenge, we do not offer one-size policy schemes but rather focus on the different elements which policymakers must take into consideration while formulating their own particular schemes. The following chapters will provide useful information and productive tools.

decisions). Supporting a biotechnology sector takes time and the policy process will go through different stages. **At each stage there will be a need to define the relevant Policy Dimensions and to make the relevant decisions.** For instance, the entry-point for the first policy scheme will be different from the scheme in the second stage of policy, which might take place some five years after the first. Thus, Chapter 5 addresses the issue of actual policy implementation and provides a framework for formulating concrete policy programs by listing all areas which require attention.

3. The Industry Life-Cycle

The TARGET approach is based on an evolutionary theory of innovation, The Industry Life Cycle. At every stage of the sector's progress, the ground work for development to the next stage is laid, and the specifics of this groundwork will influence how that subsequent stage is realized.

A biotechnology system is seen by the Industrial Life Cycle Approach as a dynamic, constantly evolving set of structures affected by:

- Spontaneous interactions between agents of knowledge creation and agents of commercialization.
- The geographic context.
- The historical context, including industrial and social history.
- The influence of the political system and agents purposely using policy mechanisms to grow the economy and exploit the opportunities presented by new knowledge and technology.

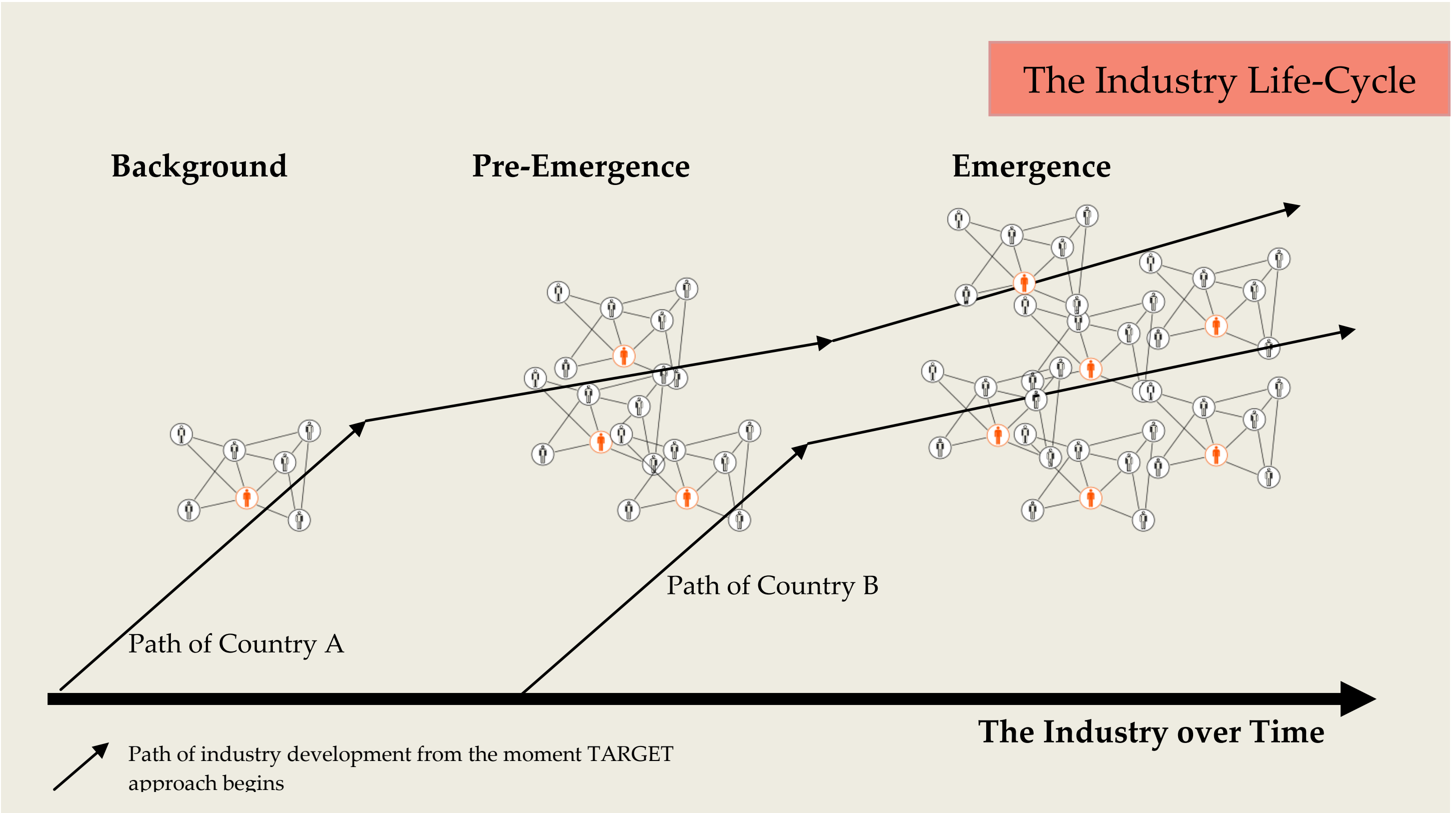
Using this approach allows policymakers to see not only how policies may have an impact on a current area of the economy, but also how it may impact events or conditions in the future, thus, it contributes to any long-term industry-building goals.

A realistic assessment of commitment is crucial, since the development of a biotechnology sector requires long timelines of more than 20 years.

The industry Life Cycle Approach, which sees different sectors as going through a life cycle of development, breaks down an industry's levels of development and maturity into three phases:

The Background Phase is the phase before the sector actually appears. **In the background phase there is as yet no biotechnology sector per se**; rather the initial seed conditions are present or being formed. At this stage there would be very little commercial activity or experience with the sector, though transferable knowledge, experience and institutional settings should be present in order to begin transitioning to the next phase. Furthermore, while actors may have rudimentary awareness of the potential for the creation of a biotechnology sector and how the current conditions encourage the emergence of the sector, there is as yet no consistent, organized interaction between actors in this regard.

The Pre-Emergence Phase is the phase in which initial activities of the sector appear. **The pre-emergence phase shows the beginning of a biotechnology sector**, **though its main feature is that the activities are not yet self-sustaining or institutionalized**; rather, the activities suggest



some specialization in the R&D sector, strong science, the development of entrepreneurial action and some initial commercial activity and investment. These activities involve some implicit exploration of the different market possibilities that the nascent sector may move towards. Actors in this phase begin showing an awareness of the sector, and interactions between actors are increasing.

The Emergence Phase is the phase before the sector becomes standardized. **The emergence phase shows the sector beginning to achieve critical mass**. Commercial exchanges begin to lose their one-off, tentative nature. Whereas in the Pre-emergence phase transactions between actors may have been exploratory or ad hoc, in the emergence phase these transactions have become more regular. Of course, activity may still be exploratory and structures may be adjusted to facilitate what is still a new market with high levels of uncertainty, but biotechnology (or its sub-sectors) does not have to "prove itself" as a commercial activity or source of investment and public policy.

An Important Note on the Idiosyncratic Nature of the Biotechnology Life-Cycle:

The path which a country/region takes towards the Emergence Phase will be idiosyncratic and contingent on the country/region's specific historical development. For example, illustrated in the above diagram, a country which begins the TARGET approach in the Background Phase (Country A) will advance differently than a country which begins in the Pre-Emergence Phase (Country B).

Previous interventions in the innovation system have created various path dependencies and trajectories that will influence both future policy as well as the development of the sector. This also shows the significance of proper assessment as to the position of the country/region. Different policy schemes will be needed for different starting points, and policymakers should be careful when comparing local progress to that made in other places, as the idiosyncratic nature of the Life Cycle means that there is no one development path to expect and imitate.

Brief Examples of the Co-evolution of the Sector Drivers

In the Israeli case, co-evolution is most clearly seen in the development of venture capital (VC) alongside the information technology sector and their later implications for the biotechnology sector. Venture capital promotion was instituted twice, with the first program (Inbal) failing in the sense that its value generated remained low. Additionally, it suffered from bureaucratic problems. The program did, however, stimulate learning in the private sector and the public sector which led to a more successful VC program under Yozma. The evolution of policy knowledge, along with the evolution of private sector experience in entrepreneurial activity, led to success the second time around. This success was also dependent on circumstances such as a high influx of skilled immigrants, and a military R&D background which provided technology to be exploited. A venture capital industry then helped to facilitate early development of the biotechnology sector, demonstrating a further link between system components.

A second clear example of co-evolution is presented in the case of Scotland and the generation of new firms in biotechnology. Academic excellence provided the source for new firm development in Scotland which continued to develop with the recognition of star scientists in the Scottish R&D system. Firms were created out of this mostly using public venture and angel money, as well as other public supports for creating new firms. Eventually, a set of Scottish companies were able to attract funding from outside of Scotland for large valuations not possible with local investors. The success of these firms, and the creation of other life science based firms in Scotland, meant that policy efforts turned away from firm creation and began focusing on firm growth. Unfortunately, a number of Scottish firms failed. With fewer firms being created, investors from abroad had no reason to stay in Scotland. In this sense, academic, financial, and policy drivers were evolving simultaneously and impacting one another. Moreover, Scotland's sector evolution was impacted by the continuing development of the Cambridge and South East England biotechnology sectors. With these sectors continuing to grow and produce new firms, a slow downturn in Scotland provided little incentive for investors from London to look for Scottish opportunities despite past promise. This experience has also meant that entrepreneurial activity in Scotland has shifted away from drug discover to lower risk endeavors.

4. The Sector Drivers

The Industrial Life Cycle Approach combined with the sector drivers provides a holistic perspective of the biotechnology sector, which assists in understanding how each of the drivers are tied together and co-evolve over time.

The Sector Drivers are the 'engines' which move the sector from one phase of the Life-Cycle to the next one. The drivers presented in this Toolkit are those which have been determined as important throughout the different phases of the life cycle: Science, Training, Commercial, Financial, Human Resources and Other Institutions. The drivers are described at each evolutionary phase to help policymakers evaluate what phase each of their own country/region's Sector Drivers is located. Mapping each of the Sector Drivers and realizing its position on the Life-Cycle is essential for the policy program to address the real needs of the country/region.

Sector Drivers at the Background Phase

Science A strong basic R&D system either public or private exists, though in most cases this will be in public institutions such as universities. This need not be in specific biotechnology areas at this stage. A scientific research base is necessary to create both absorptive capacity in R&D structures and the necessary science which would lead down a path of specialization in biotechnology or other techno-innovation paths which may appear. A funding base for R&D should also be present, preferably organized around competition to ensure that the best projects and scientists are supported and retained in the system.

Training A system of training producing skilled personnel in the sciences exists in order for the local system to maintain its R&D capacities or for utilizing science produced in the system further down the value chain.

Commercial Experience of public and private sector use of science produced by the abovementioned R&D system is a necessary background condition, demonstrating a local path for technological uptake by consumers. Additionally, industrial capacity in manufacturing, and preferably in higher value-added activities, such as product development or quality control is a good background condition as it shows experience in quality manufacturing, the presence of a skilled workforce and management and the

> An interesting example is Ireland, which has been attempting to build its life sciences industry based on its quality manufacturing experience and facilities, with science and training catching up to these features.

existence of firms which would act as either the developers of new technologies or partners/suppliers for new ventures. The Commercial driver should also include experience in transnational economic relations and collaborations, particularly as industries such as biotechnology will not be contained in one economy in the sense of knowledge creation, investment, and sales.

Financial Financial structures should be present for the transfer of capital towards new ventures or established ventures looking to take on new risk, and for investors to realize returns. This does not need to include a fully functioning venture capital market at this stage; however, the institutional structures, laws and regulations should be present to facilitate the creation of such a market if necessary.

> For example, Scotland's start-up finance was mostly centred on angel investors and public sources of support, later attracting venture capital. Sweden, on the other hand, moved forward with established public investors such as Industrifonden, direct and indirect support from established parent firms, as well as the publicly funded creation of a local VC market.

> Excellent science in conjunction with financial support for R&D and the availability of VC funds are the basic elements in the development of a biotech sector.
>
> When excellent science is not well established and there is no biotech industry in place at early stages of a biotechnology sector's development, policies targeting finance and the establishment of start-ups as an entry-point, are questionable.

Human Resources A labour market should be present which allows for the movement of skilled personnel, their attraction and retention.

Other Institutions Clarity in regulatory systems such as Intellectual Property regulations, or regulations which may impact health products should be present. Lack of clarity in these areas creates disincentives for potential investors and potential entrepreneurs, particularly in high risk sectors. Related to the abovementioned public and private use of science, a working system of health care (public or private) should be a basic background condition as it provides a system of hospitals that offer a domestic market, and potentially further R&D capacity including clinical trials. Finally, a political system with a history of cooperation is useful as this will lower the risk of erratic policy changes which affects the economic arena in which entrepreneurs and investors find themselves in.

Sector Drivers at the Pre-Emergence Phase

Science Public and private R&D sources at this stage begin specializing in biotechnology, with both basic and applied science being produced by the R&D system, particularly with an eye towards eventual commercial use. A pool of scientists in the different disciplines which make up biotechnology are present in the economy and star scientists are being recognized both locally and abroad for the work they do in the sector.

Training Graduates and new researchers in the biotechnology sector are increasing, supplying the scientific, technical and support skills necessary for both research and industry.

Commercial Closely tied to the scientific system, methods of technology transfer are generally developed more fully during this phase, facilitating the use of new knowledge by industry. Entrepreneurial activity has begun in earnest during this phase, either through the development of start-ups or spin-offs, directly from academia or from already existing firms and industry. Furthermore, key individuals with experience in the sector or who have been successful and can "reinvest" their knowledge in the sector, should become visible during this period; from these individuals the first set of serial entrepreneurs may emerge to further the sector's commercial development. Large pharmaceutical firms or other large firms in the biotechnology sector should also begin to settle in the local economy at this stage, recognizing the value of local inputs and adding a further source of attraction to other potential investors. Finally, related service and support providers should begin to appear at this stage alongside the increasing number of biotechnology firms.

Financial Finance for start-ups should not only have begun to appear by this phase but have begun to be institutionalized in some form; examples can be the formation of public venture capital schemes, more organized angel activity, or increasing private venture capital investment.

Human Resources The provision of skilled workers continues, with an increase in those with business skills, in addition to maintaining the system's R&D skills.

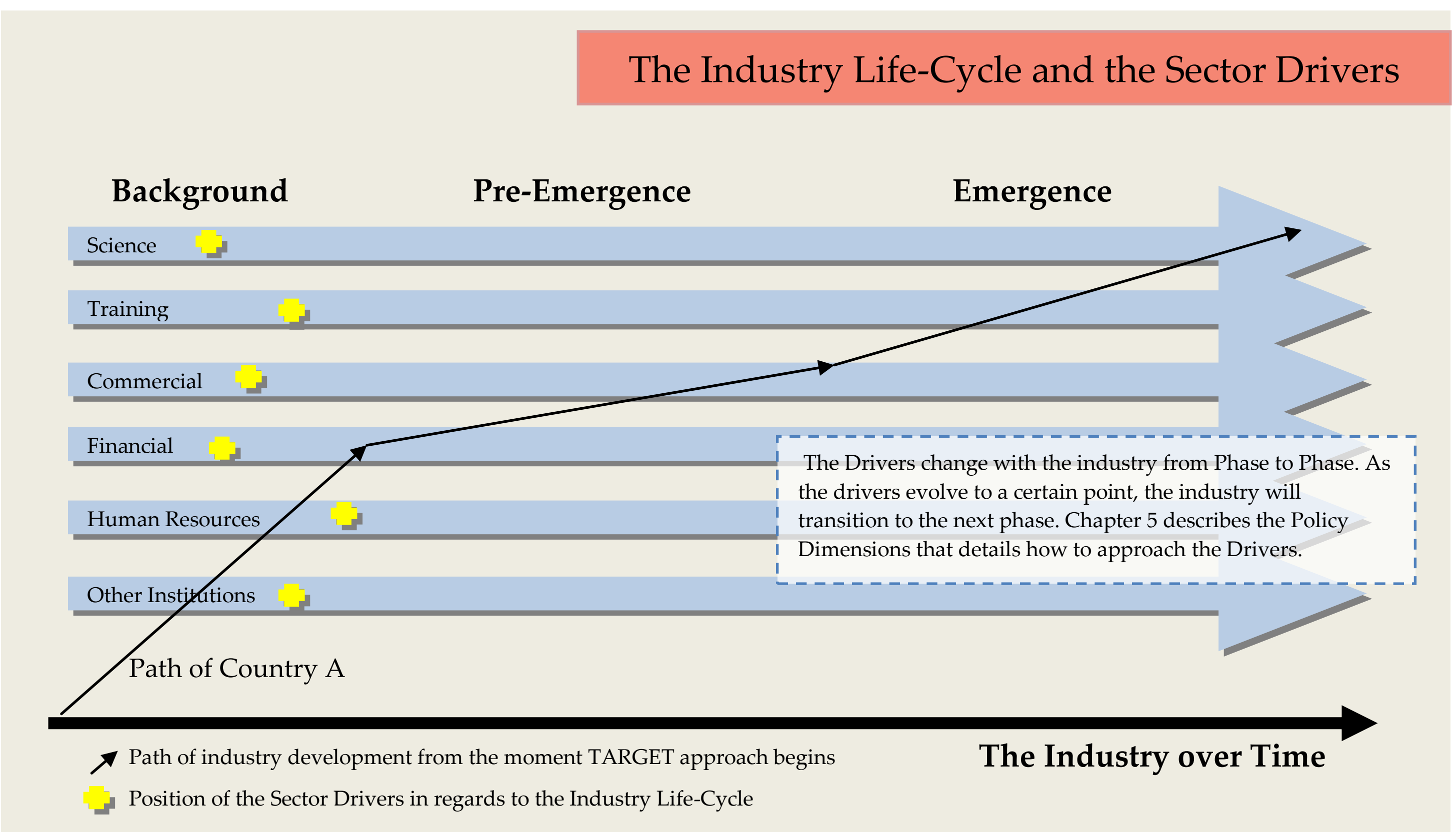
Other Institutions Trial infrastructure for new health related products will likely begin to appear at this stage. Also, while key individuals will have begun to appear in the commercial world, key individuals or champions may also appear in other areas such as the policy realm; policy support (direct or indirect) and recognition of the sector should be well-established by this phase.

Sector Drivers at the Emergence Phase

Science The science driver at the Emergence Phase is an extension of the previous phase's conditions. R&D work expands, and star scientists continue to garner recognition. Furthermore, more top quality researchers are attracted to the locality to participate in research.

Training Extension of the Pre-Emergence phase: A system of training producing skilled personnel in the science exists in order for the local system to maintain its R&D capacities or for utilizing the science produced in the system further down the value chain.

Commercial A pipeline of products is apparent and moving through the research and, more importantly, the development processes are on their way to market. Dependence on one or two products is lessened, and more companies are becoming multi-product/service providers. The emerging market for biotechnology products is gaining some stability and will not collapse with the failure of some of the companies involved, or some of the products failing to pass through different development hurdles. Manufacturing in the biotechnology sector is expanded and may involve a separation from commercial R&D entities. Links between firms at this stage become more stabilized in the sense of collaboration as well as supply relationships, and there is a growing recognition of the



local sector as a "unit" to which actors belong. Start-ups and spin-offs will continue to be created, and serial entrepreneurs should have appeared by this stage.

Financial The locality's attraction to investors becomes more established, no longer based on one-off opportunities or pleasant surprises. Start-ups and spin-offs continue to receive funding, and growth capital becomes available as well.

The existence of top quality scientific research is a key precondition for the development of the biotechnology sector. However, there have been relatively successful biotechnology firms based on less-than-revolutionary science, which highlight the importance of industry applicable science.

Simply building up the science base for the sake of having the best science may not lead to biotechnology success – the science must be applicable to industry and commercializable.

Human Resources There should be a higher amount of employment "churn", with skilled labour moving between companies, coming into the local economy as well as moving to other established biotechnology sectors abroad – tacit knowledge exchange and experience will increase in the system in this manner.

Other Institutions Some elements of public support may begin to be phased out, however new policies or concerns may emerge such as how to retain local ventures, and how to increase access to foreign markets.

Sector Drivers in each Phase of the Industry Life-Cycle; Part 1

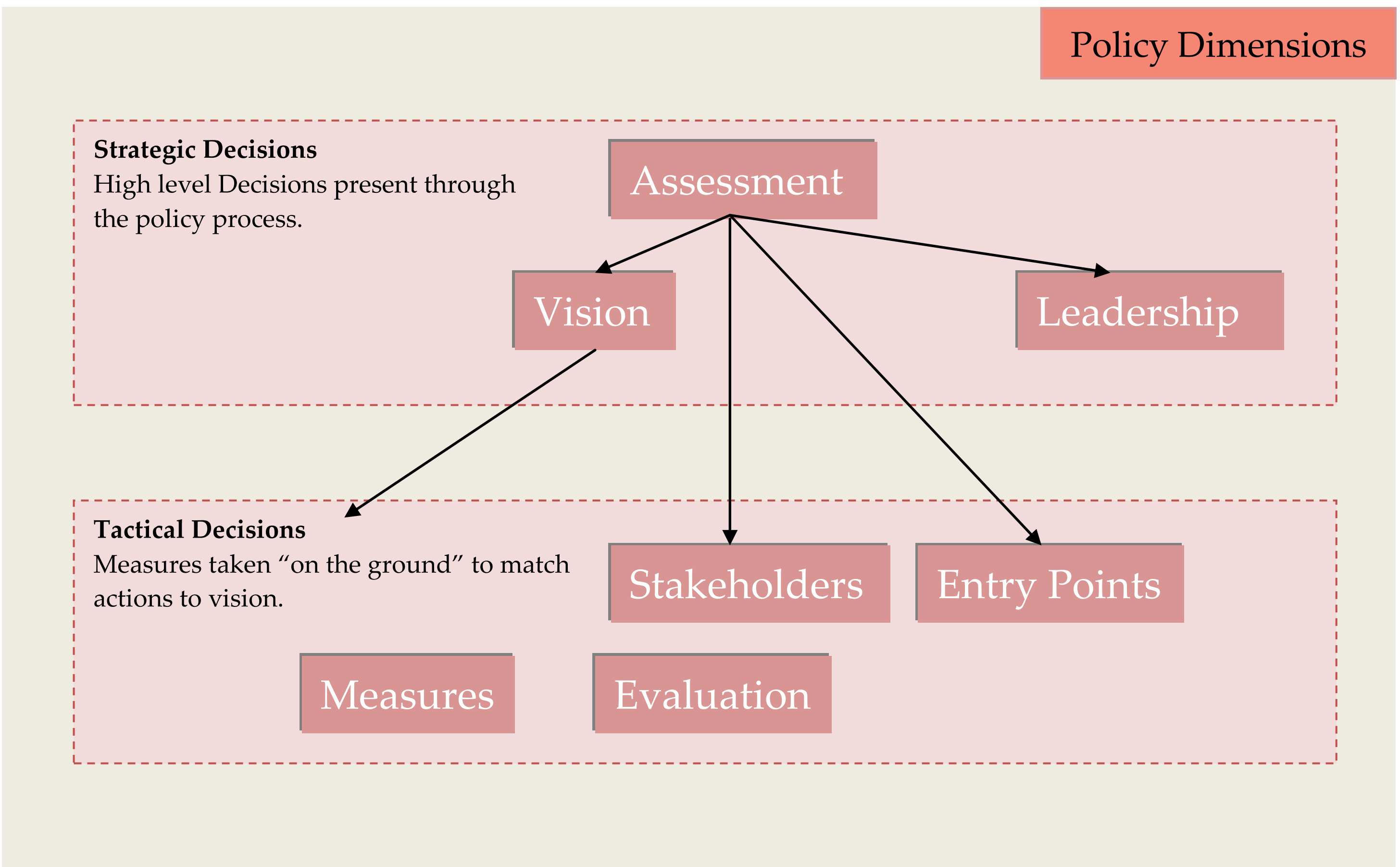
	Background Phase	Pre-Emergence Phase	Emergence Phase
Science	A strong basic R&D system (mostly in academia), not specifically in biotechnology.	Public and private R&D sources begin specializing in biotechnology, with both basic and applied science being produced by the R&D system, particularly with an eye towards eventual commercial use.	R&D work expands and star scientists continue to garner recognition. Top quality researchers are attracted to the locality to participate in research.
Training	A system of training skilled scientific personnel is present.	Graduates and new researchers in the biotechnology sector are increasing.	Extension of the Pre-Emergence phase.
Commercial	Experience of public and private sector use of science produced by the R&D system. Industrial capacity in manufacturing, and preferably in higher value-added activities. Experience in transnational economic relations and collaborations.	Entrepreneurial activity. Key individuals with experience in the sector or who have been successful and can "reinvest" their knowledge in the sector become visible. Large pharmaceutical firms or other large firms in the biotechnology sector begin to settle in the local economy. Related service and support providers begin to appear.	A pipeline of products is apparent and the development processes are on their way to market. More companies are becoming multi-product/service providers. Links between firms become more stabilized. Start-ups and spin-offs will continue to be created, and serial entrepreneurs are appearing at this stage.

Sector Drivers in each Phase of the Industry Life-Cycle; Part 2

	Background Phase	Pre-Emergence Phase	Emergence Phase
Financial	No fully functioning venture capital market. Financial structures are present for the transfer of capital. Institutional structures, laws and regulations existing.	A Finance for start-ups is institutionalized in some form: the formation of public venture capital schemes or increasing private venture capital investment	The locality's attraction to investors becomes more established Start-ups and spin-offs continue to receive funding and growth capital becomes available.
Human Resources	A labour market which allows for the movement of skilled personnel, their attraction and retention.	The provision of skilled workers continues, with an increase in those with business skills	Higher amount of employment "churn". Skilled labour moving between companies. Tacit knowledge exchange and experience.
Other Institutions	Clarity in regulatory systems. A working system of health care. A political system with a history of cooperation.	Trial infrastructure for new health related. Key individuals or champions appearing in the political or policy realm. Policy support and recognition of the sector.	Some elements of public support may begin to be phased out. New policies emerge such as how to retain local ventures.

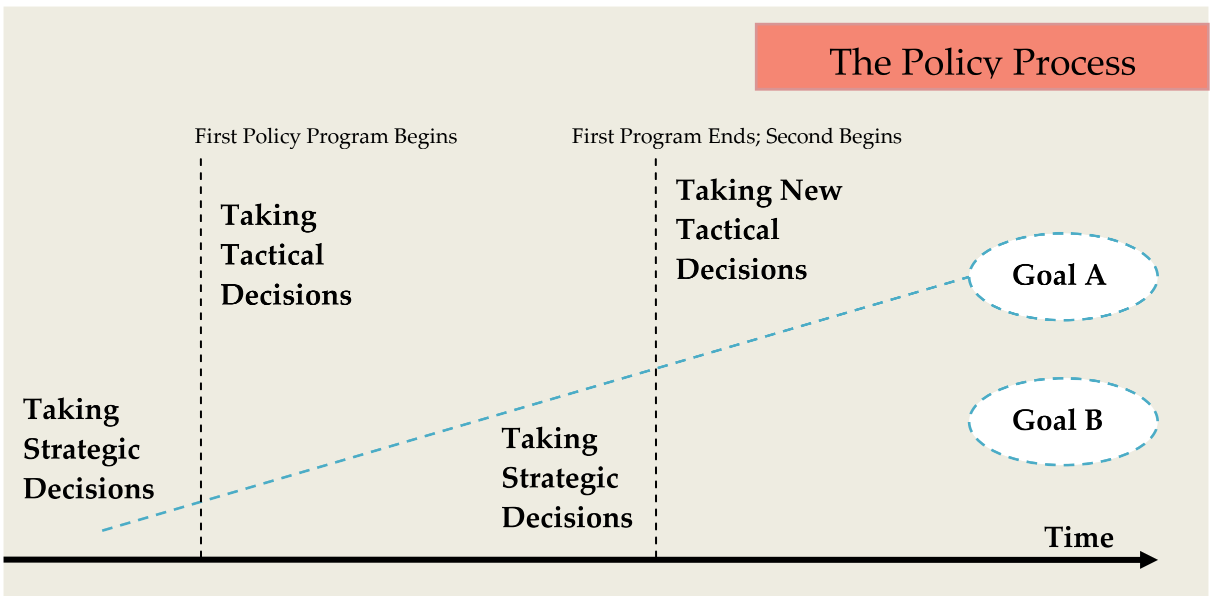
5. The Policy Dimensions

With a basic understanding of the Industry Life-Cycle and the Sector Drivers which move the biotechnology sector from one phase to the next, **policymakers are subsequently provided with a description of eight policy dimensions.** These policy dimensions are seen as key decisions points for policymakers and can be divided into **strategic and tactical decisions**.



The first four dimensions are strategic because they establish the call to pursue a biotechnology sector actively and the broad vision that efforts will work towards achieving. Once these high level decisions are made, the specific steps needed to fulfil them will have to be carried out, i.e. the tactical decisions and steps. The strategic level aspects may be determined by politicians, ministers, leaders of industry, or high ranking and influential civil servants who can influence government beyond specific policies. The tactical decisions discussed will likely be carried out by policymakers "on the ground," trying to match their actions to the vision they have been charged with working towards.

The following Diagram illustrates the policy process in terms of the different Policy Dimensions. As seen, the Strategic decisions are taken at the very beginning of policy implementation and shape the path of advancement towards the policy goal. There are different possible goals for a biotechnology sector and the Strategic decisions will determine which goal is being targeted. Once the Strategic decisions have been made, implementation begins and tactical decisions are taken. New tactical decisions are taken for each policy program. As time progresses the sector itself changes and the tactical decisions must be changed appropriately. For instance, if the country/region works under a 5-year policy program, when the first ends and a new one begins – there will be a need to revise the previous tactical decisions according to the new situation (a mechanism of on-going assessment during this period of time, not just at the end, would also be recommended). It is important to note that Strategic decisions might also need revision, especially if assessment suggests that the targeted goal might not be feasible at the moment. This will be clarified below.



Strategic Policy Dimensions

1. Realistic Sector Assessment

- **<u>A review process</u>:** Before deciding to carry out policy intervention with a functioning biotechnology sector as its goal, it is crucial that an objective assessment be carried out to establish at what phase the sector and national/regional economy is in. Using the Industry Life-cycle approach, part of the Realistic Sector Assessment must be an analysis of the Sector Drivers already existing in the economy and which could play a role in the emergence of the sector. The assessment process is given primary importance here in that it sets the targeting process on the right track. The assessment is a comprehensive review process which concerns any possible component of the sectoral system of innovation.

- **<u>Sector Drivers</u>:** The assessment should consider the Sector Drivers detailed in chapter 4: the science base (bio and medical), institutional and political framework already existing (e.g. support for targeting, tech transfer capacity), innovation policy budget, entrepreneurial capacity, industrial and public health infrastructure, small business finance, and regulation (i.e. IP, ethical approach to things like stem cells and risk-related factors especially in relation to clinical trials). The assessment process should include an assessment of global trends and competition in order to identify opportunities and competitors.

- **<u>The Capability to secure a long-term commitment</u>:** When going through the assessment, one political issue which must be determined concerns the capability to secure a long-term commitment; this is vital in the biotechnology sector, where knowledge translation and product/service development takes 10-20 years, requires major capital investments (often beyond the capacity of many countries/regions) and involves very high rate of failure. Also, concerning the science base assessment – a variety of different measures can be used, such as publications, citations, movement of skilled people, etc.; **but it is not only quantitative measures which are important, but also qualitative dimensions** such as the divisions between public and private science, the presence of networks and communication between them and the structure of the public science base. Furthermore, the assessment should consider both absolute and relative measures.

- **<u>The assessment's outcome</u>:** The outcome of this process should lead the country/region to decide:

    - Do we want to consider targeting biotechnology?

      Policymakers must take into consideration that the assessment may result in the conclusion that acting on developing a biotechnology sector may not be the best route for their particular country/region. However, if the decision is made that intervention should be pursued regardless, actors must seek to first establish pre-conditions, namely to create the missing Sector Drivers. As a result, the process will be longer and, while it may not require more buy-in from different stakeholders, will require more patience and a longer-term view by those actors pursuing the strategy.

    - What should the exact goal be? (see next point)

→ ***See the list of questions which policymakers can use as a guide to their initial assessment at annex 1.***

2. VISION

-**Definition and profile:** A decision to target a particular sector or industry requires a definition of that sector and some profile of how the sector will look after the policy is implemented.

-**Conceptualization of the policy process:** Furthermore, the conceptualization of a policy program must be multidimensional and systemic in terms of how different components in the economy influence the targeted sector, stakeholder incentives, and the potential systemic changes or adjustments needed. This conceptualization is necessary regardless of the type of interventions that may or may not take place, as it provides a long-term vision that allows for flexibility; it would allow for later interventions to be designed as necessary in a way that would not block or misalign earlier stage interventions.

-Alternative goals: The vision must address the different possibilities and capabilities of the country/region and to designate a Goal for the process. There are various forms a Biotechnology sector might take and policymakers need to take into consideration different possible goals. Alternate goals should be considered if system assessments indicate extreme difficulty in achieving a fully functioning sector, or if unintended developments arise in the life cycle requiring a change in vision.

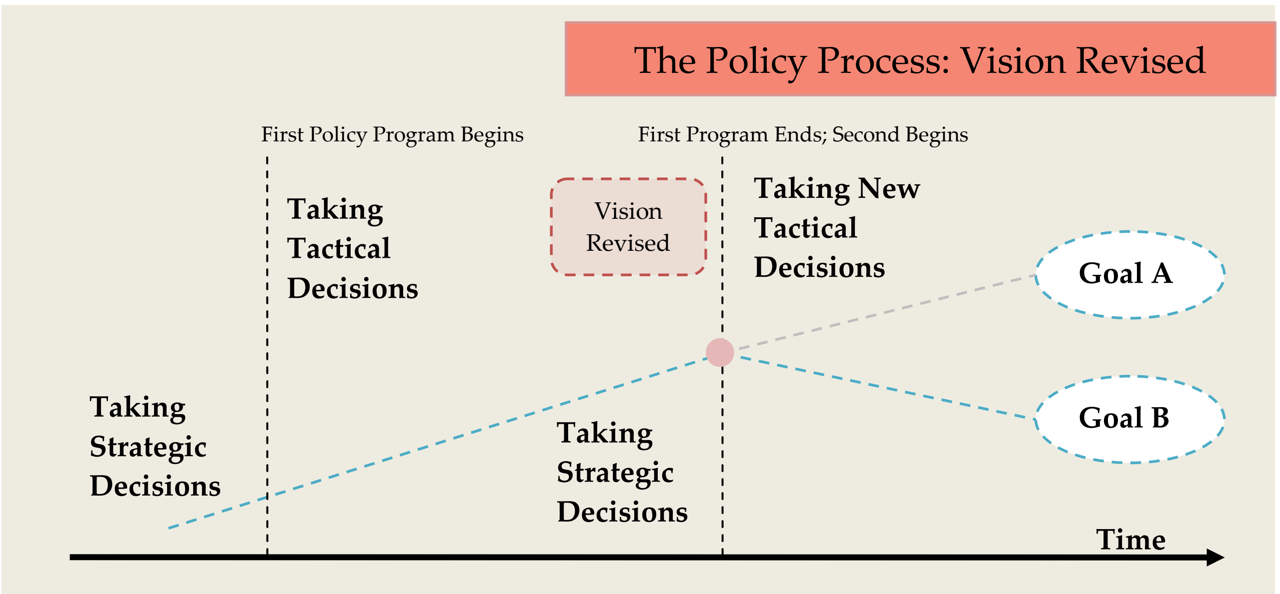
The vision should reflect not only decision-makers' "ambition to bio" but also the reality of cases assessment which delineate key capabilities of the country or region.

One of the key lessons derived from our case studies is that achieving a functioning life science cluster with any degree of critical mass will require a minimum of 20 years investment and reinvestment. It may therefore be necessary to aim for more modest goals. Such endpoints are not less valuable in that they may provide a more realistic option for return on investment, and may also lead to new potential pathways in the future.

- Full Bio cluster
- Niche Bio Cluster
- SME Generator
- Bio Supply or Service (participation in single part of value chain)
- Partner Technology (not bio, focus on a different but potentially collaborative technology)

-Broader Objectives: Just as important is the need to understand how targeting a sector forms part of broader objectives for the national or regional economy. Without this vision of its part in the broader economy, such a policy process runs the risk of being seen as a short-term fad or policy whim and would not be given the long-term resources required. Too often, high level policymakers decide to pursue their "ambition to bio," aiming for a world class, competitive, fully innovation cluster without properly understanding the timelines and resources needed.

-**Regular system re-assessments**: This is where frequent assessments become vital. In order to realize if a Goal is feasible, policymakers need to assess their progress on an on-going basis, especially when switching between policy programs. Thus, regular system re-assessments (along with policy evolution) are important features of the Target process, along with subsequent opportunities to adjust the Goals.



3. Leadership

-**Kicking-off the Target effort:** To begin the process, entrepreneurial actors are needed to kick-off the Targeted effort, regardless of whether they are involved in the management of the subsequent process. Such a decision could be taken by any entity or body that has official recognition such as a ministry, committee or even a private body that represents the field.

-Strong Unity: What is important, and creates a major challenge in achieving a coherent targeted strategy and establishing a roadmap, is the acceptance of a common mission or overarching goals by a multitude of parties. On the government/political side this means acceptance from multiple political parties, as well as other influential ministries and agencies active in the economy, but it should also include acceptance from private and third column stakeholders (e.g. universities and research institutes) in order to better facilitate coordination and less interference during the operation of the strategy itself. A minimal condition should be strong unity in either the public or private sector in this regard if not both. The condition of unity in one or both of the public and private sector should be an early part, if not precede, the early pre-implementation analysis described above.

4. A Coordinating Body

A Coordinating Body is here described as an organization (or consortium) charged with carrying out the Target strategy and delivering or advising on different policy measures necessary to achieve the Goals. As such, it involves decisions at the strategic and tactical level in terms of how to construct the Coordinating Body in terms of its institutional structure, but also in terms of how the knowledge creation, experience and data it gathers feeds back into strategic outlook and tactical policy construction. The Coordinating Body should be able to translate this information into a roadmap and to create the drive for such a roadmap to be implemented. Additionally, the Coordinating Body should be responsible for monitoring progress, ensuring on-going learning, enabling feedback from different stakeholders and constructing policy that will deal with any blank spots in the roadmap as information becomes available. Because of the undefined nature of some of the new technology markets and business plans, ideally a Coordinating Body could engage in a conscious consideration of sector context, strength and a creative process of projecting possible paths that are realistically obtainable in the economy. From that analysis, the Coordinating Body can then help to guide the next step of strategy.

> The Coordinating Body has to be able to ask the hard questions and make the difficult decisions which may not necessarily appeal to short term political interests. Without this ability, the difficulty of actively pursuing a biotechnology sector is increased.

The TARGET approach can be understood as having two chief characteristics. Recognizing that the Innovation System is non-static and develops in a non-linear way is the first and basic one. The Extended Life Cycle model described in Chapter 2 of the Toolkit captures this well. The second characteristic, which follows from the first, has to do with the way policymakers should understand their engagement with the Innovation System. Instead of envisioning the act of intervention as one which takes place during a single moment in time, policymakers should understand their involvement as an ongoing process of mutual change. This involvement is captured by the different decision points or Policy Dimensions described in Chapter 3 of the Toolkit. All policy dimensions refer to decisions that policymakers will have to address *repeatedly* as the industry develops and policy schemes change and adopt.

The different policy dimensions, such as Identification of Stakeholders or Selection of Entry Points, point to the multilayered effort which Targeting involves. In order for a biotechnology sector to develop, there are different Sector Drivers which must be addressed. These fall under the responsibility and influence of various ministries, government agencies and private entities making the process of targeting a multi-agent one. Thus, the non-static nature of the system together with the repetitive intervention process makes it clear that coordination is highly important. However, for coordination to be successful there is need for both a flow of information and the accumulation of knowledge.

The effectiveness of a designated Coordinating Body was clearly recognized in the case of Singapore. At the beginning of 2000, there was no Strategic-Level of policymaking for R&D in the country. However, headed by a prominent political figure the Economic Development Board (EDB) managed to act as a de facto Coordinating Body for targeting biotechnology. The EDB is a government agency working under the Ministry of Trade & Industry responsible for the support of business, industry and global trade. Its declared mission is to establish Singapore as a business hub of the region. Following his vision of creating a biotechnology sector, the head of the EDB at the time, Philip Yeo, acted as a 'policy champion' and negotiated a 5-year working plan for the establishment of biotechnology capabilities with different policy functions within the system.

In a sense, the EDB acted as Singapore's Coordinating Body – gathering information from different ministries, accumulating knowledge about the biotechnology sector and coordinating between elements of the innovation system to create a holistic policy program. The first phase of Singapore's BioMedical Initiative (BMI) was considered a success from a policy perspective after which the Ministerial Committee was established in 2006 to decide on the next phase. The Committee recognized the effectiveness of having a coordinating body within the innovation system and created the National Research Foundation (NRF), which acts as Singapore's Coordinating Body for the entire R&D system overseeing the progress of policy programs, deciding on new ones, collecting information and accumulating knowledge on these processes.

Although Singapore's case is unique, instances of the functioning of various sorts of coordinating bodies were recognized in other case studies. While the specific structure of the coordinating body or its institutional position within the innovation system may take different forms, there are features which such a body should be able to perform:

FEATURE 1: The Gathering of Information and Accumulation of Knowledge

Without a clear picture of 'things on the ground' it will be very difficult to realize what the proper alignment of the different stakeholders is. Without learning from past experiences, both locally and globally, it will also prove difficult to devise way of acting. Thus, as mentioned above, for coordination to take place information must be gathered and knowledge accumulated.

A. **The Coordinating Body needs to be positioned within the innovation system so it can tap into the flow of information.** This can take many shapes. Currently in Singapore the NRF is positioned at the top of the policy structure, ensuring that all information flows upwards and centers at the top. However, this does not have to be the case. Again, in 2000 the NRF did not exist and the EDB, which is positioned at the bottom of the policy structure (a government agency under a ministry), managed to tap into the flows of information nonetheless. This happened due to Phillip Yeo's personal connections. He was able to establish channels of communication with heads of other agencies and ministries above him.

Thus, while positioning the Coordinating Body at a strategic level of policy making, such as the Prime Minister's Office, there are also other alternatives. The exact position of the coordinating body will be conditioned on historical developments and contingencies which are idiosyncratic to each country and region. However, policymakers aiming for an effective body will have to ensure that it can gain access to information. Be it due to institutional power and authority, personal connections of prominent figures within the body, or other arrangements- this must be taken under consideration.

Gaining access to the flows of information will enable the Coordinating Body to perform a Realistic Sector Assessment, which is one of the most crucial policy dimensions. Having the ability to observe and follow the progress of different ministries, commercial enterprises, infrastructure, etc. will ensure that the Coordinating body can form a sound picture regarding the biotechnology cluster in the country/region in terms of its position on the Life Cycle. Ideally, dedicated personnel will be devoted to these ongoing tasks of keeping a real-time picture of progress available. This will both support assessments as well as the design of future policy programs.

B. The Coordinating Body needs to accumulate a Body of Knowledge on the process of Targeting.

Tapping into the flows on information within the innovation system is crucial, yet not enough. In order for the Coordinating Body to be able to assess incoming information it must create a body of knowledge for reference. This includes keeping record of past experimentation and policy schemes within the country and abroad, but it also includes actively researching the field being targeted.

Biotechnology is evolving all around the world and there is yet to emerge one dominant policy design, thus policymakers within the Coordinating Body need to evaluate and record progress that is being made in leading biotechnology clusters globally. This can be established in many ways. In Singapore, for instance, the EDB actively invested in foreign biotechnology companies to gain insight knowledge. This could also be performed by an outsourced committee of experts that include prominent people from different countries. Such advisory committee can exert its judgment on the information that flows inwards and provide the knowledge needed for amendments and future interventions. As with other functions, the specific institutional arrangement that materializes is less important. The issue is recognizing the need for such a function within the Coordinating Body.

FEATURE 2: Political Independence and Long-Term Commitment

The process of targeting the emergence of a sector, especially a biotechnology one, is long and challenging. In Singapore, for instance, the country has been actively investing in the emergence of the sector for more than 10 years and, arguably, it has still to reach the level of Emergence. Similarly, in Israel, the sector has been growing since the 1980s and is, arguably, on the verge of emergence. Thus, the decision to target must be understood as one for the long-term. The Coordinating Body should be the institutional framework that provides such long-term commitment. This can take different forms, but this is a key capability that must be worked out when the Coordinating Body is established.

Ideally, the body responsible for the development of the innovation system should enjoy similar political autonomy as central banks do in many countries. While this is understandably difficult to negotiated, the separation of strategic decision from short-term partisan politics should be attempted. An important point raised by many seasoned policy experts in the Life Sciences was that the Coordinating Body had to be able to ask the hard questions and make the difficult decisions which may not necessarily appeal to short term political interests. Without this ability, the difficulty of actively pursuing a biotechnology sector decreases.

FEATURE 3: Operational Role and Flexible Intervention

Ideally, the Coordinating Body should benefit from having the necessary political will (and financial support, which we will mention below) to operationalize the strategy. Furthermore, the Coordinating Body should be divided strategically and operationally, with one body or division working to determine strategic level directions and another to operationalize and deliver programs. This separation can be done by either having an umbrella organization operating alongside other organizations (as is the case in Ireland) or one organization which is internally divided (for e.g. Scottish Enterprise).

The separation of these functions requires a crucial linking mechanism in order to keep a very effective feedback and evaluative loop. The benefit of separating the functions allows for the strategic level body to maintain the strategic objectives while absorbing environmental changes and new information. This enables the Coordinating Body to adjust the details of the policy roadmap to better reach the end vision or result. Because of the undefined nature of some of the new technology markets and business plans, ideally a Coordinating Body could engage in a conscious consideration of sector context, strength and a creative process of projecting possible paths that are realistically obtainable in the economy. From that analysis, the Body can then help to guide the next step of strategy. The role of the operational side of the Coordinating Body will depend on the pre-conditions already present in the regional innovation system and whether or not market failures will be additional to structural corrections that must be addressed. An important role is that despite the business/academic/research culture in the location, the Coordinating Body must seek to build and strengthen networks between stakeholders as part of its program executions, not simply provide funding or incubation services, or other direct activities. Including network building activity would help to create opportunities for private actors to take on more responsibility or, at the very least, allow for Coordinating Body programs to have more deliverable impact through indirect spillovers.

In order for the operational side of the Coordinating Body to have positive impact in real time, it is recommended that it will be able to spend funds in a flexible way. This means that unmarked allocation of funds is necessary. While this brings difficulties from a political perspective, if Feature 2 has been established it could become easier to maintain. For instance, in Singapore, the strategic body was able to spend an agreed-upon sum of resources on 'filling gaps'. It is not possible to address all future challenges within a pre-devised policy roadmap and different problems within the innovation system are likely to manifest. Without this flexibility in the allocation of funds, these problems will only be addressed in the next funding-cycle which is locally idiosyncratic and depends on the overall budgeting cycle. A Coordinating Body that can spend resources willingly to establish new support schemes can provide better assistance to the different players and ensure that the overall strategy is being addressed. Acknowledging the dynamic nature of both the science involves as well as the development of knowledge-based sectors, flexible intervention is one of the Coordinating Body must important features.

Tactical Policy Dimensions

1. Identification of Stakeholders

While discussed at a strategic level regarding consensus for the policy process, it is important to re-state the need to identify as many stakeholders in academia, the public sector and private sector who currently, or might in the future, contribute to innovation in the sector selected, as well as any institutions which may have an indirect impact on the sector (e.g. groups which may influence ethical considerations in scientific development but are not involved in research or commercial development). This is particularly important as the most successful systems of innovation are those which demonstrate high levels of coordination between stakeholders, and take advantage of the systemic nature of innovation and technological development. This is important not only for strategy buy-in, but also to determine which policy measures should be aimed at, who they may impact, and how stakeholders may be added, disappear, or change over the course of the strategy.

2. Identification of Entry-points

Entry points for any policies or interventions in attempts to develop an industry must be defined, and there must be minimal conditions present for action at an entry-point to be effective. The entry-points are the particular areas that policy will be implemented to enact direct change or amplification of activity. Realistic chances of influence must be assessed, both in the specific entry-point and the overall system – for example, it would be pointless to select venture capital creation as an entry point if there is no knowledge available from which to create start-ups.

The decision of how to choose the particular entry-points must also consider whether the correct entry-points are those "low-hanging fruit", or those which may be more difficult but have a longer-term positive influence on the innovation system. On the one hand, while a longer term vision is encouraged for a targeted approach, the long-term planning of resources and time commitment create challenges for policymakers. Short-term goals may be an easy success, but may not be best for the system. However, a different consideration may be that low-hanging fruit can create further buy-in from stakeholders and therefore allow for more long-term commitment. Practical versus theoretical consideration must therefore be considered and policymakers should develop this awareness.

3. Design and Execution of Measures

The point above regarding effective policies at specific entry-points is important to the design of measures take to reach the selected goals. It is also important to keep in mind the stakeholders who may be involved both as providers and as 'clients' of the measures. It is recommendable to engage private sector stakeholders in the design and delivery of a measure, both because it enhances coordination and because it would help to create a realistic delivery time. For example, a measure designed to correct the funding gap for start-up firms would be hampered significantly if it was characterized by slow decision and delivery times; start-up firms would likely avoid such measures due to the resources required to fill out the necessary paper work, plus the prospect of missing market windows. On the other hand, radical systemic changes may require entrepreneurial solo action by public or private actors (e.g. an economic development agency, or a consortium of private sector actors) if potential partners are too risk-averse to cooperate. Regardless, to determine each possibility, stakeholder communication is necessary.

Proper budgeting is also important to ensure effective implementation of a Target Strategy. The main concerns regarding budgeting are the difficulty to predict how much may be needed once a measure is launched, and whether or not the budget will be maintained in the long-term or potentially be cut.

4. Appropriate Evaluation

An important but potentially overlooked part of a Target Strategy is the development of appropriate evaluation mechanisms. Evaluation is important because it allows for feedback to policymakers regarding policy effectiveness. More importantly, however, evaluation mechanisms should also provide feedback regarding the overall state of the industry as this would allow policymakers to maintain a systemic view of what is happening, and adjust the overall Target process rather than simply adjusting some specific policies. Therefore, what is necessary is a system of policy evaluation and system (re-)assessment while advanced evaluation mechanisms should be utilized, the evaluation of policies should rest both on indicators but also on a clear view of what the goal or intention the policy set rested on, whether the indicators appropriately capture that and whether these goals or intentions are still valid.

> In Lithuania, the Innovation Strategy stated that a full set of European Innovation Indicators that would be used to determine the strategy's progress. While this may be useful, relying arbitrarily on this set of indicators would be problematic as the indicators were not selected based on their appropriateness for the Lithuanian setting, and therefore would not help to provide the specific feedback necessary for policymakers at the stage of development the economy is in.
>
> In Scotland, the evaluation mechanisms for innovation were altered from quantitative measures (of how many firms were created, money invested, etc.) to mechanisms which sought to determine how policies increase national gross added value. Changing evaluation mechanisms to judge the effectiveness of policies that were not planned with such mechanisms in mind meant that some policies may have been cancelled prematurely.

III. Benefits of the TARGET Approach

Innovative activity will occur naturally to varying degrees in an economy. The degree of this activity will be directly influenced by the commercial capacity to exploit new knowledge; which in turn is affected by investments, commitments and knowledge made previously in the economy which may either fruitfully coincide with an emerging technology or conflict with it; and by external (global) market and non-market forces which affect the industry or sector. Moreover, because technologies like biotechnology encompass a fairly wide range of applications, the variety of the possible endpoints for the development of a biotechnology sector is equally wide.

The variety of possibilities means that, while we can present different examples of cases which have pursued a biotechnology sector with some success, there is no one path to that success which can be determined from these cases. The TARGET approach will offer to the policy maker a way to work through this complexity.

- The TARGET approach will help to **understand how the different components of the system are linked and work together.**

- Understanding how components are linked will help to **reduce the radical uncertainty of action**, as well as **present further opportunities for action which may move the biotechnological sector to a desired goal**.

- Understanding linkages in the context of the whole system means policymakers can try to **fill in structural or institutional gaps**, along with correcting market failures.

- By understanding linkages between system components, and how actors work, **supply and demand side policies can be applied.**

- The TARGET approach allows the policymaker to **perceive how things evolve simultaneously.** While a policymaker may be looking to cause a particular driver to evolve (e.g. science capacity), that driver will also be evolving because of the influence of other factors in the system which would have been acting upon it regardless of whether policy was directed towards it or not (e.g. past educational policy, presence of private sector R&D, R&D policy) – the question is how much change will be produced by the different influences.

- The policymaker will be able to **predict how their interventions may impact on other areas of the system**, besides their intended target. Because these drivers will evolve based on their context, an emphasis on regular and consistent system assessment will insure the necessary data flow for informed policy decision-making. Assessment will show how far the biotechnology sector has moved along its evolutionary path according to expectations derived from other cases, and help policymakers understand the importance of timing regarding interventions; and identify unique characteristics which emerge in their own case.

Policy challenges facing a Targeted approach in general

Five general challenges to effective innovation policy encountered in the case studies conducted by the research team should be kept in mind:

- **Coordination** – ensuring that stakeholders network and build on each others' efforts to facilitate the functioning of the innovation system, filling any gaps and correcting any bottlenecks.

- **Flexibility and long-term commitment** – sectors or industries that are targeted may be so new that the business plans and technology have not yet been completely determined. Therefore, flexibility in how these are addressed is essential. At the same time, many of the target interventions are systemic interventions, and institutional or system change requires a long-term view – so while flexibility is important, commitment to the overall strategy is also important. In other words, actors would ideally have the ability to change operational course if required, while maintaining long-term commitment to strategic goals.

- **Clarity, understanding and transparency** – clarity in the objectives defined and set out by policymakers and stakeholders is essential. To achieve clarity, and to properly set out a roadmap, an understanding of the national and regional context as well as the requirements of the industries in question is essential. Transparency and communication of the objectives and path is important to help coordination, and to avoid conflict amongst stakeholders which may cause long-term commitment to be more difficult.

- **The ability to create an arm's length lead organization(s)** able to separate operational from strategic concerns, and able to maintain arm's-length influence in a risk environment bound to produce a certain degree of failure.

- **Creating an environment accepting of risk and failure** and allowing cycles of failure to be formed.

Specific challenges in biotechnology

Moving an industry or sector through phases of development and facilitating innovation require very specific attention to the needs of the individual sector, as mentioned above. While a general description of a TARGET approach is useful, the development of a biotechnology industry presents challenges which are unique to it, differing from sectors such as ICT. In fact, it would be inaccurate to refer to a single biotechnology sector, as the activities which are vying for commercial space range from stem cell therapeutics to IT heavy medical devices to environmental and agricultural applications. However, because this group of activities depend on an interrelated body of scientific knowledge and skills, it is addressed by policymakers and private sector investors as a single category.

As discussed above, a Targeted approach must be flexible, market focused, whilst still giving clear indications as to how policy and industrial coordination should proceed; due to the complexity of the industry, success and failure must be expected as specific policies or solutions which are attempted, and these may need to be readjusted. The main challenges encountered in the biotechnology sector are the following:

- **Regulatory system** - The regulatory system of any potential markets will affect the risk structure and cost of developing and delivering innovation to markets, requiring any strategy to take this into consideration. Particularly for products that fall under therapeutic or drug discovery, however, the cost of pre-clinical and clinical trials drives up the cost of development and risk of failure.

- **Different risk profiles for different products** - this creates a challenge since the incentive structure for different sectors within biotechnology will exhibit different risk profiles and therefore will affect how investors behave. Products such as medical devices or diagnostics generally exhibit a lower risk profile; however, they will also generally be low on the value-added scale and long-term growth impacts. On the other hand, the risky profiles of therapeutics, and the extensive difficulty and cost of having potential products make it through all regulatory phases, means that products face a greater risk of failure during a longer period of time than other products, and investors, public and private, may simply wish to discard the risk. If particularly high risk sectors are to be pursued, then differences in incentive structures must be addressed.

- **Time-lines** - Considering costs and the process of phased trials, the timelines for new biotechnology products, particularly in drug discovery in therapeutics are much longer than other technologies, and require constant commitment and monitoring.

- **A still developing business plan** - Mentioned as one of the main challenges above for any knowledge based sector, this is perhaps one of the greater concerns in the biotechnology sectors. Much of the science is new and a large number of potential products must still pass through regulatory measures, therefore what is possible to deliver to market is constantly shifting. Furthermore, the value breakdown of projects, and the inputs and participants into the value chain are constantly being rearranged as a result of the growing complexity of science and increasing cost of research and development. The classic chemical-based large pharmaceutical firm approach can no longer be counted on as the best approach, and even the image of small firms acting as external laboratories for large pharma may need to be reconsidered. This is the main reason that, while a targeted approach may define starting points and conditions, and subsequent actions, a degree of flexibility is needed for the end goal of the industry's form. The societal goals, however, those which should be met by having a biotechnology sector, may still be defined.

- **A shifting landscape of firms** - As implied above, the multinational pharmaceutical sectors, which may form part of or anchor a national biotechnology sector, has been undergoing extensive changes. Many firms have been acquired, moved or are changing their market focus in terms of the kinds of drugs they seek to produce and research they focus on. The R&D sites that have normally been associated with these firms are constantly pressured to remain attractive, and new potential sites are competing both for R&D and high value manufacturing. While the exact impact of this on other elements of the biotechnology sector is unclear, it creates a sense of instability that will undoubtedly impact investment decisions.

- **Public vs. private systems of health** - The market dynamics for a set of products will be affected by whether there are multiple clients, a single client, competing clients or a single standard of care in a given market. Each of those has pros and cons that must be weighed, and will impact whether a product may even have a chance. For example, according to one comparison of the UK and US regenerative medicine markets, private healthcare systems may be a better environment for the development of new bio-based therapeutics because private hospitals and care providers are competing for patients and are more willing to use and advertise new technologies to attract patient/clients. In contrast, public health care is more reluctant to purchase new therapies if there is not an obvious and overwhelming difference with previous care. Another example compares the Canadian provinces of Ontario and Quebec and the public sector purchasing habits – Ontario's system preference for generic drugs used in the local hospitals and clinics has meant that generic R&D and manufacturing industry arose in the province in contrast to Quebec which uses brand-name drugs and have managed to attract more brand-name pharmacy manufacturers.

- **Niche markets vs. Blockbusters -** One of the main issues that therapeutics developers are wrestling with is whether to aim for a major blockbuster product that will be applicable to either a common disease or range of diseases and conditions, or whether they should focus on small niches in the health care system, or what may be considered orphan diseases. The risk and pay-off incentives of each differ, as well as the resources required for a company to carry something from research to the market.

- **Internal and external agglomerations of knowledge** - For the biotechnology sector, many times agglomerations of knowledge, and knowledge exchange, will occur outside of a regional or national boundary. Researchers will many times exchange ideas with colleagues in other parts of the world where there is expertise, and the setting may not be enough to sustain the knowledge requirements of an industry. As a result, scales of analysis and interaction are important to keep in mind when building and following a strategy for biotechnology.

- **Demand building** - While many policies focus on supplying the necessary inputs for an industry, it should be considered whether there are any policies that can build demand and uptake for capital, skills or the final products that may create incentives for actors to become more involved. See above point regarding public versus private systems of health and policies that may have to work around institutional limitations.

- **Judging good science** - Different cases claim to have "good science", but differ widely in comparison with each other in terms of scale and the available skills. What actually constitutes good science? And what is enough of a base for a strong biotechnology sector – whether in one niche or spanning several? This is stated in the assessment section above, but it is worth reiterating due to its importance.

IV. TARGET Case Studies

The TARGET Toolkit is based on a number of successful case studies that were conducted during the first phase of the project. These case studies included the following regions/countries: North-Carolina (The triple helix), Singapore, Scotland, Israel and Sweden (Medicon Valley). Once the first version of the Toolkit was completed, four additional case studies were conducted in: Lithuania, Slovenia, Galicia and France.

Following the completion of the first phase's case studies the research team entered a complex analytical process trying to find-out "general" elements for success. The variation of the cases and the fact that these cases represented different points on the biotechnology sector development path enabled the team to explore the importance of **the Industry Life Cycle** Phases (namely: the background, pre-emergence and emergence phases) as an approach for analysis. The cases of Israel, Scotland and Singapore, for example, demonstrated the great challenge of moving from the pre-emergence phase to emergence.

In almost all cases the development path exhibit various complexities that caused major shifts in the region/country's innovation policies. In North Carolina, the policy goal has shifted from a full-fledged cluster to a cluster that specializes in providing services to the biotechnology industry. In Israel, a shift was made from supporting the emergence of new biotech ventures to the support of public/private VC aimed at assisting companies to conduct phase III clinical trials. In Scotland failures to cross the advance phases of drug development resulted in retrenchment of local efforts towards less risky areas of the life sciences, such as medical devices and diagnostics. In Singapore, the difficulties in moving from the background phase to the pre-emergence phase and especially their failure in creating a vibrant environment of local bio-entrepreneurs, challenged policymakers and raised some important questions regarding the ability of policy, even in cases of almost unlimited financial resources, to lead the process of cultural change in the mid or even the long term.

The analysis also revealed the importance of a crucial element within the innovation system, that of a **Body of Knowledge**, to the success of the cluster creation process. The demand for a body which is responsible for processing the knowledge which is gained during the implementation of a targeted initiative and for identifying and coordinating the relevant stakeholders is of specific importance in sectors that are characterized by an unknown development path. The lack of such a body may create sever delays in the cluster development process as was demonstrated in the Israeli case, where the time lag between the identification of the need to establish a public/private VC and launching an appropriate support scheme was more than 5 years. The Israeli case study revealed that this delay was mainly due to lack of coordination between the relevant ministries and a missing function within the innovation system responsible for accumulating knowledge on the progress of the cluster creation efforts. On the contrary, the success of North Carolina to redirect its cluster creation efforts towards services was a result of an efficient body of knowledge that succeeded not only to analyze the required shift in the cluster orientation but also to reach consensus among the different stakeholders and to get their engagement to this direction. The creation of the North Carolina's Body of Knowledge resulted in an independent focal-point for strategic thinking, policy design, and implementation coordination. The structure of the Body of Knowledge enabled it to offer arm's length and unbiased evaluation and policy design.

Similarly, the success of Singapore to build the necessary drivers of the background phase could be attributed to its ability to set an effective body of knowledge which provided real time evaluation of the process, was able to direct the relevant players and in some cases to establish new agencies to bridge gaps when these were identified.

Another identified factor for success was the ability of the policy system to take **long term commitments**. The case of Scotland clearly demonstrates the vulnerability of the targeted approach in cases where the ability of the policy system to take such long commitments is limited and is subject to political changes. On the other hand, the cases of Medicon Valley (started in 1995) and the case of North Carolina (started already in 1963) demonstrate the importance of the ability to ensure a coherent and continuous development process. This stability is of highly relevant for sectors whose development trajectories are relatively unknown, since in such cases the ability to measure success by pre-defined "success indicators" is much limited. Hence, politicians may easily define an initiative as a failure with the intention of shifting its funds to other purposes, while leaving limited space for its advocators. The Singaporean case demonstrated that the ability of the government to take long term commitments was an important factor in the decisions of foreign companies (mainly big pharms) to set up research centers in Singapore and for foreign individuals to relocate.

The need for a **strong science base** is a key factor in the development of the cluster. This has been demonstrated in all cases. It was evident that the main bulk of the entrepreneurial activity, especially at the pre-emergence phase was a result of promising researchers coming out of the academic institutes. In some cases these entrepreneurs were incentivised to conduct translational research (e.g. Israel) while in other cases different actions aimed at maintaining the researcher's ownership over intellectual properties developed by him were taken (e.g. Sweden). The importance of the science base became clear when analysing the Singaporean case (where policymakers had to recruit star scientists from abroad due to lack of local competence at the beginning of the process) and when validating the Toolkit in, for example, Slovenia. In the Slovenian case the decision to target Biotechnology was in fact halted by this factor.

Our case studies also demonstrated the need to define what is meant by “biotechnology”. Many times the “ambition to bio” initially expressed by leaders may have been too ambitious for the country/region’s capacities or resources. This is why the importance of **realistic system assessment** becomes apparent. A successful targeted strategy does not have to be equivalent to the achievement of a full-fledged biotechnology cluster that covers a variety of products and services. A Target strategy may aim to achieve success in niche markets, creation of SMEs, or a more modest participation in the biotechnology value chain; the adequacy of the goals will correspond to what stage of development the region or country finds itself in terms of its scientific and commercial resources and experience. Indeed, the success of North Carolina has only appeared after its decision to focus on developing a service provider cluster. Similarly, the French case has linked the success of some of the French regions to their ability to focus on specific fields within the biotech-sector. On the contrary, part of the reason for Israel to be "stuck" at the pre-emergence phase with no real support system to take into the next phase has to do with a definition of biotechnology which was too broad and lacked clear focus.

The links between Academia, Business and Government were found to be critical to the process of cluster creation. For example, in North Carolina as well as in Medicon Valley the process of targeting biotechnology benefited from a **wide consensus** among these three elements. Such a wide consensus resulted in high level of stability and an ability to effectively coordinate the process. The case of Lithuania as well as the case of Galicia has clearly demonstrated that failing to reach consensus among the stakeholders and coordinate their action may slow dramatically the development of the cluster and in some cases may even terminate the process.

V. General Lessons

1 **The TARGET approach as an anchor for policy**

TARGET's evolutionary modeling of the biotechnology sector assists policymakers in conducting a realistic assessment of the sector. This includes an evaluation of the various drivers, the phase in which the sector is in and the measures required to lead the sector towards an emergence phase. TARGET Toolkit enables policymakers to comprehend the complexity of the innovation system, including the co-evolution of the different drivers, and therefore assist them in planning the appropriate policy measures and investments. The TARGET approach can also assist in developing shared modes of communication based on a common "evolutionary language", between the different agents and between policymakers around the globe.

2 **A long time line for achieving a functional biotechnology sector**

One of the key lessons derived from our case studies is that achieving a functioning biotechnology sector with any degree of critical mass will require a minimum of 20 years investment and reinvestment. It may therefore be necessary to aim for more modest goals. Such endpoints are not less valuable in that they may provide a more realistic option for return on investment, and may also lead to new potential pathways in the future.

3 **A variety of possible goals**

A full-fledged biotechnology sector is not the sole goal for a targeted policy in the biotechnology sector. Other alternative goals could be niche bio cluster, SME generator, bio supply or service and partner technology. In some cases, more modest goals are better appropriate in regions or nations which are located at the background phase or are lacking some of the pre-conditions for establishing a full biotechnology sector. Therefore, the desired goal should be based upon realistic assessment both of the existing state of affairs and the capability to secure a long term commitment.

4 **Good science as a necessary but insufficient condition for a successful biotechnology sector**

The variety of case studies examined in TARGET project demonstrated the erroneous nature of the assumption that good science is the key-element for an emerged biotechnology sector. The role of the science driver is indeed crucial for a functioning innovation system, but it is far from being a sufficient one, since translating science into business models requires additional necessary components, such as strong and stable financial schemes and IP regime supporting new inventions. The ability to take advantage of existing assets and establish connections between the relevant stakeholders such as scientists, entrepreneurial, VCs and industrials cannot be based on extraordinary scientific developments alone. Strong Infrastructure, qualified human resources and well-established financial schemes are required in order to attract investors and foreign companies

5 **The prominent role of public institutions and public financing**

Public institutions and public financing have a leading and evident role in establishing and promoting a biotechnology sector. The case studies have shown that the role of public finance is a crucial element for boosting the innovation system and is an inherent part of the economic development of the biotechnology sector.

6 **Investments are changing**

There is a clear shift in investment trends away from high risk projects which involve regenerative medicine, biotechnology based therapeutics and drug development, towards less risky products such as diagnostics, or device-based products.

7 **Global links as a crucial element for success**

Global links are necessary for to touching base with cutting-edge technologies, accessing global markets, achieving economies of scale, etc. MNEs can play an important role in establishing these global links.

8 **The importance of a coordinating body**

A coordinating body responsible for filling the knowledge gaps, conducting on-going assessments and coordinating between the strategic level and the tactical levels is necessary for an effective targeted policy for the biotechnology sector.

9 **Consideration of both Supply and Demand side policies**

An effective policy requires that both demand and supply side policies will be taken into account. TARGET project mainly approached supply side policy measures, due to its limited scope. However, demand side instruments, such as public procurement mechanisms, are an important component of policy for the purpose of creating and ensuring the existence of a market for the relevant technologies.

10 **A variety of sub-sectors**

While there are specific challenges to the biotechnology sector (listed in chapter III), there are also specific challenges for sub-sectors within the biotechnology sector. The lessons of TARGET project are specific lessons for the biotechnology sector as a whole. It is important to keep in mind that implementing policy measures requires supplementary efforts that take into account the variety of "sub-sectors" that might need different treatment.

Annex 1: Guiding Questions for Realist Sector Assessment

While these questions are posed as Yes/No questions, their answers are based on a thorough investigation which is composed of multiple questions detailed below. It is to the benefit of policymakers to be objective in their decision of whether or not they meet minimum criteria. While answering "No" to the questions below may not necessarily rule out a policy process aiming at support a biotechnology sector, it would mean that missing Sector Drivers will have to be accounted for in the strategy.

Precondition for a Targeted Policy

Is there a political commitment? (YES/NO)

Guiding questions:

- Is the political commitment shared by multiple stakeholders?
- What is the size of the group willing to pursue a targeted policy?
- If it is a small group, how is it able to operate successfully without broader support?

If the answer is "YES":

Since political commitment is usually tentative and may not be long-term, how would this affect the resources needed for a long-term strategy, and is it realistic to assume that a TARGET approach will be adhered to beyond a few years?

If the answer is "NO":

If there is no political commitment, is there sufficient private sector support to move a TARGET strategy forward any way?

The Science Driver

Does a strong science base exist? (YES/NO)

Guiding questions:

- Is the science base strong in a particular niche or overall?
- Is the strength based on large size or just good performance from a small but qualified group?
- What criteria are being used to judge this (e.g. internationally competitive for funding and in high impact journals; patent applications)?
- How is R&D divided between basic research and applied research and is there high quality for each category?

If the answer is "YES":

What are the possibilities of strengthening the science base in the short-term to achieve acceptable pre-conditions for the industry?

If the answer is "NO":

Is the particular sector worth pursuing through a targeted approach or are there better candidate industries?

The Training Driver

Is a training personnel program already exist or required? (YES/NO)

Guiding questions:

- Are there sufficient knowledgeable investors, researchers and managers for the range of activity needed for a functioning innovation system?
- What skills are missing?
- Which kind of programs or training can be implemented? (Keeping in mind a time lag between the start of the programs and the first qualified individuals emerging).
- Are there key individuals who can take on mentorship roles or be examples to others?

If the answer is "YES":

What are the possibilities of creating/strengthening a training program in the short-term to achieve acceptable pre-conditions for the industry?

If the answer is "NO":

Is the particular sector worth pursuing through a targeted approach or are there better candidate industries?

The Commercial Driver

Is there a strong commercial basis for a targeted policy? (YES/NO)

Guiding questions:

- What is the measure of business activity in the sector?
- What is the number of companies?
- What indicators exist for judging commercial excellence and success in industry?
- Are technically skilled people in the science base willing to work commercially or interact with commercial interests?
- Are commercial skills set in other local industries are transferable?
- What networks and existing contacts already exist?
- Does the economy have any internationally recognized firms? Any local multinationals?
- Is there foreign MNEs acting in the industry? What activities do they pursue locally? Are the activities high value-added or are they routine manufacturing/back-office work?

If the answer is "YES":

What are the possibilities of strengthening the commercial base in the short-term to achieve acceptable pre-conditions for the industry?

If the answer is "NO":

Is the particular sector worth pursuing through a targeted approach or are there better candidate industries?

The Financial Driver

Is there capacity for long run, significant financial support? (YES/NO)

Guiding questions:

- Is there any public financial policy to support life science/biomed activities?
- How much funds are dedicated to life science/biomed projects as percentage of the public R&D budget?
- Is there public investment on life science/biomed research centers?
- Are there public investments on life science/biomed incubators?
- Are there any public Venture Capital funds committed to life science/biomed?
- Do public Venture Capital funds have a special focus on any particular life science/biomed area?
- Are there any Public-Private Equity funds committed to life science/biomed?
- Are there tax incentives for Venture Capital firms with special focus on life science/biomed sector?
- Is there any specific incentive for the creation of life science/biomed focused Venture Capital firms?
- How many companies specialized in Finance Consulting exist?

If the answer is "YES":

What are the possibilities of strengthening the financial base in the short-term to achieve acceptable pre-conditions for the industry?

If the answer is "NO":

Is the particular sector worth pursuing through a targeted approach or are there better candidate industries?

The Human resources Driver

Is there human resources availability? (YES/NO)

Guiding questions:

- Are there sufficient knowledgeable investors, researchers and managers for the range of activity needed for a functioning innovation system?
- Is there at least a small number of outstanding individuals in the economy?
- Do these individuals work as "Knowledge Brokers" / "Deal Makers"?
- Do they network internationally or only locally?
- Are they active in managing firms, or also active working with or in other bodies?
- Are they ideologically committed to developing the industry or sector?
- Does the regulation enable the job mobility for Human Resources in Life science/biomed?

If the answer is "YES":

What are the possibilities of strengthening the human resource of the sector in the short-term to achieve acceptable pre-conditions for the industry?

If the answer is "NO":

Is the particular sector worth pursuing through a targeted approach or are there better candidate industries?

The 'Other Institution' Driver

Do other institutions exist in the economy for facilitating a biotechnology sector? (YES/NO)

Guiding questions:

- Is there a clear IP protection regime?
- Is there clear legislation concerning clinical testing and product regulation?
- Have actions been implemented to increase patent applications in Life science/biomed?
- Have actions been implemented to increase university patent applications in Life science/biomed?
- Are there workers at the Technology Transfer Offices (TTO) with specific knowledge for life science/biomed?
- What is the health system budget as a percentage of the GDP?
- What is the number of medical doctors in Clinical Hospitals?
- How many people are working on clinical trial activities?
- What is the annual number of clinical trials?
- What is the annual number of clinical trials in starting phases?
- Is there any specific action to promote public procurement on personalized medicine?
- Are there actions to encourage the social acceptance regarding to life science/biomed innovations?

If the answer is "YES":

What are the possible measures in the short-term to achieve acceptable pre-conditions for the industry?

If the answer is "NO":

Is the particular sector worth pursuing through a targeted approach or are there better candidate industries?

Annex 2: Stakeholder Cooperation

As discussed above, while the kick-off decision does not necessarily have to be made by the party that will eventually manage the process, it is important that as wide an agreement as possible amongst stakeholders to pursue the strategy is obtained. For policymakers involved, this will involve different steps. The first is the identification of potential partners and/or opponents to such an approach. This is not to be confused with the later, more detailed identification of direct and indirect stakeholders who will be participating in the system which occurs simultaneously to the system assessment. Rather, this can be described as an identification of the triangle of public sector organizations that may be involved or whose interests overlap (different ministries or agencies), private sector organizations or firms (such as industry bodies, manufacturing concerns, key entrepreneurs or chambers of commerce) and universities. This may also include labour organizations if there is a large industrial presence in the context of the targeted sector in case proposed policies overlap or conflict with their interests.

Briefly, according to political science theories of rationality, as well as organizational theory, different organizations have bounded rationalities which are determined by their own organizations history, learning capacity and environment. Individuals within one organization, while still rational, will not share the exact same concerns and values as individuals within another – these differences occur between firms in a field, and would be even more different between organizations such as a government ministry and a private firm. To individuals within these organizations, variables such as power, prestige, budget for activity, and profits will weigh, differently. For example, a business may consider a cut in operational budget as perfectly acceptable so long as an increase in profit follows; to a direct in a government department, a loss in budget will likely motivate them to oppose particular measures since profit does not enter into their personal gain, and in fact may be tied in to a loss in personal and departmental prestige. Operationally, therefore, a simple understanding of the different motivations of stakeholders is necessary to understand how different interests may be co-opted, or if that is not possible, overcome.

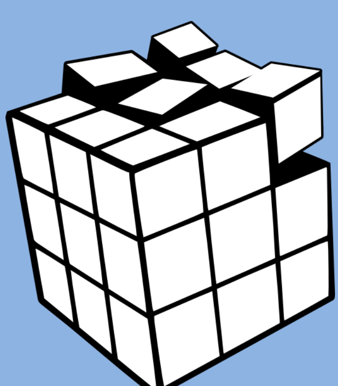
Examples of cases where agreement was relatively wide spread occurred in Ireland, Sweden and North Carolina. The agreement in these three cases to pursue an innovation strategy which included biotechnology as a key sector was held relatively widely because there was a perception of economic crisis in each case. This perception of crisis meant that, despite possible different interest and motivation sets amongst stakeholders, there was a common denominator to their interest set (overlapping interest) which meant that they collectively prioritized dealing with the economic crisis by supporting measures to foster innovation. Understanding this phenomenon goes beyond standard economic rationality assumptions for actors, and being able to do so would help policymakers and innovation policy leaders to create consensus outside of a crisis scenario.

Furthermore, the canvassing of potential partners for kicking off a targeted approach should be done as early as possible.

Besides these individual interests of different organizations, the different stages of a sector's development will have different effects on the ability to obtain agreement for kick-off at the beginning of the process. While it is more risky or entrepreneurial to kick off a targeted approach at an earlier stage of evolution, there will likely be more parties and interests at later stages with potentially more entrenched interests, which may lead to greater complications. With the stage of development in mind, it should be noted that in the cases discussed, it was mostly support for innovative sectors, not just biotechnology – in some cases biotechnology was not really a strength but a desire – perhaps not ideal to pursue. If so, how much willing is there to invest?

Also, in terms of operationalizing the kick-off agreement, what is the minimal achievement? What is the bare minimum ideal for coordination? It may be suggested that if a sufficient majority in any area can agree then this is enough agreement for at least three years initial budget commitment.

The TARGET approach presented here will help policymakers form a strategic roadmap and determine feasible interventions that lead to a functioning biotechnology system of innovation within a country or region. The goal of the Toolkit is not to present a single recipe of specific policies for success; as will be noted later on, the variety of cases and their development mean that no single path to a functionally biotechnology sector can be realistically described.



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SEVENTH FRAMEWORK PROGRAMME