National System of Innovation in Biotechnology in a Developing Country – A Gerschenkronian Approach to Biopharmaceuticals and Bioagriculture in Iran

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Declaration

I hereby declare that this thesis has not been and will not be, submitted in whole or in part to another University for the award of any other degree.

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SUMMARY

This study is a qualitative analysis to investigate the extent and characteristics of the influence of the national system of innovation (NSI) on the performance of the biotechnology sector in a developing country.

While developing country 'leapfrogging' would, at first sight, seem to contradict mainstream theorising about latecomer innovation, it fits well with a Gerschenkronian focus on the role of substitutes to overcome major stumbling blocks to economic development and the role of institutions such as banks in directing investment. This makes it compatible with an older, more traditional literature. Yet, even though such success can readily be understood for scale-intensive heavy industries with well-established technological trajectories, it does not seem so simple for biotech, where success is still highly uncertain, even for firms in developed countries, and where directed governance structures of the sort authors such as Gerschenkron highlight are not normally deemed useful.

To identify what influences the uneven performance of the bioagricultural and biopharmaceutical sectors in Iran, a parallel approach to Gerschenkron's is implemented in this thesis, to determine whether the characteristics of Iran's NSI in biopharmaceuticals differ from those of bioagricultural sector and whether these differences explain the differing performance. The study makes extensive use of interviews as well as documentation to assess the actual unfolding of events.

The findings were unexpected at the outset of the project as the uneven development in the biotechnology sector of Iran turns out to have been caused less by technological failure than by regulatory failures on the part of government. This demonstrates that while the government can speed up economic development by overcoming barriers (through for example promoting successful access to technological knowledge, research and development), it can also hamper innovation by failing to provide appropriate legislation and to adjust laws and regulations to the stage of technological development that the biotechnology sector of a developing country has achieved. Thus Gerschenkron's conclusion about the state as a substitute for 'economic backwardness' is turned on its head.

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List of Abbreviations

ABRII	Agricultural Biotechnology Research institute of Iran
ACIP	Advisory Committee on Immunization Practices
AFLP	Amplified fragment length polymorphism
ANRRO	Agricultural and Natural Resources Research Organization
API	Active Pharmaceutical Ingredient
AREEO	Agricultural Research, Education, and extension Organisations
BoP	Balance of Payment
BRC	Biotechnology Research Centre
BSI	Biotechnology Society of Iran
Bt	Bacillus thuringiensis
CGIAR	Consultative Group of International Agricultural Research
CIGB	Centre for Genetic Engineering and Biotechnology (Havana)
CIMMYT	International Maize and Wheat Improvement Centre
CPB	Cartagena Protocol on Biosafety
CSR	Centre for Strategic Research
DPD	Date Palm Developments (Limited Company)
DSCC	Department of Seed Control and Certification
EBIS	European Biotechnology Innovation Systems
EDP	Economic Development Plan
EMEA	European Medicines Agency
EMHGBN	Eastern Mediterranean Health Genomics and Biotechnology Network
EMRO	Eastern Mediterranean Regional Office (WHO)
EPO	Environment Protection Organisation
FABA	Federation of Asian Biotech Associations
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
FDD	Food and Drug Department
FDI	Foreign Direct Investment
FSH	Follicle-stimulating hormone
GAP	Gene Azma Persia Company
GCSF	Granulocyte colony-stimulating factor
GDP	Gross domestic product
GLP	Good Laboratory Practice
GM-CFS	Granulocyte macrophage colony-stimulating factor
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practice
GnRH	Gonadotropin-releasing hormone
GSB	Great Stumbling Blocks
GSI	Genetic Society of Iran
GSO	Government Support Organization
HDI	Human Development Index
HDR	Human Development Report
hGH	Human Growth Hormone
HP	Helicobacter pylori
HR	Human Resources
HTIC	High Tech Industries Development Centre
ICARDA	International Centre for Agricultural Research in the Dry Areas (Syria)
ICGEB	International Centre for Genetic Engineering and Biotechnology
ICT	Information and Communication Technology
IDRO	Industrial Development and Renovation Organization
IEASA	International Economic Affairs and Specialized Agencies
IFA-Tulln	Interuniversitären Forschungsinstitutes für Agrarbiotechnologie in Tulln
IFDA	Iran Food and Drug Administration
IFN	Interferon

IGS	Iranian Genetics Society
IMIDRO	Iran Mineral Industries Development and Renovation Organisation
INSF	Iran National Science Foundation
IPI	Pasteur Institutes of Iran
IPITT	Pasteur Institute of Iran's Think Thank
IRICA	Islamic Republic of Iran Customs Administration
IROST	Iranian Research Organization for science and Technology
IRRI	International Rice Research Institute
ISAAA	International Service for the Acquisition of Agri-biotech Applications
ISIRI	Iran's Standard and Industrial Research Institute
ISO	International Organization for Standardization
IWMI	International Water Management Institute
KTT	Knowledge and Technology Transfer
LIDCO	Life Science Industry Development Company
LMO	Living Modified Organism
mAbs	Monoclonal Antibodies
MAJ	Ministry of Agricultural Jihad
MCIG	Ministry of Culture and Islamic Guidance
MCIT	Ministry of Communication and Information Technology
MFA	Ministry of Foreign Affairs
MHME	Ministry of Health and Medical Education
MICT	Ministry of Information and Communications Technology
MIM	Ministry of Industry and Mines
MOP	Ministry of Petroleum
MPDRI	Medicinal Plants and Drugs Research Institute
MPO	Management and Planning Organization
MPTT	Ministry of Post, Telegraph and Telephone
MS	Multiple Sclerosis
MSRT	Ministry of Science, Research, and Technology
NBRC	Nano-Biotechnology Research Centre
NGO	Non-Governmental Organisation
NSBP	National Strategic Biotechnology Plan
NSI	National System of Innovation
NTC	National technological capabilities
NTD	New Technologies Division
NTDS	National Technology Development System
OIE	World Organization for Animal Health
OPEC	Organization of the Petroleum Exporting Countries
pAbs	Polyclonal Antibodies
PCT	Patent Cooperation Treaty
PFIRC	Pesticide and Fertilizer Industrial Research Centre
PGBRC	Persian Gulf Biotechnology Research Centre
PMBG	Pharmaceutical and Medical Biotechnology Group
PPDRI	Plant Pests and Diseases Research Institute
PRII	Pistachio Research Institute of Iran
PSRC	Pharmaceutical Sciences Research Centre
QTL	Quantitative Trait Loci
RAPD	random amplified polymorphic
RBRC	Reproductive Biotechnology Research Centre
RRII	Rice Research Institute of Iran
RVSRI	Razi Vaccine and Serum Research Institute
SBSRI	Sugar Beet Seed Research Institute
SBU	Shahid Beheshti University
SBUMS	Shahid Beheshti University of Medical Sciences
SCAbs	Single Chain Antibodies
SCSRT	Supreme Council of Science, Research and Technology

SPIRI	Seed and Plantlet Improvement Research Institute
SPRU	Science and Technology Policy Research
SRTC	Science, Research and Technology Commission
SSC	Shafaye Sari Company
STI	Science, Technology and Innovation
STIP	Science, Technology and Innovation Policy
SUT	Sharif University of Technology
SWRII	Soil and Water Research Institute
TAC	Technology Advisory Committee
TAI	Technology Achievement Index
TCO	Technology Cooperation Office
TDA	Training and Development Agency (under WHO)
TMU	Tarbiat Modarres University
TNC	Transnational Corporation
tPA	Tissue Plasminogen Activator
TRIPS	Trade-Related Aspects of Intellectual Property Rights
TUMS	Tehran University of Medical Sciences
U/RI	Universities/Research Institutes
UN	United Nations
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
UNEP-GEF	United Nations Environment Programme - Global Environment Facility
UNESCO	United Nations Educational, Scientific and Cultural Organization
WFCC	World Federation of Culture Collection
WHO	World Health Organization
WIPO	World Intellectual Property Organization

Chapter 1 Introduction

Developing countries are traditionally assumed to be more successful in natural resource based, and low and medium-tech industries, than in high-tech industries, where developing countries lack formal links to resources such as world-class university departments, supporting firms and specialised service provision.[1] It therefore was surprising that in 2004 Iran became the world's first country to commercialize the first variety of GM rice and appeared in the ISAAA report on the "Global Status of Commercialized Biotech/GM Crops" (James, 2005). However, for reasons studied in this project, Iran was removed from the list of GM crop producing countries in 2007 (James, 2007). On the other hand, over the past five years, the Iranian biopharmaceutical industry which was previously more in line with normal developing context expectations[2] has launched over ten modern biopharmaceutical products into the local and international markets.

The initial Iranian success with GM rice and the current success of the biopharmaceutical sector show that developing countries can catch up in the highly knowledge-based biotech industry and even take the lead. At first, this would seem to contradict mainstream theorising about latecomer innovation.[3] However, the exact processes through which the Iranian industry built up these capabilities are unclear. There have, for example, been examples of latecomer countries succeeding in some industries, like the dramatic way Europeans overtook the US in steel in the 1970s, and were themselves overtaken by the Koreans and Japanese in the next decades through government-supported investment in larger-scale production facilities that enabled lower unit cost production.

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[1] Iran is considered a developing economy according to the International Monetary Fund's World Economic Outlook Report, April 2010 (IMF, 2010). Developing countries are in general countries which have not achieved a significant degree of industrialization relative to their populations, and which have, in most cases a medium to low standard of living. There is a strong correlation between low income and high population growth. The levels of development may vary widely within so-called developing countries. Some developing countries have high average standards of living. The development of a country is measured with statistical indexes such as income per capita (per person) (GDP), life expectancy, the rate of literacy, etc. The UN has developed the Human Development Index, a compound indicator of the above statistics, to measure the level of human development for countries where data is available (UNCTAD, 2005). In the case of Iran, the Human Development Index rose from less than 0.6 in 1980 to 0.782 in 2007, moving Iran from the group of countries considered to have low human development to the ranks of those with medium human development (UNDP, 2009). Therefore Iran is placed in above the least developed and below advanced countries justifying the term 'developing'. In other words Iran falls within the group of countries with more advanced economies than other developing nations, but has not yet fully demonstrated the signs of a developed country. Chapter 4 provides further detail on Iran's level of development in comparison with selected countries.

[2] New drug formulations and development of generic products

[3] For example, Hobday has highlighted how S.E. Asian electronics firms gradually built up technological capabilities in moving from sales, to marketing, to production, to design, and only recently to R&D (Hobday, 1995). Similarly, Bell and Pavitt (1995) highlight the importance of productive capability (Bell, et al., 1995).

Such 'leapfrogging' is not incompatible with the traditional literature, and fits well with Gerschenkron's focus on the 'benefits of backwardness' and the role of establishments such as banks in directing investment. However, such success might be understandable for steel or other scale-intensive heavy industries with well-established technological trajectories that typically required firms to build larger plants, but it does not appear to be so simple for biotech, where success is still highly uncertain, even for firms in the UK and US, and where directed governance structures of the sort Gerschenkron highlights are not normally deemed useful. Even large pharmaceutical firms, for example, are moving towards a more networked, biotech-like, governance structure (Garnier, 2008). Overall, the question still remains about what caused the initial Iranian success and the subsequent slowdown in the bioagricultural sector as well as the recent success in biopharmaceuticals?

1.1 Thesis Objectives

This research uses the national system of innovation (NSI) framework to identify what influences the performance of the biotechnology 'sector' in Iran, both bioagricultural and biopharmaceutical.[4] Since the project needs to explain both initial success in rice, and also the uneven development of bioagriculture, the NSI will be complemented by a focus on sectoral systems of innovation.

The study will investigate key institutions and organizational linkages, and assess and compare the performance of these two segments of the biotechnology sector. The objective of the study is to

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[4] Biotechnology broadly means 'the application of biological organisms, systems and processes to manufacturing or service industries' (Sharp, 1996), and goes back to the first attempts of cross-breeding plants and animals and using yeast in bread making and fermenting of alcohol. Early twentieth century, a systematic attempt started to screen and categorise the role and variety of micro-organisms existing in the natural environment and to exploit those that had useful application such as penicillin. This was called the 'second generation of biotechnology'. The new or 'third generation' biotechnology dates from the early 1970s following the recombinant DNA and hybridoma technologies led the way to genetic engineering. The applications of these radical new techniques led to the emergence of a whole new generation of protein drugs based on naturally occurring proteins in the body's immune system. Further 'generations' of new products have followed developments in gene therapy and genome mapping. In this study the term biopharmaceutical refers to the use of proteins to target the underlying mechanisms and pathways of a disease: e.g. new medical therapies to treat hepatitis B, hepatitis C, cancers, arthritis, haemophilia, bone fractures, multiple sclerosis, and cardiovascular disorders; as well as production of human growth hormone, clotting factors for haemophiliacs, fertility drugs, erythropoietin and other drugs.
Biotechnology is also applied outside the pharmaceutical industry. In agriculture, genetic engineering is applied to both animal farming and plants but it has also raised difficult ethical issues. In plants it has led to the rapid development of hybrid plant species resistance to extreme temperatures, drought, fungi, pests, or particular types of herbicide. But there has also been concern that such products could lead to dangerous mutant species of plants and some authorities have moved slowly in allowing experiments. Only in the last fifteen years or so have experiments really been allowed to proceed (Sharp, 1996). However new products have already been launched in this area. In this study bioagriculture mainly refers to the use of genetic engineering technology to reduce vulnerability of crops to biotic and abiotic environmental stresses e.g. drought, salinity, insect and virus resistant, reduced dependence on fertilizers, pesticides and other agrochemicals as well as animal biotechnology e.g. cloned sheep, but also Non-GM technologies such as micro-propagation of plants.

give insights into the extent to which the performance of the Iranian biotech sector is influenced by the NSI characteristics of developing country status, and identify the possible reasons for SI failures in that sector. This will contribute to a wider understanding of the processes underlying the development of biotechnology in Iran. It also aims to increase theoretical understanding and empirical knowledge of the NSI in the context of developing countries. While the NSI approach has been widely applied, it is not itself immune from critique, and serious questions arise about the nature of causality it implies (Nightingale, et al., 2008). The NSI approach highlights how institutions are important, but this study is concerned with which particular institutions, when they are important, and from a policy perspective how their importance changes over time and across sectors.

In order to investigate whether the NSI characteristics of Iran explain the differing performance in the biopharmaceutical and the bioagricultural sectors of the country, the project looks at the following:

- Do the characteristics of Iran's NSI in pharmaceutical biotechnology differ from those of agricultural biotechnology?
- Do these differences explain the differing performance?
- What are the reasons for SI failures in the biotech sector of Iran?

Accordingly, the key research questions arising are as follows:

1. Lead question: How is the performance of the biotechnology sector in developing countries influenced by their NSI characteristics, and in which respects?

2. Sub question: Do the characteristics of Iran's NSI in pharmaceutical biotechnology differ from those of agricultural biotechnology? Do these differences explain the differing performance?

3. Sub question: What are the most plausible reasons for SI failures in the various segments of Iran's biotech sector?

The application of a Gerschenkronian approach to a country like Iran in the information age where production is based more on knowledge and the research base, suggests that the missing prerequisites for economic development may be more related to knowledge capital rather than physical capital. Consequently, the key question is how the Iranian biotech industry is going to overcome gaps in its knowledge base? Moreover, is Gerschenkron's approach applicable today?

1.2 Thesis Achievements

A key contribution of the thesis is that it explores the utility of NSI framework for developing countries and furthermore for developing countries with particular features that are not uncommon, namely those with regimes that tend towards directed governance structures of the sort Gerschenkron highlights, rather than the market-led economies that NSI was developed with in mind. The application of a parallel approach to the Gerschenkronian view emphasises that national governments are the main catalysts in overcoming stumbling blocks to development through implementing substitution mechanisms. Gerschenkron's approach to economic development, in particular the role of government in substituting missing prerequisites is shown to be a useful adjunct to the NSI model in considering how innovation proceeds in command economies perhaps developing or otherwise.

The study makes extensive use of interviews as well as documentation to assess the actual unfolding of events. Key institutions and organizational linkages are investigated; the interview data for both sectors are presented, assessed and compared to give insight into the extent to which the performance of the Iranian biotech sector is influenced by the NSI characteristics of developing country status. The empirically observed contrasts between the two sectors reveal the main reasons for the differing performance of the two sectors and identify the most plausible reasons for SI failures in the various segments of Iran's biotech sector.

A comparison of subsystems (agricultural and pharmaceutical) of a high-tech sector (biotechnology) is relatively unusual in a developing country context. This study contributes to the understanding of the reasons of success and/or failure in different sectors of the biotechnology SI, which is of value to policy-makers. Furthermore the findings of this study can be used for the understanding of the differences of biotechnology patterns in developing and developed countries. The study will give insight into Iran's technology system, which is largely overlooked in the empirical literature. The findings therefore contribute to a wider understanding of the processes underlying the development of biotechnology in Iran as well as increasing theoretical understanding and empirical knowledge of the NSI in the context of developing (and perhaps other) countries in which the state directs the economy.

1.3 Thesis Layout

In chapter 2, the concept of SI and its main dimensions are reviewed. National, sectoral, and technological SIs and the interrelationship between these concepts are discussed. Further the NSI concept is discussed in developing country context. Finally the Gerschenkronian ideas on patterns of industrialisation are described and applied to NSI in a developing country context.

In chapter 3, the research design including methods of data collection (both background and primary data), data presentation and data assessment are described and the structure of the interview sample as well as the structure and focus of the interview questions are explained. The chapter also presents limitations of gathering data in Iran and problems that arose during the project.

In chapter 4 Iran's NSI characteristics are examined. The country's economic indicators, science and technology infrastructure and capacity are described. Further, major policy making organisations and their role in the policymaking and implementation process are presented and discussed.

Chapter 5 investigates the development and attributes of Iran's biopharmaceutical and bioagricultural SIs. The chapters also present major actors promoting and financing biotechnology SI and major government policies and their impact on innovation.

Chapter 6 provides a number of product innovation journeys. The GM Bt rice and Cinnovex are selected as the main representatives of the sub-sectors complemented by other product journeys which as a set illustrate how parts of the innovation system perform.

Chapter 7 discusses and concludes the findings of the thesis. The empirically observed characteristics of the biopharmaceutical and bioagricultural sectors of Iran and the extent to which government substations have had a positive or negative influence are analysed followed by implications for theory and policy, unexpected findings, limitations of the analysis, and future studies.

Chapter 2 The System of Innovation Framework

2.1 Introduction

The theoretical background and analytical framework of this study is presented in this chapter. The different variants of the system of innovation (SI) concept are briefly explained and the national system of innovation (NSI) concept which underlies the analytical framework of this study is reviewed and discusses. Furthermore the implementation of the NSI concept in the developing country context and the issues that arise from it are examined. Finally the Gerschenkronian theory of economic development is reviewed and applied to the analytical framework of this study.

2.2 Main Dimensions of System of Innovation Concept

During the last two decades, policy makers at both the national and international level have adopted the SI and system failure concept for the formulation, implementation and evaluation of their innovation policies. The concept is attractive, as it seems to provide a sound framework for the analysis of main factors influencing the innovative capabilities and performance of national economies. It not only takes into account the major functions of production, diffusion and application of new knowledge, but also the actors and institutions within the system and the relations between them, in other words the systemic character of innovation. The SI concept broadens the rationale for government intervention as it introduces system imperfections by referring to inappropriate functioning of SI (Kern, et al., 2006).

The diversity in SI concepts raises the need for reviewing SI as a theoretical tool for innovation policy. The main dimensions of SI concepts applied to study the processes of innovation and technological change are the geographical[5], sectoral, and technological dimensions. SI categories and related concepts developed and commonly used in the literature are presented in table 2.1.

The main conceptual framework underlying this study is the NSI. Addressing the national characteristics of SI as well as the specificities of innovation processes across economic sectors and of technological fields demonstrate the complexity and dynamics of SI that need to be taken into account in innovation policies. Generally, the variants of the generic SI approach complement rather than exclude each other and it is useful to consider sectoral, regional, and technological SIs in relation to, and often as parts of, national SI (Edquist, 2004). Nonetheless, the educational system,

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[5] Focus is on a particular country or region which then determines the geographic boundaries of the system.

the R&D infrastructure, the funding system, the institutional system (including laws, regulations, and public policies, as well as behaviours, norms, cultures, and traditions), but also elements such as level of entrepreneurship mostly belong to the NSI without conceding much to specific sectors or technological fields (Kern, et al., 2006).

Table 2.1 SI categories and related concepts developed and commonly used in the literature

Conceptual Framework	Literature
National system of innovation	Freeman (1987) Lundvall (1992) Nelson (1993) Niosi et al. (1993) Patel and Pavitt (1994) Metcalfe (1995) Edquist (1997)
Regional SI	Edquist (1997)
Sectoral system of innovation	Malerba (2002)
Technological systems	Carlsson, (1995, 1997)
National technology capability (NTC)	Lall (1992)
National system of learning (NLS)	Viotti (2002)
Industrial clusters	Porter (1998)

As global economic competition is increasingly driven by technology and innovation, a keen interest in the technological advantage of nations has emerged (Porter, 1990). A notable body of scholarship has underlined the importance of country-specific institutional context in shaping national technological capabilities (table 2.1). The combination of institutions involved and their interactions, which determine the processes of technology and innovation, are believed by the proponents of the NSI concept to be the source of differences in economic and technological performance across nation states. From this perspective, technological development is considered a location-specific phenomenon, rooted in the skills, capabilities and knowledge that accumulate over time in the NSI (Freeman, 1995), (Archibugi, et al., 1995). At the same time, however, the whole concept that national economic performance is determined by domestic technological capabilities has been challenged by the view that national technological and economic frontiers are merging into a global technological system (Freeman, 1995), (Ohmae, 1990). The NSI concept is reviewed in more detail in the next section.

2.2.1 The National System of Innovation Concept

NSI was introduced into the literature by Freeman (1987) and subsequently extended and reinterpreted by Lundvall (1992) and Nelson (1993). Earlier ideas related to the NSI concept can be dated back to the 1960s (Godin, 2007). The NSI concept emerged to explain the differences in innovative performance of industrialized countries (Freeman, 1987). There is no single definition of NSI. A few of the dominating definitions of NSI in the literature are summarised in Box 2.1. All these scholars define NSI in terms of determinants of innovation processes, but point out different determinants in their actual definitions of the concept, based on what they believe to be the most important determinants of innovation. Therefore, they propose different definitions of the concept, but use the same term. This reflects the lack of a generally accepted definition of NSI (Edquist, 2004).

Box 2.1 Dominating definitions of NSI in the literature

- ... The network of institutions in the public and private sectors, whose activities and interactions initiate, import, modify and diffuse new technologies (Freeman, 1987).
- ... The elements and relationships which interact in the production, diffusion and use of new, and economically useful, knowledge ... and are either located within or rooted inside the borders of a nation state (Lundvall, 1992)
- …The interactive system of existing institutions, private and public firms (either large or small), universities and government agencies, aiming at the production of science and technology within the national borders. Interaction among those units may be technical, commercial and financial, as much as the goal of the interaction is the development, protection, financing or regulation of new science and technology (Niosi, et al., 1993).
- ... A set of institutions whose interactions determine the innovative performance ... of national firms (Nelson, 1993).
- ... The national institutions, their incentive structures and their competencies, that determine the rate and direction of technological learning (or the volume and composition of change generating activities) in a country (Patel, et al., 1994)
- …The set of distinct institutions which jointly and individually contribute to the development and diffusion of new technologies and which provides the framework within which governments form and implement policies to influence the innovation process. As such it is a system of interconnected institutions to create, store and transfer the knowledge, skills and artifacts which define new technologies (Metcalfe, 1995)
- …All important economic, social, political, organizational, institutional and other factors that influence the development, diffusion and use of innovations (Edquist, 1997).

According to Freeman the variation in national innovative performance depends on "...institutional differences in the mode of importing, improving, developing, and diffusing new technologies, products, and processes" (Freeman, 1995). Innovation and technology development are the results of a complex set of relationships amongst the actors in a network of enterprises, universities, research institutes, government, and other support organizations such as industry associations, consumer groups, business support organizations, and financial organizations (table 2.2). The networks of these economic agents whose activities and interactions bring new products, new processes and new forms of organization into economic use together with the institutions and policies that influence their innovative behaviour and performance make up the NSI (Lundvall, 1992), (Nelson, 1993) (Patel, et al., 1994).

Table 2.2 Components of the NSI

Components of the NSI		
1	Firms	State owned Private
2	Non-firm organizations	Universities, research institutes and other parts of educational sub system Industry and other professional organizations Consumer groups Bridging organisations Business support organizations Financial organizations Other interest organisations (e.g. Environmental) Government bodies
3	Societies	Learning and scientific societies Political interest societies
4	Institutions	Laws, regulations Norms, cultures, traditions, routines, established practices and common habits, standards

The relation between these components captures the non-linear features of innovation processes and is one of the most important characteristics of the SI approach (Edquist, 2004). Studies that use the NSI framework are recognized by their ability to analyse processes that are typically overlooked in the linear approach to R&D (Spielman, 2005). Due to this broader sense of analysing, policy makers are increasingly using NSI as a policy framework to support and guide them in developing effective policy measures for science, technology, and innovation (STI) at different levels of development. From an NSI perspective, the sheer number of organisations such as universities, research institutes or firms is far less important than the habits and practices of such actors with respect to 'learning, linkage formation, and investment', which form the nature and extensiveness of their interactions and their tendency to innovate (Mytelka, 2000).

The concept of 'institution' is used in SI studies both in the sense of organisational actors and in the sense of institutional rules by different authors. In this study 'institutions' refer to sets of common habits, routines, established practices, rules, or laws that regulate the relations and interactions between individuals, groups and organisations. Examples of important institutions in SIs are patent laws and norms influencing the relations between universities and firms (Edquist, 1997 p. 46). Organizations on the other hand are formal structures with a clear purpose and they are intentionally created (Edquist, 1997 p. 47). In other words organisations are the 'players or the actors' and institutions are the 'rules of the game'. Some important organisations in SIs are firms (which can be suppliers, customers or competitors in relation to other companies), universities, venture capital organisations and public innovation policy agencies. Although there is general agreement in the literature that 'organisations' and 'institutions' are the main components in SIs (see box 2.1 and table 2.2), there is no agreement what should be meant by these terms. For example, institutions for Nelson and Rosenberg are basically different kinds of organisations (according to the definition above), while Lundvall means the rules of the game when using the term institution (Nelson, 1993 pp. 5, 9-13), (Lundvall, 1992 p. 10) . Hence, the term 'institution' is used in at least two main senses in the literature and these senses are often also confused in the literature – even by the same author (Edquist, 1997 pp. 24-26).

Addressing the relations between the main components of SIs, interactions between different organisations are crucial in learning processes that are normally the basis for the development of innovations. These relations may be of a market and/or a non-market kind. Markets only co-ordinate transactions, i.e. items sold and bought. They do not deal with other kinds of relations. However, interactive learning processes between organisations concern exchange of knowledge and collaborations that are not easily handled through market transactions. Markets are important in SI, but other mechanisms such as non-market based collaborations which mediate the relations between components in the systems are also important.

The relations between organisations and institutions are important for innovations and for the operation of SI. Organisations are strongly influenced and shaped by institutions and the institutional environment or set of rules, which include the legal system, norms, standards, etc. But institutions are also influenced by organisations, for example firm specific practices with regard to bookkeeping or the relations between managers and employees which develop inside firms. Hence, there is a complicated two-way relationship between institutions and organisations, and this relationship influences innovation processes and thereby also both the performance and change of the SI (Edquist, 1997 pp. 59-60). Another type of relation between organisations and institutions is that some organisations directly create institutions, for example formulating and implementing rules also called innovation policy (Edquist, 1997 p. 60). Institutions may also be the basis for the creation of organisations, e.g. when a government makes a law that leads to the establishment of an organisation. There may also be important interactions between different institutions, e.g. between patent laws and informal rules concerning exchange of information between firms. Institutions of different kinds may support and reinforce each other, but they may also contradict and be in conflict with each other. The relations between organisations and institutions are very complex and often characterised by reciprocity. This emphasis on the complex relations between components constitutes a major advantage of the SI approach. However, it also constitutes a challenge since our knowledge about these relations is very limited. It is therefore important to specify the concepts and to make a clear distinction between organisations and institutions in order to be able to address the relations between them.

In addition to the emphasis on innovation, learning, interdependency and non-linearity, NSI's other strength is that it can include different categories of innovation, i.e. product innovation (goods and services) as well as process innovation (technological and organisational).[6] Although the main focus of innovation studies has been on technological innovations followed by goods innovations, and less on non-technological and intangible innovations, (i.e. services and organizational innovations), the SI approach is well suited to analyse all these categories of innovation (Edquist, 2004), (Johnson, et al., 2003).[7, 8]

The Nelson approach to NSI proposes that the innovative capabilities and performance of a nation are strongly influenced by nationally determined factors, where "a distinctive national character pervades the firms, the educational system, the law, the politics, and the government, all of which have been shaped by a shared historical experience and culture" (Nelson, 1993). The Nelson definition of NSI framework emphasises the analysis of the impact of national technology policies on firms' innovative behaviour. Innovative behaviour or activity is measured in terms of formal activities related to the R&D system and the science base. So the Nelson definition of NSI includes organizations and institutions involved in searching and exploring, such as universities, research institutes, R&D departments, and technological institutes (Nelson, 1993).[9]

Lundvall's approach on the other hand emphasises learning rather than the creation of knowledge itself. The concept of learning implies that the competitiveness of individual firms and entire SI reflects the ability to learn. The new trends in production and in the labour market, which are increasingly knowledge based, mean that knowledge building and learning are becoming more and more crucial for economic growth and competitiveness. It is also argued that learning and especially learning new skills and competencies is essentially a collective and interactive process which cannot thrive in a pure market economy. Hence the emphasis in this approach is more on the efficiency of networks of firms and how they undertake innovative activity than on formal activities related to the R&D system and the science base (Lundvall, 1992). Another difference between the Lundvall and the Nelson approach, as previously pointed out, is in the use of the term 'institutions'. For Nelson institutions are essentially different kinds of organizations, while for Lundvall the term 'institution' means primarily the 'rules of the game'. Consequently 'institution' is used in several different senses in the literature (Lundvall, 1992), (Nelson, 1993), (Edquist, 1997).

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[6] Product innovation is a matter of 'what' is being produced; process innovation concerns with 'how' goods and services are produced.
[7] E.g. other categories of innovation include managerial or organisational change, investment in design or skills, and the management of the innovation process (Frenz, et al., 2009).
[8] A recent study by Frenz and Lambert (2009) addresses this gap in the literature by exploring non-technological and mixed modes of innovation in nine OECD countries (Frenz, et al., 2009).
[9] It must of course be stressed that Nelson's definition of innovation is much broader than merely equating it with input (R&D expenditure) or output (patents). He defines innovation as the processes by which firms master product designs and manufacturing processes that are new to them, if not to the nation or even to the universe (Nelson, 1993).

Another approach to NSI characterised by a particular 'national' focus is the Patel and Pavitt 'path dependent learning' approach. For Patel and Pavitt differences in national innovative performance are due to: (1) different factor endowments, (2) different initial national technological conditions that firms find themselves in, where technological capabilities are built through continuous investment in education, training, and R&D. All of these are influenced by national policies and institutional environment.[10] (3) These long term investments provide national firms with an essential knowledge base of the core technology associated with particular directions of technical change (Patel, et al., 1994), (Patel, et al., 1997), (Nightingale, et al., 2008). Firms in such nations will have greater access to trained employees, specialised technical consultancy services and specialised machinery than firms in other nations.

Similar to other policy models the NSI concept is not free of criticism. The main concerns on the use of NSI framework are: (1) its national focus in an increasingly global economic setting; (2) its fuzzy and broad character resulting in the difficult execution of the framework; and (3) its neglect of sectoral characteristics (Johnson, et al., 2003), (Edquist, 2004), (Nightingale, et al., 2008).

A considerable amount of innovation involves adapting and using technology that has been developed outside the national boundaries, therefore the mere focus on how national characteristics drive the accumulation of technological capabilities within firms, limits the scope of innovation. This is particularly important for biotechnology which is very international in its scope. While the creators of NSI frameworks were clear in their interest in the diffusion of innovations from abroad, the research that has followed has tended to focus on innovations that are new to the world and are developed within a single nation (Nightingale, et al., 2008). However it should be noted that Freeman's own approach to NSI addresses the uneven nature of technological accumulation among countries and the importance of international influences on the NSI.

The creators of the approach did not specify the boundaries of the systems and did not indicate what exactly should be included in a (national) system of innovation. Nelson provided no precise direction to just what should be included in the SI, and what can be left out (Nelson, 1993). Lundvall insisted that a definition of the SI must be kept open and flexible (Lundvall, 1992).[11] Therefore at its present form, the NSI approach is not a formal theory to offer detailed suggestions

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[10] For example national corporate governance, legal, financial, accounting, and investment cultures influence how much firms invest in technology and the time scopes that they apply to their returns (Nightingale, et al., 2008)

[11] Examples of statements in favour of the broad and flexible nature of the NSI framework are the following: "The pragmatic and flexible character of the concept may be seen as a great advantage since it makes it useful for practical purposes" (Lundvall, et al., 2002 p. 221). "…heuristic concepts and focusing devices such as national systems of innovation may play a major role since they offer a broad and flexible framework for organizing and interpreting case studies and comparative analyses." (Lundvall, 2003 p. 9)

on the underlying relations between its variables, but rather an approach or a conceptual framework for the formulation of assumptions for empirical testing of the importance of several factors and actors for technological innovations. However, this has been done only to a limited degree (Edquist, 1997). Scholars within innovation studies are currently divided on whether the broad and fuzzy nature of the NSI framework is an advantage or a weakness of the concept. According to some scholars, the approach should not be made too fixed, the concept should not be 'over theorized' and it should remain an inductive one (Lundvall, 1992). Others argue that the SI approach is 'under theorized', that conceptual clarity should be increased and that the approach should be made more 'theory-like' (OECD, 2002), (Fischer, 2001). They insist that the broad and flexible nature of the NSI framework makes it difficult for policy makers to know what to focus on and the large variety in the literature does not provide much structure about what policy makers should do. Such a view has, for example, been expressed by the OECD: "...there are still concerns in the policy making community that the NIS approach has too little operational value and is difficult to implement" (OECD, 2002 p. 11).[12] In this regard however, compared to other policy models (e.g. the market failure framework), the NSI approach does make reasonably clear suggestions for policy makers to focus on by drawing attention to the importance of diffusion of existing technologies, the importance of learning and problem solving, the role of scientific research in training individuals rather than generating technology, the role of public procurement, the importance of the service sector and the limited role of high-tech innovations in the economy (Nightingale, et al., 2008), (Edquist, 2004).

A more radical position is that "...social science will never become a formalized 'general theory' and that the attempts to reshape it into such a type of theory are doomed to lead both to inconsistency and disappointments. Seen from such a perspective the kind of comparative historical approach implicit in NSI research may actually be seen as close to ideal for building the cumulative understanding of socio-economic phenomena" (Johnson, et al., 2003 p. 7). In the present context, Johnson et al (2003) conclude that "it is the flexibility, breadth and pragmatism of the innovation system approach in combination with its ability to focus on what seems to be increasingly important, i.e. learning and innovation, more than its formal theoretical rigor, which has inspired its diffusion into development thinking. It remains to be seen, of course, if this is useful or not." (Johnson, et al., 2003 p. 8). Edquist (2004) supports this view by insisting that "...at present, it is not a matter of transforming the SI approach into a 'general theory of innovation', but rather we need to make it clearer and more consistent so it can better serve as a basis for generating hypotheses about relations between specific variables within SIs (which might be rejected or supported through empirical work). Even the much more modest objective of specifying the main function of SIs, the activities and components in them and some important relations among these, would represent a

[12] A similar position is taken by Fisher (Fischer, 2001).

considerable advance in the field of innovation studies. Used in this way, the SI approach can be useful for creation of theories about relations between specific variables within the approach" (Edquist, 2004 p. 187).

The final related criticism of the NSI approach is that it fails to fully take into account the substantial differences across sectors in the nature of innovation. Malerba (1998), for example, has highlighted how industrial production and innovation within individual sectors is influenced by a range of systems factors (Malerba, 1998). He has developed a sectoral system of innovation (SSI) approach that cuts across geographic boundaries. In this regard SSI complements the national systems framework and is covered in more detail in the next section.

2.2.2 The Sectoral System of Innovation Concept

Only looking at the national level is likely to miss important aspects of innovation associated with national specialisations within global production and innovation networks. Therefore besides the national elements, this study will briefly look at some elements that are believed to be typical of specific industrial sectors and that are perceived as somewhat invariant across countries.

Sectors can be characterised by specific knowledge bases, technologies, processes of production, patterns of co-operation, demand, and demography of firms and may differ largely in several of these characteristics (Malerba, 2002). For example demand, nature of the market, and public attitudes (acceptance) to applications of biotechnology differ greatly between European biotechnology sectors (Senker, et al., 2001). In explaining these empirical differences SSI focuses on three levels of analysis and their interactions (Malerba, 2002). (1) SSI is characterised by specific (and multiple) knowledge bases, technologies and other inputs that go into the final products and processes. For example biological knowledge is essential for the pharmaceutical industry, but much less important in the financial sector. (2) SSI focuses on the different actors and networks within a system that interact (both market and non-market connections), communicate, exchange, cooperate and compete with one another. (3) SSI explores institutions, as actions within SSI are influenced by norms, routines, habits, laws, rules, etc.

Industrial organisation, sector or industry life cycles, (inter)national dimensions of R&D co-operations, character of the innovation processes and of chains of production, demand, and public acceptance are considered to belong to SSI without conceding much to national characteristics (Malerba, 2002), (Senker, et al., 2001), (Kern, et al., 2006).

2.2.3 The Technological Systems Concept

A major element of both national and sectoral concepts of SI is technological progress. Typical characteristics of technologies play an influential role in the direction and speed of innovation. To a large extent, technologies and their development follow evolutionary principles, often related to processes of economic and social progress, and in accordance with distinct life cycles. Several authors have pointed at this when discussing concepts like techno-economic paradigms (Freeman, 1987), (Perez, 1983), technological paradigms and trajectories (Dosi, 1982), and technological regimes and natural trajectories (Nelson, et al., 1982). The concept of technological SI includes evolutionary principles and aims at explaining technological and economic change through a systemic approach (Carlsson, 1997). Critical for understanding dynamics in SI concept is to acknowledge the presence of a multitude of technologies and technological systems in the SI. Technologies are not likely to develop along the same development trajectories or at the same speed. Specific technologies can be expected to have different requirements for development, such as financing, knowledge intensity or infrastructural requirements, but also different barriers that hinder full development. Moreover, the type of actors involved during the innovation process and the way they interact can also vary according to the type of technology involved (Carlsson, 1997). Therefore if, for instance, governments wish to stimulate SI by prioritising strategic technologies, they need to take into account the differences and relations between these technologies, as they probably need different sets of policy measures.

However while this is important in comparing biotechnology with another technology such as ICT, it is less significant in comparing biotechnology subsectors (biopharmaceutical and bioagricultural sectors) as they use the same science base and the same knowledge intensity in terms of scientific and technology inputs. In other words the biotechnology industry has very similar technologies in use between its different constituting sectors. Biotechnology divides into sectors according to applications to a particular industry.[13] Therefore biotechnology firms depend on firms that have already a position in the application sector. Links tend to run vertically downstream to user-industry for each sector rather than between sectors, demonstrating little technology interdependency between them (Kern, et al., 2006).

Other technology related determinants (strongly related to the issue of knowledge intensity) are the ease of entry into and commercialisation of technologies. For example at the current stage of the biotechnology life cycle, entrants need a large supply of core scientific capabilities in which a mass of scientific disciplines are combined. A strong foundation in the relevant knowledge base is needed for firms and even countries willing to enter the field of biotechnology, probably even more than the need for availability of capital (Cooper, 1994). Therefore it is of greatest importance for both new and existing biotechnology companies to build up strong relationships with universities and public research institutes (Faulkner, et al., 1995). This is interesting in comparison with other

[13] For example diagnostics and therapeutics companies make products for the pharmaceutical industry; food or enzymes producers make products and application for the food industry.

technologies such as ICT where entry seems less dependent on scientific capabilities and the extent of linkages between firms and the ICT knowledge base (Kern, et al., 2006). The specificities of technologies are in line with the argument that technologies develop by following specific trajectories and sets of requirements. Moreover, such differences justify the arguments for differentiated S&T policies, in order to achieve sustainable economic progress through the development and exploitation of different sets of technologies (Kern, et al., 2006). In the case of biotechnology SI, the technological specificities that can affect its development and dynamics are similar for its sub sectors which develop by following similar technological trajectories and sets of requirements.

2.2.4 Interrelationship between Different SI Concepts

There are various interrelationships between different SI concepts. As mentioned already, the variants of the generic SI approach complement rather than exclude each other. SIs may be international, national, or sub-national and at the same time they may be sectoral within any of these geographical demarcations. Sectors, in turn, rely on a diverse range of different technologies that can be understood in terms of technological SI. Therefore the innovative capabilities and performance of a nation are also influenced by the distinctive characteristics of specific economic sectors and technological fields. At the present state of the art, the determinants of innovation are not known systematically and in detail (Edquist, 2004). Table 2.3 attempts to summarise national, sectoral, and technological determinants that are currently found in the literature to influence the performance of biotechnology SI in the context of developed countries (Kern, et al., 2006), (Senker, et al., 2001).

Table 2.3 National, sectoral, and technological determinants of biotechnology SI

National	Sectoral	Technological
The national education and training systems; The national R&D systems (e.g. type or model of public research system); Inter firm relationships; The financial system; Role of the public sector including public policy; The moment of implementation of policies; The systemic character of policies; The balance between generic S&T policies and specific biotechnology policies; Institutional arrangements for IP rights in the public sector; National legislation and regulatory frameworks; National healthcare systems (including procurement and pricing regimes); Existence of natural resources in a country; Country's geographic position; Size of the home markets.	Industrial organisation; Sector or industry life cycles; (Inter)national dimension of R&D co-operations; Character of the innovation processes and of chains of production; Demand side, Public acceptance.	Technology life cycles; Knowledge and science intensity of technology; Interdependencies of technological development between technologies and industries; Costs of technology development and opportunities of entry; Interdependencies of technological development between technologies and industries.

The trend towards globalisation and internationalisation has challenged the significance of national dimension of SI as borders and geographical demarcations dissolve into a global technological system (Freeman, 1995). New information technologies act as a powerful medium for the diffusion of information across distant communities. The process of generating and diffusing new technologies has been shaped and strengthened by flows of information and capital. Technology has facilitated globalisation and vice versa as technological change is both a factor in globalisation and one of its most important outcomes (Archibugi, et al., 1999). International SI facilitates transmission of best-practice techniques as well as the international flow of goods and services. Because location-specific advantages are important to multinational corporations as they seek market niches with competitive advantages, these corporations have a major influence on NSI. The increasing power of TNCs and the growth of international R&D networks suggest that technological advances may be more properly viewed as products of a global technological system as globalisation is causing the integration of different NSIs that are geographically dispersed and locally specialised (Bartholomew, 1997), (Cantwell, 1999). These developments give rise to debates as to whether increasing technological globalisation signal the convergence of technological capabilities across countries, and the declining role of the nation-state in technological development or whether NSIs maintain their importance in the face of the inter-linked economy in particular in the context of a developing country. In this regard Pavitt (1999) empirically demonstrated that these concerns about the declining importance of national characteristics in an increasingly globalised economy are misplaced as the technology and innovation are not subject to globalisation to the same degree as sales or production (Pavitt, et al., 1999). Even when 'global firms' generate technology outside their home country; their technological profile is influenced by their home nation characteristics.

As already pointed out, a focus on the national nature of SI misses the importance of international aspects of technology flows, and in particular, the uneven nature of technological accumulation among countries. The importance of international interactions with the NSI is particularly significant in the developing context as problems faced by nations attempting to catch up with the technological frontier differ from the problems faced by nations that already are technological leaders (Gerschenkron, 1962), (Freeman, 1995). This will be covered in more detail in the next section.

2.3 NSI Concept in Developing Country Context

While the modern NSI concept was mainly developed in the context of developed countries (Lundvall, 1992), (Nelson, 1993), (Edquist, 1997), the history and development of the concept indicates that it can be useful for analyzing less developed economies. Some of the basic ideas behind the NSI concept go back to Friedrich List (1841) and were developed as the basis for a

German 'catching up' strategy (List, 1841). His 'national systems of production' concept took into account a wide set of national institutions including those engaged in education and training as well as infrastructures such as networks for transportation of people and commodities (Freeman, 1995), (Johnson, et al., 2003). Furthermore, Johnson et al (2003) explain that some of the most important elements of NSI actually came from the literature on development issues in the third world countries.[14]

However, in spite of all these connections between the NSI concept and economic development, it is not directly applicable to the developing context and needs to be adapted to the specific needs of developing countries. Gerschenkron points out that while developed countries may present developing (or backward) countries with possible strategies for development (for example between the middle and the end of 19th century Germany followed the road that England had begun earlier) this generalisation only presents the 'half-truth'. "In several very important respects the development of a 'backward' country may, by the very virtue of its backwardness, tend to differ fundamentally from that of an advanced country" (Gerschenkron, 1962). Gerschenkron shows that different economic development processes and institutional instruments in 'backward' countries result in differences in the speed of development (the rate of industrial growth) as well as the productive and organisational structures of industry. In other words the tendency of applying the NSI model of successful countries to developing countries ignores the fact that other processes of development may be more relevant to the catching up environment of these countries. The process of innovation in developing countries differs from that in developed countries in that the former is more diffusion of external innovations, and a process of often very high-tech and innovative adaptation to local contexts. Therefore the mere application of the Nelson, Rosenberg R&D model misses important developing country characteristics that determine the SI performance. In addition many S&T indicators are not available in developing countries or are misleading. Databases are often absent and generally practical data is limited. Different environments and lack of comparable data in developing countries often give rise to analytical problems in comparative NSI studies.

The application of a narrow definition of NSI to developing countries is particularly problematic (Viotti, 2002), (Johnson, et al., 2003). A narrow NSI concept focuses on the R&D system and on high-tech and science-based innovations. This may be quite adequate in some studies in the developed context, but it does not make much sense in the developing countries, where adequate knowledge infrastructures and IPRs, good networking capabilities and high levels of trust which are the basis for an efficient R&D system are typically missing. Therefore analyzing the details of the R&D system without concern about the connections to, and character of, the rest of the NSI is less

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[14] For example the interdependency between different sectors (Andersen, et al., 2002) and the central SI idea that institutions matter for the performance of the economy (Johnson, 1998), came from the literature on development issues in the third world, such as Hirschman (1958), Stewart (1977), and Myrdal (1968).

relevant in developing context. Viotti (2002), further points out that NSI studies generally put innovation at the core of the processes of technological change, however in the context of developing countries innovation may have a secondary role or possibly no role at all. In his 'national system of learning' concept, he proposes that national capacities to learn and absorb already existing techniques[15] and to generate improvements in the area of acquired techniques are more essential in developing NSI context (Viotti, 2002). Therefore national activities, institutions, and relationships associated with learning, absorption[16], linkage formation, and incremental innovation are the major elements of national systems of technical change in the developing context. NSI studies on newly developed countries confirm Viotti's view that the dynamic engine of late development is technological learning. Looking at successful newly developed countries such as Korea, Taiwan, and Singapore, an important facilitator of technological catching up processes appears to be their intensive learning ability (Intarakumnerd, et al., 2002b).

A further dissimilarity between the developed and developing SI contexts is that the need and opportunity to build on local and traditional knowledge may be relatively bigger in the developing countries than in the developed countries. The existence, nature and value of such knowledge may not be well known to national and international firms and policy makers. Therefore it is essential to underline the importance of tacit knowledge[17]. Local knowledge is easily forgotten when economies are opened up to international competition too quickly and societies are restructured accordingly (Nightingale, et al., 2008). A broad NSI concept helps to see the importance of the development of different kinds of knowledge and the ways they complement each other.

That a broad NSI concept is useful for analyzing less developed economies is also suggested by Johnson et al (2003) which show that integrating three recent tendencies in development thinking into the NSI approach makes it more relevant for development studies: (1) an increasing focus on capabilities rather than resource endowments as the main instruments and values in development, (2) a new focus on knowledge as the perhaps most crucial resource driving development, and (3) a tendency to underline the primary importance of institutions as the 'root causes' of development reducing the importance of all other factors such as geography and policies. This integrated perspective on development is already implied in the broad version of the NSI approach.

As mentioned before, it is potentially misleading to think of NSI at the national level, without considering the relative international technological position of the nation (Nightingale, et al., 2008). Technological leaders start from a position where they have no rivals and levels of technology are low. But in technological catch up context, firms start in a position where competitors exist and

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[15] I.e. the absorption of innovations produced elsewhere.
[16] Absorption is the process of diffusion perceived from the perspective of the recipient of the technique.
[17] I.e. mostly not codified and undocumented local competencies (Nightingale, et al., 2008).

levels of technology are advanced. For example in biotechnology, attempting to follow the US success by adopting the same policies as the US should be avoided, because the US has already succeeded and certain opportunities will no longer be there. As Gerschenkron suggests the policies aimed at 'backward' countries are unlikely to be successful if "...they ignore the basic peculiarities of economic backwardness." In Gerschenkron's view, policies aimed at 'backward countries' should "in addition to general experiences of the past" take into account "the degree of endowment with natural resources, the climatic disabilities, the strength of institutional obstacles to industrialisation, the pattern of foreign trade, and other pertinent factors" but also "the climate of the present century which in so many ways has added new and momentous aspects to the problems concerned" (Gerschenkron, 1962).

However this doesn't mean that firms that are not at the forefront of international technology are at a disadvantage and they may hold some important advantages. Because technologies have already been developed, firms in developing countries can often acquire and use the latest technology at lower costs than firms that developed it, because it is possible to transfer the technology, exploit inward investment and recruit rather than train skilled workforce (Gerschenkron, 1962), (Gerschenkron, 1968). Therefore, it can be argued that uneven development at the international levels can have a major influence on the national institutions that emerge and are successful (Gerschenkron, 1962), (Freeman, 1995). This may be particularly important for understanding Iran's NSI in biotechnology. As Iran is a catching up country compared to, for example, the US, it is likely to have a different SI, and will require different policies than if it is a technological leader. Gerschenkron and Freeman's emphasis on the role of uneven international development and the resulting differences in both starting positions and institutional requirements, provides a useful alternative to the extensive focus on micro-level determinants of innovation that is found in most literature.

2.3.1 Catching Up/Developing Processes in the Context of Developing Countries

In the early stages, industrial development needs basic human capital (literacy and numeracy, with some professional skills); the period needed to absorb simple industrial technologies is short and needs little protection or external support. At this stage, relatively non-selective educational interventions may be appropriate (Lall, 1992). As development progresses, more complex technologies are used and the need for more sophisticated and specialized education and training grows "...to the extent that the education 'market' lacks information on these specialized needs, or under invests in providing facilities of the right kind and quality, there arises the need for selective intervention. Moreover, since there is a serious risk of private under investment in training at the firm level when labour is mobile, human capital development requires measures to induce more investment to support employee training, by firms individually or cooperatively, or by governments where private agents consistently under-invest. These measures maybe functional, applied to all activities, or they may be selective, targeting emerging sectors" (Lall, 1992).

The application of biotechnological techniques to a number of industries such as pharmaceuticals and agriculture has transformed the knowledge base of these industries. By deepening the science base of these industries, the enhanced role of research in relevant innovation has set off "new competitive practices and international regulations of knowledge appropriation, market access and the use of innovation-related policies" (Mytelka, 2006). However traditional views believe that such changes have no effect in developing countries, which were considered as users of product and process technologies from developed countries (Mytelka, 2004). Catching up processes in developing countries are believed to mainly involve imitation and absorption of innovations from abroad (Viotti, 2002), (Kim, 2004). The processes of catching up in developing countries have been traditionally expected to proceed along a pre-established trajectory.[18]

In a knowledge based economy, knowledge creation and appropriation increasingly shape opportunities for learning, for innovation and consequently for growth and development (Mytelka, 2004). In this context the role of developing countries as technology users will result in increasing differences between developed and developing countries, particularly in science-based industries (such as biopharmaceuticals and bioagriculture). Many developing countries lack strong scientific training and a well-established scientific research base. However while universities and research institutes are clearly required in the development of biotechnology SI, focusing the incentive mainly on the provision of researchers and research outputs may not necessarily lead to innovation. The development of capabilities is the outcome of complex interaction of incentive structures with human resources, technological effort and institutional factors (Lall, 1992). From an NSI

[18] For example catching up in biopharmaceutical production in developing context is often a process of incremental capacity building through reformulation of drugs using imported active ingredients. The slow build-up of capabilities in reverse engineering has enabled some firms to emerge as producers of products (Hobday, 1995) (Mytelka, 2004), (Mytelka, 2006). For example in biopharmaceuticals, India started by reproducing a range of drugs developed abroad and slowly, through the mastery of GMP, became supplier of generic drugs to large multinational pharmaceutical firms. Incentive created by a set of public policies made the entry of low-cost Indian producers possible. In addition IP rights were less of an issue in pharmaceutical industry as product patents were not granted in all countries and patent lives were much shorter. With the application of biotechnology, biopharmaceutical industry today makes use of a wider range of science bases that has made laboratory research a central element in the discovery and development of new products and processes. High research costs, continuous innovation, and patent-intensity have added to the difficulties developing countries face in pursuing traditional catching up strategies. The rising costs in the development and marketing of drugs and the emergence of new international trade, investment, and IP rules have resulted in high prices of imported anti-viral drugs (Mytelka, 2006). Strong patents with longer patent lives have made working around a patent or accessing patented knowledge more difficult thus reducing opportunities for local researchers to leverage knowledge gained in research and production to design or discover new drugs.

perspective, transformation from technology consumer to knowledge producer and innovator cannot be achieved without important changes in the traditional institutions and norms of economic agents in developing countries, particularly those related to learning, linkages, long-term investment and innovation (Mytelka, 2000).

The main difference between the NSI concept and traditional production system perspective is that the latter attempts to assess the contribution of S&T to development by emphasising inputs and outputs such as numbers of engineering and science graduates or patents, but not what these graduates did or whether patents were put into use (Mytelka, 2006). From the NSI concept's non-linear perspective on innovation processes, the presence of large number of engineers and scientists in a country does not necessarily result in high levels of S&T outputs or innovative performances, The supply of research by local universities or public sector research institutes does not automatically lead to products in the market, nor does the co-location of knowledge producers and users automatically result in their interaction (Freeman, 1988), (Metcalfe, 1995), (Mytelka, 2006). In the NSI framework the presence of large number of organisations such as universities, research institutes, and firms is far less important than their performance and practices with respect to 'learning, linkage formation and investment' which shape the nature and extensiveness of interactions between the actors of NSI and their tendency to innovate (Mytelka, 2006).

2.3.2 Growth and Structural Change in Developing Countries

Technological innovation continues to be highly concentrated in the developed world; nonetheless some developing countries have been able to undertake original R&D in some high-tech fields such as biotechnology. While in the context of developed countries productivity growth mainly relies on technological innovation, for developing countries growth and development are much less about pushing the technological frontier and much more about changing the structure of production towards activities with higher levels of productivity (UN, 2006). This kind of structural change can be achieved largely by adopting and adapting existing technologies, substituting imports, entering into world markets for manufacturing goods and services, and through rapid accumulation of physical and human capital.

Differences in the nature of the growth process between developed and developing countries remain subject to extensive debate among economists. The more traditional perspective that accumulation of capital is the key to economic development is increasingly being complemented by explicit recognition of the role of external economies in human capital formation and technological innovation, dynamic economies of scale associated with learning by doing, and institutional factors in the growth process. These as well as an increased linking of policies to economic growth performance are among the most important analytical developments in recent decades. However these analytical developments don't provide meaningful criteria for determining which variables found statistically important should be considered the core determinants of economic growth, and fail to grasp the importance of context-specific factors, particularly those associated with institutional development (UN, 2006). In addition it should be taken more into account that the growth impact of policies tends to differ across countries and time periods (the issue of non-linearity) (Gerschenkron, 1962). The focus of such studies has been on the growth process in developed countries, rather than developing economies where underutilization of labour (and other factors of production) and the coexistence of modern and traditional production technologies are common. Economic growth in developing countries is believed to involve structural change towards high-productivity sectors and industrialization plays a key role in that process (Gerschenkron, 1962).

Innovations and sectoral linkages are all factors that influence productivity positively when growth accelerates. As the economy expands, these factors become more important for productivity growth as more resources become available for investment in new technology and for the training of workers. "The development of the modern industrial sector contributes more in dynamic terms to overall output growth, because of its higher productivity growth which results from increasing returns to scale and gains from incremental and radical innovations" (UN, 2006). Learning by doing and experience accumulated during the production process by both entrepreneurs and labourers are also essential for productivity growth and these factors become increasingly important when growth is dynamic. Growth will lead to better utilization of existing resources by improving the structure of employment. Resources are shifted from low- to high-productivity activities (Lall, 1992).

As economies develop, the services sector also gains in importance. Modern service sectors are a source of productivity gain and are essential for the achievement of industrialization. As international trade for services grows, they also offer a new opportunity for export development (UN, 2006).

Dynamic structural change involves more than just growth of industry and modern services. It is about the ability to constantly generate new activities as well as about the capacity of the new activities to absorb surplus labour and to promote the integration of production sectors within the national economy (i.e. to strengthen 'national linkages'). Strengthening national linkages further influences the size of the national market as well as the degree of technological and other spill-over effects that exports and FDI can create for national economic activity and in this way, it influences the extent to which a country is able to benefit from international trade and investment. In this sense, linkage to the world economy can only generate rapid technological progress and contribute to high and sustained growth when it is based on or can help create strong national linkages.

2.3.3 Processes of Technology Transfer

Spin offs from universities and other forms of university-industry linkages, contract transfer, licensing, imitation, spill-over, training and education at the source of technology, research partnerships, multinational companies, FDI and joint ventures are all types of linking to sources of technological knowledge. In order for technology transfer to lead to the process of catching-up in developing countries, improvements in NSI's absorptive capacity and learning ability are necessary (Viotti, 2002), (Mytelka, 2000). Therefore knowledge and technology transfers are greatly influenced by the institutional and organisational structures that support technological learning, development, and innovation.

The context for knowledge transfer extends beyond national frontiers and technological development needs technology imports from advanced countries (Lall, 1992). Gerschenkron (1962) shows that in the context of catching up, 'borrowed' technology is a primary factor in high speed development of a 'backward' country. "...the contingency of large imports of foreign machinery and know-how, and the concomitant opportunities for rapid industrialisation with the passage of time increasingly widened the gulf between economic potentialities and economic actualities in backward countries" (Gerschenkron, 1962 p. 8).

The idea that nations at the technological frontier have a local source of technical change, while nations attempting to catch-up have to import and 'grow' sources of technical change was originally developed by List in his analysis of the 18th century Germany (catching up country) compared to the 18th century England (technological leader) (List, 1841).[19] List demonstrated that for a nation well behind the technological frontier, there has to be a much greater focus on the interdependence of domestic and imported technology. Formal and informal interactions between national and international SIs, in the form of organisations, institutes, and individuals are part of the NSI process of accessing, generating and diffusing new technologies, which is shaped and strengthened by the flows of information and capital across the borders. Thus foreign linkages, such as research partnerships constitute a potentially important addition to knowledge transfer.

The extent of reliance on imported technology and the form that technology imports take, affect the development of 'national technological capabilities' (NTC). "A passive reliance on foreign skills,

[19] List argued that Germany required distinct policies because of its backward technological position. Adam Smith could therefore focus on the role of the division of labour and learning when understanding what policies were appropriate as England went from a trade to manufacturing based economy. For a nation behind the technological frontier, like Germany, there had to be a much greater focus on the interdependence of domestic and imported technology. Thus, List promoted policies that differed substantially from Smith, for example, promoting the protection of emerging and new industries and adopting policies to accelerate the diffusion of existing technology within the nation and from abroad.

knowledge and technology lead to NTC stagnation at a low level[20], while selective inputs of foreign technology into an active domestic process of technology development can lead to dynamic NTC growth" (Lall, 1992 p. 22).

Therefore technology transfer from foreign sources must support local efforts rather than suppress them. Unfavourable effects can arise from a massive foreign presence in the form of multinational corporations that keep their main R&D functions overseas. They can, however, also arise from licensing or use of foreign consultants in ways that do not transfer know how to local firms, and that transfer all the benefits of learning abroad. These sorts of foreign linkages have a more unclear relationship to the dynamics of learning and innovation (Mytelka, 2006). "Licensing can be ... a stimulus to local learning or a drain on it: NTC development requires appropriate information selection and negotiation. Thus specific interventions are needed to promote NTC development, and these will have both selective and functional aspects" (Lall, 1992).

2.4 Gerschenkron Approach to Economic Development

2.4.1 Historic context of Gerschenkron

Gerschenkron's view of economic development fits well with the NSI concept as Gerschenkron's unit of observation is the nation state which historically tends to have common languages, laws, policies, cultures and other institutions. Gerschenkron saw the government and a certain type of bank[21] as particular agents of economic development in countries characterised by economic 'backwardness'. These are part of a more general concept of 'substitutions for prerequisites' of economic development that were missing in 'backward' countries that nevertheless developed. Gerschenkron also viewed 'ideologies favouring economic development' as another agent of economic growth that tends to be stronger in 'backward' countries (Gerschenkron, 1962), (Gerschenkron, 1967). For example during the latter half of the nineteenth century British industrialists were forerunners in industrialization and did not face strong international competition. The technological trend during the 'First Industrial Revolution' was also not so much towards increasing capital-output ratios as that during the 'Second Industrial Revolution' when Germany and Russia began their catching-up efforts. It was thus enough for the British commercial banks to provide industrialists with only operating or working capitals (Gerschenkron, 1962).

However, Germany and Russia required special institutions to mobilize scarce resources in order to implement their catching-up strategies. The mixed banks carried out this role in Germany, a moderately backward country, because the banking sector had already developed to a certain level

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[20] I.e. low rate of growth in national technological capabilities.
[21] German banks, i.e. mixed banks that combined commercial and investment banking, are an important agent of economic development in Gerschenkron's approach (Gerschenkron, 1962).

although the country was far behind Britain in industrialization and per capita income. In Russia, an extremely backward country there was little to expect from the private sector. The Russian state took over the entire role of devising a catching-up strategy and implementing it. A main driver in Gerschenkron's views is competition among nations. If Germany and Russia were content to remain in dependent status, they would not have needed to adopt strategies to catch-up. The strategy was pursued because they wanted and needed to compete with Britain in terms of industrial and military might. In a world where industrialization had come to exist, economic backwardness was also a threat to national security. Gerschenkron's central concept of 'substitutes' was derived from this competition for supremacy and ensuring security among the European powers. The different strategies and institutions adopted by the latecomers were substitutes for the lack of the supposed 'prerequisites' for economic development like capital, technologies, or efficient financial intermediaries, which were present in the forerunners.

Gerschenkron's approach suggests that while a number of countries led the industrialization process, others, lacking a variety of prerequisites for spontaneous industrial development, lagged behind. Their 'relative backwardness' subsequently induced creative tensions which led them towards more rapid economic growth, and to types of institutional innovation which supplied 'substitutes' for the missing developmental prerequisites. Gerschenkron's theory implies that the government can speed up economic development by overcoming the barriers, for example through financial innovation such as a 'mixed bank' or the very power of the state. The Gerschenkronian approach is generally considered to contribute to understanding the rationale for numerous cases of state-led development where state practices can achieve catch-up development such as facilitating access to resources and directing resources suitable to development project.

Gerschenkron's view on 'substitutes for the needed prerequisites' to overcome the 'great stumbling blocks' to economic development differentiated his view from contrasting 'linear' dynamic models (linear conceptions of development), which implied one fixed way to growth (e.g. Rostovian stages[22]). Gerschenkron's methodology suggests that strategies and practices from past cases are only part of the problem, the other part depends to a large degree on the social structures in any given society on the 'eve of their catch-up attempt', and how they influence processes of institutional innovation. In contrast to Rostow, Gerschenkron argued that it is essential to look at the differences in stages between individual countries and to analyse in detail the dynamic processes

[22] Ideas of stages of economic growth were made popular by Rostow. Stages analysis assumed a fairly linear, uniform path of development and that 'prerequisites' had to emerge before a society would move from one stage to another (Rostow, 1960). The opposite extreme to Rostow's stages of growth is the emphasis on the uniqueness of each case of economic development with no lessons to be learned from studying other cases (Sylla, et al., 1991). Gerschenkron's approach is somewhere in between the above two views, emphasising many uniformities in the economic development across societies but also demonstrating many deviations from the prerequisites of economic development (Gerschenkron, 1962), (Gerschenkron, 1967).

of change. He focused on the role of different institutions (e.g. the function of banks in central European industrialization and the importance of the Ministry of Finance in Russian industrialization) in promoting industrialization. Regarding general prerequisites for industrial growth (e.g. the provision of social overhead capital and a favourable 'value system'), through his own research on latecomer development, Gerschenkron showed that these prerequisites were sometimes not present or only present to a limited extent in latecomer economies which had gone on to develop. Indeed, in some cases the great 'spurt' occurred without them.

Gerschenkron derived a number of hypotheses from his concept of relative backwardness about the patterns of European industrialisation which are generalised here in six points. The more backward an economy is at the start of economic growth in comparison with the economies of more advanced countries at the same point in time: (1) the greater will be the discontinuity with previous economic experience, (2) the more rapid the 'great spurt' in economic growth which enables catching up; (3) the greater the role of industrial banking and the government; (4) the greater will be the reliance on technological borrowing and financial assistance from aboard; (5) the harsher the associated repression of living standards and the agricultural sector; and (6) the more influential the political regime and modernizing nationalism (Sylla, et al., 1991), (Fishlow, 2001).

Gerschenkron argued that there are no automatic stages of development and that countries cannot pass through the same stages of development that others have passed through before them, precisely because others had passed through them. As a result, barriers to entry and opportunities for development have changed. Each latecomer economy therefore faces a very different external environment in terms of markets, technologies and opportunities for growth.

Gerschenkron's view was that latecomers had to plot their own distinctive path of development. These paths had to take account of how other earlier developers had progressed, including the markets and technologies they had created and influenced. He also argued that the starting position of the latecomer economy (or stage of backwardness as Gerschenkron called it) had to be taken into account. In particular, his research showed how the particular conditions of backwardness shaped the nature, depth and path of state intervention with respect to enterprise, technology, institution building, resource mobilization etc.

2.4.2 Operationalisation of the Gerschenkron ideas

The Gerschenkron idea central to this study is that the government can speed up economic development by providing 'substitutes' for the missing prerequisites of development. The views of Gerschenkron have important implications for innovation and development. They imply that development is an active process involving economic action and reaction, as well as heavy investments in learning, technology and the institutions of development. This type of purposeful strategy contrasts with market-led processes or passive approaches to development. Hoping simply to 'pass through' the stages of development that earlier developers had followed was highly unlikely to bring about development. Indeed, Gerschenkron emphasized the importance of variety and difference in the development paths of nations. In Gerschekron's model, new strategies in relation to government policy, development path, technology acquisition etc. are a central part of economic development. Only by choosing and successfully following distinctive paths (and therefore stages) of development can latecomer nations meet the new circumstances presented to them by the actions of earlier developers. While he also recognized that any development path followed will not be entirely new, it will have to embody at least some innovative features to cope with the new environment (Hobday, 2003). In this way Gerschenkron has linked innovation to the development process in general. A number of substitution methods are outlined in table 2.4.

Table 2.4 – Potential Substitution Methods

Prerequisites in market-led economies	Potential substitution in directed economies
Financial Capital	Government-funded capital FDI Inflows/TNC subsidiaries
Knowledge Capital	Government research laboratories Government capital, fund, and consultancy services (access to local banks or alternatives) Link to foreign organisations (knowledge/capital)
Strong entrepreneurial and managerial capacity	State support for start-up creation/businesses
Large internal markets/markets via FDI/trade	Export-led growth Government support for local brands

In the case of Germany, Belgium, and mainly Russia, the technology was at hand, but the capital was absent. In Gerschenkron's view, the prerequisite was capital (bank), and substitutes included government-funded capital (as in Soviet industrialization under Stalin) or FDI inflows (Gerschenkron, 1962). The application of Gerschenkron's idea to the information age in a country like Iran is more about the knowledge or the research base where the 'great stumbling blocks' seem to be more knowledge capital rather than physical capital, so the key question is where are the substitutes going to come from? In a Gerschenkronian sense the industry has 3 choices to overcome the gap in knowledge base:

(i) Government research laboratories
(ii) Government capital, fund, and consultancy services (access to local banks or alternatives)
(iii) Link to foreign organisations (knowledge/capital)

Gerschenkron's emphasis on differential development in response to different initial conditions suggests that the state should be allowed to remain strong and active in economy matters to promote successful industrialization. Gerschenkron sees in the government of a nation a potential agent of economic development which is essential in conditions where markets fail to promote economic development. Gerschenkron suggests that in situations of backwardness where market share is absent or insufficient, the net economic impact of direct government intervention is likely to be greater than where markets are well-developed (Gerschenkron, 1962).

Gerschenkron's concept of economic backwardness is too broad to be fitted into standard procedures of empirical testing.[23] It essentially means the stage of economic development that a country has reached. Scholars have for example used GNP per capita to rank countries relative backwardness. Socio-economic indicators are rough measures of the differences in the degree of backwardness and should be used with great caution in comparative analysis. Use of different sources, indicators and methodologies may arrive at quite dissimilar results. In addition Gerschenkron's 'index of economic output' is only statistical and doesn't demonstrate the causality (Sylla, et al., 1991).

In a Gerschenkronian sense evaluation of Iran's economic condition provides an assessment of its 'stage of development' or its 'backwardness'. However, economic performance indicators such as GDP, GERD or number of patents, provide a narrow understanding of NSI. In a developing country context, a wider set of indicators is appropriate, including, in particular, information on the education system and S&T capability of the country (Viotti, 2002), (Johnson, et al., 2003). Iran's macroeconomic setting, S&T infrastructure, and innovation policy framework are presented in chapter 4 (based on availability) including some comparisons of selected countries. However these statistical indicators don't demonstrate the causality (Sylla, et al., 1991).

The study tries to overcome the methodological difficulties in 'measuring the relative backwardness of a country' as there is little guide on how to judge the relative backwardness of countries in particular fields, through a qualitative analysis of Iran's specific NSI characteristics including economic and S&T structures (with comparison to selected countries) and the study of knowledge, supply, demand, and financial components of Iran's biotechnology NSI through identifying actors, institutions and their linkages.

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[23] "Gerschenkron's broad definition of backwardness was meant to supply an explanatory variable in the literal meaning of the word. A backward country not only was less endowed with such factors of production as skilled labour, up-to-date technology, infrastructure and financial capital but was likely to be burdened with a ruling class whose very interests would be at least partially jeopardized by successful industrialisation. Such a country was likely to encounter many obstacles on its way to industrial progress. Moreover, the majority of its ruling class would not perceive the advantages of such progress. In these circumstances market forces alone would be rather slow in generating conditions of rapid economic growth. A short-cut along the road of industrialisation could be taken if those among the ruling class who could see the advantages of taking the road could also get hold of a tool capable of surmounting the major obstacle to industrialisation. Those tools might be a financial innovation such as the 'mixed bank' or the very power of the state, according to the country's degree of backwardness" (Sylla, et al., 1991).

The operationalisation of the insights of Gerschenkron necessitates that the progress of Iran's biotechnology SIs be interpreted as a pattern of substitution of missing prerequisites, in line with Gerschenkron's view of European latecomer industrialization. More broadly, the progress of Iran's NSI should not be viewed as repetitions of earlier industrialization experiences as they involve significant deviations from the latter, usually entailing distinctive institutional, technological, and development. The thesis tries to interpret Iran's biotechnology development in the light of Gerschenkron's argument "that European history should be seen as a pattern of substitution governed by the prevailing—and changing—degree of backwardness" (Gerschenkron, 1962 p. 359). By examining the biopharmaceutical and bioagricultural sectors of Iran, the thesis assesses the extent to which the development of Iran's biotechnology sector can be viewed as a pattern of substitution for prerequisites of economic development. Chapter 3 (Methodology) addresses factors identified as significant for innovation in the conceptual framework of this study (which parts make up the system) and how the conceptual framework will be useful for opening up parts of the Iranian NSI for analysis the effect of state's substitution.

2.5 Summary

In recent years the NSI concept has gained popularity in developing countries providing an analytical tool as well as a tool to regulate policy. It is in "contextualizing the innovation process in terms of policies and institutions" that the NSI approach makes its most important contribution to knowledge and to policy-making (Mytelka, 2006). NSI frameworks emphasise the importance diffusion of existing technology, the importance of learning and problem solving, the role of scientific research in training individuals rather than generating technology, the role of public procurement, the importance of the service sector and the limited role of high-tech innovations in the economy (Nightingale, et al., 2008). The analytical framework underlying this study employs a combination of the Nelson (1993), Lundvall (1992) and Viotti's (2002) NSI approaches, emphasising the impact of national technology policies on the innovative activity of firms, as well as taking into account the interaction of firms with various elements in the system, for instance with the higher education sector, and the national capacities to learn and absorb already existing technologies and to improve the acquired techniques.

Further, a Gerschenkronian approach to the NSI concept is aimed at making the framework less of a US based market-led economy model and take more into account different processes of growth and development based on differing initial socio-economic conditions, such as the state led economy of Iran.[24] The central Gerschenkronian idea is the role of state in substituting the missing prerequisites for economic development. This approach investigates the role of the Iranian

[24] A detailed presentation of Iran's economic characteristics is available in chapter 4.

government in facilitating technological catching up in the biopharmaceutical and bioagricultural sectors. The application of Gerschenkron to the information age is more about the knowledge or the research base where the great stumbling blocks seem to be more knowledge capital rather than physical capital, so the key question is where are the substitutes going to come from? Iran is making efforts to move from being a major importer of high-tech products such as modern biopharmaceuticals to producing them locally; therefore access to technological knowledge is an important focus of this study. How does Iran subsidise knowledge or research?

It is particularly important to stress the significance of international interactions with the NSI as biotechnology is a global system, as well as Iran is a developing country and problems faced by nations attempting to catch up with the technological frontier differ from the problems faced by nations that already are technological leaders (Gerschenkron, 1962), (Freeman, 2002). Therefore nations attempting to catch up with the technological frontier cannot simply copy the international leaders and adopt similar institutional set-ups. The role and importance of foreign actors in Iran's NSI such as foreign technology transfers and other interactions with foreign U/RIs as well as industry are emphasised in this study to overcome the concern that a national focus on SI misses the importance of international aspects of technology flows. The substantial differences in the nature of innovation across sectors are also taken into account by complementing the NSI framework with the SSI, investigating sectoral characteristics of the biotechnology subsectors of Iran. Developing countries have often limited records available on individual sectors. A qualitative approach to the developing NSI is assumed to complement scattered and unreliable quantitative records and shed light on causality of the differing NSI performances in Iran's biopharmaceutical and bioagricultural sectors. The study makes extensive use of semi-structured interviews as well as documentation to assess the actual unfolding of events in the biotechnology subsectors of Iran. Interview questions are designed to look at systemic linkages and investigate the role of government in supporting and facilitating access to technological knowledge. Chapter 3 outlines the methodology of this study in more detail.

Chapter 3 Methodology

3.1 Introduction

The research design and methodology of the study are presented in this chapter. The method of data collection (both background and primary data) is outlined and the make-up of the interviewee sample as well as the structure and focus of the interview questions are described. The chapter also presents limitations of gathering data in Iran and problems that arose during the project.

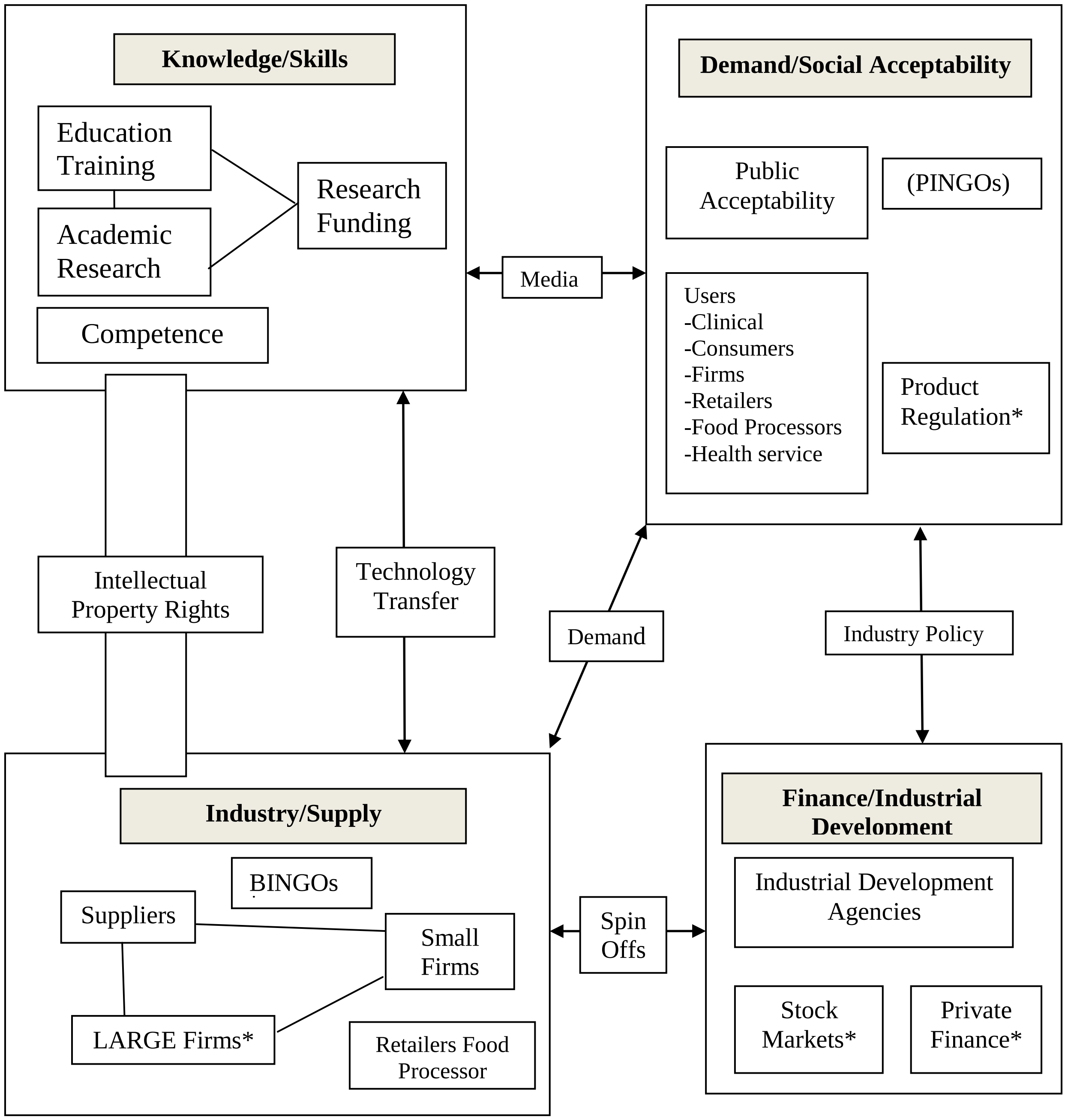
3.2 Operatanalisation of the NSI Framework

Gerschenkron's substitution method suggests that government substitutions of needed prerequisites may be able to explain the performance of the biotechnology sector in a country like Iran. For example how does the Iranian government substitute the knowledge capital required in the development of science-based sectors? For this purpose a comprehensive NSI framework specific to science-based sectors is needed. Such a framework includes significant factors for innovation. This study will then investigate these factors and/or their substitutions in the biotechnology sector of Iran.

Such a comprehensive NSI framework specific to science-based sectors is provided by the EBIS study (Senker, et al., 2001). This framework, presented in figure 3.1, outlines factors identified as significant for innovation, the four main networks within which institutions and organizations are embedded (knowledge and skills, industry and supply, demand and social acceptability, and finance and indusial development), and their links.

The characteristics of the knowledge and skills network is studied through the review of the wider S&T capacity, higher education and research and technological infrastructure in Iran's industrial sector (chapter 4). This is complemented with the study of sectoral characteristics and selected product journeys presented in chapters 5 & 6, to see how Iran substitutes for the required knowledge capital. From the supply side perspective, the study looks at organizations active in promoting research and educational activities as well as in the promotion of innovation-based high-tech industries in the biotechnology sector. Processes of technology transfer and IP issues are important elements of science-based sectors affecting the linkages of knowledge network to the industry. The demand Side looks at government policies and their impact on innovation in the biotechnology industry. Finance and industrial development in a country like Iran is believed to be mainly through government capital, fund, and consultancy services (access to local banks or alternatives). These will be investigated in the empirical chapters.

Figure 3.1 Networks of Key Factors influencing innovation (Senker, et al., 2001 p. 20)



* International Influence
BINGOs = Business Interest non-governmental Organization
PINGOs = Public Interest non-government Organizations

3.3 Case Study Methodology

A 'case methodology' is implemented as the main research strategy of the study. The 'type of primary evidence' used in this case methodology is qualitative data and the 'type of data collection method' is interviews and documentation. Interviews were arranged with 42 key contacts (including key researchers, entrepreneurs, consultants, etc. with strong linkages to different elements of the NSI) at 38 organisations (U/RIs, GSO's and firms).

The case- methodology approach has no operational formula and different approaches are applied in different studies. This lack of specific set of guidelines has opened it up to criticism (Miles, 1979). Yin (1981) however shows that case methodology can be conducted systematically (Yin, 1981). Also Ragin and Sonnett (2004) argue that comparative case-oriented work has its own logic and rigor. "Because it is explicitly 'intersectional', the examination of different combinations of conditions is essential to this type of research. This type of logic and rigor is lacking in most quantitative research, where matching cases undermines degrees of freedom and statistical power" (Ragin, et al., 2004).

As a research strategy, the distinguishing characteristic of the case study is that it attempts to examine a contemporary phenomenon in its real life context, especially when the boundaries between phenomenon and context are not clearly evident (Yin, 1981).[25] The case study strategy is implemented to attempt to explain a phenomenon through an accurate interpretation of the facts of the case, some consideration of alternative explanations of these facts and a conclusion based on the single explanation that appears most fitting with the facts. There are no fixed recipes for building or comparing explanations. Yin compares the process of building an explanation to doing detective work where a detective must construct an explanation for a crime:

> Presented with the scene of crime, its description, and possible reports from eye-witnesses, the detective must constantly make decisions regarding the relevance of various data. Some facts of the case will turn out to be unrelated to the crime; other clues must be recognised as such and pursued vigorously. The adequate explanation for the crime then becomes a plausible rendition of a motive, opportunity, and method that more fully accounts for the facts than do alternative explanations (Yin, 1981).

The biopharmaceutical and bioagricultural SIs studied here are in the same national setting making the case study strategy a multiple case analyses within a single national environment. A 'within' case

[25] For example case study differs from experiments in that it does not deliberately dissociate a phenomenon from its context and it differs from history in that it is not limited to a phenomenon of the past where relevant informants of the past may be unavailable for interview and relevant events unavailable for direct observation (Yin, 1981).

analysis of the individual sectors provides a rich familiarity with each case which facilitates the 'between' case analysis where the findings of the two cases are combined and compared.

The interview data on factors potentially affecting biotechnology innovation activities and inter-agent linkages (in particular the role and effect of government on innovation activities at public and private organisations) are presented in chapters 5 & 6 in support of the secondary data. Particular pieces of evidence are cited as the study shifts from data collection to within-case analysis and finally to concluding results and policy implications (presented in chapter 7). The product cases for study are selected to represent the main issues of the biotechnology SI. These cases are chosen in consultation with experts in the IPITT as the most representative of the issues that innovating firms have to face in Iran's biotechnology SI.

Table 3.1 List of Product journey studies in the biotechnology subsectors of Iran

Product	External support	Evidence of Success
Cinnovex	Bioengineering and production up to the pilot scale was optimized at Fraunhofer IGB in Germany	Major revenue generation for Cinnagen, established in the Iranian market and being imported to 22 countries worldwide
Buserelin	Developed by Cinnagen with Russian consultation at the IPI	Cinnagen's second most successful product in terms of sale and revenues
Cellcept	Developed by Roche in Switzerland and transferred to Zahravi for production	Zahravi's highest source of revenues
Hepatitis B vaccine	Technology transfer from Cuba's ICGB to IPI	Major import substitution, made the vaccination of a large proportion of Iran's children possible
Imod and Angipars	Developed in collaboration with Russians partly in Moscow (bioengineering) and partly in Iran (pilot scale and testing)	Following regulatory approval were copied and replaced by cheap imitations affecting the sale and revenue for the company
GM rice	Fully developed by ABRII's scientists	Achieved regulatory approval in the previous government and was released to a limited number of farmersin 2004, but was put on hold after 2005 change in the government and in still awaiting licence for full commercialisation
Barvar II Phosphate Bio-fertiliser	Fully done at Iran's public U/RIs and transferred to industry	Main source of sales and revenue for ZFS company, exported to over two countries in the region.
GMO Detection Services	No external support, Connercialise at a spin-off from NIGEB	Government is the main client of this service making the service successful and a source of growth for the company, but company needs to enter new markets to sustain growth
Micro-propagated Date Palm Plantlets	Government mediated technology transfer from UK firm	One of the largest producers in the world

Cinnovex and GM rice are the main representative cases of the biopharmaceutical and bioagricultural sub-sectors respectively. Cinnagen is considered Iran's most successful private biotechnology firms in terms of revenues and export success. Cinnovex as well as Cinnagen's other prominent product Buserelin are presented to demonstrate sources of technological knowledge in Iran's biopharmaceutical innovation activities, the characteristics of the external factors to innovating firms such as the system of approval for biopharmaceuticals in Iran and marketing issues and the governments substitutions to overcome these.

Cellcept is also an interesting case of import substitution as it has significantly reduced the cost of drug and once again highlights the main mode of access to technologies in Iran. Imod and Angipars are particularly interesting as they are original drugs based on native herbs and reveal interesting issues on the IP system of Iran.

Barvar II bio-fertiliser is one of the few modern bioagricultural products commercialised in the private sector and the innovator is a central figure in Iran's bio-agricultural developments with strong links to academia, industry, and NGOs. It is representative of the bio-agricultural products in Iran's market and shows the mains sources of technological knowledge in the sector. The GMO detection services provided at GAP is also included as it demonstrates common problems in Iran's bioagricultural SI and the innovation is a central figure at NIGEB. Finally Micro-propagated date palms are also covered in the case studies as these are produced by Iran's larges bioagricultural firm which is also one the frontrunners in this sector in globally. This product represents the activity of most firms involved in non-GM crops and also shows the important of government mediated technology transfer.

The effects of IPR (an important element of knowledge based SI) are investigated by asking researchers and entrepreneurs how Iran's current IPR affects their R&D and innovation activities at both public and private biotechnology organisations.

Data on private SMEs are largely missing from the existing reports and documents. To address this gap, data from a sample of eight biopharmaceutical and six bioagricultural firms are presented in chapters 7 and 8, studying the current position of SMEs within Iran's biotechnology SI, the operational environment of the firms, the role of other actors in their innovative activities (systemic linkages) and reasons for systemic failures.

The second part of the interview questions addressed the type, importance, and success of inter-agent linkages studying the role of 'other actors' (both national and international) towards innovation activities at U/RIs and firms. In particular, the role of government in the biotechnology development at public and private organisations is investigated. Analysis of inter-agent linkages are also used to outline sources of knowledge and technology and the importance and success of different forms of technology transfers.

A pattern emerges from the within and between case analyses, revealing sources of success and failure in biopharmaceutical and bioagricultural development of the country. All data including field notes, quotes, and other field data are used to improve the quality of the case study.

3.4 Methods of Data Collection

Background data (qualitative and quantitative) were collected through extensive use of national and international publications, reports, internet (websites of ministries, firms, scientific societies, universities, research institutes, and GSOs) as far as available. In addition to national reports, documents, and websites, main sources of macroeconomic indicators in the study are the UNDP Human development report 2007/2008 and UNDP 'build your own tables' facility[26], the UNCTAD STIP report 2005, the World Development Indicators 2009 from the World Bank reports 2009/2010, ECO 2006, WIPO 2009.

Data on SMEs, an essential element of any NSI, is largely missing from the available material. Therefore interviews are the main source of qualitative data on biotech activities of SMEs in Iran and the role and effect of other actors in the system towards their innovation activities.

Initially internet was used to identify actors of the Iranian biotechnology SI and obtain an overview of their roles and contact details. However there were limitations as many of the organisations do not have up to date websites.

Following a pilot study in summer 2007, including visits to the biotechnology departments of U/RI's, consultation with the experts at IPITT and members of the Sharif University of Technology's department of Management and Economy, prominent locally produced biotechnology products (in terms of R&D intensity, sales and profit, and novelty)[27] were identified to be Cinnovex (Iran's prominent IFN-β based MS treatment medicine), other IFNs (IFN-α, IFN-γ, pegylated IFN), hepatitis B vaccine, erythropoietin[28], erythromycin, IMOD, Angi-Pars, Cellcept, Barvar-II bio-fertilizer, and Iran's first GM crop (the stem borer resistant Bt rice). The focus on these products pointed towards major actors involved in innovation in the two sectors.[29]

Out of the 81 firms in Iran involved in biotechnology activities, 30 are in the private sector. The product focus led to identification of Cinnagen, Shem enzyme, Pars Roos, Pouyesh Darou,

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[26] UNDP build your own tables facility is available at http://hdrstats.undp.org/en/buildtables/

[27] An explanation of R&D and innovation activities in the context of this study should be provided here. R&D defines "creative work undertaken on a systematic basis in order to increase the stock of knowledge, including knowledge of man, culture and society, and the use of this stock of knowledge to devise new applications" (OECD, 2002 p. 81). R&D here includes basic research, applied research and experimental developments. Innovation defines new or significantly improved products and technological processes. Innovation here does not mean something entirely new to the world, but new to a given firm or country, the ability to understand and master a new technology and adapt it and apply it to the specific national or sectoral context. R&D and innovation activities are studied at public (mainly research institutes) and private organisations (mainly SMEs).

[28] Effective in increasing the production of red blood cells and lowering the mortality rate among cancer and chronic renal failure patients

[29] While a detailed list of interviewees and their roles were prepared and presented to the research supervisors and examiners, the identity of these interviewees are protected in this publication.

Rastadaroo, Zahravi, Shafaye Sari, Zist Fanaveare Sabz, and Rana Agro Industrial Corporation were short listed for interview (not all however cooperated). Further the new spinoffs from NIGEB in the biotechnology incubator (17 companies) were found to be very interesting in terms of the challenges they faced with regards to survival, growth and expansion stages and were also approached for interviews. HTIC, LIDCO, and biotechnology incubator were identified as important GSO's. Details of the firms who agreed to take part in the interviews is presented in tables3.2. The biopharmaceutical firms in the interview sample consist of 6 established firms (older than five years) and 2 start-ups (younger than five years). The bioagricultural firms in the sample include 2 established firms and 4 start-ups.

Table 3.2 Biopharmaceutical firms' details

Biopharmaceutical Firms				
	Sector	**Year of establishment**	**Spinoff**	**Size of firm**
Biopharma Firm 1	Private	1994	No	Medium
Biopharma Firm 2	Private	1992	Yes, from TUMS	Medium
Biopharma Firm 3	Private	2001	No	Medium
Biopharma Firm 4	Private	1986	No	Large (250)
Biopharma Firm 5	Private	1996	No	Medium
Biopharma Firm 6	Private	1994	No	Medium
Biopharma Firm 7	Private	2007	Yes, from NIGEB	Small
Biopharma Firm 8	Private	2005	Yes, from NIGEB	Small
Bioagricultural Firms				
Bioagri Firm 1	Private	1993	No	Medium
Bioagri Firm 2	Private	2003	Yes	Medium
Bioagri Firm 3	Private	2005	Yes	Small
Bioagri Firm 4	Private	2007	Yes	Small
Bioagri Firm 5	Private	2007	Yes	Small
Bioagri Firm 6	Private	2007	Yes	Small
Bioagri Firm 7 [30]	Private	2006	Yes	Small
Bioagri Firm 8	Private	2006	Yes	Small

While initially questionnaires were intended to be the main method of primary data collection, preliminary attempts to contact interviewees during a five week pilot fieldwork in June/July 2007 revealed that interviews had many advantages over questionnaires. Participants did not show much interest in completing questionnaires and would rather talk. Therefore semi structured interviews were chosen as the most suitable method of primary data collection. Parallel questionnaires which were previously developed for firms, U/RIs, and GSOs were used as an 'interview guide'. This guide included the list of questions and topics (NSI headings) that needed to be covered during the conversation, and the particular order in which questions needed to be asked. While following the

[30] Interviews were also carried out at bioagri firm 7 which designs and produces laboratory and semi-industrial fermenters and bioagri firm 8 which designs and produces Fitotron plant growth chambers. The interviews provided interesting information and are therefore included in the list.

guide, semi-structured interviews allow additional questions to be added wherever appropriate to suit the experience and role of the interviewee, and they allow interviewees the freedom to express their views in their own terms. Semi-structured interviewing is best suited when there is only one chance to interview someone (Cohen, et al., 2006). Interviews were recorded unless requested otherwise by the interviewee, where notes were taken instead. The recorded material was then transcribed for presentation and assessment. Interviewees also presented letters, documents, internal reports and news articles on major events in the biotechnology sector's recent development. Interviews were carried out over a 26 weeks fieldwork period in Iran from 14th March 2008 to 12th September 2008. Many of the interviewees were not on the initial list of contacts, but were approached as a result of snowball effect causing the number of interviews to increase to 42.

The contribution of interviewees varied according to their role, experience and degree of cooperation. Eleven of the interviewees had experience in the bioagricultural sector, 21 in the biopharmaceutical sector, 6 in both sectors, and 4 in other biotechnology subsectors (bio-environment, bio-industry and bio-equipment). Interviewees were active at 12 U/RIs, 16 firms, 7 GSOs, and 3 NGOs (table 3.3).

Table 3.3 Number of interviewed organisations/institutes

	Biopharmaceutical sector	Bioagricultural sector	Both Sector	Other Sectors	Total
U/RI	7*	2	2	1	12
Firms	8	6	-	2	16
GSOs	2	2	3	-	7
Other (NGOs)	-	-	3	-	3
Total	17	10	8	3	38

*SBU and SBUMS are considered separate universities

3.5 Structure and Focus of the Interview Questions

Interviews aimed at investigating U/RIs, firms, and GSOs' biotechnology related activities (e.g. R&D, innovation, technology transfer, and IP related activities). The central questions were on the role of other actors (e.g. government, national and foreign U/RIs, industry, and foreign companies and consultants) in the innovation activities of U/RIs and firms.

To identify barriers and obstacles to biotechnology innovation in Iran, questions to U/RIs addressed issues of access to technological knowledge, government policies and regulation, human resources, funding, technology transfer, and any other issues interviewees would like to mention.

Similarly firms were asked on access to technological knowledge, financing, marketing, partnerships, skills, sources of business advice, government policies and regulations, competition, taxes, market acceptance of new products or technologies, and IP issues. In addition, to address firm's operational environment, questions were asked on firms' ownership, management, human resources, business strategy, and external factors.

GSOs were asked on human resources promotion and other support activities and obstacles to the Iranian biotechnology development.

The questions were prepared in English and translated into Farsi. Table 3.4 presents an overview of the topics addressed at the interviews. Interview questions are available in detail in Appendix 1.

Table 3.4 List of NSI factors to study through secondary and primary data

Key topics	U/RI	Firms	GSOs	NGOs
Biotech related activities	R&D Innovation Technology transfer IP	R&D, Innovation Technology transfer IP	Support for biotech related research and innovation at U/RI and firm level	Support for biotech related research and innovation at U/RI and firm level
Firms' operational environment		Ownership Management Human resources Business strategy External factors		
Role of other actors in innovation activities	Role of government Role of other national U/RI Role of foreign U/RIs Role of industry Role of foreign companies and consultants Role of other actors not mentioned above	Role of government Role of national U/RI Role of foreign U/RIs Role of foreign companies and consultants Role of other actors not mentioned above	Interactions with foreign organisations/ companies/ consultants to promote biotech in Iran,	Interactions with foreign organisations/ companies/ consultants to promote biotech in Iran
Sources of success in biotech SI	Main strengths	Main strengths	Main strengths	Main strengths
Barriers and obstacles to biotech SI	Access to technological knowledge Government policies and regulation Human resources Funding Technology transfer Other (biosafety)	Access to technological knowledge Financing Marketing Partnerships Skills Business advice Government policies and regulations Competition Taxes Market acceptance of new products IP issues (Other)	Human resources promotion activities Obstacles to the Iranian biotech innovation	Human resources promotion activities Obstacles to the Iranian biotech innovation

3.6 Methods of Data Presentation and Assessment

In a Gerschenkronian sense evaluation of Iran's economic condition provides an assessment of its 'stage of development' or its 'backwardness'. Standard economic performance indicators (e.g. GDP, GERD, number of patents) are used together with the wider set of indicators, in particular, information on the education system and S&T capability of the country to avoid a narrow interpretation of NSI (Viotti, 2002), (Johnson, et al., 2003). Iran's macroeconomic setting, S&T infrastructure, and innovation policy framework are presented in chapter 4 including some comparisons of selected countries. Interview data is used to support secondary sources and fill the gaps. The interview data is also used to provide a number of product innovation journeys to illustrate how parts of the innovation system perform. These help to identify sources of technological knowledge, role of national government and institutions, and other factors leading to success/failure of biotechnology innovation in Iran.

The data are analysed to assess the performance of the different elements of the NSI: knowledge and skills, industry and supply, demand and social acceptability, and finance and indusial development, their links, and the effect of government substitutions for knowledge capital, financial capital, strong entrepreneurial and managerial capacity, and access to large markets via FDI/Trade.

3.7 Limitations of Gathering Data in Iran

A major limitation in gathering data in the political environment of Iran was the interviewees' cautious approach to providing information. Interviewees were reluctant to talk about issues related to the government and often chose their words carefully, in particular when the recorder was on. In addition interviewees with strong ties to the government were wary of providing information to a student of a British institute therefore formal introductions through influential personalities were necessary. Also some firms who agreed to take part in the study did not wish to give detailed information on any particular product, but were happy to answer questions in general.

Another challenge was to gather data on Iran's economic environment. Detailed and reliable sources of quantitative data such as data banks are limited/non-existent. The available STI data are often in an unpublished form, scattered and not up-to-date. In other cases the figures provided are contradicting. For example the Iranian government had specified in its 4th EDP that by 2008, 2% of the GDP would be allocated to R&D. However there are many different figures as to how much has been actually spent. While all effort has been put into gathering trustworthy quantitative economic data from official reports and sources for the background chapters, the possibility remains that official figures paint a rosier picture than the reality (e.g. unemployment and inflation figures), none the less these figures demonstrate the trend of the economic development of Iran.

3.8 Problems Arising During the Project

This project was originally based on Iran's commercialisation of the world's first GM rice in 2004. However, during the course of this project, Iran's GM crop production and genetic engineering activities slowed down while the biopharmaceutical sector marketed over ten products using modern biotechnology. As a result, the focus of the project had to be adjusted to investigate why the bioagricultural sector failed to fully commercialise the GM rice, while the biopharmaceutical sector which initially had been more in line with developing country expectations, has started to market locally produced modern biopharmaceuticals.

Conducting a fieldwork in Iran proved very challenging. Initial attempts to contact key interviewees through email and telephone were unsuccessful and formal introduction proved to be the only way to arrange interviews with key individuals at U/RIs and GSOs. Arranging interviews at private biotechnology firms was equally difficult due to trust issues. The breakthrough came when the innovator of the Iranian GM rice agreed to a series of interviews on the details of the case. Further opportunities arose as a result of introduction to head of the Biotechnology Society of Iran who proved very knowledgeable and influential in the sector. Subsequent formal introductions and extensive networking efforts led to a snowball effect resulting in 42 interviews.

3.9 Summary

A comprehensive NSI framework specific to science-based sectors is implemented including significant factors for innovation, four main networks within which institutions and organizations are embedded (knowledge and skills, industry and supply, demand and social acceptability, and finance and indusial development), and their links (Senker, et al., 2001). This study will then investigate the performance of these factors and their substitutions in the biotechnology sector of Iran.

The characteristics of the knowledge and skills network is studied through the review of the wider S&T capacity, higher education and research and technological infrastructure in Iran's industrial sector. This is complemented with the study of sectoral characteristics and selected product journeys, to see how Iran substitutes for the required knowledge capital. From the supply side perspective, the study looks at organizations active in promoting research and educational activities as well as in the promotion of innovation-based high-tech industries in the biotechnology sector. Processes of technology transfer and IP issues are important elements of science-based sectors affecting the linkages of knowledge network to the industry. The demand Side looks at government policies and their impact on innovation in the biotechnology industry. Finance and industrial development in a country like Iran is believed to be mainly through government capital, fund, and consultancy services (access to local banks or alternatives). This will investigated in the empirical chapters.

In a Gerschenkronian sense evaluation of Iran's economic condition provides an assessment of its 'stage of development' or its 'backwardness'. Standard economic performance indicators (e.g. GDP, GERD, number of patents) are used together with the wider set of indicators, in particular, information on the education system and S&T capability of the country to avoid a narrow interpretation of NSI (Viotti, 2002), (Johnson, et al., 2003). Iran's macroeconomic setting, S&T infrastructure, and innovation policy framework are presented in chapter 4 including some comparisons of selected countries. Interview data is used to support secondary sources and fill the gaps. Sector specific data and a number of product innovation journeys are presented in chapters 5 & 6 to illustrate how parts of the innovation system perform. These help to identify sources of technological knowledge, role of national government and institutions, and other factors leading to success/failure of biotechnology innovation in Iran, and the effect of government substitutions for knowledge capital, financial capital, strong entrepreneurial and managerial capacity, and access to large markets via FDI/Trade.

The main limitation in gathering data in the political environment of Iran was the interviewees' reluctance to provide information. Formal introductions through influential individuals were the only way to arrange interviews and gain the interviewees trust. The interview strategy was to keep any influence on the interviewees' responses to a minimum. Interviewees were promised anonymity, censorship, and confidentiality on specific parts of the interview as per their requests.

Chapter 4 Iran's National System of Innovation

4.1 Introduction

NSI framework implies that to successfully transform an economy to compete in technology- and knowledge- intensive sectors such as biotechnology, countries need to successfully create and strengthen the network of economic agents whose activities and interactions bring new products, new processes and new forms of organization into economic use. The key agents in this network include firms, U/RIs, the government and other support organizations (e.g. industry associations, consumer groups, business support and financial organisations). Continuous interaction between these actors and the learning opportunities created as a result are critical for innovation.

This chapter outlines Iran's economic setting, S&T infrastructure, and the policy framework that underlies its NSI within which firms and sectors operate.[31]

4.2 Economic Characteristics

Iran is largely a natural resource-based economy[32] and has used its oil revenues to build up a significant industrial base, mainly by licensing technology from abroad. However, the non-oil export base is narrow and developments in the oil market largely explain Iran's economic growth performance. The rapid increase in Iran's output during the 1970s had been caused by the two major increases in oil prices coordinated by OPEC. While Iran's per capita GDP as well as non-oil GDP increased steadily during 1960-1976 while oil income was rising, the decline in per capita oil revenues which started in the late 1970s slowed the economy (Salehi-Isfahani, 2000). The fall in the price of crude oil is not entirely responsible for the one-third decrease in per capita GDP in 1977-1982. Disruptions due to the 1979 revolution and the war with Iraq also contributed to economic decline (Salehi-Isfahani, 2001), (Amuzegar, 2005). After a temporary increase in 1990, oil prices continued a declining trend up to 1999, pushing Iran and many of the oil-exporting countries of the region into deep recessions and generating high levels of unemployment (Salehi-Isfahani, 2001) (Amuzegar, 2005). Thereafter, oil prices rose sharply again and have stimulated a strong economic recovery (Amuzegar, 2005).

[31] Sources of data are national and international publications and websites, including UNCTAD 2005 STIP report on Iran, the World Bank Development Indicators, The UNDP human development reports as well as websites of Iranian ministries, GSOs, U/RIs, publications and reports in both Farsi and English.

[32] Iran ranks as the fourth largest oil producer and the second largest gas producer in the world.

During the 3rd Five-Year Social, Cultural, and Economic Development Plan (EDP), Iran received more than US$130 billion from crude-oil exports while the forecast had been only US$64 billion. The average price of Iranian crude-oil exports fluctuated between US$21.4 and US$44.7 per barrel during 2000-2005, compared to an estimated US$12 per barrel (Amuzegar, 2005).

Iran's level of income fluctuates due to the close association between per capita income and per capita oil revenues. High dependence on oil and gas make Iran's economy highly vulnerable to external shocks and declining terms of trade (Salehi-Isfahani, 2001). In addition the exhaustibility of natural resources and the fact that Iran has been under different forms of sanction for the past three decades have strengthened the Iranian government's incentive to diversify the economy and further broaden the industrial and export base (UNCTAD, 2005). The government's 3rd (2000-2005) and 4th (2005-2010) EDPs have specifically emphasised capability building in high-tech areas such as biotechnology to accomplish the shift to a more knowledge-based economy (Amuzegar, 2005), (Atieh, 2005). In 2002, Iran's Expediency Council approved the '20-year Vision Plan for Economic, Social and Cultural Development 2005-2025 (20-Year Vision Plan) which sets the strategies for Iran to become a developed country in twenty years, and achieve the first economic, scientific and technical rank in the region (Kabganian, 2006). To meet the objectives of the 20-Year Vision Plan, a 'Comprehensive Plan for Science'[33] was prepared in 2008 with particular emphasis on specific high-tech sectors. This plan lays down qualitative and quantitative objectives supporting the long-term socio-economic development strategies (SCCRI, 2007).[34] The plan promotes industry–university research partnerships to convert ideas into new commercial processes, products and technologies and focuses research and science education on achieving high-level innovation in the specific high-tech areas, including biotechnology and nanotechnology. The plan also promotes public understanding of science, increased focus on S&T parks, and private-sector investment in science. Since 1990, Iran's EDPs have emphasized a gradual move towards a market-oriented economy and development of the private sector. The 3rd EDP (2000-2005) committed the government to a programme of liberalization, diversification and privatization (Amuzegar, 2005) (UNCTAD, 2005). Subsequently, a number of reforms were approved, in particular:

- Approval of the Foreign Investment Promotion and Protection Act, aimed at simplifying the inflow of foreign capital and easing of technology transfer from abroad[35]
- Liberalization of foreign trade through the elimination of non-tariff barriers and regulations for contract deposit

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[33] نقشه جامع علمی کشور

[34] The Plan is available in Farsi on the website of the Supreme Council of Cultural Revolution: http://www.iranculture.org/commission/cscm_map/Files/Full_MAP_p3_870828.pdf

[35] In May 2002, the Expediency Council approved the 'Law on the Attraction and Protection of Foreign Investment' to encourage inflows of foreign investment through streamlined procedures and profit repatriation guarantees. The law was sent to the government for implementation in January 2003.

- Equalization and reform of the system of exchange rates, aimed at increasing transparency in the government budget and subsidies
- Reform of the Direct Tax Law, reducing corporate taxes from 54% to 25% and personal income tax rates from 54% to 35%
- Reform of the Banking System, through the establishment of non-banking credit institutions and private banks.

Iranian government declared its intention to privatize most state industries after the Iran–Iraq War in 1988, in an effort to stimulate the stagnant economy. The sale of state-owned factories and companies has been slow, mostly because of opposition by a nationalist majority in the Iranian parliament. Most industries, comprising 70% of the economy remain state-owned. The majority of heavy industries[36] are in the public sector, while most light industries are privately owned. In recent years, the role of the private sector has increased. An amendment of Article 44 of the Iranian constitution[37] in 2004 authorized 80% of state assets to be privatized (Shaghaghi, 2008).[38-39] The remaining 20% will stay in the government sector. Despite the slow reforms and delays in the implementation of these structural changes, progress is reflected in the general improvement in macroeconomic indicators (tables 4.1 and 4.2).

Table 4.1 Iran's macroeconomic indicators – growth pattern

	Average annual growth (%) 1986-96	Average annual growth (%) 1996-06
GDP	4.5	5.4
GDP per capita	2.6	3.6
Exports of goods and services	6.7	7.5
Non-oil sector GDP	3.1	5.3

Source: UNDP HDR 2007/2008[40], UNCTAD (2005), Amini (2008).

Table 4.2 Iran's macroeconomic indicators – annual trends (1999-2008)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
GDP growth rate (%)	1.93	5.14	3.67	7.52	7.11	5.08	4.62	5.89	7.82	5.6
Non-oil industrial production growth rate (%)	4.4	4.5	5.5	8.0	5.9	5.1	3.2	4.8	---	---

[36] Heavy industries include steel, petrochemicals, copper, automobiles, and machine tools.
[37] A summary of the Iranian constitution is available at http://mellat.majlis.ir/archive/1383/10/15/law.htm
[38] 40% of asset privatization is to be conducted through the 'Justice Shares' scheme and the rest through the bourse organization.
[39] In the industrial sector, 102 out of the total of 130 companies affiliated to IDRO were privatized by March 2009 (Iran Daily 3103, 2009). Leading automakers Iran Khodro and Saipa were privatized in March 2008 (Iran Daily 2938, 2007).
[40] UNDP HDR is available at http://hdr.undp.org/en/media/HDR_20072008_EN_Complete.pdf

Source: World Development Indicators (2009), Central Bank of Iran, (2009), and ECO (2006).[41]

Iran's GDP per capita increased by 3.6% per annum from 1996 to 2006, while it fell in the 1970s and 1980s by 0.6% (UNDP, 2007), (UNCTAD, 2005). Annual GDP growth for the same decade averaged 5.4% due to fixed investments in upstream oil/gas and downstream industries (mainly petrochemicals and steel), stronger energy prices, increased export volumes and government spending, and improved business confidence (UNCTAD, 2005), (Siddiqi, 2003). Iran's non-oil sector's average annual GDP growth from 1996 to 2006 was 5.3% reflecting increased manufacturing, construction and agricultural output, and upbeat domestic demand. The non-oil export saw a growth of US$ 13 billion in 2006-2007 (Amini, 2008).[42] However this reasonably high rate of growth has caused large budget deficits that are, at least partly, the result of large-scale subsidies[43] provided by the state on consumer items such as foodstuffs[44] and gasoline. The state also subsidizes imported input costs incurred by the industry (UNCTAD, 2005).

4.2.1 Human Development

Significant improvements have taken place in health and education standards in Iran. Due to the government's commitment to reducing poverty and improving basic living standards and education, the UNDP human development index (HDI) values for Iran rose from less than 0.6 in 1980 to 0.782 in 2007, moving Iran from the group of countries considered to have low human development (HD) to the ranks of those with medium HD (table 4.3).

Table 4.3 Human development indicators – historical trends

	1960	1980	1990	2000	2007
Adult literacy rate (%)	14.5	49.7	57.1	74.5	82.3
Life expectancy (years)	48.47	58.94	64.80	68.91	70.95
GDP per capita (US$, PPP)	1985	2620	3730	5950	10955
Annual population growth rate[45] (%)	2.5	3.47	2.18	1.65	1.31
Human development index trends	---	0.561	0.672	0.738	0.782

Source: UNCTAD 2005, UNDP HDR (2007/2008, 2009)[46], World Bank[47]

[41] GDP growth rate data from World Bank (WDI, 2009); Non-oil industrial production growth rate from Central Bank of Iran (Economic Research and Policy Department of the Central Bank of the Islamic Republic of Iran, 2009), Economic Cooperation Organization Country Profiles 2006 (ECO, 2006).
[42] The non-oil export increased from US$ 84,000 billion in 2006 to US$ 97,500 in 2007.
[43] Amounting to about US$4.7 billion per year
[44] Wheat, rice, vegetable oil, bread and sugar
[45] Percentage change of resident population compared to previous year
[46] UNDP Human development report 2009 Indicators available at http://hdrstats.undp.org/en/indicators/
[47] Data Source available at http://datafinder.worldbank.org/

Iran has radically improved its adult literacy rate as well as the youth literacy rate (age 15 to 24) which has risen from 86.3% in 1990 to 97.4% in 2005 (table 4.4).

Table 4.4 HDI – comparisons of selected countries (2007)

HDI Rank 2007		HD index value	Life expectancy at birth, annual estimates (years)	GDP per Capita (PPP US$)	Adult literacy rate (% aged 15 & older)	Youth literacy Rate (% aged 15-24)	
		2007	2007	2007	2007	1985-1995	1995-2005
High Human Development							
26	R. Korea	0.937	79.2	24,801	..	..	..
51	Cuba	0.863	78.5	6,876	99.8	..	100.0
53	Mexico	0.854	76.0	14,104	92.8	95.4	97.6
66	Malaysia	0.829	74.1	13,518	91.9	95.6	97.2
75	Brazil	0.813	72.2	9,567	90.0	..	96.8
Medium Human Development							
79	Turkey	0.806	71.7	12,955	88.7	92.5	95.6
88	**Iran**	**0.782**	**71.2**	**10,955**	**82.3**	**87.0**	**97.4**
92	China	0.772	72.9	5,383	93.3	94.3	98.9
123	Egypt	0.703	69.9	5,349	66.4	63.3	84.9
134	India	0.612	63.4	2,753	66.0	61.9	76.4

Source: UNDP HDR 2009 Indicators[48]

There is no gap in higher education between adult men and women. Out of the total number of higher education students[49] enrolled in the academic year 2004-2005 (2.1 million) 54% were women compared to only 31% in 1978.[50] The government's commitment to HD and poverty reduction through innovation and application of modern technologies is reflected in the activities of the national biotechnology research centres working on curing the diseases common in the native communities (UNCTAD, 2005).

4.2.2 Employment

Iran's population growth rate dropped from an all-time high of 3.94% in 1985 to 1.31% in 2008 (WDI, 2009). To keep growth rates low, Iran's government continues to emphasize the social value of smaller families. However as almost 50% of Iran's population is under the age of 20, population momentum is strong and growth in the immediate future is inevitable. The growth in the labour supply is now at a high rate of 5% per year, mainly due to the 'demographic bulge' in the early 1980s (Amuzegar, 2005). Around 800,000 skilled work force enter the labour market every year. Iran's labour force totalled 24.3 million in 2008, around 10.3% of whom were unemployed (unemployment has doubled from 1.5 to 3 million during 1991-2007). The unemployment rate

48 UNDP Human Development Report, 2009 Indicators available at http://hdrstats.undp.org/en/indicators
49 Both government and private sector
50 Data from MSRT website at http://www.msrt.ir/default.aspx

reached 11.8% in 2009 (table 4.5). To improve the current situation Iran is trying to diversify its economy and move away from its dependence on the oil and gas sector (UNCTAD, 2005).

Table 4.5 Iran's Unemployment rate as a % of labour force

	2000	2005	2006	2007	2008	2009
Unemployment rate (%)	12.8	11.5	---	10.5	10.3	11.8

Source: UN data (2010)[51], CIA World Factbook (2010)[52]

At present, the manufacturing sector employs almost 30% of the work force, although it makes a relatively small contribution to the national product. Public services and social services (with relatively low salaries) are the biggest employers, along with agriculture, mining, trade and transport. The automotive sector is important as a major source of private-sector jobs, employing half a million people (UNCTAD, 2005). The trend in the number of persons employed in the non-oil sector shows an increase from 13 million in 1991 to 19.8 million in 2007, with most of the increase occurring in the later years (table 4.6).

Table 4.6 Non-oil sector employment

Sector	Number of employed persons (thousands)			Avg. Growth (%)	Avg. Growth (%)
	1991	1996	2007	1991 - 1996	1996 - 2007
Agriculture	3,205	3,357	3,878	0.9	1.6
Manufacturing	3,616	4,473	6,420	4.3	4.0
Services*	6,276	6,741	9,582	1.4	4.0
TOTAL	13,097	14,571	19,880	4.2	3.5

Source: UNCTAD (2005), (Barnameh 261, 2008). * Including unregistered jobs.

4.2.3 GDP and Export Composition

Privatization and minimizing the government's role in the economy is underlined in article 44 of the Constitution and in the 20-Year Vision Plan. 80% of the shares of state enterprises, covered under article 44, are to be moved to the private sector, with share prices determined through the stock exchange. According to article 145 of the 4th EDP (2005-2010), at least 3% of the responsibilities of executive organizations – whether social, cultural or productive – should be handed over to the private sector every year. As a result, funds for public-sector related firms are expected to decline by 2% per year and the number of state employees to decrease by 5% by the end of the 4th EDP (Iran Daily, 2007). At present, the Iranian economy is dominated by the state and is still largely dependent on the primary sector. As there are many public–private enterprise

[51] UN data on Iran is available at http://data.un.org/Search.aspx?q=Iran
[52] CIA World Fact Book on Iran available at https://www.cia.gov/library/publications/the-world-factbook/geos/ir.html

variations, it is difficult to assess the exact contribution of the private sector but its contribution to GDP value-added is estimated at 15%.[53]

Iran's non-oil GDP comes primarily from services, then manufacturing and agriculture. In 2007, when oil prices were very high, oil accounted for only 27% of the total GDP, which indicates that the economy is relatively diversified (table 4.7), (Salehi-Isfahani, 2009). Iran allocated US$250 million for the establishment and development of high-tech industries during the Iranian calendar year 2009/2010.[54]

Table 4.7 Sectoral contribution to GDP in Iran (%)

Sector	1990	1995	2000	2005	2006	2007	2008
Agriculture	19.10	18.37	13.72	10.19	10.36	10.22	10.06
Industry (of which Oil and Gas)	28.70 (10.8)	34.24 (16.1)	36.74 (13.4)	44.71 (---)	43.64 (25)	44.47 (27)	44.92 (---)
Services	52.19	47.39	49.53	45.10	45.66	45.31	45.01

Source: World Development Indicators (2009), UNCTAD (2005), Salehi-Isfahani (2009).[55]

Historically, as national economies mature, the share of agriculture in GDP declines while those of manufacturing and services rise sharply. Comparison to newly developed and developing countries shows that sectoral contribution to GDP in Iran, was similar to that of Malaysia in 2007 (table 4.8). The services sector's contribution to Iran's GDP was below that found in the Republic of Korea, India, and Egypt. With the state dominating the economy, much of the service sector in Iran is comprised of government employment and its services. Manufactured exports represented only 8.81% of total merchandise exports in 2005 and Iran is far behind the countries of comparison in this respect (table 4.8).

Table 4.8 Comparison of Iran to developing and newly developed countries in sectoral contribution to GDP (2007) and manufacturing share of total merchandise exports % (2005)

	Sectoral contribution to GDP (%) 2007			Manufacturing exports as % of total merchandise exports 2005
	Agriculture	Industry	Services	
Iran	**10.22**	**44.47**	**45.31**	**8.81**
Malaysia	10.24	47.72	42.05	74.62
Republic of Korea	2.88	37.12	60.00	90.84
China	11.13	48.50	40.37	91.88
Egypt	14.07	36.34	49.59	30.61
India	18.11	29.51	52.38	70.32

Source: World Development Indicators (2009), nationmaster.com[56]

[53]Private sector companies are mainly concentrated in food processing, textiles and carpets, light manufactures and automotive components (UNCTAD, 2005).
[54] Source: Website MIM: http://www.mim.gov.ir/.
[55] Source: World Bank Development Indicators (WDI, 2009), Oil and Gas data from Statistical Centre of Iran and UNCTAD (2005), 2007 figure from (Salehi-Isfahani, 2009)

The value of total exports of goods and services (as % of GDP) has been growing since the early 1990s (table 4.9). However, even though by adopting strategies of self-reliance and import-substitution over the years Iran has developed a broad industrial base[57] its export base is still narrow.[58]

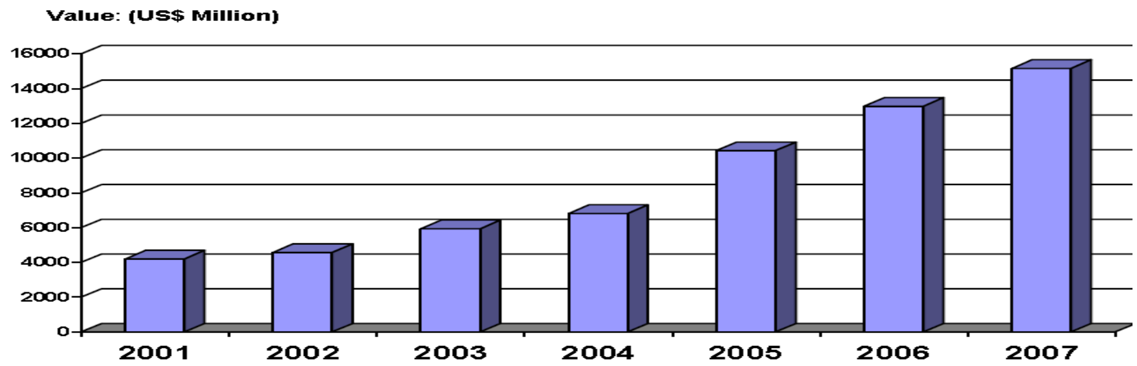
Table 4.9 Iran's balance of trade (1990-2008)

	1990	1995	2000	2005	2006	2007	2008
Import of goods and services (% of GDP)	23.1	13.1	17.4	24.7	24.4	21.5	22.6
Export of goods and services (% of GDP)	14.5	21.7	22.7	33.1	32.4	32.2	32.6
High-tech exports (% of manufactured exports)	---	---	1.89	2.54	6.17	---	---

Source: World Development Indicators (2009)

Primary commodities (oil and gas sector) continue to account for 85% of exports.[59] In 2006 manufactured products accounted for 9% of total exports and exports of high-tech products were 6% of manufactured exports. Iran's annual non-oil exports during Iranian calendar year 2007/2008 showed a growth of 15.1% compared to the same period of the previous year. Figure 4.1 shows Iran's non-oil export trends.[60]

Figure 4.1 Iran's non-oil export trends (2001 to 2007)



Source: Iran's Customs Administration (IRICA)[61]

[56] http://www.nationmaster.com/graph/ind_man_exp_of_mer_exp-industry-manufactures-exports-of-merchandise.

[57]Including automotive, telecommunications and consumer electronics manufacturing

[58] Iran currently has only the item "oil and other petroleum products" in the export 'champions' segment. Some agricultural products such as grapes, saffron and fresh fruit have some dynamism. These products can be quickly added to the champions segment by further processing (UNCTAD, 2005).

[59]The oil and gas industry itself is currently operating below the pre 1979 level of 5.5 million barrels per day. Most importantly, most of the oil extracted is exported crude and only a small proportion is transformed locally into refined oil and higher value-added petrochemical products or technology-intensive products. As a result, Iran has become a net importer of refined petrol (UNCTAD, 2005).

[60] Iran's annual non-oil exports during Iranian calendar year March 2007 to March 2008 reached US$15.2 billion (excluding US$5.8 billion liquid gases).

[61] Iran's non-oil exports statistics report is available at

The 20-Year Vision Plan has set an investment target of US$3.7 trillion, of which US$1.3 trillion should be in the form of foreign investment (Iran Daily, 2007). FDI in Iran reached US$750 million in 2007 from US$40 million in 2000 and US$17 million in 1995. This is very negligible in comparison to countries such as Malaysia and Republic of Korea (table 4.10). In the early 2000s the Iranian government liberalized foreign investment regulations. However FDI has been hindered by unfavourable or complex operating requirements and by international sanctions. Iran only absorbed US$3.82 billion of foreign investment from 1991 to 2007 (WDI, 2009).

Table 4.10 FDI comparison of Iran to developing and newly developed countries

	FDI net inflows (BoP, billion US$)		
	2000	2004	2007
Iran	**0.04**	**0.31**	**0.75**
Malaysia	3.79	4.62	1.58
Republic of Korea	9.28	9.25	8.46
Egypt	1.24	1.25	11.58
India	3.58	5.77	22.95
China	38.4	54.94	138.41

Source: World Development Indicators (2009)

4.2.4 The effect of Sanctions on Iran

Since 1979, numerous sanctions have restricted/banned dealings with Iranian banks and individuals, including businesses and members of the Revolutionary Guard. These sanctions have made it difficult for Iran to access technologies and equipment from abroad. In the past countries such as Iraq, North Korea, and Cuba have been under similar sanctions. The main effects of these sanctions are inflation, unemployment, mounting shortages, unsteady supply chains and disrupted exports.

For ordinary businesses these sanctions have caused unpredictability, from failing to move goods from ports to opening letters of credit. Operating costs have risen dramatically for importers of industrial machinery because of new shipping and insurance restrictions on Iran-bound cargo. Many foreign firms around the world have suspended or limited their transactions with Iran. For example in the pharmaceuticals, increasing time and cost of importing raw materials have caused company owners to lay off employees and curb production.

In the biotechnology sector these sanctions have made both technology transfer as well as access to machinery and equipment difficult and lenghty. The case studies of GM Bt rice and Hepatitis B Vaccine presented in chapter 6 demonstrate these limitations. For example access to common research equipment such as biolistic guns, incubators, -80°C freezers, and ultra-centrifuges have

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http://www.iranembassy.com.pt/fa/Docs/endoc/Non%20oil%20Export%20Statistics%20of%20Iran.pdf been extremely difficult and time consuming. Some of these equipment had to be produced in the country and some were imported through third parties.

Recent cuts to government subsidies have boosted prices of subsidized food items such as wheat, rice, oil, milk and sugar. The IMF estimates inflation in Iran at about 10%, but warns that the subsidy cuts could send the rate to 30%. However some economists and analysts say inflation is already over 25%.

Sanctions have also hindered FDI has been hindered even though the Iranian government liberalized foreign investment regulations in the early 2000s. Iran only absorbed US$3.82 billion of foreign investment from 1991 to 2007 (WDI, 2009).

4.3 Scientific and Technological Capacity

Iran has built up substantial S&T capacity (U/RIs, scientists and engineers), and production capability. According to the Technology Achievement Index (TAI) developed by UNDP to assess technological capacity of a country by investigating how it is creating and diffusing technology and building a human skills base[62], Iran is ranked 50 out of 72 countries assessed in 2001. The countries that rank highest on TAI are described as technological leaders. The second level is potential leaders in technology which includes a larger number of developing countries. The third level of TAI (including Iran) is dynamic adopters.[63] Iran is ranked higher than some main dynamic adopters (e.g. India and Egypt) but after China, Brazil, Malaysia, South Africa and Mexico (table 4.11).

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[62] TAI is a combination of four elements: creation and use of new knowledge (with indicators for patents granted and licence fees received per capita), diffusion of recent innovations (internet hosts per capita and tech-based exports as share of all exports), diffusion of old technology (log of telephones and electricity consumption per capita) and human skills (mean years of schooling and enrolment at technical tertiary levels). TAI also provides indicators to measure potential direct and indirect inputs into an innovation process (e.g. share of educational expenditures in total government expenditures, number of scientists engaged in R&D per million inhabitants, and share of R&D expenditures in GNP (UNCTAD, 2005).

[63] TAI leaders includes Finland, US, Sweden and Japan, Republic of Korea and Singapore. TAI potential leaders include Malaysia, Mexico, Argentina, Costa Rica and Chile. TAI dynamic adopters include Iran, South Africa, Panama, Brazil, China, Egypt, Indonesia, Sri Lanka, and India.

Table 4.11 Knowledge and innovation related indicators – comparison of selected countries

Technology Achievement Index		Public expenditure on education (% of GDP)		Public expend. on education (% of total government expenditure)			Tertiary students in science & engineering (% of tertiary students)		Internet users (per 1000 people)	
		1991	02-05	1991	98-00	00-07	95-97	99-05	2001	2005
Leaders										
2	USA	5.1	5.9	12.3	..	13.7	13.9	16	501	630
4	Japan	..	3.6	..	9.3	9.5	10.0	19	384	668
5	R. Korea	3.8	4.6	25.6	17.4	15.3	23.2	40	521	684
7	UK	4.8	5.4	..	..	12.5	..	22	..	473
8	Singapore	3.1	3.7	18.2	23.6	..	24.2	..	411	571
11	Germany	..	4.6	..	9.7	9.7	14.4	..	374	455
Potential Leaders										
29	Poland	5.2	5.4	14.6	11.4	12.7	6.6	20	94	262
30	Malaysia	5.1	6.2	18.0	26.7	25.2	3.3	40	273	435
32	Mexico	3.8	5.4	15.3	36.2	25.6	5.0	31	36	181
34	Argentina	3.3	3.8	..	11.8	13.1	12.0	19	101	177
Dynamic Adopters										
39	S. Africa	5.9	5.4	..	25.8	17.4	3.4	20	65	109
40	Thailand	3.1	4.2	20.0	..	25.0	..	..	..	110
43	Brazil	..	4.4	..	12.9	14.5	3.4	16	47	195
45	China	2.2	1.9	12.7	..	13.0	3.2	..	26	85
50	**Iran**	**4.1**	**4.7**	**22.4**	**20.4**	**19.7**	**6.5**	**40**	**16**	**103**
57	Egypt	3.9	..	..	..	12.6	2.9	..	9	68
63	India	3.7	3.8	12.2	12.7	10.7	1.7	22	7	55

Technology Achievement Index		Patents granted to residents (per million people)			R&D expenditure (% of GDP)	Researchers in R&D (per million people)	High-tech exports (% of manufactured exports)		
		1999	2001	2008	2000-2005	1990-2005	1997	2002	2006
2	USA	300	307	254	2.68	4605	31.7	31.5	30.0
4	Japan	1057	860	1188	3.14	5287	25.9	24.4	21.6
5	R. Korea	929	461	1257	2.64	3187	26.4	31.3	32.0
7	UK	49	47	33	1.89	2706	27.2	31.4	33.6
8	Singapore	12	41	103	2.25	4999	56.8	60.4	58.0
11	Germany	142	139	153	2.49	3261	13.8	16.9	16.7
Potential Leaders									
29	Poland	26	22	38	0.58	1581	2.5	2.8	3.8
30	Malaysia	1	0.7	6	0.69	299	49.0	58.2	53.8
32	Mexico	1	1	1	0.39	268	17.5	21.4	18.9
34	Argentina[1]	4	3	3	0.41	720	4.5	7.44	6.7
Dynamic Adopters									
39	S. Africa	...	....	...	0.76	307	7.5	5.2	6.5
40	Thailand	<1	<1	<1	0.26	287	30.7	30.8	27.4
43	Brazil	2	3	1	0.98	344	7.3	17.0	12.3
45	China	2	4	35	1.44	708	12.7	23.3	30.3
50	**Iran[2]**	**2**	**8**	**8**	**0.67**	**1279**	**0.1**	**2.6**	**6.2**
58	Egypt	<1	<1	1	0.19	493	0.2	0.8	0.5
63	India	<1	<1	1	0.84	119	4.8	4.8	5.0

Sources: UNDP HDR (2007/2008, 2009); World Bank (2009, 2010); UNCTAD (2005); Desai et al. (2002); WIPO (2009).1 (1 2000 data; 2 Latest data from on Iran 2001)

Table 4.11 shows that Iran has a relatively high expenditure on education as a proportion of total government expenditure (22.8%) and a high ratio of science enrolment in tertiary education, compared to several other developing countries (rising from 6.5% in the period 1995-1997 to 40% in the 1999-2005 period). However, it has a very low proportion of technology-based exports (2.6% of total goods exported). Comparatively, even India, which is ranked below Iran, has a higher proportion of technology-based exports (4.9 %). Iran spends 0.67% of its GDP on R&D which is considerably below the average 3% spent by developed countries (ASTI, 2008). In this respect, it is lagging behind several other emerging economies such as Brazil, India and South Africa.

Although Iran's tertiary science enrolment ratio of 40% compares favourably with other developing and developed countries, the experience of countries such as the Republic of Korea and Singapore suggests that, to transform into a knowledge-based economy, other TAI indicators such as ratio of technology-based exports and R&D expenditure also need to be raised substantially (UNCTAD, 2005). Nonetheless, Iran has made a noticeable progress in building its S&T capacity. The number of researchers in R&D is high compared to other developing nations and the number of research institutes has doubled in the last two decades. As a result of the growth in the country's S&T capacities, Iran has also made huge progress in its scientific output in recent years (see next section).

4.3.1 Higher Education and Research

Due to severe emigration of scientists from Iran after the 1979 revolution and during the subsequent eight year Iran-Iraq war, Iran experienced a severe brain drain for almost a decade. In 1988 the Graduate Study Bill was put into action to internalize and expand the education at graduate levels. The scientific production of the country began to rise after a decade of decline and stagnation. The growth was six fold one decade after the Graduate Study Bill and around 45-fold by 2007 (Etemad, et al., 2008). The number of researchers (including PhD students) per million inhabitants increased from 340 in 1996 to 1280 in 2006. Iran is expanding its research output more rapidly than China and is now approaching Singapore in volume of world publications (UK Department of Trade and Industry, 2007). What is not known is how this growth has altered the distribution of researchers across private and public sector institutes.

Iran's EDPs as well as the 20-Year Vision Plan have emphasised the national goal of self-sufficiency in all scientific fields. These plans consider S&T essential for sustainable national development. At present, Iran's human resources have provided a strong base for research and technological development. The country's output in scientific articles published in international journals has quadrupled over the past decade (Etemad, et al., 2008). The number of annually published ISI papers grew from less than 500 in 1995 to 6748 in 2006 and 9061 in 2007 (Noroozi Chakoli, et al., 2008).[64]

Iran's scientific output has currently placed it second amongst the Islamic countries after Turkey (Shamsipur, 2008). Detailed ISI field rankings for Iran in the 1996–2005 period are available in Appendix 2. During this time, the Iranian scientists published 19,900 papers in ISI journals with an average of 2.79 citations per paper. Iran seems to have reached the threshold of self-sustainability in basic sciences during the 3rd EDF (Etemad, et al., 2008). In 2005 Iran's scientific production was behind that of Turkey by a factor of 3 and behind that of South Korea by a factor of 5.5. Turkey and Iran have considerable demographic indices in common. Comparison with South Korea becomes meaningful if one considers that both are among the emerging nations in S&T.

The Pasteur Institute of Iran (IPI) was the country's first research institute established in 1920. By 1982 Iran had 86 research institutes and in 2001, the number of public-sector research institutes had risen to 216. 112 of Iran's research institutes are associated with the Ministry of Science, Research and Technology (MSRT) including the Iranian Research Organization for Science & Technology (IROST)[65] and the National Institute of Genetic Engineering and Biotechnology (NIGEB).[66] The number of private technical and engineering research institutes has also increased from 1 in 1971 to 76 in 2001 (Abbasi, 2003).

At present Iran has a large network of public and state-affiliated universities offering degrees in higher education. These comprise of 54 state operated universities and 42 state medical schools which are primarily the top choice for students in national University entrance exams, and have the largest and most prestigious programs. In addition there are 289 major private universities operating in Iran such as the Islamic Azad University. State-run universities of Iran are under the direct supervision of the MSRT for non-medical universities and Ministry of Health and Medical Education (MHME) for medical schools. In 2008, the private sector accounted for 48.6% and the public sector accounted for 51.4% of all enrolments in university degree programmes.[67] The state-run universities, however, are academically stronger and account for nearly all students enrolled in PhD programmes. One quarter of all university enrolments are in engineering and a further 10% in pure sciences, while medical sciences account for an additional 9.3% of the students enrolled at the tertiary level (UNCTAD, 2005). The universities largely operate on state budgets. Except for private universities such as the Islamic Azad University, tuition, room, and board are also mostly paid for

[64] Source available at http://www.collnet.de/Berlin-2008/NoroozichakoliWIS2008eis.pdf

[65] IROST was founded in 1980 and subordinated initially to the Revolutionary Council. Later it was affiliated with the Ministry of Culture and Higher Education and now with the MSRT.

[66] In biotechnology research, MSRT thus plays an important role, though there are other major research centres such as the IPI which fall under the MHME and the Razi Vaccine and Serum Research Institute (RVSRI) which comes under the Ministry of Agricultural Jihad (See chapters 5 and 6 for details).

[67] Data from MSRT Website.

by the government. Furthermore there are institutes like Payame Noor University that offer long distance and online degrees. Some schools offer degrees in conjunction with European Universities. The University of Chabahar offers Political Science programs under the guidance of London School of Economics, Goldsmiths University of London, and Royal Holloway.[68] Other schools, such as the Institute for Advanced Studies in Basic Sciences in Zanjan, have close collaboration with the International Centre for Theoretical Physics in Trieste, Italy for workshops, seminars, and summer schools. The Iranian government also offers intensely competitive but fully paid scholarships for successful applicants to pursue PhD level studies in the UK.

Iran's university population was 100,000 in 1979, 2.1 million in 2006, and 3.5 million in 2008.[69] The total number of graduates in science increased nearly six-fold between 1991/92 and 2004/05 academic years. The total number of graduates in engineering also increased four times in the same period. Number of University graduates in sciences and engineering from 1991/1992 to 2004/2005 are available in Appendix 2.

During the past two decades, the high level of research in chemical and biological sciences together with support from the Iranian Scientific Societies have strongly influenced the promotion of interdisciplinary sciences, including biological chemistry, biotechnology, and nanotechnology. During this period, the government of Iran increased investments in support of fundamental and applied research especially in the fields of biotechnology and nanotechnology. Since the mid-1980s, several highly productive research institutes have been established where bioscientists play key roles (e.g. NIGEB and ABRII).

4.3.2 Technological Infrastructure and Capacity in the Industrial Sector

In the information age, internet access is argued to contribute greatly to technological capacity. Telecommunications infrastructure and the internet are considered to be particularly essential for access to knowledge, for learning and for the kind of networking that leads to competitiveness (UNCTAD, 2005). The Iranian government has made great efforts to improve the country's technology infrastructure. In 2001, the Supreme National Council for ICT Agenda (TAKFA)[70] under the leadership of the President's special envoy initiated some 40 national projects in the fields of ICT infrastructure, commerce, governance, human resource development and employment (Jahangard, 2004). With high priority given to transforming Iran into a knowledge-based economy during the 3rd EDP and a budget of US$1 billion allocated for intensive ICT work, Iran has made significant progress in ICT (table 4.12). Iran's telecommunications infrastructure is particularly

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[68] Data from Universities websites: http://www.iuc.ac.ir/aboutus-aboutus-fa.html; http://www.iasbs.ac.ir/
[69] Data from MSRT's website.
[70] TAFKA is an acronym of Farsi words representing the Iranian National ICT Agenda.

successful in connecting people via telephone mainlines. The number of internet users has also increased substantially between 2001 and 2005, but it is still behind Mexico and Kuwait.

Table 4.12 Telecom diffusion - Iran in comparison with other oil-producing countries

	Telephone mainlines (per 1,000 people)			Cellular subscribers (per 1,000 people)			Internet users (per 1,000 people)		
	1990	2001	2005	1990	2001	2005	1990	2001	2005
Egypt	29	104	140	0	43	184	..	8.4	117.0
Kuwait	156	208	201	10	386	939	..	87.9	276.1
Iran	**40**	**169**	**278**	**0**	**32**	**106**	**0**	**15.5**	**178.0**
Indonesia	6	111	58	0	242	213	0.1	20.1	35.8
Mexico	64	137	189	1	217	450	0.1	71.7	188.7
Saudi Arabia	75	145	164	1	113	575	..	47.3	129.8
Syrian Arab Rep.	39	103	152	0	12	155	0	3.5	56.5
Venezuela	75	109	136	0	263	470	0.1	46.6	126.2

Source: UNCTAD (2005), World Bank (2009)

Two specific policies introduced during the period of reconstruction attempted to reorient research more towards industry. The first was to promote applied research with a view to make university research applicable to industrial needs. During 1990s, the Ministry of Industry and Mines (MIM) also sought to promote R&D activities directly in large and medium-sized companies, most of which were state-owned. By 1996, 158 companies had received official operating licences for their R&D centres. In 1996, the total number of researchers, research assistants and technicians amounted to 68,385, of which 82% were employed in public sector institutes and 18% in private sector research centres (UNCTAD, 2005). By 2000, 76 technical and engineering research institutes had been created in the enterprise sector (public and private). In order to encourage U/RIs to increase their collaborative activities with the industry, promote demand-driven research and boost government investments in R&D in all sectors of the economy, the Parliament has instructed all public (non-research) agencies to spend at least 1% of their current budget on research through contracts with universities and other research institutes (ASTI, 2008).

In addition to building up capacities in the knowledge system, Iran has also built up substantial technological capacity in the manufacturing sector. It has a fairly well developed manufacturing capacity in the automotive industry, telecommunications and pharmaceuticals. Large state enterprises still dominate contribution to the national product. Unfortunately, Iranian statistics relating to SMEs are scattered and incomplete. The Guilds Board and Ministry of Commerce cover service and trading businesses that employ around one million people. The Ministry of Agricultural Jihad (MAJ) is responsible for small agro-based and rural industries. About 345,000 small/medium industrial enterprises that employ 1.6 million or about 10% of the total employed work force are registered with the MIM (UNCTAD, 2005).

4.4 Policy Framework

4.4.1 Characteristics of Iran's Innovation Policy System

The 3rd (2000-2005) and 4th (2000-2010) EDPs have promoted the transformation of Iran to a knowledge-based society by strengthening the role of S&T in the innovation process. The main technology policies contained in Iran's five year EDPs are summarizes in table 4.13.

Table 4.13 Technology policy content of Iran's Five-Year Economic Development Plans

First EDP (1990-1995)	Second EDP (1995-2000)	Third EDP (2000-2005)	Fourth EDP (2005-2010)
Selecting appropriate technology with minimum dependence on foreign suppliers. Setting quality standards for manufactured products. Upgrading industrial and engineering research capacities and technology capabilities. Attracting and developing new technologies.	Creating quality control systems to improve the quality of products through co-operation between research centres and higher education centres. Assisting the establishment of in-house R&D units in large and medium-sized factories as well as R&D centres for specific industries. Providing credit facilities for doing research.	Stimulating dynamic and continuous communication and linkages between scientific organs, industrial centres, state manufacturing units, and related organs to attract higher levels of technology. Creating a competitive Environment.	Enhancing innovation, internal and external sources of R&D and mechanisms for building technological and innovative capacity. Improving overall goal and priority setting within an integrated innovation-based framework.

A national vision in S&T and its role in innovation have been prepared and national priorities have been set. As a result Iran's innovation policy is primarily entrusted to the Ministry of Science, Research and Technology (MSRT). Other Ministries also involved in the innovation policy process include the Ministry of Industry and Mines (MIM), the Ministry of Health and Medical Education (MHME), the Ministry of Agricultural Jihad (MAJ), the Ministry of Information and Communications Technology (MICT), and the Ministry of Petroleum (MOP) (Abbasi, 2003). Most goals and priorities are set within these individual ministries through traditional top-down bureaucratic decision making processes. Recent attempts have been made to introduce a bottom-up approach involving experts in the definition of goals and short term priorities. One attempt was undertaken by the High Tech Industries Centre (HTIC) for a number of high-tech sectors such as biotechnology. Another attempt involved a survey conducted by IROST in collaboration with the Management and Planning Organisation (MPO) to establish a list of technology priorities in 14 different fields to serve as the basis for planning and investment in research and technology development activities in the 4th EDP (Atieh, 2005).

Unlike production-oriented ministries such as MIM, MSRT has no state-owned companies within its organizational structure. Education and scientific research linked to MSRT are two of its main mandates. In addition, within the MSRT, IROST focuses on technological development up to the pilot stage and then seeks industrial partners to whom technology can be transferred. The main strength of the MSRT lies in its knowledge of the research process and its ability to work closely with universities and networks across the research divisions and departments of other ministries. MSRT has also started recent efforts to bring research activities to the market. For example the Biotechnology Incubator supports the creation of private spin-offs from NIGEB.

Operations at production-oriented ministries such as MIM, MOP, MAJ or Ministry of Energy are related more directly to the activities of firms. However internal organizational problems still prevent these production-oriented ministries from being centres of excellence in innovation support services and policies.[71] This has contributed to innovation policies and practices in which firms in traditional sectors and SMEs are excluded from consideration. Moreover due to traditional habits and practices, governmental bodies and research institutions in Iran work in parallel rather than in collaboration with each other.[72] Having multiple projects of this sort is not in itself negative. However, there is a lack of cross fertilization and information flows across projects and ministries/institutions in which they are located. Therefore there is a critical need to improve communications within as well as between ministries.

Policies and programmes developed by main actors in the innovation policy system of Iran focus on the supply of human and knowledge capital as generated by the education, scientific research and technological development processes (linear). The conceptual approach to innovation in terms of a 'National Technological Development System' reinforce this focus on the supply of research and technology, whether from within the developing system or through international collaboration and licensing from abroad, and on the role of technology in the growth of industrial output. Recent policies, however, are directed more towards stimulating the learning and technological mastery needed for innovation.

In 2003, the government established the Iran National Science Foundation (INSF), which provides grants to researchers at U/RIs to carry out interdisciplinary and multi-institutionary research, to patent innovations and technologies, and to scale up and market industrial research results[73]. INSF is managed by the President's Office, has its own research council, and operates different technical committees to review and assess priorities and quality of the research proposals (INSF, 2008). INSF

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[71] For example, in the case of MIM, there is a serious lack of information exchange and collaboration between the HTIC, line divisions and departments within the MIM.
[72] For example in biotechnology, research in the same areas and sometimes on highly similar projects is under way.
[73] Source: http://www.insf.org/Ayeename-Siasatha.php?

has an annual funding budget of up to US$100,000 for individual research projects. In 2007, the total value of research projects approved by the fund was US$5 million (ASTI, 2008).

The 4th EDP and the 20-Year Vision Plan demonstrate a change from the traditional emphasis on production to underline innovation as the core of development process. These plans pay more attention to the need for domestic capabilities in Iran. The change of focus from transfer of hardware technology and equipment to transfer of know-how, with more focus on developing technological capabilities has also affected licensing practices. Licensing has been practiced in Iran as a means to produce a variety of products for the domestic market. Industries which practice licensing such as the pharmaceuticals have bought technology from foreign companies and did not have to strategically prioritize R&D. The 20-Year Vision Plan has moved away from short-term economic benefits of cooperation and licensing to getting the most out of these agreements in the long term. This creates incentives for learning through licensing and more recently through joint ventures which improve the opportunity to exploit the knowledge base of a license through co-ownership. In addition, international strategic partnerships have become popular in recent years among enterprises and research institutes as a means of acquiring new knowledge, technologies and learning. Some Iranian research institutes already have such partnerships with foreign research institutes on a smaller scale. There is no record of Iranian enterprises entering into such partnerships either with foreign enterprises or with research institutes.

Iran has also programmes in place to develop clusters and incubators of knowledge-based activities. Currently there are three free industrial and trade zones already established in the Persian Gulf, and three others are in the planning stages.[74] In addition, 20 special economic zones have also been created.[75] In Iran, free industrial and trade zones were developed mainly for job creation purposes, and therefore set up in poor and underdeveloped regions to attract both domestic and foreign investment through duty-free access to imports (but not exempt from labour and financial regulations). Most of these are still at an early stage of operation. More recently, Iran has also started to develop incubators for early-stage enterprises and technology parks for commercializing research outputs.[76]

Over the past decade a division of labour has begun to emerge with respect to high-technology sectors in the economy and in programmes currently under way in MICT and MIM to support private enterprises. S&T policies are almost exclusively focused on 'high-technology sectors' as

[74] Free industrial and trade zones already established in the Persian Gulf are Qeshm, Kish and Chabahar and those in the planning stages are Abadan-Khoramshahr, Jolfa, Bandar Anzali.
[75] e.g. Petzone
[76] The biotechnology incubator at NIGEB, the IT incubators at Isfahan Science and Technology Town, and in Kerman (which includes Darya, the first venture capital fund), and the Pardis Techpark under construction near Tehran are promising developments.

drivers of the economy. Naturally this may not be always desirable (von Tunzelmann, et al., 2005). This creates a disincentive to develop policies that stimulate linkages between these 'high-tech sectors' and traditional industries and downstream productive activities.

The following section examines the main ministries involved in the policy making and implementation in more detail.

4.4.2 The Ministry of Science, Research and Technology

MSRT is historically involved in higher education and scientific research. Building upon its earlier knowledge base in tertiary education and scientific research, the government added the function of technology to the renamed Ministry of Science, Research and Technology. The connection of the 'Iranian Research Organization for Science and Technology' (IROST) to the new MSRT in 2000 enlarged its functions beyond the higher education and scientific research components that were at the core of its earlier activities to include technology development. This new ministry was nominated as the coordinator for S&T policymaking for innovation across a large number of vertically integrated ministries operating in the manufacturing sector but maintaining few horizontal linkages among themselves. The approval of the 'Bill on Objectives, Missions and Structure' of the MSRT by the Parliament in 2000 has enabled MSRT to play its coordinator role more effectively. With the approval of the MSRT Bill and the establishment of the 'Supreme Council for Science, Research and Technology', problems are expected to be resolved more effectively. Such problems include: (1) overlap of functions amongst the expanding players with a direct role in STI policymaking; (2) weak goal and priority setting with respect to STI policy coordination, monitoring and evaluation; (3) financing technological upgrading in traditional sector enterprises; and (4) policies aimed specifically at shaping the demand for scientific research and innovation through demand-pull strategies. MSRT also has the objective of encouraging public-sector research organisations to link more closely to industry. For example, the biotechnology incubator at NIGEB promotes and supports bioscientists to engage in entrepreneurial activities.

MSRT's main roles are in higher education, scientific research, and technology development. Each role falls under a vice minister who has responsibility for planning, goal-setting and policymaking and finance. MSRT's policymaking and planning responsibilities are carried out primarily with respect to public-sector universities, research centres and research institutes affiliated with MSRT. The latter fall under the vice ministry of technology and include IROST, 10 provincial research centres now converted into cores for technology parks, and NIGEB. MSRT's functions in planning, goal-setting and policymaking and finance differ considerably across the education, research and technology sectors.

Higher education has by far the broadest set of such functions. It plays an important role in goal-setting, policymaking, monitoring and evaluation.[77] Some higher learning institutes, such as the University of Tehran and the Sharif University of Technology (SUT) are considered to have achieved a high educational level in the field of S&T and students graduating from these universities easily find places in PhD programmes in Iran and abroad. The number of patents obtained by universities in Iran has increased 10-fold in the last decade. The higher education sector within MSRT has a comprehensive plan for the development of qualified researchers, and its implementation appears to have been successful.

Planning in the MSRT for the expansion of research seems to be less comprehensive than education. The focus is mainly on academic research, and activities are only weakly linked to the National S&T Plan and the broader development plans. The role played by the vice ministry for education in setting standards, monitoring and evaluation in the education sector is not replicated in the research sector. Monitoring of research projects is inadequate, and the evaluation of research quality makes use of a scientometric approach based on the Science Citation Index which has a limited scope.[78] The distribution of R&D funding among ministries is proposed to the government by the 'department of research support and logistics' within the office of vice minister of research (table 4.14). The state provides 96% of the research budget and enterprises provide 4%. Approximately 0.5% to 0.7% of the GDP is spent on R&D, and of this 7% to 8% is dedicated to basic research. The 'department of research support and logistics' also helps research institutes under other ministries to secure additional funding for their work. First, a peer evaluation of the request is made on the basis of the relevant ministry's priorities, and if the outcome is positive, the department negotiates with an Iranian bank to obtain a loan for the institute at low interest rates. The government pays part of the interest rate as a subsidy. The department is also planning an insurance system in the area of S&T to protect institutes that cannot repay their loans or keep up interest payments.

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[77] Policies and goals, for example, have been established with respect to the number of students/year/discipline/university/public or private; the programmes for the different levels – graduate, MSc and PhD; projections for the number of students to be sent abroad; the research to be carried out at universities and the corresponding capacity for its realization; and the procedures for monitoring both public and private universities.

[78] The number of citations does not necessarily reflect the importance of the knowledge generated in a given country. Thus, citation indices are useful mainly to assess the results of basic research that fall within the worldwide mainstream of knowledge, but they are not appropriate as a tool for evaluating applied research or research results that have a national or local impact and consequently are of national importance. Therefore, basing evaluations of research quality and impact mainly on scientometrics is not only insufficient but creates a major disincentive for researchers to link to industry, where projects are less likely to produce the kind of theoretical publications that invite citations (UNCTAD, 2005).

Table 4.14 Iran's R&D budget distribution as % of research funds

	R&D budget distribution as % of research funds
Universities under the MSRT	20
Medical Universities	10
Agricultural sector	40
Other sectors	30

Source: UNCTAD (2005)

Despite the attention paid to standard-setting, monitoring and evaluation in the education sector, little effective monitoring or evaluation is undertaken with regard to research expenditures, their outcomes or the impact of R&D projects. Even data such as a list of the most important R&D results in Iran over the past several years, which might make such an assessment possible, is not available. The lack of specific goals and desired impacts of the research activities funded through the MSRT and the absence of monitoring and evaluation capabilities and activities are serious weaknesses in the innovation policy management system.

Within MSRT, technology development falls under a separate vice ministry from that of research. Despite the absence of formal guidelines and policies in the area of technology development, MSRT has carried out a series of studies S&T as the basis for the design of new policies in this area. In the development of linkages between producers of research and technology development and the industry, IROST plays a central role. Established in 1980, IROST's main mission is to support private-sector inventors, innovators and researchers, financially and intellectually. IROST provides technical and some financial support to start-up companies, particularly those manufacturing products that substitute for imports. IROST therefore acts to some extent as a granting council, receiving proposals from researchers in SMEs when they require funds to develop a prototype, peer reviewing the proposals and making awards. This is part of a joint programme involving the MSRT, IROST, MPO, and the private sector to support innovation projects up to the experimental development scale and encourage public-private partnerships in the process. To do this, 40 % of the funding comes from private industry and 60 % from the MPO. MSRT and IROST are the intermediaries. IROST outlines some technological development priorities through these grants and is oriented towards support for SMEs.

IROST also provides a range of support services to inventors and innovators. These include recommending them to banks for low interest loans, assisting in the transfer of technologies developed by researchers to third parties, and obtaining production licences and production facilities from the MIM for innovators following the pilot plant stage. More substantial policy instruments, low-interest loans, tax incentives such as exemptions amounting to 0.02% of total annual sales for firms that establish their own R&D units and a US$30 million fund for research, technology development and innovation in high-tech sectors are administered by the MIM. IROST, therefore, does not have sufficient funds to move products to market or create spin-off companies in most sectors, though it does provide technical and intellectual support to researchers for this purpose. MSRT thus plays a relatively small role in the funding of innovation generally, but it has a strong position in scientific research and technological development in biotechnology.

Following the experience in setting up the 'Isfahan Science and Technology Town' which grew out of IROST's Isfahan Research Centre, IROST decided to turn its other provincial branches into S&T parks. These new S&T parks took their funding with them, thus leading to a decline in IROST's budget in recent years. In view of the range of actors currently involved in setting up science, technology or industrial parks in Tehran area and in the provinces, including a large number focused on high-tech sectors, it is uncertain what role IROST will be playing in this field in the future. TCO, for example, established the 'Pardis Technology Park' near Tehran in 2001, and the 'Iran Industrial Estates Corporation' was set up by MIM to develop knowledge-intensive industries within urban areas. A 'Software Technology Complex' and a 'Telecom Research Centre' were also established under this programme which seems to have become part of the mission of HTIC.

There is a separation of scientific research from technological development in policy planning and programming within MSRT which shows the persistence of a linear approach to the innovation process. Prior to the 3rd EDP (2000-2005), the position of the vice minister for technology in MSRT was held by the head of IROST. Now there are two separate posts. IROST receives its budgetary allocation from MPO, with which it negotiates directly. Its budget is thus not included in that of the MSRT, and to some extent its activities are independent of the ministry to which it is attached. This distinction between MSRT and IROST was reflected in work on the National Technology Development System (NTDS), a project stemming from the tasks assigned to MSRT under the 3rd EDP (2000-2005) and intended to provide the basis for infrastructure, legal framework, goals, strategies and priority setting in the area of STI. At the request of MSRT, a Technology Advisory Committee (TAC) was established within IROST to review the NTDS and to advise the Iranian government on long-term technology development planning (Abbasi, 2003). As part of this mission, IROST commissioned a number of innovation studies both in-house and from outside consultants to benchmark technological development in Iran. Its approach, however, was not coordinated with that of the vice minister for research. The latter contracted the 'System Engineering and Management Company' to develop a management system for the development of science (Abbasi, 2003). This reinforces an artificial distinction between research and technology development, adding to the already problematic exclusion of traditional sectors and downstream industries from the NSI.

4.4.3 The Supreme Council for Science, Research and Technology

Under the previous government (1997-2005) a council for planning, priority-setting and granting was established in the SCSRT. Eleven commissions provide consultation to this council on scientific matters. Under the 3rd EDP (2000-2005) MSRT was assigned a number of broader functions including a role in proposing S&T policies to the Supreme Council for Science, Research and Technology (SCSRT) and coordinating S&T policy. The formation of the SCSRT intended to overcome a legacy of weak horizontal linkages among ministries and enable MSRT to carry out its coordinating function. SCSRT under the Presidency is responsible for formulating policies, strategies, and overall guidance on S&T as well as planning and identifying national S&T priorities. MSRT, MHME, and MAJ are amongst the ministries represented at SCSRT meetings on S&T development. SCSRT reviews and allocates annual public research funds to the various ministries and organisations following approval by the Iranian parliament. SCSRT's new plan is to assess the relative role that each sector plays in the Iranian S&T and how government S&T funding can best be allocated. The goal is to increase public spending on S&T development to more than 1.5 % of GDP. Newly emerging technologies such as biotechnology, stem cell research, information technology, and nanotechnology are priority areas for public S&T funding, and in recent year's significant progress has been made in the application of these new technologies.

4.4.4 The Technology Cooperation Office

The former 'Office of Scientific and Industrial Studies' was founded in 1984 and given the task of providing scientific and industrial advice to the President. At the time, there were few scientists and technicians in the bioscience sector, and no infrastructure existed to produce the enzymes and reagents needed for biopharmaceuticals. Policies and programmes to stimulate and support collaborative R&D partnerships in Iran or abroad did not exist. This office therefore began to fill these gaps with a focus on the 'technology' side rather than on research. Over time it developed its contacts with foreign scientific research institutions and was renamed the Technology Cooperation Office (TCO) to emphasize its mandate in promoting international cooperation in advanced technologies. TCO promotes joint research projects between Iranian institutions and foreign industrial and scientific research centres. TCO has begun to engage in technology foresight activities at the national level and to assess policy proposals and strategic programmes that are brought before the President and Cabinet.

The sector-specific departments and the Research and Planning Department within TCO maintain very light staffing structures. Technically, TCO's sector-specific departments cover a broad range of technologies, but in practice its current focus and strength lies mainly in biosciences, nanotechnology and advanced (compound) materials.[79, 80]

In 1998 TCO created a Research and Planning Department to meet the growing need within TCO for technology support and advisory services. The department is mandated to study the technology sourcing and finance problems of the private sector as part of the government's growing interest in promoting private-sector involvement in the development of high-tech industries. The department has expanded to include research, planning and supervision, jurisdiction and contracts, technology evaluation, information and library, and training divisions.[81] The latter five divisions have technical support functions in the transfer of technology process, including preparation of contracts, dispute settlement and project evaluation, and in providing planning, budgeting and monitoring as well as data management and training services for TCO itself. The research division is mandated to undertake studies of policies and development plans in successful countries, analyse the factors affecting development and progress in Iran, provide assistance in developing the technological culture; carry out fundamental research on technology, develop concepts and methods for technology transfer; evaluate the existing status of technologies in Iran, forecast the process of technology development in Iran and other countries, help set up technology analysis centres and establish relations with similar centres and among researchers[82]. A number of these tasks overlap with those of HTIC affiliated with MIM.

4.4.5 The Ministry of Industry and Mines

Policy making and monitoring for industrial sectors are two functions of MIM's line departments. These line departments are involved in comprehensive strategic planning processes in collaboration with other ministries.[83] MIM also contains a number of departments composed of established organizations and companies that support technology development in industrial firms.[84] MIM supports technology development through several financial programmes.[85] In addition MIM includes HTIC, created in 2001 as part of the changes introduced under the 3rd EDP, to stimulate the creation of enterprises in high-tech sectors. Like IROST, its annual budget of US$35 million to

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[79] In addition to these three areas, TCO covers aerospace, IT, software, industrial processes, civil engineering, infrastructure and energy, and also undertakes studies on technology development and technology management. http://www.tco.gov.ir/tco-briefe.html

[80] See chapter 5 and 6 for TCO's activities in biopharmaceuticals and bioagriculture.

[81] Source: http://www.tco.gov.ir/tco-briefe.html

[82] Source: http://www.tco.gov.ir/tco-briefe.html

[83] E.g. developing a strategic plan for the automobile industry in close collaboration with the Ministry of Petroleum (UNCTAD, 2005).

[84] These include the Industrial Development and Renovation Organization (IDRO); Small Industries Organization; Iran Mineral Industries Development and Renovation Organisation (IMIDRO); and Iran's Standard and Industrial Research Institute (ISIRI).

[85] MIM's financial programmes include the auto industry fund, the industrial technology assistance programme, the electronic development fund, the industrial research and IT training programme, the productivity programme, the study of SMEs research programme, and research production programme.

US$40 million comes directly from the MPO and does not pass through MIM, thus artificially creating a separation between HTIC and its host ministry. HTIC consists of nine committees, each headed by a project leader contracted to HTIC. Several of HTIC project leaders are also adviser-consultants to TCO. Collectively, the network of scientists and other experts associated with these committees constitutes a group of around 300 collaborators. Six of the HTIC's committees are sector-based (technology) and focus on biotechnology, software and IT, electronics, civilian aerospace, laser and optics, and new materials.[86]

In addition to its sector-specific committees, HTIC has three research divisions with a focus similar to that of TCO. One of these divisions has been set up to survey development models in other countries to understand the factors that enabled them to advance technologically. This task is identical to that being undertaken by the TAC within IROST. The other research divisions focus on economics and management of technology, an area that is not central to the work of either TCO or IROST. Within the technology management group, tools for technology assessment and technology foresight applicable at the sector level are being developed. The training of MSc students in the technology management programmes at SUT and Allameh University provides an important addition to tertiary education in the field of STI policy and practice in Iran.

4.4.6 Iran's Intellectual Property Rights

Data on patent application shows an active interest among non-residents in seeking patent protection in Iran (table 4.15). This may be a reflection of the importance of the Iranian market for inventors. To award a patent no substantive examination of the invention are conducted. The material is published to see if there are any objections from the public, in other words it is a purely declarative process. The time period from the application to the award is only one to three months. Publication is in Persian language.

Table 4.15 Data on patent and trademark applications in Iran

	1998	1999	2000	2001	2002*
Patents					
Total Applications	496	543	616	993	1,199
residents	337	366	410	691	910
non-residents	159	177	206	302	289
Total Registration	241	322	448	881	840
residents	64	152	241	529	440
non-residents	177	170	207	352	400
Trademarks					
Applications	6,278	9,494	10,220	11,082	12,880
Registration	2,528	3,796	3,750	4,437	5,187

Source: WIPO; (*2002 data from UNCTAD)

[86] See chapters 5 and 6 for HTIC's biotechnology specific activities.

The law relating to patents and trademarks comes under the judiciary department of Ministry of Justice. The department headed by a deputy minister (who is also a judge of the Supreme Court) houses the 'Patent and Trademarks Office and Registration of Companies'. The legislation relating to copyrights comes under the Ministry of Culture and Islamic Guidance (MCIG). Iran's first law on patents was ratified in 1931. In 1957, executive regulations were added and modifications made. In 1958, Iran became a party to the Paris Convention on Patents. In 1978 the Paris Convention text was revised, but Iran joined the revised convention in 1998.

Iran enacted legislation for copyright protection in 1969, but it did not join the Berne Convention on Copyright. In 1980 and 2000, it enacted other laws to protect literary and artistic works. In 2001, it enacted legislation for software protection considered to be compatible with international practices, which was drafted by a committee of experts from the legal and software sectors. Under this legislation, if a piece of software is a new invention, it can be granted a patent, otherwise it can apply for copyright protection.

In 2000, a 'Legal Consultative Committee' was appointed to revise the IP laws in Iran as per the model law developed by WIPO. A year later, Iran became a member of WIPO. In August 2003, the Iranian Parliament approved two bills to join the Madrid Agreement and its Protocols (trademarks). The Madrid Agreement and the Madrid Protocol entered into force in December 2003. In 2005 new legislation incorporating 16 different international conventions on IP was submitted to the Parliament. A 'High Coordination Committee' composed of deputy ministers of relevant ministries was created to revise IP policies.[87] This legislation aims to provide stronger IP protection by incorporating enforcement as part of the legislation.

The new IP law in compliance with the WIPO model IP law was ratified by the Iranian parliament in January 2008 and became effective in May 2008 for a probationary period of 5 years. The law provides protection for Industrial Designs as well as Patents, Trademarks and Trade Names and has been praised for meeting the requirements of the TRIPs Agreement (Baines, et al., 2009). This law introduces civil and criminal penalties for patent infringement. Another significant improvement over the previous legislation is the addition of inventive step to the novelty and utility patenting conditions. Also under the new law the patent office is committed to substantive examination of patent applications.

However, some procedural and substantive inconsistencies remain. For example utility models and traditional knowledge have not been provided for and there is no provision for an open system of patent examination (Baines, et al., 2009). It is envisaged that a more limited examination system will be implemented instead, based on peer review of inventions by academics based at a number of

[87] These ministries included MSRT, MCIG, MIM, MAJ, and Ministry of Post, Telegraph and Telephone.

universities and science parks. The law provides free access to patent documents; however, the Industrial Property Office has tried to restrict access to these records by asking individuals to obtain the agreement of the inventor to access the documents, contrary to the public disclosure requirements of most modern patent systems.

It is too early to draw any firm conclusions on the new law's application and effectiveness. It will be interesting to see whether it will strengthen patent protection, which is the stated goal of the government.

While the legislation on patents and trademarks corresponds to international regulations, the legislation on copyright is different from the international norm. Although it has a good standard of protection for national properties, protection for foreign artistic and literary works was previously considered to lead to cultural competition. This has now changed in the 2008 IP law as a result of government awareness of the importance of IPR in attracting FDI. Three seminars on copyright and international conventions were held at the national level, in cooperation with WIPO, which helped to create awareness in Parliament and the Guardian Council of the importance of protecting foreign property. Iran is not a member of the Patent Co-operation Treaty (PCT).

There are now at least five different courses on IPR law at the Masters level (e.g. University of Tehran and SBU) and many students have completed their theses on topics relating to IPR.

4.5 Summary

Iran is a middle-income developing country, with a broad industrial base, a reasonably well developed S&T infrastructure and well-educated scientists and engineers. Iran has pursued a development strategy of self-reliance with some degree of success. Nevertheless, the Iranian government adopted an import substitution policy using its oil revenues to acquire foreign technologies to industrialize. Diversification of Iran's natural-resource-based economy is an imperative for the Iranian government, not only because natural resources are exhaustible but also as export success in world markets increasingly demands knowledge-intensive production and innovation-based competition. Above all, there is need to provide quality jobs for 800,000 skilled work force that enter the labour market every year. These development strategies of the Iranian government fit Gerschenkron's view on 'ideologies favouring economic development' as an important agent of economic growth. In this regard the 3rd and 4th EDPs (2000-2010) have promoted the transformation of Iran to a knowledge society by strengthening the role of S&T in the innovation process. The focus of the Iranian government on building a strong S&T infrastructure in high-tech areas is favourable for knowledge intensive sectors such as biotechnology. At the current stage of the biotechnology life-cycle, entrants need a large supply of core scientific capabilities in which a mass of scientific disciplines are combined. A strong foundation in the relevant knowledge base is needed for firms and even countries willing to enter the field of biotechnology, probably even more than the need for availability of capital (Cooper, 1994).

The main actors in Iran's NSI are government ministries, U/RIs, and enterprises. Many of the U/RIs have built up impressive capabilities ranging from basic research to product and process development. A unique feature of the system is that almost all U/RIs and the majority of enterprises are state-owned. Largely due to this government ownership, there are close links between U/RIs, enterprises (mainly large) and government. As a result government ministries interact strongly with U/RIs and large firms. The nature of these interactions ranges from prioritization of research areas by the relevant ministries to the funding of specific research projects. U/RIs, in turn, monitor technological developments and provide feedback to ministries to facilitate decisions relating to research priorities. To coordinate interactions, activities, and objectives amongst the U/RIs, the government has established research councils and coordination committees to prioritize research programs and allocate tasks between different organizations. For instance, in the biotechnology sector, different U/RIs, which are under different ministries such as MSRT, MHME, and MAJ collaborate in providing postgraduate education. TCO under the Presidency has strong links with the research institutes, mainly through funding of research projects that can be commercialized by Iranian firms.

The link between U/RIs and large firms is also strong. Many large enterprises in Iran do not have in-house R&D capacity and tend to rely on research institutes for product development and process innovation. The government lays down R&D programs and projects to be undertaken by U/RIs. As a result, decisions on R&D priorities tend to be based on perceived immediate economic or social needs rather than based on consumer demand or long-term strategy. Due to the weak R&D capabilities of firms, U/RIs also carry out downstream R&D activities such as product and process development and testing. As a result, research projects take a long time to complete (Abbasi, 2003).

Another unique feature of Iran's NSI is the marginal role played by TNCs in the economy. TNCs are almost non-existent in Iran and therefore contribute very little to the development of the NSI. To address this issue the government has established free zones where foreign companies can locate operations.

Iran's export base is narrow relative to its industrial base and technological capabilities. Iranian authorities have recognized the need for policies that will stimulate diversification, technological upgrading, learning and innovation. The 4th EDP (2005-2010) places emphasis on the adoption of policies for enhancing innovation, internal and external sources of R&D and mechanisms for building technological and innovative capacity. The creation of SCSRT chaired by the President, and the establishment of a coordinating secretariat within the MSRT provide a basis for overall goal and priority setting within an integrated innovation-based framework. Iran has already made some progress in building a support structure for innovation. In recent years, the idea of establishing science parks and incubators has gained momentum with both national and regional government. MSRT first established the Isfahan Science and Technology Town and following a successful experience decided to establish new science parks in different provinces by converting the existing branches of IROST. MIM also took up the idea and established a couple of technology parks. These S&T parks and business incubators are geographically close to U/RIs to assist start-up firms and increase the role of SMEs which currently play only a small role in the economy. Start-up firms set up by students and researchers from U/RIs are the main residents in science parks. As a result, science parks have strong ties with U/RIs. MSRT, MIM, MCIT, and TCO provide research loans and grants to some firms located in these science parks. Provincial officials are making efforts to mobilize financial resources and obtain necessary approvals for developing science parks in their respective provinces. However these S&T parks are still in their experimental stage.

While Iran's STI policies reflect its efforts to transform into a knowledge-based economy, a linear approach to the innovation process still characterizes its policymaking. This is reflected in the separation of scientific research from technological development in policy planning and programming. Dominance of academic criteria as the standard for evaluating research quality derives from the link between higher education and scientific research. Research institutes[88] lose relevance if their researchers do not collaborate closely with industry. Yet to do so is against long-standing prejudice in academic circles against research that builds upon theory as opposed to producing theory. There is need to better link the S&T infrastructure to the needs of the manufacturing sector generally. In addition due to traditional habits and practices governmental bodies and research institutions in Iran work in parallel rather than collaborating. Where collaborative linkages remain weak, ministries do not provide the demand or subsequently supply the users for the output of research and technological development when they are not involved as collaborators in projects.

[88] E.g. Iran Composite Institute

Chapter 5 Key Features of Iran's Biotechnology SI

This chapter presents the key features of Iran's Biopharmaceutical and Bioagricultural sectors. Major actors promoting and financing biotechnology SI and major government policies and their impact on innovation in these sectors are discussed. Secondary data from national reports and publications, the websites of ministries (e.g. MHME, MSRT, MAJ, and AREEO) and major U/RIs is supported by the interview data to provide a comprehensive picture of Iran's Biotechnology SI. Data on biotechnology SMEs are largely missing from the existing reports and documents. Therefore the current position of SMEs within Iran's biopharmaceutical SI, the role of other actors in their innovative activities (systemic linkages) and reasons for systemic failures is based on the primary data from interviews.

5.1 Development and Attributes of the Biopharmaceutical SI in Iran

Iran's first activities in traditional biopharmaceuticals were conducted at the Pasteur Institute of Iran (IPI) founded in 1920, followed by the Razi Serum and Vaccine Research Institute (RSVRI) in 1925. These institutes started producing vaccines through traditional biotechnology methods for both veterinary applications and human use. Pharmaceutical companies in Iran started their operations by licensing products and processes from TNCs and manufacturing them locally. The operations mainly involved importing mass drugs and formulating them locally (Cheraghali, 2006). However the TNCs left Iran after the Revolution of 1979 and subsequent political developments including numerous sanctions made it difficult to access technologies from abroad. At this point, all the pharmaceutical companies were nationalized. The subsequent Iran-Iraq war in the 1980s led to severe shortages of medicines (Basmanji, 2004). This led the government to move towards the production of generic drugs.[89] The government invested large sums of money in both firms and research institutes to develop this capability (INDP, 2004). This led to a complete bureaucratic centralization in policy and decision making within the pharmaceutical sector of Iran with the MHME in charge of decisions on policies and resource allocation, particularly distribution of subsidized hard currency. The price of pharmaceutical products was also firmly controlled by the government.

The 1st EDP, which began in 1990 as a reconstruction plan after the end of the war with Iraq, introduced the first steps towards privatization of the industry (EDP, 1990). The privatization policy was given additional momentum in the 3rd EDP (2000-2005) during which, many companies were acquired by NGOs including religious charitable foundations and societies such as insurance

[89] Generics are those on the WHO's list of generics, as well as those products that are not patented in Iran

and pension funds. The National Social Security Organisation[90] is the major stakeholder in the industry. Today, about 35% to 40% of pharmaceutical companies are owned by these NGOs (Basmanji, 2004).

From an NSI perspective, ministries, national U/RIs, and biopharmaceutical firms are the major actors in the Iranian biopharmaceutical sector (Sanati, 2004). Apart from the general medical and biotechnology U/RIs, Iran also has disease-specific medical research centres.[91] The role of support organizations such as industry associations and venture capital firms is limited. Private financing for start-ups seems to be largely absent. In place of venture capital, governmental funds from HTIC, LIDCO, and TCO in form of research grants and low interest loans seem to be playing a critical role.[92] Bank credit is also available for industrial operations. However, even the government-owned development banks have not started venture capital operations or other low-risk financing mechanisms (UNCTAD, 2005). Private sector business support and consultancy organizations only started emerging in the past 5 years.[93]

While there is an absences of TNCs in the biopharmaceutical sector as TNCs have no manufacturing or distribution facilities of their own in Iran, there are two types of collaboration between TNCs and local firms. One is the purchase and import of a whole formulation from a TNC by a local distributor (in this case a government agency) and the other is importing drugs in bulk, repackaging them locally and marketing them with both the TNC's and the local company's names on the label. These approaches have no significant learning opportunities for local firms, but the latter helps to reduce costs, create local jobs and improve availability of drugs. In addition to TNCs, contract research organizations which carry out and manage multi-centre clinical trials are absent in the Iranian biopharmaceutical SI.

Initial research activities in modern biotechnology started in 1981 at the University of Tehran's Biophysics and Biochemistry Research Institute followed by the Biotechnological Research Centre of IROST in 1985. NIGEB was established in 1987 and gradually research institutes such as RSVRI and IPI started activities in modern biopharmaceuticals (Sanati, 2004). Parallel with the establishment of modern biotechnology research centres in the country, educational centres also started offering official courses in biotechnology.[94] Appendix 8 provides a list of biotechnology

[90] 'Sazemane Tamine Ejtemaee'

[91] Disease-specific medical research centres include the 'Research Centre for Skin Diseases and Leprosy', 'Kerman Neuroscience Research Centre', and 'Research Centre for Gastroenterology and Liver Diseases'.

[92] From interviews.

[93] E.g. Peyman Assistance, Consultation and Technology Transfer (PACTT) International Company.

[94]The first biotechnology related degree was established in 1990 at the master's level followed by PhD level degrees at TMU and IPI in collaboration with NIGEB, IROST, Iran's blood transfer organisation, RSVRI, and Tehran University of Medical Sciences' (TUMS) faculty of Health. This trend continued with other major universities such as Sharif University of Technology, Amir Kabir University, and Universities of Mashhad, Tabriz and Isfahan introducing biotechnology related courses. In 1998, a 'medical biotechnology' degree was

postgraduate degrees initiated during 1995-2000 period. Table 5.1 presents the number of institutes active in biopharmaceutical R&D in Iran and other developing countries in the region.

Table 5.1 Number of biopharmaceutical R&D institutes in selected regional countries

	Disease diagnostic	Drugs, therapeutics and products	Bioinformatics	Vaccine development	Total
Iran	14	10	4	5	33
Egypt	3	3	3	3	12
Oman	3	1	3	0	7
Pakistan	2	1	1	2	6
Sudan	2	1	1	1	5
Jordan	2	0	1	0	4

Source: EMHGBN (2007)

A unique feature of the Iranian biopharmaceutical sector is the manufacturing and marketing activities of major state-owned research and education institutes, much like firms (mainly vaccines and diagnostic kits). These are integrated organizations combining research, education and commercial production of drugs (RVSRI, IPI), therefore the results of research at these organisations are passed onto their own production units for manufacturing. In addition most research organizations have pilot-scale or full plants supplying raw materials to drug manufacturers.

Public research institutes are the main sites to conduct advanced biopharmaceutical R&D in Iran. MHME and MSRT have done well in building specialised research institutes and centres conducting basic and applied biopharmaceutical research. Close collaboration between local U/RIs result in distribution and integration of the technological knowledge in the education and R&D system. The main challenge of the current government is to translate the R&D outputs into products and services beneficial to the public. In particular, increased collaboration with the private sector is considered crucial emphasising that private firms' business management capabilities are much more effective than the government sector.

R&D is also rated as increasingly more important to private biopharmaceutical firms' activities, the majority of which use a combination of in-house R&D and outsourcing. The main role of GSOs is to act as a bridge and establish the link between academia and industry, in particular the private sector. The efforts of such organisations were rated as important and successful by private biopharmaceutical firms studied in this project though more support such as diversified sources of funding are required.

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established at TUMS. A New Route PhD in biotechnology was also introduced to attract outstanding students to biotechnology through the national university entrance examination and science Olympiads. These efforts created considerable interest in biotechnology related subjects and a pool of graduates interested in the industry, attracting entrepreneurial activities in the field. (Interview, June 2008)

Biopharmaceutical R&D activities at major U/RIs range from isolation, identification and purification of biologically active molecules/compounds from plants, micro-organisms and marine resources with use in medical/pharmaceutical applications, to development and production of recombinant biopharmaceutical products of all kind.[95] Research areas and activities of key biopharmaceutical departments are available in detail in Appendix 6. All major U/RI studied in this thesis are government organizations with the exception of Royan Institutes. However Royan collaborates with MHME and is currently conducting three research projects requested by MHME. Royan Institute's innovation activities in the use of molecular methods in diagnosis of genetic disorders and use of stem cells in the treatment processes are unique in the region (Morrison, et al., 2007).

Basic research at U/RIs includes studying gene mutations and diversity among different ethnic groups in Iran. Such research helps in the prevention of hereditary diseases and in designing effective drugs to treat the diseases. Iranian researchers have been very active in the herbal medicine sector, particularly in identifying, isolating and extracting active ingredients. Worldwide, there is a high demand for these herbal compounds (UNCTAD, 2005). Iran has a vast variety of flora and a study of these plants would provide thousands of molecular structures. Consolidating all the compounds identified (including through future research) in different research institutes and building up libraries of such compounds will provide Iran with a unique business opportunity. In order to build up biotechnology capabilities, Iran needs to strengthen the process of producing the critical inputs efficiently by producing the critical reagents needed for research locally.

Researchers at these research institutes suggest their own research projects to the institutes for approval unless the institute suggests a ministerial/industrial project in which case if interested individual researchers or research groups will take on the project.

The list of novel and notable inventions at U/RI are impressive, however the majority of these inventions are not commercialised. There is a lack of entrepreneurship among scientists, partly because of the lack of modern methods of financing that offer low-risk capital to start-up firms.

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[95] NIGEB has 40 completed and 7 on-going projects in the areas of molecular diagnosis of genetic diseases (in particular pre-natal diagnosis and identification of carriers of defective genes), determination of genomic diversity of communities and patients, gene therapy and genetic consultation, understanding the defence mechanisms of the body, new vaccines, designing serologic molecular diagnostic methods, increasing the level of body immunity, tissue and organ transplantation, and understanding molecular mechanisms of human pathological diseases (e.g. cancer) and infectious and parasitic diseases in order to find ways of diagnosing, preventing and curing.

IROST is currently active in isolation of micro-organisms producing anti-virus and anti-cancer substances, production of the calcitonin hormone by cloning, and laboratory production of cyclosporine.

The biotechnology research centre of IPI deals with molecular detection of prevalent genetic disorders and various infectious diseases in Iran as well as the development of recombinant vaccines and pharmaceutics (e.g. protein expressions, interferon and vaccine for H. Pylori).

The commercialisation of research outcomes are either through transfer to the industry or spin-off creation. However even research institutes with their own production units face financial, administrative, and bureaucratic obstacles which make the route from lab to production unit challenging.

> "...as soon as the pilot activity falls into government bureaucracy it slows down or fails. This happened to the Growth Hormone project which [we were] a pioneer at. Unfortunately it fell victim to government inefficiency and its production was delayed ten years. ...In the government sector, heads of institutes change all the time, policies change, funding is not continuous; often researchers get frustrated and leave the project or the institute, or even get a better offer from a foreign institute and leave the country. Sanctions also affect Iran..." (Interview at research institute 1)

> "We have hampering regulations that don't support SME set up. Problems start with the bureaucracy involved in obtaining a production license from MIM [...] Decades ago someone at MIM decided that as Tehran was growing, no manufacturing firm should be set up within 120 km of the town Centre. This might be a good idea for polluting factories but does not apply to high-tech firms... These laws need to be updated... We evaluate our academics by putting a form in front of them which says how many papers have you published, not how many technologies have you transferred to the industry... If academics want to advance their career they will concentrate on publication. This is one reason why our academics don't go towards industry. We need to meet the industry's needs. It's no use to the industry if the researcher has published one hundred academic papers. We have had about 40 patents at the institute, none has been commercialised [...] Often the industry just wants to make money and doesn't see the point of investing in R&D... The government can play an important role in solving this problem by lowering industries' risk and fear of investing [...] in R&D, for example through financial support or subsidies [...] Only recently has the government started to address this issue. Article 45 of our constitution states if the industry invests 40% in R&D projects, the government will contribute 60% without taking any part of the profit generated. ...Now the industry is interested in what we do, they have been a few investments from the industry. The institute is very willing to interact more with the industry and has set up a collaboration office [...] Another problem is that the government still has an import strategy in place. We had a Chinese product in the market at 8000 IRR. The Iranian product entered the market at half that price. Soon the Chinese reduced their price to 800 IRR. How could we compete with that price [....] The Ministry of Commerce should put taxes on imports or stop them when there are domestic producers." (Interview at research institute 1)

> "...Most of my work [ ] involves novel ways of fast diagnosis of genetic disorders [......] It is however slow due to financial problems. Most of our projects at [the institute] have a novelty factor but the majority are not commercialized..." (Interview at research institute 2)

The techniques mastered by research institutes include the isolation, identification and purification of biologically active molecules/compounds from plants, micro-organisms and marine resources. In this activity IPI, NIGEB, IROST and SBU are very advanced and are aiming to build up an internationally competitive industry, extracting active ingredients and developing products on this basis or even supplying organic chemicals to world markets as raw material. In the medicinal plant sector NIGEB is working on a very advanced technique of cell culture (i.e. culturing plant material, like bacteria). If successful, these technologies could help Iran establish a competitive industrial sector, as the world's demand for plant-derived compounds is growing. Among the most notable achievements are the development of human growth hormone (the first recombinant product in Iran, developed at NIGEB and transferred to Samen Pharmaceutical Company for commercial production), GM-CF (a cytokine that functions as a white blood cell growth factor) at NIGEB, and novel vaccines against Leishmania and H. Pylori at IPI and RVSRI. These examples demonstrate Iranian research institutes' innovation capabilities.

In 1994, the need for centralizing activities and requests from research organizations to receive funds for biotechnology related research led to the establishment of a council for coordinating and assessment of proposals in the 'Bureau of Scientific and Industrial Studies of the Presidential Office'. A delegation from the 'State Department of Budget and Planning' submitted a written proposal in 1996, titled 'Organizing Activities in Biotechnology in Iran' and a biotechnology commission was established within the 'National Research Council' amongst other specialized commissions (Sanati, 2004). Following the president's 2000 decree, a 'National Biotechnology Committee' started its activities within MSRT's framework of responsibilities and authorities. This committee, with the participation of ministers, deans of universities and heads of major research centres became responsible for directing and promoting biotechnology related research and activities in the country. As a result a 'National Strategic Biotechnology Plan' (NSBP) was prepared by the 'National Biotechnology Committee' and ratified by the council of ministers to outline Iran's goals in the development this sector and the strategic plan to achieve its goals[96] (table 5.2).

[96]NSBP was prepared as an integrated program for establishment of a national biotechnology coordinating organization and budget allocation, as well as development of human resources, research activities, technology developments, production efforts, and commercialization promotions. NSBP includes the application of biotechnology in agriculture, medicine, environment, livestock and marine life, industry and mining, and bioethics.

Table 5.2 Medium and long term biopharmaceutical related goals outlined in NSBP (2006)*

Application of biopharmaceutical technology in Iran			
	Current situation	Medium term goals	Long term goals
Preventive technology	Relatively good	Achieve modern vaccine technologies and prepare the ground for export.	Export of modern biopharmaceutical products.
Diagnostics	Major parts of diagnostics are currently imported. Current efforts concentrate on growth of domestic production of diagnostics, using modern biotechnology in national laboratories, and setting national standards.	Production of 50% of the domestic need.	Production of 80 % of the domestic need.
Treatment	Currently 3% of the drugs used in treatment are imported which are mainly specialised drugs produced through modern biotechnology. In terms of value, these imports account for a third of the national drug budget.	Production of 10% of the domestic need for modern biopharmaceuticals.	Production of 30% of the domestic need for modern biopharmaceuticals.

*The content of table 5.2 are translated from the NSBP, drafted by 'Higher Council of Biotechnology of Iran'

Local production of high-tech biopharmaceuticals is a new development in Iran. In addition to state owned organisations such as IPI and RVSRI, a number of private companies (e.g. Cinnagen, Shem Enzyme, Pouyesh Darou, and Pars Roos) have started to produce modern biopharmaceuticals and the number of start-ups and spinoffs joining this industry is gradually increasing. Starting in 2001, MHME lifted the compulsory generic production of the medicines and encouraged pharmaceutical companies to produce branded generic medicines. Firms are encouraged to propose products for licensing based on their own perception of market needs. This policy has created a more competitive environment for biopharmaceutical companies and is expected to improve quality of locally produced medicines (Cheraghali, et al., 2004). Locally produced modern biopharmaceutical products have already entered the market (FDO, 2005).[97]

Despite the presence of medical insurance scheme, imported medicines which are mainly high-tech biopharmaceuticals, receive direct government subsidies. This means that the government pays direct subsidies to the importers of these medicines in order to reduce their costs. The subsidy mechanism has made essential medicines available and affordable for more than 90% of the population (Cheraghali, et al., 2004). The government determines which product needs to be produced and licenses it to companies for manufacture with a production allowance established for each firm. Multiple licensing avoids dependence on a single supplier. The companies manufacture

[97] Locally produced modern biopharmaceuticals in Iran include: hormones, growth factors, IFN α, IFN β, IFN γ, pegylated IFN, streptokinase, erythropoietin, erythromycin, human growth hormone GM-CFS[97], Hepatitis B vaccine, vaccines against Leishmania and H.pylori and diagnostic kits and reagents.

the product with a generic label. Drug prices are controlled by the government and the price of a drug is the same all over the country, whether it is sold by a private or a public company (IPHR, 2004). Currently, the pricing system is based on cost analysis and rigid profit margins for producers, distributors and pharmacy outlets (Cheraghali, 2006).

As a consequence of government subsidies compensating companies for the low fixed prices, companies have no motivation to compete on the basis of brand name or quality. This also has implications for profit margins and R&D investments. The government subsidies have been very high, thus, even after many years of experience in drug production, the technological capability of Iranian pharmaceutical companies remain mainly limited to manufacturing and development of new drug formulations. The processes, in most cases even the delivery systems, is developed by national research institutes and transferred to companies. Post market research is also carried out by national research institutes.[98] Once a product was identified, the government funded the development of that drug (mainly new processes and formulation). After developing the product, research institutes transfer the know-how to pharmaceutical firms on a royalty basis. R&D carried out by pharmaceutical firms is mainly limited to the testing of product quality (UNCTAD, 2005).

However recent emergence of private biotechnology firms with R&D capabilities such as Cinnagen and Shem Enzyme is changing this trend. Under the 3rd EDP (2000-2005) there has been a change in the government's intervention and it is now less involved in strategy-setting at the firm-level. To promote competition in the industry, in parallel to the privatization act, the government is trying to reduce its intervention by removing fixed subsidies from the local industry and replacing them with targeted subsidies (Basmanji, 2004), (FDO, 2005). Currently only a few imported medicines, such as blood factors and medication for cancer treatment still benefit from government subsidies. The government also supports the local biopharmaceutical industry through imposing high tariffs on imported medicines which are also produced locally (Cheraghali, et al., 2004). The total value of the drug market in Iran was estimated at US$750 million in 2006 (Cheraghali, 2006). With the government looking to privatize the drug import sector, experts predict imports to reach US$1.2 billion by 2015 (NSBP, 2006), (NSBP, 2009).

Iran's reliance on imports for raw materials (including APIs)[99] and many specialized drugs, despite the rather developed national pharmaceutical production capability, has motivated the government to encourage the local industry to produce these drugs. Iran's local pharmaceutical industry produces more than 97% of the market needs and only 3% of drugs are imported, however in

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[98] Post market research is the process of monitoring new drugs launched in world markets.
[99] More than 70% of raw materials used in the manufacture of drugs (including APIs) are still imported from Europe, China and India.

terms of value, these imports account for a third of the drug budget (Annual Statistics Report, 2005). This situation has opened up an opportunity for new companies to emerge to develop and/or to manufacture these high-value drugs, which will reduce the outflow of foreign currency and reliance on imports which could always be affected by political turbulences. Table 5.3 shows Iran's medium and long term goals in biotechnology as stated in the NSBP. The goals are ambitious and show the previous government's drive to develop biotechnology.

Table 5.3 Iran's medium and long term biotechnology goals as stated in the NSBP

	2005	2008	2015 (medium term goals)	2020 (long term goals)
Total number of biotechnologists with MSc and PhD	1,400	1750	3,500	16,000
Total ISI biotech publications	250	700	1,500	5,000
Total national biotech publications	2,000	1600	5,000	18,500
Number of biotech patents	16	85 (incl. 5 internat.)	15 internat. patents	50 internat. patents
Number of biotechnology research centres and institutes	43	93 (public and private)	15% growth	30% growth
Biotechnology product market value	US$ 400 million	US$ 902 million	US$ 1 billion	US$ 2 million
Biotechnology contribution to GNP (%)	0.6	0.6	1.4	1.5
Export (% of total biotechnology production)	insignificant	insignificant	30	50
Number of firms producing biotech products and machinery	30	81 (30 private)	Over 80	150
Private sector share of biotech production including machinery and equipment (%)	NA	55 (short term goal was 65%)	75	85
Private sector share of biotech R&D activities (%)	Insignifican t	Insignifican t	15	30

Source: (NSBP, 2006), (NSBP, 2009)

5.2 Development and Attributes of the Bioagricultural SI in Iran

Bioagricultural development too has received particular attention by the Iranian government during the 3rd EDP, through intensive investment in education and creation of public-sector bioagricultural research institutes and modern plant modification methods, to increase crop/food yield in the limited fertile land space of Iran. Currently only 12% of the country's total land area of 1,636,000 km^2 is under cultivation. In addition most of the present farms are being used with only 50% to 60% capacity (Shobha Rani, 1998).[100] 12.5 million ha are cultivated annually with a wide range of crop species. Wheat, rice, other grains, sugar beet, fruits, and nuts are the country's most

[100] With 35% of Iran's landscape covered by deserts, salt flats and bare-rock Mountains, 11% by woodland, and 7% by cities, towns, villages, industrial areas and roads, the majority of Iran's landscape is not suitable for agriculture.

important crops, with a total value of US$13 billion (Mousavi, et al., 2007). In addition to water scarcity and areas of poor soil, seed is of low quality and farming techniques are old. All these factors have contributed to low crop yields and poverty in rural areas (Shobha Rani, 1998). Moreover, after the 1979 revolution many agricultural workers claimed ownership rights and forcibly occupied large, privately owned farms where they had been employed. The legal disputes that arose from this situation remained unresolved through the 1980s and many owners discontinued large capital investments that would have improved farm productivity, further deteriorating production. In 1979, 65% of Iran's required food crops had to be imported (James, 2005). Declining productivity was also blamed on the use of modern fertilizers, which had scorched the thin Iranian soil. Unresolved land reform issues, a lack of economic incentives to raise surplus crops, and low profit ratios drove increasingly large segments of the farm population into urban areas.

Since 1979 commercial farming has replaced subsistence farming as the dominant mode of agricultural production. Some northern and western areas support rain-fed agriculture, while other areas require irrigation for successful crop production (James, 2005). The government has sought self-sufficiency in food as part of its overall goal of decreasing economic dependence on the West. Higher government subsidies for grain and other staple foods and expanded short-term credit and tax exemptions for farmers complying with government quotas were intended by the new regime to promote self-sufficiency (Mousavi, et al., 2007). Irrigation is very expensive and highly subsidized. Much of the newly irrigated land is used to grow wheat, at a cost higher than that of imported wheat, but it aims to reduce the country's dependence on imports and improve food security (Seifi, 2007). However the government efforts in self-sufficiency have been inconsistent and in the past two decades, Iran has actually been more dependent on agricultural imports than in 1970s (Mousavi, et al., 2007). To address these problems more efficiently, in 2001, the 'Ministry of Constructional Jihad' and the 'Ministry of Agriculture' merged under the national legislation to form the new 'Ministry of Agricultural Jihad' (MAJ). The government's current focus areas for agriculture related policies are to ensure self-sufficiency in the provision of national food requirements[101], to set budgets for agro-industrial projects in the food processing, packaging, and irrigation sectors, to provide financing and low-interest loans for investment in agriculture and agro-industrial projects, and to provide agricultural machinery and equipment with emphasis on local production by making technology transfer a required clause in foreign contracts[102] (ASTI, 2008). To address agricultural research policy, the 'Agricultural and Natural Resources Research

[101] Under article 18 of the 4th EDP, the government is to prepare a plan for the development of agriculture and natural resources with a view to attain self-sufficiency in the production of basic agricultural products, improve food security, increase export of agricultural products, and generally enhance growth in the sector (Atieh, 2005)

[102] In 2008 foreign loans and investments in the agro sector exceeded US$500 million (ASTI, 2008).

Organization' (ANRRO) was established in 1975 as a central entity for policy formulation, prioritisation of research areas and coordination of the activities at existing research institutes. ANRRO's main objective was to increase production of agricultural and horticultural crops in the country. In 1990, ANRRO was reorganized and merged with 'Agricultural Education Organization and Extension Directorate', creating the 'Agricultural Research, Education and Extension Organization' (AREEO) responsible for agricultural research, education and development in Iran. Currently AREEO operates under MAJ and runs the network of Iranian agricultural research institutes including those active in biotechnology R&D.[103] Three commissions of biotechnology, agriculture, and soil and water within SCSRT provide consultation to this council on bioagriculture issues. Table 5.3 presents Iran's medium and long term goals in bioagriculture as set out in the NSBP (2006).[104]

Table 5.4 Medium and long term bioagricultural goals outlined in the NSBP (2006)

Technology	2005	Medium term goals (2015)	Long term goals (2020)
- Tissue culture	Average application in production (limited production in the private sector) and relatively good application in research.		Export of tissue culture products to the Middle East and Central Asia
- Molecular markers	Application is almost totally limited to classification. Short term goal is setting grounds for the development of technical knowhow. (Molecular markers have different applications from localization of a gene to improvement of plant varieties by marker-assisted selection. Genome analysis based on molecular markers has generated a vast amount of information).	Extensive application in the genetic manipulation of plants to at least 2 applications of molecular marker technology.	Extensive application in the genetic manipulation of plants to at least 10 applications of molecular marker technology.
- Biological fertilizers and pesticides	Production and consumption of 1% of the total amount of pesticide and fertilizer needed by the country	To produce 3% of the country's need for bio-fertilizers and bio-pesticides (replacing chemical fertilizers and pesticides)	To produce 10% of the country's need for bio-fertilizers and bio-pesticides (replacing chemical fertilizers and pesticides)
- Gene transfer and transgenic plants	Application is limited to research and laboratory scale production. Short term goal is creating technological knowhow.	Cultivate 0.2% of the world's transgenic plants.	Cultivate 0.5% of the world's transgenic plants.

[103] Source: http://www.areo.ir/HomePage.aspx?TabID=3881&Site=DouranPortal&Lang=fa-IR
[104] The content of table 5.3 is translated from the NSBP, drafted by a consortium of bioscientists.

Other goals stated in the NSBP (2006) include:

- Production of 10% of the national demand for livestock by the end of 2015.
- Production of 5 kinds of new vaccines against livestock diseases and an export target of 30% of total production by the end of 2015.
- Production of 15% of the country's need for biological products used in the food industry by the end of 2015.

The establishment of agricultural research institutes in Iran date back to RVSRI (1925) followed by other major agricultural research institutes.[105] Modern bioagriculture and plant modification research departments were established during 2nd and 3rd EDP at IROST, NIGEB, Seed and Plant Improvement Research Institute, Research Institute of Forest and Rangeland, and faculties of agricultural sciences. The 'Agricultural Biotechnology Research Institutes of Iran' (ABRII) was established in 1999 which soon became a pioneer in the field and produced Iran's first GM crop. On the educational side, postgraduate degrees were introduced by faculties of agriculture at various Universities in Iran during the 2nd and 3rd EDP.[106]

Over 20 biotechnology research institutes (in whole or in part) are involved in modern bioagricultural research in Iran (Mousavi, et al., 2007). Research areas and activities of Major bioagricultural research departments are available in detail in Appendix 7. Plant and crop improvement (through genetic engineering as well as non-GM technologies) and bio-fertilizer/bio-pesticide projects dominate modern bioagricultural research activities at public research institutes. Other activities include isolation, identification and purification of biologically active molecules/compounds from plants, micro-organisms and marine resources.[107]

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[105] Animal Science Research Institute (1933), Plant Pests and Diseases Research Institute (1943), and Seed and Plant Improvement Institute (1959).

[106] PhD degrees in plant modification, molecular genetics and genetic engineering were introduced in 1994 at the 'Faculty of Agriculture of University of Tehran' followed by a Master degree in 'Agricultural Biotechnology' in 1997. These were followed by degrees in Genetic Engineering of Plants at the Faculty of agriculture of TMU, Genetic Engineering of Crop Plants at the Faculty of Agriculture of University of Hamedan, Agricultural Biotechnology at the Faculty of Agriculture of University of Kermanshah, and Advanced Genetics and Molecular Biology of Plant Breeding at the Faculty of Agriculture of University of Gilan.

[107] ABRII focuses on the use of molecular markers for the study of genetic diversity and characteristics of the germ plasma of plants, micro-organisms and agricultural pests; micro-propagation, plant tissue culture and transfer of useful genes into plants; genetics and growth of plants using cellular and molecular techniques; micro-organisms needed in the production of bio-pesticides and bio-fertilizers, and identifying genes responsible for plant resistance to environmental stress.

NIGEB's research activities at its plant biotechnology department include identification of plant viruses and diseases through molecular methods, optimization and establishment of plant transformation techniques for production of transgenic virus resistant and salinity/and draught tolerant plants, molecular farming by using plant as a factory for production of important pharmaceutical proteins and industrial enzymes.

IROST's bioagricultural research is on preparation of bio-fertilizers, production of lysine amino acid as a food supplement for livestock and poultry, production of single-cell proteins from agricultural waste, and use of bacteria and fungi as microbial pesticides.

Iran became the world's first country to release a GM Bt rice to national farmers in 2004. However the full commercialization which was planned for 2006 has still not taken place due to reasons studied in chapter 6. None the less this crop is a landmark development in biotechnology, since it was the first time that a biotech version of rice, one of the world's most important food crops, legally went into production. The Bt rice program was only one of Iran's several GM crop initiatives. Other biotech crops which reached field trial stage were virus resistant sugar beet and herbicide tolerant canola at NIGEB, and pest resistant cotton at ABRII. Further, insect-resistant maize, cotton, and potatoes, salinity and drought tolerant wheat, and blight-resistant maize and wheat are currently produced only in laboratory scale. A list of Iran's GM crop projects at U/RIs is available in Appendix 4.

Over 40 GM crop projects have been completed at bioagricultural research institutes of Iran over the past decade, however only very few have been commercialised (Appendix 4). These products demonstrate Iran's technological capabilities in the field of crop improvement using modern as well as conventional methods. However due to the ban on GM activities, a major part of the R&D projects at research institutes are not translated into products for public use. Genetically engineered crops have been restricted from commercialisation/release and are still awaiting production licences. During the 4th EDP (2005-2010), use of genetic engineering and recombinant DNA technologies has been limited to lab-scale production and not applied in projects for commercial use. Therefore commercial plant improvement has been mainly through tissue culture, plant breeding, and gene transplant methods.

Public bioagricultural research institutes often have large scale production facilities and give the crops directly to farmers for production. Those institutes who don't have large scale production capacity transfer the technology to state firms.

In the private sector 1/3 of the 35 biotechnology companies produce bioagricultural products such as tissue cultured plants, bio-fertilizers, bio-agents for crop pests and disease control, and biomaterials mainly for feed, food, and pharmaceutical purposes (Mousavi, et al., 2007).

The Rice Research Institute of Iran's (RRII) biotechnology research is on production of inbred and hybrid rice varieties using mutation and recombinant DNA technologies, in addition to conventional breeding. The research objectives are to improve grain quality and yield potential; improve resistance to pests/diseases/drought/salinity; develop early maturing varieties; conservation and utilization of rice germ plasma; biological control of major pests and diseases using beneficial organisms (predators, parasitoids, pathogens and antagonists), mass production and preservation methods of Trichogramma as bio-control agent of striped stem borer (Chilo supperssalis), as well as new sources of resistance to blast and sheath blight diseases. Basic studies are on biology and genetic diversity of rice diseases and introduction of alternative control methods to chemical control against rice pests, diseases and weeds.

5.2.1 Iran's (bio)agricultural R&D expenditure, research staff, and research focus

Bioagricultural research is primarily funded by the national government.[108] The AREEO affiliated national and provincial research institutes and government centres are much more dependent on government support than other government agencies.[109] The national research institutes receive all of their funding directly from Tehran, mostly through AREEO, although a number of institutes receive funding from other units affiliated to MAJ, other ministries or the SCSRT. Each year, the national and provincial AREEO-affiliated research institutes submit funding proposals to AREEO headquarters. After approval by AREEO, the proposed budgets are passed on to the Iranian Parliament for review and approval in line with Iran's EDP. After parliamentary approval, SCSRT reviews and allocates public research funding to the various ministries and organizations. In 2007, total public funding allocated to S&T development was estimated at around US$1 billion, of which the agricultural sector received 20% (ASTI, 2008).

The provincial research centres also depend mostly on funding from Tehran (about 90%). In addition they also receive some funding from the provincial government entities, mainly for projects addressing local problems.

Funding for 'university-led' agricultural research is also derived primarily from the Iranian government but through a variety of sources including direct university appropriations and funds from INSF and other government agencies, as well as from provincial government entities.[110] Each province has its own S&T council and can financially support research proposals targeting local challenges. AREEO's provincial research centres and universities usually compete for R&D funding based on the priorities identified by the provincial government. The provincial funds, however, have not yet become a substantial and reliable source of research funding in Iran and these institutes have to rely on funding from the national government.

Public (bio)agricultural[111] R&D investments (excluding the private sector) grew steadily during the 3rd EDP at an average annual rate of 3.3% (from US$390 million to US$432 million).[112] Iran's

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[108] In 2000, the government supplied the funding for 94% of the government and non-profit agencies' expenditures (ASTI, 2008).

[109] During 2000–2004, the non-profit agencies combined received roughly 70% of their total funds from public/private enterprises and 30% was generated internally. For example, sugar beet research at Khorasan Sugar Beet Research and Agronomic Services Company (KSRAS) was entirely financed by the sugar industry (ASTI survey data).

[110] In 2007 agricultural projects accounted for 19% of INSF's total budget of US$5 million (INSF, 2008).

[111] The use of brackets in (bio)agriculture is to indicate the limitations of the available secondary data on Iran's bioagricultural sector.

[112] In 2004, Iran invested US$432 million in public agricultural R&D (or 0.91% of the country's agricultural GDP). Together with private-sector agricultural R&D investments (6% of Iranian agricultural R&D

intensity of investment in (bio)agricultural R&D is well above some countries in the region, such as Pakistan and Syria but below Jordan (table 6.1).

Table 5.5 Investment in (bio)agricultural R&D - comparison of selected countries (2004)

	(Bio)agricultural R&D investment as % of agricultural GDP
Iran	0.96[113]
Pakistan	0.31
Syria	0.53
Jordan	2.83
Developed countries (Average)	0.53

Source: ASTI (2004 Survey)

Public agricultural research is largely conducted by AREEO and its affiliates (Ghareyazie, 2004). 4,700 full time scientists were involved in public agricultural research in 2004, which represents an 18% increase over data recorded in 2000 (table 6.2). AREEO employs 75% of Iran's agricultural scientists. The provincial government agencies are engaged in all types of agricultural R&D in a particular province, while their national counterparts tend to focus on one particular commodity or discipline.

In terms of the average qualification levels of research staff, the intensity of public-sector investment in agricultural R&D (table 6.1) and average expenditures per researcher, Iran has outperformed many of its neighbours (ASTI, 2008).[114] Iran's share of researchers with postgraduate education (71%) is much higher than other countries of the region, such as Jordan (61%) and Syria (25%) (ASTI, 2008).[115] Iran's non-AREEO government research and higher education agencies play a more modest role in public agricultural R&D, accounting for just 8% and 11% of total FTE agricultural research staff in 2004, respectively (ASTI, 2008). The 2004 survey data on the composition of agricultural research institutes and FTE research staff is presented in Appendix 3.

Over 50% of Iran's FTE researchers are involved in crop research, 16% in livestock research, 9% in each natural resources and fisheries research, and 3% in forestry research. AREEO's research staffs are more involved in crop research compared to their non-AREEO counterparts. Livestock

investments), agricultural R&D investment was about 0.96% of the agricultural GDP, bringing Iran's total (public and private) agriculture R&D expenditures to US$457 million (ASTI, 2008).

[113] Share of public sector is 0.91% and share of private sector is 0.05% of agricultural GDP.

[114] Agricultural R&D expenditure per researcher at national research institutes averaged around US$144,000 during 2000-2004, which was considerably higher than the corresponding levels at provincial government centres (US$61,000) and other government and non-profit agencies (US$109,000). The higher spending per researcher at national research institutes partly results from their function of providing technical support, organizing workshops and procuring research equipment at provincial research centres. Average expenditure per researcher totalled at US$580,000 at RVSRI given increased financial support from government for infrastructure and facilities including construction of new laboratories and buildings for production of vaccines (ASTI, 2008).

[115] In 2004, 21% of FTE researchers in public agricultural R&D agencies held a PhD degree, 50% held MSc degree, and 29% held BSc degree.

research was more prominent in the private and higher education sectors.[116] In 2004, 14% of Iran's crop researchers were working on crop improvement through genetic engineering methods, 12% on crop pest and disease control, and 16% on other crop-related areas. The remainder of the researchers focused on livestock and natural resources-related areas, while only a small portion of researchers focused on postharvest, soil, and water areas. Research on crop genetic improvement was more important for government agencies than for the private and higher education sectors. 20% of private-sector research staff focused on postharvest themes, compared to 1% at AREEO. The share of FTE researchers involved in socio-economic as well as policy research is very low both at government and private agencies (ASTI, 2008).

The private sector accounts for only a small share of agricultural R&D conducted in Iran (ASTI, 2008). Notably, much of the private research relates to quality control and testing and the research results are not accessible through publications, internet, or other means. The private sector agricultural research staff showed consistent growth during the 3rd EDP (table 6.2). The number of agricultural researchers rose 62% during this period, which was much higher than the overall growth in the public sector throughout the same period (18%). Despite this impressive growth rate, the overall share of private sector in agricultural R&D staff rose only marginally, from 4% in 2000 to 5% in 2004.

Table 5.6 Agricultural research staff by sector (2000 and 2004 data comparison)

	Total agricultural research staff (FTEs) 2000	Total agricultural research staff (FTEs) 2004
Public	3971	4696
Private	172	277
Total	4143	4973

Source: ASTI

The role of private sector in financing public sector (bio)agricultural R&D is negligible.[117] However, the private sector has become increasingly involved in conducting its own (bio)agricultural R&D. Unfortunately, time-series data on private (bio)agricultural R&D spending are not available. In 2004, it was estimated that 34 private agencies involved in agricultural R&D spent a combined total of around US$25 million. Of particular note is the high number of private-sector agencies involved in livestock research given the relatively limited contribution of livestock to agricultural GDP. Iran has a number of relatively large companies that produce, process, or market livestock products, and these companies have established small research units to support production and test quality.

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[116] Unusually high share of researchers focusing on other research topics in the non-AREEO and non-profit institutes stems from the high number of researchers focusing on pesticide research at PFIRC (ASTI, 2008).
[117] Private share of (bio)agricultural R&D investments is only 6% of the country's total agricultural R&D investments (2004 ASTI Survey)

Iran's government does not have specific policies in place to stimulate private-sector participation in bioagricultural research. Moreover, no incentives are in place for private financing of public-sector agricultural research (ASTI, 2008). The private sector has initiated research in specific areas that fall outside the public sector's mandate, the results of which are proprietary and hence not available in the public domain. These areas include food processing, high-value crops and the adoption of imported seeds from abroad. In recent years, the government has tried to encourage private-sector investment in bioagricultural R&D, such as in seed production, fertilizer use and production, plant pest and diseases management, food processing, and marketing. Nevertheless, Iran still lags behind other transition economies such as Argentina, India, Malaysia, and Turkey when it comes to private-sector involvement in agricultural R&D (ASTI, 2008), (Mobasser, 2003).

5.2.2 Iran's Agricultural Products

The wide range of temperature fluctuation due to the three distinct agro-ecological zones (humid, semi-arid, and arid regions) make it possible to cultivate a diverse variety of crops in different parts of the country.[118] These include cereals (wheat, barley, rice, and maize), fruits (dates, figs, pomegranates, melons, and grapes), vegetables, cotton, sugar beets and sugarcane, pistachios (40% of the world's output in 2005)[119], nuts, olives, spices, saffron[120] (82% of the world's total output in 2005), tea, tobacco, and medicinal herbs. Over 2,000 plant species are grown in Iran. Wheat, rice, and barley are the country's major crops.[121] Wheat and barley have a large portion of the cultivated land with wheat accounting for 53% of the cultivated land in Iran in 2005.[122] Iran's forests cover about one ninth of its total surface area, approximately the same amount of land for its agricultural crops. The largest and most valuable woodland areas are in the 'Caspian Sea' region and the northern slopes of 'Alborz Mountains', where many of the forests are commercially exploitable and include both hardwoods and softwoods. Forest products include plywood, fibreboard, and lumber for the construction and furniture industries.[123] Iran also has a large dairy industry and imports close to two million tonnes of feed grain annually.[124] Production of livestock increased to reach 11.3 million tons in 2008 from 10.6 million tons in 2007, and 9.9 million tons in 2006.[125]

Major agricultural exports include fresh and dried fruits, nuts, animal hides, processed foods, and spices. In agricultural exports, pistachio, raisins, dates, saffron, tea, and caviar are the six largest

[118]Source: http://www.fao.org/countryprofiles/index.asp?lang=en&iso3=IRN&subj=4
[119] Source: http://www.bbc.co.uk/persian/business/story/2006/10/061013_oh_pistachio.shtml
[120] Source: http://www.idosi.org/wasj/wasj4%284%29/7.pdf
[121] Source: http://faostat.fao.org/site/339/default.aspx
[122] Source: http://www.atiehbahar.com/Resource.aspx?n=1000013
[123] Source: http://www.rifr-ac.ir/index.aspx, accessed in December 2008.
[124] Iran's livestock mainly consist of sheep, followed by goats, cattle, donkeys, and horses.
[125] Source: http://www.zawya.com/printstory.cfm?storyid=EIU20080501212100777&l=000000080303

export products in terms of value.[126] In addition Iran also exports medical and industrial plants, decorative plants, as well as livestock products. Pistachio is Iran's third biggest export product (after oil and carpets).[127] The total value of Iran's agricultural exports was US$3.2 billion in 2008, which showed a 6.1% increase over 2007 (Barnameh, 2008)

Even though agricultural products constitute Iran's main export items after oil, Iran is one of the major food importing countries (table 6.3). While the Iranian government's policy is aimed at self-sufficiency, Iran has struggled to provide enough basic food commodities to meet its local market demands following a significant population increase over the past two decades (James, 2005). Agricultural production stood at 108 million tons in 2008, which indicates a 20 million ton increase from 2007 (Barnameh, 2008). Nonetheless the national produce does not meet the national consumption and Iran remains one of the largest importers of agricultural products (Ghareyazie, 2004), (Mousavi, et al., 2007). The import of rice, for example, has increased dramatically in the last three decades, partly because of population growth (from 19 million in 1956 to 72 million in 2010). Iran is currently importing about 1 million tons per year making it one of the largest importers of rice in the world (Mousavi, et al., 2007). Limited available land for agriculture and limited supply of water (average annual rain fall of 240 mm compared to the 860 mm in the world) put restrains on increasing national rice production.[128] In addition rice is susceptible to several insect pests including striped stem borer, the major insect pest of rice in Iran causing an estimated crop loss of up to 20% (Mousavi, et al., 2007).

Table 5.7 Iran's largest agricultural food imports in million tonnes, 2005

Product	Quantity (Million tonnes)	Value (US$ 1000)
Maize	3,089,731	437,880
Rice	945,729	276,316
Soybean oil	923,384	514,508
Oilseed	845,560	234,833
Soybean	828,000	225,041
Wheat	406,365	168,466
Sugar	406,365	81,210
Palm oil	126,970	60,055
Sunflower oil	117,856	789,382
Potatoes	33,189	3,362
Rapeseed oil	19,974	12,369

Source: Abdolabad, 2007

Looking at other countries where bioagricultural products are multiplying in number and cultivation area and are considered by many to be a remedy for food shortages, many Iranian scientists believe

[126] Source: http://www.presstv.ir/detail.aspx?id=38184&sectionid=351020102
[127] At over 200,000 tons for US$840 million in 2008. Source: http://www.sahravi.com/news_dates-raisinspistachio.htm#Iran,%20Turkey,%20USA%20 major%20 raisin%20 exporters
[128] For example Iran's total area of rice cultivation is about 630,000 ha, which only produces 1/3 of its rice consumption (Mousavi, et al., 2007).

the country's food problems can be solved more rapidly and efficiently through bioagricultural innovation. But despite the local production capacity through modern biotechnology, Iran carries on importing a large amount of its food requirement (Ghareyazie, 2004).

5.2.3 Development of Iran's Biosafety Regulatory Framework

Prior to ratification of Iran's National Biosafety Document in 2009, the environment safety in Iran was regulated by the Environmental Protection Law of 1974 which did not contain legal and administrative regulations on biotechnology or GMO/LMO. In 1996, Iran joined the Convention on Biological Diversity. According to Paragraph 8 of this convention, Iran committed itself to the creation and maintenance of tools necessary for supervising, managing and controlling risks in the use or release of LMOs resulting from modern biotechnology with regards to human health and the environment (NBFI, 2004).[129] In August 2000 the National Biosafety Committee (NBC) was established at MSRT in order to compile biosafety laws and develop a system for biosafety control.[130] NBC's prominent functions have been the decision on joining the Cartagena Protocol on Biosafety (CPB) and related issues, and preparing the draft of the national biosafety laws and regulations for safe utilization of modern biotechnology and its products in order to reduce possible risks to the environment, biodiversity, and human health (Mousavi, et al., 2007).

Iran signed the CPB in April 2001 and the protocol entered into force in February 2004.[131] Consequently, the government formed the NBC at a higher state level, composed of 6 ministers and 2 deputies of the president as chairman and secretary.[132] The new secretariat involved in year-round negotiation with representatives of several state organizations to draft the national biosafety

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[129] Available at http://www.unep.org/Biosafety/files/IRNBFrep.pdf

[130] NBC's duties included biosafety macro policy formulation; formulation of regulations and directives regarding biosafety measures; approval of biosafety standards and criteria; high biosafety supervision in accordance with the CPB and other related international treaties; biosafety supervision in cooperation with the Ministerial Biosafety Committees, certification of higher-level laboratories and control facilities; instructions for assessing the risks of microorganisms which have been designated for controlled use; supporting the collection and development of methods and instructions for assessing the risks of microorganisms selected for field trials and commercial release; appointment of members of departmental biosafety committees with the help of centres involved in genetic engineering and foreign species under the supervision of relevant heads of organisations.

[131] Iran signed the CPB on 23rd of April 2001, which was the beginning of a series of formal procedures for ratification of the protocol and the Iranian Parliament ratified CPB. Based on the date of official registration at the secretariat of the protocol (20th of November 2003), it entered into force on 18th of February 2004 (Mousavi, et al., 2007).

[132] NBC members are the Minister of Science, the director of the Environment Protection Organization, the Minister of Foreign Affairs, the Minister of Health, the Minister of Agriculture, the Minister of Industries and Mines, the Minister of Commerce, four specialists from medical biotechnology, agriculture, environment and basic sciences backgrounds, the representatives of the network of NGOs and private organisations, and representative from the Strategic Council of Biotechnology.

law in order to provide the required mechanisms for risk assessment and risk management for contained use, release, handling, import, export or transit of LMOs and their products.[133]

NBC includes the focal point of the CPB and the Biosafety Clearing House (BCH) located at its secretariat office. The focal point of CPB is a point for all international contacts, including that of the protocol secretariat. The focal point was initially located at MAJ and then moved to the Environment Protection Organisation (EPO). BCH's function is to facilitate information exchange in risk communication and experience with LMOs to promote scientific understanding on biosafety issues and to share information and experiences in different aspects of biosafety.[134]

Under NBC's supervision, five Ministerial Biosafety Committees (MBCs) are responsible for processing requests for the use of LMOs from their specific points of views and national missions, responding to specific enquiries, forwarding proposed regulations based on their role, and reporting to NBC the activities going on in their area.[135] Similar to CPB, requests for the use of LMOs could be classified as application of LMOs for food, feed, and processing, contained use, or release to environment. Some requests might require the review of 2 or more national competent authorities (NCAs) as judged by NBC secretariat based on the type of application.[136]

Although efforts towards a national biosafety document for approval by the parliament where initiated during the 3rd EDP, the parliament did not ratify the national biosafety document until May 2009.[137] According to this recent law a representative from scientific communities is added to the NBC. Environmental release, commercial production, import, export and use of LMOs are allowed and no obligatory labelling is required for commercialized LMOs. R&D is exempted from the limitations of this law. In addition rejection of application for commercialization of any LMOs should be based on scientific evidence only (Ghareyazie, 2009). As this law is recent the effects on the development of Iranian bioagriculture remain to be seen, however it is expected that approval

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[133] Although the use of LMOs for pharmaceutical and research affairs are exempted from this law, these are covered by other governmental laws and regulations, in particular those by MHME and MSRT.
[134] For this purpose BCH provides information and documents related to general scientific biosafety developments at national and international levels, developments related to the biosafety protocol and national policies and laws, experts and authorities in Iran, capacity building needs and priorities. BCH also publishes the seasonal biosafety bulletin. Source: http://ibch.nrcgeb.ac.ir
[135] MBCs are located at MIM, MHME, MAJ, MSRT and EPO.
[136] Relevant articles of the law declare a judiciary regime according to which the holder of permission is liable for possible damages regardless of their improper action unless they prove accountability of the third party. On the other hand, permission holders are forced to obtain responsibility insurance for the duration of the permit, which ensures compensation for damages to individuals, farms, and the environment. Failure to obtain permission or inappropriate actions will be judged as an offense and penalized accordingly. Additionally, NCAs are responsible to monitor the use of LMOs that may lead to suspension or even termination of a permit. In such cases, the holder's right to appeal the decision by referring to different levels of the judiciary system is preserved.
[137] Data on Iran's biosafety issues and the Case Study on Iran's GM rice are presented in chapter 8.

of this law will benefit R&D as well as innovation activities in the field of genetic engineering (Ghareyazie, 2009).

5.3 Actors Promoting Biotechnology Development in Iran

The main governmental agencies promoting research and educational activities as well as innovation in the biopharmaceutical sector of Iran are MHME, MSRT, MIM, TCO, and Ministry of Justice for IP rights. Within MHME, the 'Department of Research and Technology' and the 'Department of Medical Education' play vital roles in promoting biopharmaceutical innovation in the country.[138] The Network of Herbal Medicine NGO has also played an important role in developing herbal medicines. In bioagriculture the main actors promoting the development of the sector are AREEO under MAJ, MSRT, TCO, and non-governmental scientific organisations related to biotechnology (Biotechnology Society of Iran, Genetics Society of Iran, and Biosafety Society of Iran).

5.3.1 Ministry of Health and Medical Education

5.3.1.1 Department of Research and Technology

The 'Department of Research and Technology' under MHME manages research in medical sciences, monitors research and technology development, sets priorities among research projects, and provides funding for projects, most of which are allocated to governmental organizations. About 30% of the funding is allocated to basic research and the rest to applied research, for example process development. The department funds research projects in both universities and research institutes. In 2008 over US$10 million were allocated to S&T Parks by MHME and MSRT together (Etemad, et al., 2008). The criteria adopted for the selection of research projects are based on the priority of diseases (based on assessment results of medical school laboratories that collect information on health issues) and existing local capabilities.

The Department has also established a 'Cardio-vascular Research Centre' and an 'Endocrinology and Metabolism Research Centre' at TUMS. Another 'Endocrinology Research Centre' has been established at SBUMS. Even though these research centres are affiliated with medical universities, they are provided with separate budgets by MHME, a practice which is similar to that of MSRT and IROST. The particular universities selected as the location for the above research centres were chosen because they have built up expertise in these specializations through previous research.

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[138] MHME consists of five departments, headed by deputy ministers: Department of Medical Education; Department of Food and Drugs; Department of Health; Department of Logistics; Department of Research and Technology.

The 'Department of Research and Technology' has also formed three networks for basic research in order to promote coordination, knowledge exchange and prevent duplication. These networks are the 'Medical Biotechnology Network', the 'Molecular Medicine Network', and the 'Herbal Medicine Network of Iran'. The Molecular Medicine Network is the largest of these networks with 34 member research organisations. In general, there is no duplication of work, but in some cases the research requires further analysis and parallel research in several laboratories are carried out.

The 'Medical Biotechnology Network' was established in 2002 to manage and direct research and production efforts in this field. This network currently includes ten major research areas with priorities in production of vaccines as well as pharmaceutical and medical diagnostics through recombinant protein technology; production of transgenic animals for use in drugs, monoclonal antibodies, and enzymes; recovery of bio-products from microorganisms and other natural resources for preventive biotechnology; establishment and development of cell banks; and strengthening of the medical biotechnology R&D infrastructure in the country.[139]

Similarly, molecular medicine and herbal medicine networks of Iran were established in 2001 to promote interests and activities in the field, collaboration in research and clinical practice, educational workshops and technology transfer. They are also involved in planning and priority setting activities, bioinformatics, HR development, budgeting, resource mobilization and allocation.

5.3.1.2 Department of Medical Education

The 'Department of Medical Education' under MHME is another significant player in Iran's biopharmaceutical SI. In 1985, the responsibility for medical education was transferred from MSRT to this department. In general, there is no shortage of doctors and specialists in Iran. However, while there is an over-supply of general practitioners and mid-wives, a shortage of doctors is being experienced in some sub-specializations in certain rural and urban areas (INDP, 2004). The department is responsible for curriculum planning, teacher training and accreditation of medical schools. It also conducts the national examination for all students, including those at private universities, as well as the examinations for super specializations and approval of foreign degrees.

5.3.2 Ministry of Science, Research and Technology

MSRT's major role in biopharmaceutical sector is in promoting research and educational activities. Even though responsibility for medical education was transferred to 'Department of Medical

[139] Major Members of the Iranian Medical Biotechnology Network include: Biotechnology Research Centre of IPI, Department of Pharmacy of TUMS, Cellular and Molecular Research Centre of SBUMS, Biotechnology Research Centre of SBUMS, Jahad-e Daneshghahi of SBUMS, Avicenna Research Complex, Cancer Research Centre of Shiraz University of Medical Sciences, Bu Ali Research Complex of Mashhad University of Medical Sciences, Endocrinology and Metabolism Research Centre of TUMS, and Faculty of Basic Sciences at TMU.

Education' under MHME in 1985, MSRT-affiliated research institutes are still active in biopharmaceutical research and education, including herbal medicine. MSRT also plays an important role in promoting research and educational activities in the bioagricultural sector similar to that in the biopharmaceutical sector. Even though responsibility for most agricultural research institutes lies with AREEO, MSRT-affiliated research institutes such as IROST and NIGEB are active in research and education in plant genetics. NIGEB is one of Iran's two pioneering institutes focusing on GM food crops R&D. Similar to ABRII, NIGEB also provides postgraduate programs in molecular genetics and bioagriculture.

The main responsibilities of MSRT are comprehensive planning and policy making for the expansion of higher education and research to train skilled and specialized manpower;[140] preparing and presenting S&T policy proposals to SCSRT; policymaking with regard to overseas training of students, their support and supervision, as well as their employment after return to the country; regulation and supervision of higher education and research at universities and research institutes.

5.3.3 Technical Cooperation Office

The role of TCO in biopharmaceutical SI is in research, project development and funding, and analysis and planning. TCO's activities in bioagriculture are mainly concentrated on assays to screen and develop wheat and rice resistant to fungal infections.

The 'Biotechnology Studies Centre' within TCO, launched in 1994, is a non-profit organization responsible for comprehensive and comparative survey of biotechnology development in Iran and the world, enhancing the infrastructures required for the private sector to get involved in manufacturing of biopharmaceuticals (TCO promotes the creation of biotechnology spin-offs from existing companies and U/RIs through low-interest loans), facilitating relations between Iranian scientists/research centres and well known institutes in the world, reviewing and assessing national policy documents in the area of S&T. In addition, as technology advisor to the presidency, TCO helps other governmental bodies to achieve their role and priorities.

'Biosciences' and 'Advanced Materials' are currently TCO's most active departments. The Department of Biosciences was established in 2000 and is active in development, coordination, and examination of biotechnology related projects, international collaborations in the field of biosciences, and policy analysis and planning in the development of biotech sector. The department consists of five areas (medicine, agriculture, biopolymers, nutrition and environment) but has only 10 staff members. The bulk of individuals involved in the department's activities are advisers to

[140] policymaking with regard to establishment, expansion, merger and termination of any higher education and research institutes

TCO for specific projects (about 20 per field). For the most part, these advisers are researchers based in their home institutes and each adviser manages at least one international project. TCO's planning and support activities in biosciences include identifying and supporting new projects (identifying national and international partners for collaborative research and funding) in both state and private sectors. TCO supports projects that may result in a commercial technology/product. TCO also supports technological capability building activities by training PhD students abroad and developing training courses and workshops in Iran.

TCO further supports biotechnology development by publishing a bulletin to inform policymakers of recent findings in biosciences and their economic utility.[141] TCO helps to shift the government thinking away from a 'factory/production' approach towards a 'knowledge and innovation' approach, building linkages between firms and university faculties to support local knowledge transfers.[142]

5.3.4 High-Tech Industries Centre

HTIC under MIM is active in promoting applied research and supporting the emergence of high-tech firms. The 'Biotechnology Department' of HTIC focuses on developing benchmarks in industrial policy, S&T policy, IP rights, coordination between government and private agencies, policies targeting the improvement of industry-university relationships, educational policies, promotional and protective policies such as domestic product tax exemptions or relaxation and foreign product tax increases, coherence of policies in such areas as taxes and rules,[143] and special funding policies.

The department's work is further sub-divided into five areas of medical/pharmaceutical, agricultural, industrial, biomaterials, and bioinformatics. These areas closely resemble those that are the focus of TCO activities. However, the tasks undertaken by HTIC differ. In particular, HTIC is involved in surveying the strengths and weaknesses of the sector in relation to global market and technology trends and creating consensus among different high-tech industry agents (primarily R&D centres and universities) on a set of priorities for the development of the sector. The action plans that are being drawn up go beyond the strictly scientific to include technical, marketing, investment, legal, management and engineering information and assistance, equipment for laboratories, creation of incubators, and identification of tax laws and regulations needed to strengthen the private sector.

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[141]TCO also created the Biotechnology Website of Iran to link researchers throughout the country and distribute its bulletin to them. In addition TCO has organized four electronic workshops to link isolated researchers in the provinces with those in Tehran.
[142]For example TCO has advised MHME to launch eight centres of excellence across the country.
[143] Through the analysis of policies in the United States, Europe and the Far East.

HTIC supports private biotechnology firms by encouraging scientists to establish biotech start-ups, encouraging foreign investment, launching a national medical biotechnology strategy, establishing research centres and incubators next to major universities, facilitating regulations and policies relating to biotechnology exports and raw material imports, supporting IP protection, prioritizing and protecting national biotechnology production, promoting and encouraging joint ventures with foreign private and government sectors, relaxing or eliminating tax laws, facilitating and supporting technology transfer and collaboration with foreign experts.[144] Many of these activities are still in the early stages and it is not clear whether milestones have been established for follow-up activities in these priority areas.

HTIC organises workshops to promote research activities based on the industry's needs and provides grants to promising research projects. These projects often consist of one or two senior researchers and their students. HTIC helps and consults researchers to commercialise their results and facilitates links to the industry by putting researchers in contact with the right people in the industry as well as provides low interest loans to entrepreneurs.

HTIC's main support function is to assist in the establishment of new start-ups through financing (low interest loans), consultation, and networking activities. Amongst the specific accomplishments of HTIC are funding of established and successful biotech companies such as Cinnagen (HTIC provided both low interest loan for commercialisation of Cinnovex as well as grants for Cinnagen's other research projects). In addition HTIC helps private firms to access sources of technological knowledge (e.g. HTIC helped linking Cinnagen with the Fraunhofer Institute in Germany for IFN-β technology transfer). HTIC has also helped in the construction of three biotechnology laboratories[145] in three major universities in Tehran.

HTIC is directly involved in policy making and advices MIM on policies that support biotechnology innovation in the country particularly through promoting commercialisable research and linking sources of technological knowledge to industry.[146] HTIC has also been active in organising international biotechnology seminars in Iran for academic researchers to gain entrepreneurial skills. These workshops are organised in cooperation with the industry and if possible with participation of foreign organisations and reported increased interest in entrepreneurship as a result of these programmes (e.g. short MBA programs for potential entrepreneurs in collaboration with French experts and a number of national institutes and industry experts).

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[144] From interviews at HTIC

[145] Protein engineering, industrial biotechnology and biopolymers

[146] At the interview numerous reports and documents were provided on the general functions of HTIC which were used in outlining the centres activities in chapters 4, 5, and 6.

HTIC supporting the formation of a joint venture company between Iran and Germany, , , In 2007 the biotechnology department of HTIC started a close collaboration with LIDCO to support private biotechnology start-ups.[147]

5.3.5 Life Science Industry Development Company

LIDCO is a subsidiary of Industrial Development and Renovation Organization of Iran (IDRO). IDRO founded LIDCO in 2003 to implement its policy for promotion and investment in biotech companies. LIDCO is a holding company providing consultancy and investment in life sciences. LIDCO also has private investors (Rena investment group and Ayandehsaz funds). LIDCO's main activities are in provision of a suitable platform for rapid commercialization of biotechnology research results; collaboration with people who have ideas or capital to start production facilities in biotech; investment in technology incubators and research parks; and support for the development of industrial activities in biotechnology and life sciences in Iran.

As the consulting arm of IDRO in biotechnology development issues, LIDCO is responsible for funding, overseeing, and commercializing R&D and pilot studies. LIDCO also carries out market research, prefeasibility and feasibility studies and prepares business plans for projects suggested by IDRO from 'Small Business Development Centres' at over 100 U/RIs as well as projects coming from U/RIs, and private sector. LIDCO's 'Small Business Development Unit' and 'Innovation Unit' are responsible for evaluation and supervision of projects from funding to commercialization. These units collaborate with consultants from universities, industry and legal sector. LIDCO is currently involved in five commercial projects with an investment of US$20 million.

LIDCO invests in entrepreneurial researchers in biological sciences and supports commercialisation of research activities in providing feasibility tests, business plans, and consulting services in industrial and research projects. LIDCO's main function is to act as a bridge between U/RIs and the industry by supporting projects through funds and expert business advice:

> "...biotech industry needs access to the results of applied research but currently the system to access these research activities is broken. Also researchers lack an industry oriented mind-set... and financial means. This is where we come in and provide our support activities..." (Interview at Lidco)

LIDCO supports entrepreneurial scientists/researchers to commercialise the results of their research. In the absence of any business knowledge or business minded partners, LIDCO teams up with these scientists and guides them on how to start the commercialisation process. In addition to

[147] From interviews at HTIC

low interest loans, LIDCO provides feasibility tests, business plans, and business advice all along the way (box 7.5, quote 2).

> "Often when we do the feasibility test, the projects prove not to be suitable for commercialisation in their current form... Unfortunately this happens most of the time and the research projects conducted are not ready for commercialization... However, if the project has potential, our biotech experts guide the scientists on how to make the project suitable for commercialisation. In recent years we have made the screening process for projects tougher as many researchers apply for grants and use the money to pursue their academic interests or buy new equipment for their labs..." (Interview at Lidco)

Overall LIDCO has been active in 20 projects. LIDCO takes up a 40%-49% ownership of the venture. So far, LIDCO has invested in 5 successful biotech companies, three of which are active in biopharmaceuticals. The Royan Stem Cell Company was set up to commercialise Royan Institute's research on Stem cells. This project was introduced to LIDCO by IDRO directly and has been very successful. LIDCO has a 49% ownership. Out of the five biotechnology firms supported by LIDCO, Kara Biotechnology Company is the only firm active in bioagriculture, producing Azetobactor based bio-fertilizers. LIDCO has invested US$2.2 million in the company and has a 40% ownership. Seven of the 17 firms at the Biotechnology incubator are active in the bioagricultural sector.

5.3.6 Biotechnology Incubator

The biotechnology incubator under MSRT was established in 2005 next to NIGEB and focuses on commercialisation of research activities conducted at NIGEB by supporting private spinoff creation through low interest loans, provision of offices and production space, business advice and consultation, feasibility reports, and networking support. Biotechnology Incubator supports researcher's whose R&D projects or ideas have commercial potential, in particular those that are innovative and new and have an emerging market. After a proposal is presented to the Incubator, the committee will decide if the proposal is feasible, this means if it is financially viable and whether there is a market for the product. Researchers are supported financially through loans, as well as provided with the location for their start up at the incubator. The Incubator also facilitates links to other organisations.

There are currently 17 companies at the incubator, many of which have already entered their products in the local market. These companies are involved in biopharmaceuticals, bioagriculture, and bio-equipment production. The incubator would like to provide more support but it is still young and learning from experience. Nonetheless the majority of these spinoffs have already marketed their products. Young start-ups at the incubator find access to funding as their main obstacle and improved provision of loans is greatly desired. Other difficulties are the bureaucracy involved in obtaining production licence and competition with imported and established foreign brands. Young firms also pointed out that the biotech incubator needs more financial support, a bigger and more equipped laboratory facility and increased authority.

> "…Our diagnostic kit is unique in the world but kits have a short product life span and need to be marketed fast... The customer is waiting to purchase our products but the paperwork never ends. It's like going in a circle sometimes... The bureaucracy is ridiculous. Kits have a very short product life cycle. Time is valuable and our products can quickly become out of date before they even enter the market. Getting licence from MIM was so difficult... Finance is another problem. I am IRR 20 billion in debt... Getting a loan is very difficult. The incubator tries its best but its resources are limited.'"' (Interview at biopharma firm 8)

> At present, the incubator is a backbone for us and provides us with office space and workshop for a minimal rent..., but it has limitations and its financial resources are not sufficient... Biotech incubator is still young and has limited resources; authorities are still unfamiliar with the functions of the incubator" (Interview at biopharma firm 7)

> "Finance was a big problem for us. Without Biotechnology Incubator's support we couldn't start the production. We still need more funding but it's hard to find capital funds in Iran. Banks demand huge deposits..." (Interview at bioagri firm 8)

> "Without the incubator our ideas would have never turned into products. The incubator helps us out the best it can... but its resources are still limited..." (Interview at bioagri firm 4)

5.3.7 AREEO

AREEO is the largest organisation responsible for agricultural research and education in Iran and is also involved in policymaking, funding, and supervision of the activities of public agricultural research institutes. AREEO oversees the major share of government-led agricultural R&D and is supervised by a board of trustees headed by MAJ. Other board members represent MSRT, EPO, and MPO. The board oversees AREEO's performance, formulates policies, and approves the overall budget and regulations. The head of AREEO is 'Deputy Minister of Research and Education' at MAJ, supported by other deputies and directors at AREEO headquarters.

AREEO plays a critical role in the development of the agricultural sector through the generation of appropriate technologies for food, feed, and fibre production by its affiliated research institutes and centres. It is also involved in sustainable management of natural resources and conservation of biodiversity. AREEO is responsible for general administration, coordination, and international collaboration of 22 semi-autonomous national agricultural research institutes, which are either commodity, multidisciplinary, or farming system oriented. These are further linked to a network of 34 regional or provincial agricultural research centres also under AREEO. This extensive network of national and regional research institutes work on different crops and agro-ecological regions. Six of the semi-autonomous agricultural research institutes under AREEO are active in bioagricultural R&D (Table 6.5). National agricultural research institutes affiliated to AREEO are presented in Appendix 5.

Table 5.8 AREEO affiliated biotechnology research institutes

Crop-specific research institutes	Discipline-specific research institute
Rice Research Institute of Iran (RRII) Sugar Beet Seed Research Institute (SBSRI) Pistachio Research Institute of Iran (PRII)	Agricultural Biotechnology Research institute of Iran (ABRII) Seed and Plantlet Improvement Research Institute (SPIRI) Soil and Water Research Institute (SWRII)

AREEO supports R&D and education to increase agricultural production, improve food quality, save biodiversity and manage natural resources through policies, strategies, research programmes, and funds under MAJ's guiding principles. ABRII is in charge of monitoring and coordinating bioagricultural R&D in all AREEO affiliated institutes and centres. Special support is provided to innovative R&D projects with potential for commercialisation in the form of funding and expert assistance to turn initial ideas into research projects, including help with proposal writing. ARREO's division for human resources development supports education and training of researchers by collaborating with national and international U/RIs. Appendix 9 provides AREEO's main international collaborations. In addition ABRII organizes workshops for advanced training of experts who are involved in bioagricultural R&D.

5.3.8 Non-Governmental Scientific Organisations

The three scientific societies of 'biotechnology', 'biosafety', and 'genetics' collaborate with each other and national and international U/RIs to promote sound policy making, collaborative research and educational activities as well as public awareness of biotechnology related issues. Interviews revealed that the Biotechnology Society of Iran (BSI) often in collaboration with biosafety and genetics societies has played an important role in supporting development of the sector, and in particular in adjusting the draft of Iran's national biosafety law. These societies are further active in networking, public awareness campaigns[148], drafting the NBSD, and consulting authorities in national biotechnology issues. The activities of these societies are similar and there is a strong collaboration between them.

BSI is the largest and most influential of these societies. The sharp increase in the number of bioscientists and experts in Iran made it necessary to create a national biotechnology society BSI was founded in 1997 by a council of senior researchers and academics active in different fields of biotechnology to help develop and improve biotechnology research and education in Iran. Currently BSI has around 400 members, of which 102 are regular, 77 affiliated, and the remaining are students and institutional members. BSI is active in establishing scientific and cultural relations between biotechnologists at national and international levels, collaborating with U/RIs, government, and the industry to boost biotechnology education, research, and innovation, encouraging researchers and honouring successful biotechnologists, offering biotechnology related research and educational services, publishing scientific books and journals, and cooperating with private sector in biotechnological projects. BSI provides expert advice to the government in biotechnology related issues, publishes a quarterly newsletter, and organises (in collaboration with other institutes) conferences at national, regional and international levels. For example BSI organises the annual 'National Congress of Biotechnology' (since 2000) in collaboration with national U/RIs such as NIGEB, ABRII and TUMS. The private sector's willingness to invest in biotechnology is not as strong as in other industries (like petroleum, electronics, and construction), therefore BSI involves in promotional activities to attract private investors to this sector.

The Genetics Society of Iran (GSI) was founded in 2000 as a non-profit, non-governmental, scientific organization with the main purpose of bringing together professors and researchers through providing a forum for sharing various issues in all fields of genetics. The plant genetics group of GSI actively encourages collaborations among Iranian plant geneticists, supports efforts for preservation of plant germplasms, collects indigenous knowledge especially for endemic plants, monitors the usage of transgenic plants in Iran, and provides financial assistance.

The 'Biosafety Society of Iran' which is the newest of the three societies was founded in 2006 by Dr Ghareyazie, the innovator of the Iranian GM rice, in order to address biosafety issues and create a network for interested parties. The society investigates national and international biosafety developments, issues and concerns, informs and advices policy makers, academics, scientists, as well as the public on biosafety matters, and promotes biosafety awareness based on scientific facts and evidence.

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[148] Student and academic media networks also engage in educating the public on bioagricultural issues, benefits, and concerns through emphasising scientific evidence and global developments in the sector.

In addition to the above NGOs interviewees mentioned the role of the Network of Herbal Medicine as important towards biopharmaceutical innovation activities. Interviewees pointed out that the efforts and campaigns by members of the network is what made the government realise the importance of this sector and initiate support programmes.

> "Personal connections are a necessity in Iran. I have good linkages to scientific networks such as the Plant Medicine Network which is one of the most successful scientific networks in Iran and links over 80 private and public organisations. Currently we are trying to link national Plant Medicine laboratories through this network." (Interview at NIGEB)

5.4 Government Policies and Their Impact on Biopharmaceutical Innovation

The main actor involved in biopharmaceutical related policies and regulation is MHME. MIM also has influence in shaping demand for innovation in the biopharmaceutical industry. Further MAJ and Ministry of Justice also play a role in the biopharmaceutical sector.

MAJ is the main actor in Iran's bioagricultural policy system. The official and national standards in the bioagricultural sector come under the 'National Standards Committee of Microbiology and Biology' under MHME.

5.4.1 Ministry of Health and Medical Education

MHME is the main agency for the regulation of pharmaceutical industry, including biopharmaceuticals and herbal medicines. MHME's mission is to 'provide access to sufficient quantities of safe, effective and high quality drugs that are affordable for all the population' (INDP, 2004). In order to achieve this mission, Iran adopted a full generic-based drug system as part of its drug policy. The national drug policy of 2004 reflects the import-substitution principle that is visible in the overall development of the biopharmaceutical industry. The main features of Iran's National Drug Policy are vigorous GMP inspections, fully generic-based drug system, promotion of herbal medicine industry, high regulation of producers, licensing for local production of imported pharmaceutical products, supporting local production of pharmaceuticals (promoting national pharmaceutical companies), price controls, and self-sufficiency in vaccine production (Cheraghali, et al., 2004).

The pharmaceutical regulatory system of Iran consists of the 'Office of Pharmaceutical Affairs' which supervises all manufacturing, distribution, and import of medicines and the 'National Quality

Control Laboratory'.[149] Registration is the main prerequisite for marketing of pharmaceuticals in Iran. Iran's has a national drug list based on generic names, which are drawn up by the 'Drug Selection Committee'. The committee consists of medical specialists, pharmacists, and drug regulatory and control authorities and meets regularly to review and evaluate new drugs based on their generic identity, efficacy, safety and cost effectiveness (Cheraghali, 2006). Once a new generic drug is identified, some local companies are given production licenses by MHME. The firms that have the innovation capabilities necessary to develop processes and formulations produce the drug by themselves, but most companies require the support of national U/RIs in developing products and processes (Nikfar, et al., 2005). In order to reduce costs and improve affordability, the drug procurement process is centralized. State-owned and two semi-private companies are given the responsibility for procurement of most imported drugs. Only drugs that are on the drug list may be imported. Price controls (on the prices at which drugs are sold to patients) also extend to imports.

More than 85% of the population is covered by medical insurance that reimburses expenditures for drugs. In order to keep drug prices low, the government has subsidized the production of essential drugs, making them available and affordable for more than 90% of the population (Cheraghali, 2006). However as part of the changes introduced under the 3rd EDP (2000-2005), MHME declared a new policy of withdrawing subsidies from the industry and transferring them partly to public insurance companies (Cheraghali, 2006). Another plan to promote therapeutic specialization among companies is the 2001 MHME policy, demanding companies to develop a ten-year plan within which they would identify a number of therapeutic areas for specialization. The registration of a new product by a company would then only be accepted if it fell within this ten-year plan. Otherwise, the company would be obliged to convince the authorities to change the plan, or it would pass the product on to another company that already has the relevant therapeutic area in its plan (Cheraghali, 2006).

The promotion and regulation of herbal medicine also falls under MHME. Iran has a vast variety of flora and fauna, and the government has placed emphasis on the development of biopharmaceuticals through herbal compounds. Iran is one of the few developing countries to regulate herbal medicine (UNCTAD, 2005). Since 1994, the government has regulated the production in this sector to ensure that GMP is followed. In the case of well-established herbal medicine products, the regulatory aspects apply only to safety and not to effectiveness, but any new formulation that is not prescribed in the olden texts must have proof of effectiveness. MHME encourages entrepreneurs in this sector by organizing conferences and bringing together investors and scientists. Herbal products are registered by MHME before they are launched in the market. So far over 200 herbal products have been registered by MHME. Compared to other countries, this is

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[149] Source: www.fdo.ir

a relatively small number and herbal medicines account for only 5% of the total drug market, but MHME is encouraging insurance companies to include herbal medicines among reimbursable items under health insurance plans (Cheraghali, 2006).

5.4.1.1 Department of Food and Drugs

From biopharmaceutical policy and regulation perspective, the 'Department of Food and Drugs' (DFD) under MHME is the most important agency. DFD is the only supervisory board for the production and import of drugs in the country. DFD consists of the three departments of 'Food and Cosmetics', 'Pharmaceuticals', and 'National Quality Control'. The 'Department of Food and Cosmetics' is involved in registration and inspection of both imports and domestic production. The 'Department of Pharmaceuticals' issues permits for the release of drugs and pharmaceutical material and equipment as well as for the establishment of pharmaceutical firms, supervises manufacturing, carries out GMP inspections and ensures the registration of drugs (both small molecules and biological compounds, and domestic and imported drugs). DFD also carries out regulatory, standard setting, and quality control functions for all pharmaceutical-related industries. The 'Department of National Quality Control' has a testing laboratory to which the pharmaceutical directorate sends samples before a product can be registered. In addition, the 'Office of Rational Drug Use', which distributes drug information to doctors and promotes rational use among doctors, patients and consumers, is located within this department.

DFD has played a major role in the development of biopharmaceutical R&D and SI. Prior to 1990 there were a few biotechnologists such as faculty members and members of scientific boards, but a coordinated and organised system of education and research in biotechnology did not exist. The 1990 establishment of the first biotechnology related degree in the country was a systemic effort by a number of different institutes (IPI and IROST under MHME supported by DFD, NIGEB under the MSRT, Iran blood transfer Organisation, TUMS' faculty of health, and RVSRI under MAJ). In parallel, between 1988 and 1990 DFD set up a state of the art biotechnology laboratory at IPI. The main function of DFD is to support commercialisation of biotechnology research activities (Quote on R&D issues from interview at DFD).

> "In 1990s biotechnology education in Iran became systematic and organized and the basis for its expansion in the country was set. Biotechnologists started producing basic products, for example enzymes such as the crucial taq DNA polymerase. Since 2002, with the help and effort of national experts and in some instances with the collaboration of foreign organizations biopharmaceutical products have started entering the market. The increasing number of firms active in biotechnology production, currently over 80 public and private firms, the increase of specialized biotechnology courses at TUMS and TMU and the advances in life sciences' expertise show the development of this sector..." (Interview with biotechnology industry expert)

DFD assists innovation through policy regulation, funding, and technology transfer from foreign sources to IPI. The hepatitis B vaccine project mediated by DFD was the first project to transfer biopharmaceutical technology to the country and produce high-tech biopharmaceuticals locally. DFD also mediated the transfer of three other biopharmaceutical technologies to Iran. The history of the transfer agreement is presented in box 7.4. The establishment of IPI's biotech lab also attracted a number of biotechnology experts from Russia who came to work at IPI and organised workshops for students and young professionals.150 Attracting these Russian scientists to Iran (through important collaboration with TCO) strengthened biotechnology R&D activities at IPI. These Russian scientists became actively involved in education, research and supervision in various departments of IPI, in particular in the biotechnology laboratory. The Russian bioscientists transferred a high standard of knowledge and organisation to the institute (see quote on biopharmaceutical innovation support at DFD).

> "... The level of knowledge of the Russian scientists, who came to work here, was so much higher than our level of knowledge. There were a few biotechnology graduates from foreign institutes who came back and started working in the research institutes here, but they didn't have the systemic organisation of the Russians..." (Interview with biopharma industry expert).

DFD mediated important technology transfers to IPI. In 1993, the deputy of research and innovation under MHME (later appointed as director of IPI) contacted European countries for the purpose of technology transfer collaborations, but due to sanctions most of Europe would not grant firms export licence to Iran. Finally Cuba was chosen as the source of technology and Iran signed the first biopharmaceutical technology transfer contract with Cuba in 1993 and three more technology transfer contracts in 1998 (box 7.18, quotes 2 and 3). However IPI faced many challenges in restructuring its Karaj production site to meet the production requirements of the new technologies. Government organization, foreign sanctions, and changes in the size and capacity of some machinery and equipment, all created problems along the way. The projects were finally completed in 2005.

5.4.1.2 State Department of Standards and Industrial Research

From the demand-side perspective in bioagriculture, the regulatory, standard-setting and quality control aspects are also important. One government department under MHME carries out these functions for bioagricultural products. The 'National Standards Committee of Microbiology and Biology' at the 'State Department of Standards and Industrial Research', which is the official

[150] These Russian scientists were free to travel after the collapse of Soviet Union and became resident in Tehran.

authority for determining, publishing and implementing official and national standards of the country for the biotechnology industry (excluding the pharmaceutical-related sector)[151], helps improve production methods and efficiency and enhance the quality of domestic production by carrying out research and setting up national committees. The committee determines the guide to the study of purity, biological activity and stability of products containing micro-organisms, and standards related to transgenic organisms and their release into the environment.

5.4.2 Ministry of Industries and Mines

The biopharmaceutical industry, like other industries, must follow MIM's regulation on permits and licenses needed in order to set up manufacturing operations (e.g. industrial zoning and pollution control). Through such regulations, MIM is potentially able to influence the demand for innovation and stimulate technological capability building in the biopharmaceutical sector. However, it has few policy instruments at its disposal to influence innovation directly, such as inducing greater efficiency and lower prices in the biopharmaceutical industry.

Although MIM has developed a strategic plan for the automobile sector from an innovation-oriented perspective, the same cannot be said for biotechnology. Considering Iran's eventual entry into WTO, there is a clear need to build a biotechnology SI by expanding production capabilities in the industry, supporting linkages to research (and to the healthcare system in biopharmaceuticals), and developing policies to stimulate and support entrepreneurship and innovation. For this to take place, line departments at MIM must overcome their production-orientation and the confusion over concepts such as 'manufacturing', e.g. when it comes to biopharmaceutical products where, in value terms, critical inputs such as active ingredients are not produced locally but imported.[152]

5.4.3 Ministry of Justice - Intellectual Property Rights

Iran's IP regulation has no comprehensive law for full protection of IP in the pharmaceutical sector. MHME licenses medicines from different producers and importers. A pharmaceutical company can market or manufacture a product, only after obtaining a license from MHME. MHME registers 'copied' products based on patented medicines (IPHR, 2004). The law does not say anything about 'compulsory licensing', presumably because a pharmaceutical company can market or manufacture a product only after a license from MHME is given.

Trademarks are registered for medicines. A separate law governing the pharmaceutical industry requires that along with the brand name, the generic name of the product must be published on the package.

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[151] The Department of Food and Drugs under MHME is responsible for all pharmaceutical-related industries.
[152] From interviews at HTIC and LIDCO

Article 28(3) of the 'Trademarks and Patent Registration Law' of 1931 prohibited the award of patents to a 'pharmaceutical formula or arrangement'. This implied that product patents could not be granted for pharmaceuticals. However a patent application could be filed for processes related to the manufacture of pharmaceuticals.

Article 28 (2) prohibited patent protection for 'a new invention, or the development of an existing invention harmful to public order, morals or public health'. The law itself did not mention anything about the patentability of living organisms, so biotech products obtained through genetic engineering were presumed to be patentable in Iran.

According to section 4 of the new IP law which came into force in July 2008, genetic resources and their constituent as well as biological processes for their production and the knowledge of diagnosis and treatment of human and animal illnesses are not considered as 'inventions' and hence are not eligible for protection.[153] The new law is currently undergoing its five year probationary enforcement period and is too early to draw any firm conclusions on its application and effectiveness. However interview data suggest that researchers are reluctant to disclose their scientific and technical data and firms are discouraged to spend time, effort, and money on R&D and innovation, when it can be easily copied. Scientists prefer to patent their inventions abroad but this is costly. Currently the sector is focusing on accessing existing technologies, however as the sector progresses IPR is gaining in importance. Lack of biotechnology experts at the patent office and lack of specialised judges and courts to deal with patent infringements are mentioned as major gaps in the IP legal protection system. Additionally, the new IP law prevents patenting of genes, promoters, and bioprocesses which researchers consider a new obstacle in the bioagricultural SI.

> "Patent protection in our country is weak and discourages the innovator to spend time, effort, and money on R&D and innovation, when it can be easily copied... If you go to the patent office you will see what is wrong with it... They deal with all kind of patent applications in any field at the same desk. This shows the lack of importance of patent in our country. The government needs to introduce harsh regulations to protect it. Only then will everyone else trust and respect the patenting system and take it seriously... They are working on the patenting system but in biotechnology there are weaknesses... Currently GM products cannot be patented locally but can be patented abroad..." (Interview with biopharma researcher)

In 2005 Iran became an observing member of WTO. Although the full joining process may take up to ten years, it would have drastic impacts on the biopharmaceutical industry and market of Iran. Restrictions on copying patented pharmaceuticals would force the government to allocate

[153] Source: http://www.ip-watch.org/weblog/2008/06/13/irans-new-law-on-ip-protection-moves-it-onto-international-stage/

additional resources especially for novel and high-tech products such as biopharmaceuticals and to boost the national technological capabilities of the pharmaceutical industry (Cheraghali, 2006). The majority of biopharmaceutical interviewees believe joining international IP regulation will hinder copying activities of foreign technologies and strengthen the presence of foreign brands in the local market as Iran's biopharmaceutical sector has not yet reached the capacity to compete globally. However the majority of interviewees in the bioagricultural sector believe that joining PCT and WTO will have a positive impact on the national system of patent protection and implementation in compliance with WTO regulations and will benefit national bioagricultural innovation activities.

> "...Entering international patent systems are only valuable when you see yourself capable of competing internationally. ...Now we have the opportunity to benefit from copying, we should not enter international patenting systems until we have acquired existing technologies, reached the global level of knowledge, and increased our potential to compete..." (Interview with biopharma researcher)

> "Iran is not part of any international patent organisation... We will benefit from our innovations more if they are internationally patented, however international patent applications are expensive for our scientists and so foreigners can also copy our products. ... [The] GM rice is neither patented nor [covered by] any Material Transfer Agreements. This is an opportunity for anyone who wants to use it..." (Interview with bioagri researcher)

5.4.1 Ministry of Agricultural Jihad

MAJ is the primary policy making organisation in the agricultural sector and employs 20% of the country's total employees in the sector. [154] MAJ's objectives and programmes were restated in 2002 at the cabinet meeting of MPO. The ministry's biotechnology related research training and innovation policy objectives include: "to benefit from advanced biotechnology techniques and genetic engineering in agricultural sector, to develop suitable methods and apply modern technologies in agriculture and livestock, suitable for climate and geographical conditions of country".[155] Following the 2001 merger of the Ministry of Constructional Jihad and the Ministry of Agriculture, the responsibility of overseeing affiliated research institutes of the two ministries was

[154] MAJ is active in policy making, planning and supervision; research, training and innovation; national resources and watershed management; agricultural infrastructure and rural development; agricultural, livestock and aquatic affairs, and agricultural support, promotion and investment. Source: http://www.maj.ir/english/AboutUs/program.asp?p=aboutus

[155] Source: http://www.maj.ir/english/AboutUs/program.asp?p=aboutus

entrusted to AREEO. AREEO is involved in both demand and supply side. AREEO's demand side activities include policy making, funding and supervising agricultural R&D activities in its affiliated research institutes.

The seed prices of major agricultural crops are determined by the 'Economic Council' of MAJ. The price of seed distributed by the public sector is lower than free market prices. For private companies price is determined based on supply and demand, particularly for vegetable seeds where there is better competition. The agricultural bank provides credit with low interest rates to farmers. Credit is available for contract growers to encourage contract seed production and for establishing seed drying and cleaning facilities. However, credit is not available for purchase of certified seed because the government is already subsidizing its production (Mobasser, 2003).

As biotechnology is a generic technology and its techniques can be applied in developing products for both humans and animals MAJ can also influence the demand for innovation in medicines designed for human consumption through its role in shaping the demand for vaccines in the veterinary sector. This is clearly reflected in the case of RVSRI, which, under the control of MAJ develops and produces vaccines and serum for both human and veterinary applications.

5.5 Summary

The biopharmaceutical R&D has been slowly but steadily progressing during the 2nd, 3rd, and 4th EDPs. Production activities such as manufacturing of drugs are financed through the government budget. Production levels are decided by the government, and the budget is provided accordingly. The government's strategies to promote the national biopharmaceutical sector include optimizing resource allocation, replacing fixed drug subsidies with targeted subsidies, supporting private sector activities, and promoting national and international investment in biopharmaceutical industry (FDO, 2005). Iran's local pharmaceutical industry produces more than 97% of the market needs and only 3% of drugs are imported. However, in terms of value, these imports account for a third of the national drug budget. The government's import substitution strategy together with a focus on the private sector development has resulted in the emergence of private biopharmaceutical firms during the 3rd and 4th EDPs with a strategy to replace expensive imported drugs and has adopted a growing role in biopharmaceutical R&D and innovation. Therefore the private sector's role is becoming increasingly important in introducing modern biopharmaceuticals to the Iranian and the regional markets. Access to highly qualified personnel is not a problem for established firms in both sectors, while it is a moderate problem for start-ups mainly due to financial constraints; however brain drain is also a problem in both sectors. The market niche for the firms' products is competitive in both sectors. However biopharmaceutical firms compete with established and powerful foreign brands in a market that is reluctant to accept local products. MHME has started addressing this problem by introducing a levy on selected imported biopharmaceuticals that are also produced locally. Bioagricultural firms on the other hand find the market demand for local bioagricultural products strong. Competition is mainly with local firms as the number of local producers is increasing. During the 4th EDP (2005-2010), over ten modern biopharmaceutical drugs have entered the market. Major sources of funding for the firms studied are own funds and bank loans with low interest. In both sectors, start-ups and small firms suffer from similar obstacles such as a macroeconomic environment of high inflation[156] and high interest rates, burdensome and out of date regulations, lengthy and difficult procedures for securing bank loans and lack of diversified sources of funding, and the dominance of large state enterprises in industrial production.

One unique feature of Iran's biopharmaceutical sector is that large organizations that produce a major portion of drugs required by Iran (e.g. IPI and RVSRI) are not companies but unique integrated research, education, and production institutes. Another unique feature of Iran's biopharmaceutical SI is the complete absence of TNC operations.

The main ministries supporting biopharmaceutical innovation (MHME, MSRT) have built up significant capabilities in this sector by investing in state of the art research institutes/centres. However most of these capabilities remain at the research institutes as the knowledge system has not integrated into the production system properly. State firms mainly undertake production and do not perform innovation activities. Moreover, even large manufacturing enterprises rely on imports for inputs. This is mainly because of the absence of strong supplier networks in the form of SME's.

The previous IPR law enacted in 1931 did not refer to issues such as compulsory licensing nor clearly distinguished product and process patents. The new IP law (2008) is more comprehensive and aims to strengthen both legislation and implementation. Entering international IP systems is generally perceived to hinder the progress of the biopharmaceutical sector by protecting foreign technologies from being copied in Iran. However bioagricultural scientist/entrepreneurs insisted that only by joining international IP systems would the national legal system of IP protection become efficient.

The government's self-sufficiency policy is also the basis for Iran's incentive to develop the national agricultural production efficiency using biotechnology methods. Unsuitable landscape and shortage of water make Iran one of the largest importers of food crops in the world with maize, rice, soybean-oil, oilseed, and soybean annual imports alone adding up to US$1.67 billion. Iran's goal to grow over 0.5% of the global area of GM crops by 2015 as stated in the NSBP, emphasises the strong incentive towards bioagricultural development including the use of LMOs during the 3rd

[156] Inflation was 25% in 2008 (measured by the annual growth rate of the GDP implicit deflator) (WDI, 2009).

EDP. The government's major focus on bioagriculture during 2nd and 3rd EDPs (1995-2005) resulted in a 'development spurt'. R&D capabilities and technological knowledge at public research institutes caught-up with developed countries in genetic engineering of GM crops and plants as well as non GM technologies.[157] However, despite the advanced research capabilities in modern bioagriculture the results of the state of the art R&D in GM crops which were due for commercialisation in the 4th EDP have failed to enter the market.[158,159] For example, insect resistant cotton and rice and salinity-resistant wheat developed at ABRII and GM sugar beet and Canola developed at NIGEB have completed field trials and are awaiting full commercialisation. The GM case study in chapter 6 explores the reasons for the delay in the release of these GM crops. In addition to GM crops, Iran's research institutes have also produced bio-fertilisers and bio-pesticides (e.g. nitrogen bio-fertilizers for rice fields at ABRII, phosphate bio-fertiliser at NIGEB and Tehran University) as well as transgenic animals (IPI, Royan Institute).

The main player in Iran's bioagricultural policy and regulation system is MAJ and its affiliated ARREO. The majority of Iranian agricultural research institutes operate under AREEO. However NIGEB (under MSRT) and to a smaller extent universities also conduct advanced bioagricultural R&D activities. Public R&D is mainly funded by the government. The role of private sector in funding public agricultural R&D is limited. Nonetheless, the private sector has become increasingly involved in conducting its own agricultural R&D. Private sector's contribution to bioagricultural R&D and innovation is still marginal, but SMEs are increasingly entering this sector and the majority of the companies in the sample studied are young start-ups.

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[157] This rapid development of the sector fits Gerschenkron's definition of 'development spurt'.
[158] Commercialisation here means full release of the GM crop to farmers for cultivation
[159] Some of Iran's GM crops have been ready for commercialisation since 2004

Chapter 6 Biotechnology Product Innovation Journeys

6.1 Introduction

This chapter provides a number of product innovation journeys. The GM Bt rice and Cinnovex are selected as the main representatives of the biopharmaceutical and GM crop sectors complemented by other product journeys which as a set illustrate how parts of the innovation system perform. Selected quotes from interviews are presented wherever appropriate to further demonstrate SI issues in Iran.

6.2 Cinnovex

Cinnovex is the commercial name for an IFN-β-1a drug used in multiple sclerosis (MS) therapy and its Cinnagen's most important product in the market so far. Iran is the third country in the world to produce IFN-β in after Germany and USA. MS is the most common disease of the central nervous system and estimates put the number of people suffering from it at about 2.5 million worldwide (Fraunhofer IGB, 2007). The only therapeutic successes achieved so far have been with IFN-β, which is a protein produced naturally in the body (IFN-β-1a is produced by mammalian cells while IFN-β-1b is produced in modified E. coli). It slows down the progression of the illness and reduces the relapse rate through its anti-inflammatory properties and strengthening of the blood-brain barrier. Biotechnology makes it possible to engineer this endogenous protein in bacterial or mammalian cells. Innovation in IFN based biopharmaceuticals are based on two factors: increased effectiveness of the drug in the treatment of MS symptoms and/or reduced side effects of the drug.

6.2.1 About Cinnagen

Cinnagen was founded in 1994 as a biotechnology start-up company, with four scientists manufacturing restriction enzymes for local research institutes and diversified its production line to blood group typing reagents and kits, various other diagnostic kits, including biochemistry, PCR and ELISA for infectious diseases, and DNA-extraction kits. The company went into the manufacture of diagnostic kits for learning purposes and as a way of build-up capacity. Since 1994, Cinnagen has expanded its total staff strength from 4 to currently 120 scientists, technicians and employees on the production side and has structured itself into the 4 divisions: Biopharma Division delivers biopharmaceuticals, generic peptides and active pharmaceutical ingredients (API) to the market. Molecular Biology division produces and distributes genetic engineering and molecular biology R&D laboratory tools. Diagnostics division offers a wide variety of diagnostic kits and reagents for a routine clinical laboratory. Cinnagen consulting helps new companies and institutions to start a new solution or facility for production, diagnostic lab or quality management.

Biopharma is the biggest division within Cinnagen and delivers modern biopharmaceuticals such as Cinnovex. Cinnagen Biopharma was established in 1999 and started producing and marketing generic peptide hormones. Using the experience of the hormone production Cinnagen Biopharma started producing human IFN-β1a and erythropoietin and is now a major producer of biogeneric and biosimilar drugs in the region. Currently Cinnagen Biopharma employs a team of 50 biopharmaceutical experts and technicians. In 2007 Cinnagen launched Cinnovex in the market, its most important product using recombinant DNA technology. Cinnovex is a recombinant IFN-β1a used in MS treatment. So far Cinnovex has been registered in 5 countries including two European countries. Currently 411 Cinnagen products are in the local and international markets. Cinnagen is the currently known as the most successful Iranian biotechnology firm. The financial growth rate of Cinnagen has been more than 30% annually from 1999-2005 and more than 300% since 2006. Cinnagen's annual turnover is over US$ 2 million.

Box 6.1 List of important events in Cinnagen's development history:

- 1994 Establishment of the Cinnagen Company
- 1995 Marketed Taq DNA polymerase
- 1997 Marketed Molecular Diagnostic kits such as HIV, HBV, HCV, H.pylori, and MTB (PCR based technology)
- 1999 Marketed PCR based research kit such as RT-PCR system
- 2000 Marketed synthetic peptides for Veterinary use, Luliberin (GnRH analog)
- 2002 Marketed T4 DNA ligase, restriction enzymes (EcoRI, BamHI, HindIII, HindII, NotI)
- 2003 Marketed monoclonal antibodies for blood group typing (Anti-A, Anti-B and Anti-D)
- 2005 Marketed DNA and RNA extraction kits (RNX™, DNG™ and DNP™)
- 2006 Launched Cinnagen's products in more than 18 countries
- 2007 Launched Cinnovex (recombinant Interferon beta 1a) in the market in collaboration with Fraunhofer Institute of Germany, as the second manufacturer in the world after Biogen. Started registration of Cinnovex in 5 countries including two European countries.

  Launched Buserelin acetate based on synthetic peptide technology for human use.
- 2008 Clinical studies of EPO and CinnaRelief (IFN-ß 1a); re-Hu FSH and PTH in the pipeline.

Source: http://www.cinnagen.com/History.aspx

Cinnagen was founded in 1994 by two biotechnologists from IPI and has increasingly involved skilled scientists and industry experts in its growth stage. In the first 5 years of its establishment due to limited financial resources, Cinnagen did not engage in innovation activities. Cinnagen's initial strategy was to strengthen the firm's financial and human resources and pursue capacity building within the firm and the local industry.

> "When we started, the market was not ready for local biotech products. Foreign brands were highly established in the market... In early 1990s, biotechnology, molecular biology, and genetic engineering activities in the country were weak. In addition to production activities we engaged in capacity building through organizing educational workshops to contribute to the development of relevant knowledge in the country..." (Interview at Cinnagen)

Cinnagen's next strategy was to focus on process development to produce imported biopharmaceuticals locally as process innovation was easier, faster, and better suited to CC's financial situation. CC's strategies have proved successful and the company has grown significantly in recent years Cinnagen started manufacturing of diagnostic kits for learning purposes and as a way of building up capacity with a long-term focus on biopharmaceuticals (e.g. peptides). Cinnagen's current innovations are process innovations.

> "When we reached the phase of producing new products, we changed our strategy accordingly. To produce imported drugs locally, we wanted to master entire technologies and be able to develop them in house. We did that through training abroad and collaboration with European and Russian institutes..." (Interview at Cinnagen)

Collaboration with foreign scientists and research institutes has proved very important to the company's growth stage. The company has expanded in the past 5 years and now employs over 100 personnel including bioscientists, manufacturing staff, business and marketing experts, and administrative staff.

6.2.2 The Market for MS treatment

The market for MS treatment is dominated by three brands: Avonex produced by Biogen, originally under the Orphan Drug Act in the US (competition protection act), Betaseron produced by Berlex Biopharmaceuticals[160], and Rebif produced by the EMD Serono.

Avonex has the highest share of the global MS market at around 55%. It was approved in the US in 1996 and in Europe in 1997, and is registered in over 80 countries. Avonex is sold in two formulations, a lyophilized powder requiring reconstitution and a pre-mixed liquid syringe kit. It is administered once per week via intramuscular injection. Rebif is a disease-modifying drug used to

[160] Berlex Laboratories Inc. is a Montville, New Jersey-based subsidiary of the German Schering AG.

treat MS in cases of clinically isolated syndromes as well as relapsing forms of MS and is similar to the IFN-β protein produced by the human body. It is co-marketed by EMD Serono and Pfizer in the US under an exception to the Orphan Drug Act. It was approved in Europe in 1998 and in the US in 2002 and is also registered in over 80 countries. Rebif is administered via subcutaneous injection three times per week and can be stored at room temperature for up to 30 days. The new formula for this drug has the same treatment effects as Avonex but with less side-effects and has become a serious competitor for Avonex (26% of the global Ms Market share). A one month supply of Avonex or Rebif can cost anywhere from US$1,600 to more than US$3,000.

Closely related to the above IFN-β-1a drugs is IFN-β-1b, which also may be used for MS treatment with a very similar drug profile. IFN-β-1b was previously marketed only by Berlex in the US as Betaseron and outside US as Betaferon by Schering AG. In 2009, Extavia, another new brand of IFN-β-1b was marketed by Novartis for the treatment of early and relapsing forms of MS.

All the above are brand drugs. The first biosimilar/biogeneric recombinant IFN-β-1a drug, under the commercial name of Cinnovex, was manufactured by Cinnagen in Iran in 2007. Cinnovex was developed at 'Fraunhofer Institute for Interfacial Engineering and Biotechnology' (IGB) in Stuttgart in collaboration with Cinnagen and is the first therapeutic protein from a Fraunhofer laboratory to be approved as biogeneric/biosimilar medicine. Iran has one of the highest MS rates in the world with 15% share of the world's MS drug market. Until 2007, the main drug for MS treatment in Iran was Avonex with an average annual sale of US$50 million. Thus, Cinnagen's strategic choice to produce an IFN-β based drug as its first biogeneric was a good decision for the following reasons:

- IFN-β is the first choice for the treatment of MS
- Iran has a large home market for the drug
- IFN-β was patented, preventing the world's largest biogeneric producers, China and India, from entering the market, which would affect the price of the drug substantially.

6.2.3 Access to IFN-β Technological Knowledge

Cinnagen assigned a group of 4 to study all available information on IFN-β technology using the internet, including reports, papers, patents etc. over a period of three month. This group found that recombinant IFN-β was initially produced by Fraunhofer IGB of Germany in collaboration with the American Biogen. The group also found that there had been a disagreement between Fraunhofer IGB and Biogen, where the latter was accused to have undermined Fraunhofer with regard to the IPR of the drug. Biogen has the sole rights of commercialising the drug. Cinnagen therefore found in Fraunhofer IGB a potential source of technological knowledge as, even though it could not sell the drug under the TRIPs law, Iran which is not a member of WHO could sell the technology. HTIC assisted Cinnagen in establishing the link with Farunhofer institute.

The next step was to decide whether to use mammalian cells (nucleus) or bacteria (no nucleus) for the production of IFN-β. While bacteria replicate faster, the protein produced in the mammalian cells is more similar to the human protein. To match the quality of Avonex, Cinnagen opted for the mammalian cells even though these are of much higher maintenance and the extraction of the protein from them is more difficult.

Following the first meetings between Cinnagen's founder and director of marketing with the Fraunhofer IGB, Cinnagen bought the first ingredient of the technology, the cells. Produce these cells at Cinnagen would have taken too long and since an essential element in high-tech marketing is timing; the main reason for purchasing the cells was to save time. Cinnagen saved 2 years by buying the cells which is crucial in biopharmaceutical product life cycle. Cinnagen also acquired all the information on downstream (production of the molecule of interest from the purchased cells), upstream (purification of the molecule in ppm-parts per million), maintenance of the cells, and setup of the production line.[161]

After biotechnological engineering and production up to the pilot scale was optimized at Fraunhofer IGB and upon the access to all the necessary knowledge, Cinnagen introduced IFN-β-1a to MHME in 2004. MHME started the process of standardizing the product in accordance with FDA and EMEA. Cinnagen provided the proof of its clinical effectiveness, including appropriate quality control and clinical trials. This was a lengthy process due to weaknesses in MHME's system for the approval of biopharmaceuticals. Finally in 2007 the drug entered the market under the commercial name of Cinnovex.

6.2.4 Challenges in Market Acceptance of Cinnovex

The initial reaction to the sudden entrance of the domestic product in the Iranian market was a resistance towards using Cinnovex by the medical community who carried on prescribing Avonex. Cinnagen's numerous seminars on the quality, safety, and cost benefits of the drug to overcome this

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[161] Fraunhofer IGB's genetic engineering project group under Professor Bernd Otto in Hannover, successfully cloned the human protein into a suitable expression vector and established the production of the natural protein by a stable transfection in a mammalian cell line. The resulting IFN-β-1a is glycosylated similar to the human protein and shows a higher biological activity than IFN-β-1b in vitro, which is produced in bacteria and is not glycosylated (Fraunhofer IGB, 2007). In the Fraunhofer IGB Stuttgart laboratories a multi-disciplinary team developed the production of this pharmaceutical protein up to the pilot scale. Fraunhofer IGB developed the fermentation process as well as the downstream processing resulting in a highly purified protein and identified the protein by amino acid sequencing and proved its antiviral effects (Fraunhofer IGB, 2007).

resistance remained ineffective and competition with the powerful and established Biogen who had also started a massive campaign against Cinnovex seemed impossible.

Cinnagen assigned a research group to find the source of this resistance. The research group found that Biogen had allocated a budget of US$3 million to protect its Iranian market from the locally produced rival product. Biogen's representatives in Iran rewarded the medical community who prescribed Avonex to MS patients, with benefits such as commissions and travel opportunities abroad. All of Cinnagen's effort's in the battle with these hidden and powerful networks proved unsuccessful and following failure to establish itself in the local MS treatment market Cinnovex faced eradication from the market altogether.

Finally, MHME's intervention helped Cinnovex to overcome this massive obstacle. Following the lengthy standardization and approval of the drug, MHME let both drugs to be used by patients during a probationary period and subsequently stopped the import of Avonex in June 2007 to help the establishment of the domestic product in the local market. The Ministry's reason for this step was the realisation that soon China and India would produce cheap IFN-β Biogenerics, possibly with lower quality and the cheaper drugs would eventually find their way into the Iranian market. MHME's action did not only give a local producer the chance to enter the local and (global) MS market but also helped MS patients, access to a more affordable drug.

6.3 Buserelin

As part of its R&D activities, Cinnagen has developed a drug analogue of GnRH jointly with Russian scientists and launched Buserelin acetate in 2007 based on synthetic peptide technology for human use. Buserelin acetate is an analogue of GnRH with similar properties. It is used for the suppression of testosterone in the treatment of malignant neoplasms of the prostate; it is also used in the treatment of endometriosis and as an adjunct to ovulation induction with GnRH in the treatment of infertility. It has also been used in precocious puberty and has been tried in the treatment of uterine fibroids.

Since the company already had the capacity to manufacture a synthetic peptide, it entered into this partnership in order to diversify into other products. As Buserelin was imported as a high-value, low volume API by Iranian pharmaceutical companies, a business opportunity existed for this API in Iran. Cinnagen's objective was to develop the best possible process from among those available. In this project, the company also collaborated with the biochemistry department of the Pasteur Institute. Cinnagen does not have a synthetic lab, so it approached Pasteur Institute with a proposal to develop the product in the latter's lab, together with Russian consultants. Cinnagen paid for the rent and reagents.

6.4 Hepatitis B vaccine

The industrial production of hepatitis B vaccine was achieved by the Biotechnology research centre of the Pasteur Institute of Iran in collaboration with the Centre for Genetic Engineering and Biotechnology (CIGB) at Havana. The hepatitis B vaccine technology transfer made the vaccination of a large proportion of Iran's children possible.

The strengthening of Iranian-Cuban cooperation began shortly after the Cuban aid to the Iranian earthquake of 1990. In 1993, Cuba and Iran signed their first biotechnology transfer agreement for recombinant hepatitis B vaccine at a cost of US$15 million per annum. In the same year, IPI (under MHME) established its biotechnology research centre. However international sanctions greatly hindered the import of laboratory equipment and machinery.

> "Iran is under sanction by US and Europe. We encountered many hardships in access to machinery and equipment from Europe. In a few instances we managed to obtain the required equipment, for example we imported an equipment to purify water for injection purposes from 'Chris' in Germany. They only agreed because the technology is used in many different industries, not solely in Biotech. The entire Europe avoided giving export licence for Iran and wasted our time and energy. At first the sanction was on fermenters but it expanded to other products. For example to purchase clean-room software and liofilizator we communicated with the 'Telstar' of Spain for a long period, opened an LC for them and so on but they could not obtain the export licence. For fermenters we contacted different suppliers in Switzerland, Germany and Italy they couldn't obtain the export licence to Iran. Purification systems were very essential for us... Building bio-labs for research purposes is not difficult, but building a bio-lab for industrial purposes was a different story and we obtained the machinery with lots of difficulties through third parties. Even now we have problems with maintenance and spare parts. Learning quickly how to maintain and repair them is essential... (Interview with biopharma industry expert).

> "Due to sanctions only Belgium [Smith Kline and Beecham] agreed to talks to us. […]. [We] visited the manufacturing site and signed a general agreement with the Belgians. However they either were not ready to transfer the complete technology to us or wanted to drag the technology transfer on for a long time. [...] So we decided that collaboration with Cuba would be more useful [...] and signed the contract for Hepatitis B vaccine technology transfer [...] In 1998, the new Minister of Health travelled to Cuba to sign new technology transfer contracts for streptokinase, erythropoietin, and IFN-α [...] It is good to transfer foreign knowledge as far as this is based on a thorough and long term strategy and vision [...] For Hepatitis B vaccine we sent around 50 staff for training in different areas of the production system such as protein chemistry, purification, fermentation, disruption, QA, QC,

> and validation to Havana... Where we don't have the essential knowledge and technology, it is recommended to access foreign sources, but as soon as technology is obtained it has to be integrated and developed further. Especially young scientists and students should access this knowledge and develop it..." (Interview with biopharma industry expert)

In addition to the transfer of know-how, the collaboration agreement included training of personnel, on-going work of Cuban scientists and technicians in Iran, and shipment of necessary production equipment to Iran. So far, Cuba has provided advanced training in biotechnology to over 300 Iranian scientists (e.g. a senior scientist at IPI pursued advanced biotechnology studies in Cuba, completing postdoctoral training in protein characterization at Havana's CIGB from 1997 to 1998). MHME has provided grants for students on both sides.

In 1996 IPI formed a joint venture with Cuba's CIGB. Cuba provided the intellectual capital and technology and Iran provided the financing in the amount of US$60 million. This modern biotechnology production plant near Tehran has five units built on 14,000 square meters. The plant took 5 years to build (1996-2001).

In 1998, the Iranian Minister of Health visited Cuba and arranged the transfer of recombinant IFN-α, Streptokinase (used in the treatment of cardiac arrest), and Erythropoietin (used in the treatment of kidney failure). In 2000, the Iranian President Khatami (1997-2005) visited CIGB to support continuous scientific collaboration between Havana and Tehran. The above technology transfer projects were finally completed in 2005.

The technology transfer from Cuba's CIGB to IPI has played an important role in the growth of modern biopharmaceutical sector of Iran. Currently the production plant at IPI has a production capacity as follows:

Modern Biopharmaceutical	Annual production capacity
Hepatitis B vaccine	16 million doses
Erythropoietin	300,000 doses
Recombinant IFN-α	1.5 million doses
Streptokinase	120,000 doses

While these MHME mediated transfers of hepatitis B vaccine, IFN-α, streptokinase, and erythropoietin technologies from Cuba have boosted the technological capability of the sector. However government style administration and bureaucratic management practices are found unsuitable for commercialisation giving government additional incentive to support privatisation (e.g. case of IPI's production unit).

> "…We need to increase and promote collaboration with the private sector. Private firms manage business much more effectively than IPI... If we had

> transferred the technology for Hepatitis B vaccine to the private sector, it would have been commercialised much faster and more efficiently... Unfortunately, the huge potential of the hepatitis B plant in meeting domestic needs and export possibilities are being ignored. This is also happening in the case of erythropoietin, IFN, and streptokinase. Government's hampering and slow administrative practices and allocation of insufficient resources have held back the proper operation and expansion of this capable factory... I strongly recommend that we should collaborate more seriously with the private sector and use their efficiency to get the best outcome from such projects... Experience from Pasteur Institute has shown that government is successful in setting direction and supporting R&D but should leave production to the more suitable organisation, competence, and effectiveness of the private sector. I really do hope that this unit is transferred to the private sector, where, under adequate managerial practices and the allocation of sufficient resources the factory realises its massive growth potential. ...From the start it was obvious that under government management this project would encounter deficiencies and progress very slowly. We mentioned this many times. ...[The previous Minister of health] agreed that the government style management practices would not benefit the projects and it was finally decided to hand the projects over to a semi private organization [Social Security Organisation]. By the time Social Security agreed to the take over and we received the approval of the President's consultants in industry matters...the government changed again. The new government was new to the whole idea and it took again some time to get the approval for the handover and there were disagreements in finding a takeover partner so the whole process was delayed until the projects were completed. At present we observe again that government administration is not adequate for the operation and maintenance of an industrial factory of this scale and with such high level of technological knowledge..." (Interview with biopharma industry expert)

6.5 Cellcept

Mycophenolate Mofetil marketed under the commercial name of Cellcept is new to the Iranian market. Cellcept is Roche's leading immunosuppressant drug used extensively in the prevention of organ rejection in patients receiving kidney, heart, or liver transplants. Zahravi Pharmacuticals is the first producer of immunosuppressive drugs in Iran acquired the technological knowledge for Cellcept through a technology transfer agreement with Roche in 2004 and.

Cellcept is patented abroad till 2011 and Zahravi Pharmaceuticals is the first Iranian biotech firm to produce an internationally patented drug in Iran. During the two year technology transfer Roche organised a number of workshops for Zahravi's staff both in Switzerland and Iran. A production unit was set up on 498 square meters under the supervision of Roche.

> "Roche's representatives visited us twice for inspection... In one inspection the production site for Cellcept was ready but we had to make modifications until it was approved... Then we sent three batches to Switzerland for inspection and analysis until we finally got the all clear for production. It took 2 years until Roche granted us the production permission." (Interview at Zahravi)

Roche enters into partnerships with emerging pharmaceutical companies in order to create life cycle expansion opportunities for Cellcept and continued business development.[162] Zahravi has experienced significant growth through expanding the organization to support the development of Mycophenolate Mofetil in autoimmune indications. Currently Zahravi exports its products to Iraq and is in the process of expanding to other countries.

Zahravi also produces cardiac drugs which previously were imported in large scale. (e.g. Ciclosporin). Before Zahravi started producing Ciclosporin locally it was imported from Switzerland at an annual cost of SFr 55 million, but now Zahravi provides the entire local need for Ciclosporin for only SFr 10 million.

6.6 IMOD and AngiPars

IMOD and Angipars are unique in the world as they are made of completely native Iranian herbs. Pars Roos' conducts R&D activities on novel herbal drugs for treatment of non-curable diseases (e.g. AIDS, bedsore, hepatitis, diabetic foot ulcers, and cancers). Its R&D affairs are managed in an independent department under direct supervision of the strategic committee and the managing director. The R&D department's main activities are primary studies on formulation and production of new experimental products through nano-biotechnology, and correcting the formulation or production method of existing products. PR outsources some of its research to research institutes.

IMOD (Immuno-Modulator Drug) was Pars Roos' first innovation, which is an herbal drug (made of seven completely native Iranian herbs) to control or reduce the spread of HIV infection in the human body. The drug was tested by the 'Iranian Research Centre for HIV/AIDS' and approved by MHME.

Angipars is Pars Roos' second innovation, a Semelil based drug which is a novel herbal-based compound containing extracts of Melilotus officinalis, formulated for treatment of chronic wounds,

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[162] For example in October 2003, Roche entered into collaboration with Aspreva Pharmaceuticals (now Vifor Pharma) to further develop Cellcept in autoimmune diseases. Aspreva licensed Cellcept from Roche for use in the treatment of lupus. Through this partnership with Roche, Vifor Pharma currently has two phase III MMF clinical trials underway for the treatment of two autoimmune diseases: lupus nephritis and pemphigus vulgaris.

in particular diabetic foot ulcer. It took 5 years to develop the drug and it has been tested on over 200 patients.

IMOD and Angipars were developed in collaboration with Russian scientists at toxicology laboratory of Moscow. A Russian expert then came to Iran to work alongside 4 Iranian experts. Pars Roos has collaborated with TUMS, SBUMS, ARI, and the Iranian Research Centre for HIV/AIDS to conduct to study effects of IMOD and Angipars and conduct clinical tests. Pars Roos actively seeks collaboration with research institutes to outsource some of its research projects.

In the case of Angipars, due to the weak national IP system, a cheap imitation of the drug entered the market within month of its launch.

> "When we introduced Angipars to the market at a high price... soon a low quality cheaper replica entered the market... In absence of a functioning monitoring systems fraud is widespread. Our patent office... is only for registration not for examination, so anyone can register anything. We don't even have specialized lawyers and judges in this area. In US and Europe from the day you register a patent you are protected. In Iran this is not the case... ...They will say they produced it independently and the formula used is different so the [IPR] system is not able to decide whether this product is copied or not. Our courts are so busy with everyday family disputes that they won't bother with IPR issues; we need specialized courts for that..." (Interview at Pars Roos)

6.7 Iran's GM BT Rice

In September 2004, the world was taken by surprise as Iran became the first country to commercialize transgenic Bt rice. A local variety of rice called 'Tarom Molai' was genetically modified with Bacillus thuringiensis (Bt) to become resistant to stem borer pest. The Iranian rice variety transferred with the Cry1Ab gene (extracted from the Bt bacteria) produces the Cry1Ab protein in its stem and leaves which results in resistance to stem borer and other lepidopteran pests. This innovation was not only the first variety of GM crop using the biolistic gun gene transfer method, it was also shown by numerous immuneblot analysis to be the only variety of GM rice that does not contain the Cry1Ab protein in its corn. This is due to the use of PEP Carboxylase promoter in the production of GM Tarom Molai (Ghareyazie, et al., 1997), (Alinia, et al., 2000). Technical characteristics of the Iranian GM rice are available in Appendix 10.

The Iranian scientist, Dr Ghareyazie, mastered the technology in 1995 during his PhD at IRRI. The first national announcement that an Iranian scientist had produced Bt transgenic rice and was working toward the availability of this crop for cultuivation was made on the 6th of March 1996.

However the commercialisation did not take place until 2004, after numerous field trials and risk assessments. Following the initial release, Iran appeared in ISAAA's annual report on "Global Status of Commercialized Biotech/GM Crops: 2005" (James, 2005). Large scale release was planned for 2006, instead Iran disappeared from ISAAA's annual report in 2007 (James, 2007). The case of the Iranian GM rice shows how a developing country overtook the world in producing the first GM rice, but it also demonstrates how national systemic failures deprived Iran from benefiting from this achievement.

6.7.1 Source of Technological Knowledge for Iran's GM rice

The Iranian transgenic rice 'Tarom Molai' was the result of Dr Ghareyazie's PhD project at IRRI in Philippines. Prior to that, he was on the Guilan University's scientific board where he observed the lack of any relevant expertise in genetic engineering. In early 1990, bioagriculture was very new in Iran. At that time Guilan University only had a few tissue culture researchers. In addition to shortage of modern biotechnology experts, Dr Ghareyazie's other motive for choosing this project was to help Iranian farmers who are highly exposed to chemical pesticides. Therefore in 1992, he started a doctoral study in genetics with an IRRI-administered research scholarship from MSRT. He worked in the Genome Mapping Laboratory of IRRI to classify Iranian rice germpalsm using DNA markers. In January 1994, he joined IRRI's Plant Molecular Biology Laboratory where his key activities in gene transfer into rice began and where he completed his project.

In the early 1990s the only attempts to produce putative transgenic plants were those of the Japanese researcher, Fujimoto, who had published a report in 1993 in which he described to have transferred the Bt gene into rice using Agro-bacterium gene transfer method. However, attempts to replicate Fujimoto's Bt rice failed. In addition Fujimoto's GM rice showed no resistance to stem borer (Fujimoto, et al., 1993). In 1994, Dr Ghareyazie started his gene transfer research at IRRI using 16 varieties of rice (including certain Iranian varieties). His supervisor, Dr Bennett, disapproved of the gene transfer into Iranian varieties of rice. Dr Ghareyazie who was keen to produce and Iranian transgenic variety agreed to work on both the Iranian as well as an international variety provided to him. After 823 unsuccessful attempts to produce a transgenic plant, in 1995, the lines 824 to 827 proved to be transgenic. The key to this success was in the selection process.[163] The line 827 of his putative transgenic plants showed a 'single' band in the

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[163] The previous few transgenic plants which contained the marker and reporter genes had undergone a two week selection in a culture of 50mg/litre Hygromycin-B. Dr Ghareyazie, however, continued the selection process throughout the bombardment period and extended it until after the regeneration and rooting period of the plants. This method resulted in a reduced number of putative transgenic plants (from 100s to only a handful) all of which were found to be positively transformed. This proved that the weak selection process used previously damaged the transgenic plants due to the advantage that the non-transgenic, healthy cells had over the bombarded and injured transgenic cells. In other words, the weak selection process caused an overgrowth in non-transgenic cells and destroyed any chance of survival for the transgenic cells.

southern blotting analysis.[164] The immunoblotting (western blotting) analysis which starts with protein extraction and quantification showed a clear band which meant that the gene was successfully transferred and expressed. This blot was published in future papers (Ghareyazie, et al., 1997). It was the first time that 'Biolistic' gene transfer method was used successfully to produce transgenic rice.

Dr Ghareyazie carried on with a bioassay analysis to establish whether the transgenic plant was resistant to stem borer pest. As entomology was outside his expertise, Faramarz Alinia, another Iranian PhD student at the entomology department of IRRI under the supervision of Dr Michael Kohen, the head of the entomology department of IRRI, assisted in the bioassay tests. Five bioassay tests were carried out with Alinia and Kohen's collaboration and showed that the Iranian GM rice 'Tarom Molai' caused a 100% mortality of Lepidopteran pests. Dr Ghareyazie's thesis was approved in January 1996.

Later, Alinia was given the responsibility to analyse the pest-resistance characteristics of all GM crops produced until then. He showed that the rice produced by Fujimoto in 1993 and the rice produced by Wunn in 1996 (Wunn, et al., 1996) had no resistance to lepidopteran pests (Alinia, et al., 2000). Dr Ghareyazie's rice on the other hand, showed a high resistance. Studies also showed a reduced expression of Cry1Ab protein in aging plants, a desired effect as old and dying plants don't need to express Cry1Ab protein (Alinia, et al., 2000).

Numerous studies were carried out on this GM rice by researchers at IRRI from different perspectives, as it was the first of its kind. 26 tests were conducted over 10 years which confirmed the resistance of the Bt transgenic Tarom Molai to any Lepidopteran pest at any larva stage. The most comprehensive of these studies were those by Alinia and Kohen.

Another unique characteristic of this rice was the use of a special promoter to control the expression of the Cry1Ab protein. Tests showed that the Iranian GM rice only expressed the Cry1Ab protein in the green tissues and the corn was Cry1Ab free at all times. Chen, et al., 2005 analysed all existing GM rice worldwide and confirmed that the Iranian GM Tarom Molai was the only GM rice to use PEP Carboxylase promoter resulting in a selective expression of the protein in the green tissues (Chen, et al., 2005).

The Iranian Minister of agriculture had visited IRRI to monitor the progress of Iranian students and had been following the GM rice research project with interest. In 1996, upon completion of his research at IRRI, Dr Ghareyazie was employed by the Ministry of Agriculture. Under the ministry's

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[164] If there are multiple copies of the gene, there will be no gene expression (silencing of the gene), therefore a single band is optimal.

instructions, Dr Ghareyazie returned to IRRI for a further two years as a post-doc to acquire further skills in molecular physiology, gene isolation, identification and characterisation. When he returned to Iran in 1998, interest in genetic engineering technology had increased significantly.

6.7.2 Initiation of GM Rice R&D Activities in Iran

Upon his return, Dr Ghareyazie established ABRII in June 1998 under the orders of Ministry of Agriculture, with four branches in Karaj, Isfahan, Tabriz, and Rasht. Ministry of Agriculture and MPO allocated extensive funds to ABRII. These funds were further increased by the Parliamentary Islamic Council in the subsequent years. With government's support an impressive research institute was built including a Genetic Engineering department. ABRII's graduates were employed in research positions. Today, these students are successful and important scientists in the field. ABRII's researchers started to produce transgenic plants under Dr Ghareyazie's supervision. Sanctions against Iran made access to common research equipment such as biolistic guns, incubators, minus 80°C freezers, and ultra-centrifuges very difficult. Some of these had to be produced in the country and some were imported through third parties with difficulty. Finally the Bt transgenic rice was produced by Dr Ghareyazie's MSc students who mastered the whole technique and the gene transfer became a routine procedure in the lab. Three and five year field trials were carried out in the Rasht province, confirming Bt Tarom Molai's resistance to Stem-borer and other Lepitobteran pests on the field. Other characteristics of the Bt transgenic rice showed analogy to the Tarom Molai control rice. Tests carried out included allergeneticity tests, animal feeding trials, proteomics analysis (to establish substantial equivalence), and field trials.

The merger of Ministry of Agriculture and Ministry of Constructional Jihad in 2000, worried scientist at ABRII that certain non-scientific departments of the latter ministry would hamper the GM rice project. However the new ministry (MAJ) provided extensive support for the Bt rice project and bioagriculture and genetic engineering technology in general. Dr Ghareyazie was appointed as Deputy of Education and Research of the new Ministry. This increased his responsibilities and reduced his presence in the lab and on the rice field; however his students and colleagues carried on with the GM rice research activities. On the other hand his new position at MAJ made it possible to access facilities at other institutes (e.g. important animal feeding trials were carried out at the 'Institute of Cattle Studies'[165]). In 2003 (after 2.5 years) Dr Ghareyazie resigned from his post as MAJ's Deputy of Education and Research to resume his research activities.

[165] Moassesseye Olume Dami

6.7.3 Field Release of Iran's GM Bt Rice

After numerous national and international tests and field trials[166], the vice president of Iran officially launched the release of GM rice in September 2004 on 2000 hectares. This initial release was to ensure provision of seed supplies for larger-scale commercialization on 10,000 to 20,000 ha, in 2006. The release of Iran's GM rice was published in the Journal of Science in 2005 under the title: An Islamic science revolution (Stone, 2005). No company was involved in the release of the Bt transgenic rice and the farmers received the crop for free.

6.7.4 Problems and Obstacles after Initial Release of the GM Rice

In 2000 the 'Office for International Economic Affairs and Specialized Agencies' (IEASA)[167] at the Ministry of Foreign Affairs (MFA) started negotiations on Iran's membership in the CPB. However, the head of this office adopted a cautious position towards genetic engineering and warned the president in a letter (signed by MFA), of GM technology's potentially hazardous consequences. This letter was criticized by scientists and scientific societies as unfounded and speculative. The head of IEASA was later appointed as 'Deputy of Natural Environment and Biodiversity' of EPO and transferred his conservative views towards genetic engineering to EPO.

As a result of these initial biosafety concerns, NBC was established at MSRT in 2000, under direct orders of the president, and Iran joined the CPB in 2003. However, NBC's Secretariat and later, CPB's National Focal Point became sources of power struggle between MSRT, MAJ and EPO and were moved in 2004 from NIGEB (under MSRT) to ABRII (under MAJ), and following the 2005 change in the government from ABRII to EPO, leaving the conservative EPO in charge of drafting the National Biosafety Law.[168] GM production was put on hold until a national biosafety law was in place to regulate different aspects of GMO and LMO production.

Following these developments, the three non-governmental scientific societies of biotechnology, genetics, and biosafety combined efforts to inform the authorities of the international empirical evidence on GM biosafety, the growing global cultivation of GM food and its effects on Iran, and the obstruction caused to the progress of Iran's bioagricultural sector by the conservative

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166 Tests include biosafety assessments, comprehensive molecular characterization of the transgenic plant, establishment of substantial equivalence of the GM rice with its parental conventional cultivar, 5 years of multi-location field trials and insect bioassays, nutritional and biochemical composition analysis, animal feeding trials, and environmental studies including the effect of GM rice on non-target organisms.

167 IEASA communicated with the 'Biodiversity Convention', 'Cartagena Biosafety Convention', and the 'Basel Convention' as a national focal point.

168 In scientific societies' opinion MSRT and MAJ are more suitable locations as they apply a scientific approach to biosafety concerns and have access to adequate expertise.

approach.[169] In addition these societies organised a working group of ten senior researchers, who carried out a comprehensive biosafety assessment of Iran's pest-resistant GM rice. The results of this assessment were published in 2007 confirming the results of previous tests.

Conflicting views on GM technology and power struggles within Iran's regulatory system turned the biosafety policy making process into a national political dispute. On one hand MHME and MSRT continued their pro GM attitude based on scientific evidence and global advances in this technology[170]. On the other hand MAJ adopted a cautious approach and EPO opposed to GM technology as potentially risky to the environment and human health. These conflicting interests within the government as well as disagreements between government and non-governmental scientific societies delayed the National Biosafety Law by five years. Drafts of the law prepared by EPO were strongly opposed to by the scientific societies who argued the documents dealt primarily with trade issues of GM crops, rather than with S&T development and national requirements. In 2007, EPO handed the 4th draft of this document to the parliament for authorization. The nongovernmental scientific societies, however, tried to stop its ratification, by suggesting that it would hamper national progress in genetic engineering and promote an import strategy rather than self-reliance in bioagriculture. Consequently this draft of national biosafety law was rejected by the parliament in 2008. Following this rejection, BSI in collaboration with the biosafety society of Iran and IPI made comprehensive suggestions to address the document's gaps and flaws. The adjusted draft was approved by the 'Parliamentary Commission of Agriculture' and handed to the parliament for ratification. However disagreements did not stop. In a speech at a parliamentary meeting, head of EPO once again opposed to genetic engineering and GM crop production. This speech was criticised by BSI for lacking scientific proof and misleading the parliament.

Finally, in May 2009, the adjusted draft of National Biosafety Document was ratified by the Parliament. Scientific societies are delighted with this progress which is five years overdue, and hope this will have a positive effect on Iran's bioagricultural growth. Currently producers of the GM rice and other GM products are still waiting for a production licence from NBC. The effects of the new law on Iran's GM food production remain to be seen.

6.8 Phosphate bio-fertilizer Barvar-II

Barvar-II phosphate Bio-fertilizer, marketed in 100-gram package per hectare by the Zist Fanavar Sabz Company can replace all chemical phosphate fertilizers used in the region. Zist Fanavar Sabz

[169] The Centre for Strategic Research also prepared two reports on global developments in the production and use of GM crops, and Iran's GM crop developments and issues.

[170] For example MHME who is responsible for human health aspects of GM technology announced in Sobh News on 16th of November 2004, that GM rice was a healthy alternative to chemical pesticides which put the health of farmers and consumers at risk.

was founded by the head of Barvar-II project[171] in 2003 for the mass production of Barvar-II which was successfully commercialised in 2003. Successful collaboration between bioscientists, industry experts and engineers and farmers is the key to the company's growth.

The technology for Barvar-II was transferred to Zist Fanavar Sabz Company from the public sector research institutes. Barvar-II was developed over 8 years at Tehran University's Department of Applied Microbiology in collaboration with NIGEB and Zist Fanavar Sabz. Each 100-gram package of the product per hectare has replaced 70% to 100% of phosphate chemical fertilizer.

The Phosphate Bio-fertiliser Research project was funded by the National Research Council of Iran. Four research teams of 25 researchers and Biotechnologists including Microbiologists, Plant Physiologists, Crop Physiologists, Plant Geneticists, Soil Biologists, Bioprocess and Industrial Design specialists completed this project in 8 years. BARVAR II phosphate Bio-fertiliser contains two types of phosphate solubilising bacteria (PSB):

1) Bacterial strain P5 that release phosphate form inorganic compounds by producing organic acids.

2) Bacterial strain P13 that release phosphate from organic compounds by secreting strong phosphates enzymes.

The development of BARVAR II phosphate Bio-fertiliser involved three stages:

1) A series of microbiological and biochemical studies to determine the genus and species names of the isolates.

2) Design of the preservation formula that allows the survival of bacteria for long term storage.

3) Preparation of instructions for using Phosphate Bio-fertiliser and its application in over 30 field trials. 2000 reports on experimental field trials in different climates were conducted in a five years period.

The product was patented in 2003 at the department of Companies and Industrial Ownership. Zist Fanavar Sabz is the only company in the sample studied which has patented its product both nationally and internationally, however the innovator of the Barvar-II bio-fertiliser the national IP protection system as weak and unreliable.

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[171] Dr. Malboobi, Associate professor and researcher at NIGEB since 1996 and Research Vice President of NIGEB from 1997 to 2001

> "R&D in biosciences is time taking and complex, but once it is done it's like a solved puzzle and copying it is easy... The current national legal system is not very useful in providing IP protection... Recently a law was ratified by the parliament which prevents the patenting of genes, promoters, and bioprocesses; this does not support innovation activities in biotechnology..." (Interview with bioagri researcher)

Zist Fanavar Sabz produces and packages the products and provides sale services and supports as well as after sale monitoring to ensure appropriate use of the product and farmer satisfaction. The company already exports the product to Iraq and Afghanistan. ZFS is also trying to strengthen its export activities in order to reduce reliance on the local market in case of any changes in government regulations.

Zist Fanavar Sabz Company's R&D, support, and monitoring units provide general and professional information on applying Barvar-2 phosphate bio-fertiliser for best results. Zist Fanavar Sabz transfers the technology in any desired level from know–how to turn-key to interest parties. The company's activities currently include formulation of bio-fertilisers; production of bio-fertilisers; consultation on bioagricultural technology transfer, biosafety issues, bioinformatics, contract research and development programs; partnership in marketing Barvar-2 phosphate bio-fertiliser; transfer of Barvar-2 phosphate bio-fertiliser technology from know–how to turn-key, transfer of any genes with a reproducible method, in partnership with NIGEB.

Since 2005 ZFS in collaboration with NIGEB also provides modern Sugar beet transformation to the regional market. This product is also patented nationally by the company.

6.9 Micro-propagated Date Palm Plantlets

The eight years of war with neighbouring Iraq in the 1980s resulted in the loss of 3 million date palm trees in Iran. Based on the opportunity that arose from many government initiatives in the early 1990s to restock the lost groves of date palm RAI was established with government's help in 1993. The Iranian Ministry of Agriculture supported RAI with funds (from the Iranian bank of agriculture) and assisted in the transfer of the technology for micro-propagation of date palms to the company from UK. With the Ministry of Agriculture's support, RAI set up a joint-venture agreement with the Date Palm Development Company (DPD) in the UK in 1993 to facilitate the transfer of date palm micro-propagation technology to Iran over a period of 3 years. The technology transfer was successfully completed in 1996 and was certified by DPD's parent company, former 'International Plant Laboratories'. RAI subsequently acquired 100% ownership of the technology and has been producing high quality micro-propagated date palms for over a decade.

Rai is the first private plant biotechnology firm in Iran to use direct somatic embryogenesis technique for the micro propagation of date palm varieties and is currently one of the largest producers of tissue cultured plantlets worldwide. There are a wide range of superior date palm varieties and a selection of banana cultivars currently in production at RAI's micro-propagation unit. Date palm varieties include, but are not limited, to Barhi, Pyarom, Thory, Dairy, Zahedi, Mazafati, Kalas, Deglet Nour, Rabi, and Ashrasi. RAI has expanded its marketing activities into foreign countries in the region and competes on a global level.

The owners/directors of RAI are family members and have degrees in economy (2MScs from Iran) and biotechnology (2 PhDs from UK). The management at Tehran head office consists of internal and foreign procurement managers, and chief and second accountants. RAI's plant biotechnology laboratory complex has a site manager, a laboratory manager, and a glasshouse manager.

6.10 GMO Detection Services

There is an increased demand for GMO detection services for agro-food products since genetically modified food products have entered the Iranian market through unregulated imports. Lack of proper regulation resulted in GM food being imported to Iran from GM producing countries (mainly Argentine, Brazil and Canada) at competitive prices and compete with conventionally produced local products.

> "We are importing and using transgenic oil from Argentine, Brazil and Canada. We can't stop the import because we have a shortage in the country..." (Interview with bioscientist)

Gene Azma Persia (GAP) is the first private firm in Iran to provide GMO detection services. GAP offers consultation and scientific advice to government as well as private sector.

> "We are the first company to obtain a certificate for these services... A part of my company is a medical plant clinic. There are 22 other medical plant clinics in Tehran, but we are the only one to conduct high-tech molecular research at such advanced level because our clinic is a spinoff from our research at NIGEB..." (Interview with bioscientist)

Gap started in 2007 to offer GMO testing and consultation services in agricultural products and processed food based on international standards. The company tests imported food for GM products. GAP also started to provide toxin residue testing services in 2008 and is the first private company in Iran to collaborate with the Plant Quarantine Organization under MAJ and the National Laboratory of Department of Food and Drugs under MHME as a reference laboratory. GAP's Plant Disease Diagnostic Clinic also works closely with MAJ. GAP also collaborates with the Seed and Plant Health Institute of Iran. GAP's main customer is the government (MAJ and MHME), therefore the company relies on government's demand for its services.

> "In 2008, Ministry of Agriculture decided to outsource the testing of toxin residues to the private sector. The government created this position and is our main customer, so it plays an important role in our company. Maximum [pesticide] residue levels in agricultural products and processed food are extremely regulated, so we collaborate with the Department of Food and Drugs of the Ministry of Health and the Ministry of Agriculture to on detection of pesticide and heavy metal residues in agricultural products, especially nuts and vegetables, in accordance to international standards..." (Interview with bioscientist)

GAP's founder finds difficult access to large scale production facilities, government regulation, and lack of funds as major barriers to start-up activities. These obstacles caused the firm to change its focus from diagnostic kits to GMO and LMO testing services.

> "We turned our technological knowledge into a diagnostic kit and started looking for clients. The problem was we couldn't mass produce the kit because we didn't have the manufacturing facilities. So we either needed companies who would buy our kit (basically our technological knowledge) and produce it themselves or we had to form an alliance with a manufacturing firm. These sorts of alliances need personal connections or else you have to try so many companies until finally someone trusts you. Getting loan was another problem..." (Interview with bioscientist)

The founder is a senior researcher at NIGEB (with partners). GAP's 'Plant Disease Diagnostics Clinic' is a facility of NIGEB's 'Department of Incubation'. This alliance allows GAP to maintain a strong connection with leading researchers in the field of plant pathology and biotechnology and helps GAP to provide accurate and timely plant disease diagnosis, specialized services, and modern control recommendations. Also in its tissue culture activities GAP collaborates with NIGEB to access facilities such as green houses, walking chambers, tissue culture cabinets, particle gun and other instruments for high-quality gene transfers. NIGEB also contracts parts of its projects out to GAP. GAP rates these collaborations as very important to its innovation activities. GAP started with 2 staff and expanded to 8 including graduate biotechnologists, plant medicine experts, biochemists, industrial food specialist, and chemical engineers. GAP's strategy has been to switch from product innovation to process innovation and become the first private firm to address the national need for GMO testing services. GAP engages in continuous modern R&D to offer quality services in plant disease diagnosis and treatment, GMO testing of both imported and exported food products, tests for pesticide residues and relevant consultation and advice (box 8.9, quote 1).

> "We concentrated mainly on providing services because production in Iran is very difficult. You need to have private funding, because government loans are not easy to obtain and need huge deposits which I couldn't afford... Our other strategy is to market ourselves in the private sector so if we lose government support we have other customers..." (Interviews with bioscientist)

The firm is advancing from start-up stage of growth to expansion as the founder is opening two new branches. The firm's director only hires her graduate students and avoids hiring anyone she doesn't know. GAP is also trying to obtain ISO standards. A recent strategy is to diversify the company's clients and reducing its reliance on the state sector as uncertain developments in government regulations are a concern for GAP. While GAP started as the first provider of GMO testing services, since its establishment, five new laboratories have started offering these services and the initially monopolised market has become competitive. The company's main external concern is any changes in government strategy as the government is the main client for its services. GAP is trying to reduce its reliance on the government's demand by looking at opportunities to expand into new markets including international clients.

> "One problem is that government employees cannot engage in business with the government. This is in contradiction to the privatisation act. On one hand they want to encourage researchers to setup private firms, on the other hand these researchers are government employees and cannot do business with the government. The industry is dominated by the government so you have to find someone you can trust and register the company in their name to do business with the government... ...If government regulations change we might even have to close down, so we are constantly trying to find new customers... For example if we receive offers from international inspection agencies to be their reference laboratory we won't have to rely on the Ministry of Agriculture anymore..." (Interview with bioscientist)

6.11 Summary

The GM Bt rice and IFN-β product journeys demonstrate that the main barriers to both these innovations were at the commercialisation stage, however for different reasons. This finding is representative of most Iranian biotechnology product and established as well as start-up firms (e.g. in the biotechnology incubator) face difficulties in the commercialisation stage. However, while in the biopharmaceuticals this is mainly due to competition with established foreign brands, the bio-agricultural market is very welcoming of local products and barriers are mainly government regulations and bureaucracy. In the case of Iran's GM rice, ministerial regulations posed the main barrier to its full commercialisation. The conservative approach of the post 2005 government (MAJ and EPO) to GM technologies resulted in a ban on the full commercialisation of GM rice. A national biosafety law was ratified by the parliament in 2009 allowing local GM production subject to the attainment of a production licence from NBC. The GM rice is still waiting for a production licence. In contrary, ministerial regulations played a constructive role in the case study of Cinnovex. The main barrier in the commercialisation of Cinnovex was the battle with hidden and powerful networks run by large foreign corporations aiming to immediately eradicate Cinnovex from the market. Cinnovex is a quality product at a fraction of the foreign brand's price. This has massive effects on the foreign brand's share in the Iranian and international markets. MHME interventions helped establishing Cinnovex in the national market and compete with the foreign brand.

The case studies reveal that foreign sources of technological knowledge (mainly foreign research institutes) are very important in the biopharmaceutical innovation activities of both government and the private sector. Access to technological knowledge is facilitated through contract technology transfer from abroad to national research institutes (e.g. hepatitis B vaccine technology transfer from Cuba to IPI, followed by IFN-α, erythropoietin, and erythromycin), which upon adoption and adaption to local circumstances, are transferred to state and private production units. Government support organisations assist firms to locate and contact foreign sources of technological knowledge (e.g. role of HTIC in the Cinnovex case study). The majority of modern biopharmaceuticals on the market have involved technology transfer from foreign sources.

Angipars, a novel drug based on native herbs developed by Iranian scientists in collaboration with Russians is another interesting case demonstrating the importance of foreign collaborations as well as the weak national IP protection system allowing the a cheap copy of the Pars Roos's innovation to appear on the market within month of its commercialisation. The bioagricultural cases are varied however they confirm the miss-regulation of the sector which allowed GM food being imported to the country while banning local production. The local technological knowledge is strong and with the exception of RANA there have been no formal technology transfers from foreign sources involved in innovations. The finding from empirical data is discussed in more detail in chapter 7.

Chapter 7 Discussion and Conclusion

7.1 Introduction

This chapter analyses the empirically observed findings within the conceptual framework of the study and a Gerschenkronian focus on 'the role of government as an agent of economic development' to demonstrate how parts of Iran's NSI are performing and the extent to which state's substitutions have had a positive or negative influence. Further, the implications of the empirical findings for the significance of NSI in the light of internationalisation and increasing popularity of sectoral systems of innovation are discussed. In addition the chapter presents unexpected findings, limitations of the analysis, policy implications, and future studies.

7.2 Factors Influencing Biopharmaceutical Innovation in Iran

The empirical examination of national strengths and weaknesses in the key factors influencing innovation found that Government funds allocated to public sector research, the increasing number of university departments and Research Institutes carrying out research, and the post-graduate students being trained in relevant areas have positively contributed to building an impressive R&D base in biotechnology. Also investment of funds in relevant research and research training in both subsectors during the 2nd and 3rd EDPs has been essential to the sectors' development.

However the innovation activities based on 'domestic R&D activities' have been modest in the biopharmaceuticals due to a linear approach to innovation and lack of incentive for academics to enter commercial activities (weak link between academia-industry). The government is trying to overcome this linear approach by introducing the biotechnology incubator at NIGEB and development of S&T parks. Although the incubator is very young it is supporting 17 firms, over half of them have already marketed their product. The government (MHME) has substituted the gap in technological knowledge in the industry by mediating contract technology transfers from abroad to integrated state organisations combining research, production and marketing. In addition MHME and TCO's efforts in attracting Russian collaboration with Iranian research institutes has been an important step towards developing systemic innovation activities in the sector. Some private firm's with strong links to national research institute (e.g. spin-offs or firms whose founders work at U/RIs) make use of these links with foreign sources of technology (e.g. Cinnagen and Pouyesh Darou). In addition Iran has introduced a new IP law which is more comprehensive than the previous law, however biotechnology firms still distrust the national system of IP protection.

The IP system should be strong both in legislation and in implementation in order for biotechnology firms to protect their R&D investments.

Due to political turmoil and sanctions in the past three decades, Iran has failed to attract foreign pharmaceutical multinationals to establish research active subsidiaries in the country. Also activities of sectoral business interest non-government organisations (BINGOs) to represent the interests of the business community are weak and limited to 'non-governmental scientific societies' with limited resources to support entrepreneurship amongst academics. BINGOs are substituted by government industry support organisations such as HTIC and LIDCO which have been which were described by scientists and entrepreneurs as a step in the right direction.

The size of the national market is large and the regimes followed for procuring pharmaceuticals by the national healthcare system clearly influence the activities of companies. Government subsidies compensating companies for low fixed prices gave companies no motivation to compete on the basis of brand name or quality. This also has had implications for profit margins and R&D investments. The government subsidies have been very high, thus, even after many years of experience in drug production, the technological capability of Iranian pharmaceutical companies remained mainly limited to manufacturing and development of new drug formulations. The processes, in most cases even the delivery systems, are developed by national research institutes and transferred to companies. Post market research has also been carried out by national research institutes. Once a product is identified, the government funds the development of that drug (mainly new processes and formulation). After developing the product, research institutes transfer the know-how to pharmaceutical firms on a royalty basis. R&D carried out by pharmaceutical firms has been mainly limited to the testing of product quality.

Recently, to promote competition in the industry, in parallel to the privatization act, the government is trying to reduce its intervention by removing fixed subsidies from the local industry and replacing them with targeted subsidies. This has had a positive effect on the private firm's activities and the private sector is playing an increasingly more important role in Iran's biopharmaceutical SI.

Market's resistance to domestic biopharmaceuticals has challenged local products, trying to eradicate local versions of imported high-value drugs from the market. The government has supported the local production of these high value drugs by imposing high tariffs on the foreign brands and restricting their market share.

While there are technology policies to support the development of biotechnology firms in Iran, including mechanisms to encourage technology transfer, such as government promoting joint venture creation, the political environment and sanctions on Iran have discouraged foreign firms to invest in the country. Availability of financial capital strongly affects the creation of start-up firms and diversified modern methods of financing that offer low-risk capital to start-up firms are required to support privatisation.

To sum up: Iran has an environment where Government is the main factor in driving innovation in biopharmaceuticals and the development of the sector. There are still several areas which have so far acted as a brake on innovation, although recent policy is attempting to address these handicaps, such as the high subsidies and the strong control of pharmaceutical prices. The mixture of both positive and negative influences has resulted in a slow growth, but the positives in the demand as well as the supply side factors have outweighed the negatives in supporting biopharmaceutical innovation. Iran's strengths in knowledge and skills and strategies encouraging public-private R&D cooperation promise continuous growth in the sector.

7.3 Factors Influencing Bioagricultural Innovation in Iran

Public sector research related to bioagriculture has received strong funding from the government during the 2nd and 3rd EDPs and Iran has built a strong scientific base in its public research institutes. Private investment is still marginal and mainly in the non-GM technologies. Public sector research has focused on GM plant biotechnology but these investments have not generated commercial activity. With 40 GM crop projects in the pipeline during the 3rd EDP, this area was at the forefront of bio-agricultural development in Iran concentrating on crops resistant to biotic an abiotic stresses. There is public demand for the applications of GM technology to crops and food as sanction and inflation have tremendously increased the price of food crops. In addition to GM crop technology, Iran has built capabilities in bio-fertiliser production and animal cloning (e.g. Royan institute).

Public interest non-governmental organisations are absent in Iran's demand side NSI factors. BSI's public awareness campaign has been the closest to such activities.

Despite high demand in the local market and no public opposition to GM crops (at least until now), MAJ and EPO have adopted a more conservative approach to GM products in the 4th and 5th EDP. Further ministerial power struggles delayed the national biosafety document by five years further delaying the fate of the GM products awaiting production licences by the national biosafety committee. However GM products have been imported to the country due to a weak monitoring system, demonstrating miss-regulation in Iran's bioagricultural SI. Bioagricultural innovation is currently limited to tissue cultured seeds and plantlets, bio-fertilisers, and bio-pesticides. Major GM crops including rice, cotton, sugar beet, potato, canola, maize, wheat, lentil, and chick pea resistant to insects, diseases, viruses, and abiotic stresses are still awaiting production licences from the NBC in accordance to the 2009 National Biosafety Law.

To sum up, the development of the agricultural biotechnology sector is greatly influenced by the government activities. The government's large investment in a strong science and technology base and world class research institutes, a large domestics market and absence of public opposition to GMOs caused the fast development of national strength in this sector. However, while there has been a national emphasis on commercialising this science base prior to 2005, the GM crop projects at public research institute have neither generated commercial activity nor been employed to achieve the country's self-sufficiency strategy. The brake on the development of the sector is due to MAJ and EPO banning local GM production in the 4th EDP while importing such crops to the country due to lack of proper regulation. There are very few small biotechnology firms involved in GM technologies. Private firms mainly involve in micro-propagation of seeds and plants. In the non-GM sector the dominance of the state sector, weakness of private investment in R&D, together with no availability of venture capital to support the formation of small firms are the main barriers to growth.

7.4 Substitutes for Missing Prerequisites in Iran's Biotechnology Sector

The empirical data reveal the following key substitution strategies for the missing prerequisites as demonstrated by an arbitrary developed country (e.g. USA or Japan):

The establishment of Government Support Organisations such as HTIC, LIDCO, and Biotechnology Incubator, the gradual replacement of fixed drug subsidies with targeted subsidies, and the low-interest government loans for new business start-ups are all attempts to substitute for a strong entrepreneurial and managerial capacity and a competitive environment. These GSO's have had a positive effect on the development of the private sector, and the gradual removal of the subsidy system has encouraged competition amongst firms based on brand name and quality, however the low-interest government loans have only partially substituted for diversified methods of financing that offer low-risk capital to start-up firms. Easier access to seed capital is essential for the further development of the biotechnology sector.

Restriction on imports of selected foreign brands and/or imposing high taxes on selected imported biopharmaceuticals which are also produced locally substitute for access to export markets. This is important as access to the large internal market is crucial for biopharmaceutical firms in the absence of TNC subsidiaries and export-led growth possibilities in the sector (however many firms are hoping to achieve export-led growth as many important patents for bio-similar products have expired or are about to expire). The Iranian government has also tried attract FDI inflow through liberalising FDI regulations in the early 2000s, however this strategy has not been successful and FDI has been hindered by international sanctions as well as unfavourable or complex operating requirements. Iran only absorbed US$3.82 billion of foreign investment from 1991 to 2007 (WDI, 2009).

Government funded research activities at public research institutes, government mediated technology transfer to integrated research, production and marketing organisations such as IPI and RSVP, as well as promotion of private sector research collaboration with foreign sources of technology are positive substitution method for the lack of technological knowledge in the industry. In addition to government mediated contract technology transfer from abroad (e.g. ICGB in Havana), other interactions with international centres (most notably ICGEB of Trieste, including its New Delhi component) have helped Iran by training scientists, funding research projects at NIGEB, and transferring technologies for biotechnological vaccines and drugs to Iranian companies.

The government's directed governance structure in Iran's NSI has mixed effects on the biotechnology sector's development. Both biopharmaceutical and bioagricultural sectors have benefitted from government's prioritization of biotechnology during the 2nd and 3rd EDPs. Iran's strategies of self-sufficiency and reduced dependence on the 'West' are in line with the type of 'ideologies favouring economic development' that Gerschenkron sees as an important agent in development. Allocation of major funds for the establishment of state of the art research institutes and laboratories, introduction of biotechnology related degrees at postgraduate level and government funds for biotechnology R&D helped the development of the R&D base. These ideologies are also reflected in the National Strategic Biotechnology Plan of Iran and the 20-year Comprehensive Plan for Science and Technology promoting long-term sustainable growth in science. Iran's core strength lies in its human resources. Its bio-scientists and engineers are well trained, and many of them have studied abroad. Their knowledge of the subject is comparable to the best in the world. Iran is drawing advantage from its appreciable human capital, initially with producing generic products, since many important patents for such products have expired or are about to expire, and has started to produce novel products and processes more specific to the country and the region. Also Iran has a vast variety of flora and fauna and Iranian researchers are very active in the herbal medicine sector, particularly in identifying, isolating and extracting active ingredients.

The government's initial focus on the production of restriction enzymes needed for research and production purposes, as well as low-tech diagnostic kits has offered vast learning opportunities. Although these technologies are now available at low cost worldwide, the complexity lies in adapting diagnostic kits to suit the kind of strains of bacteria and virus common in Iran.

The study also identified the following areas where government strategies have been slow in achieving the desired effect:

Universities and industry still work independently of each other. Industry's investment in R&D is marginal and there is a lack of incentive for scientists to become entrepreneurs. In addition scientists don't have commercial knowledge. The biotechnology incubator is a step in the right direction but is still very young and new in the NSI of Iran.

Government support for projects is discontinuous. Hampering government bureaucracy and slow administrative practices slow down progress of projects. Out-dated government laws and regulations, in particular the law preventing government employees from engaging in business activities with the government; and the Law stating companies should be set up within 120 km of the town centre. The latter is found to put a geographical distance between Industry and U/RIs.

Iran's previous IPR system was weak both in legislation and implementation therefore firms were reluctant to invest in R&D. The previous legislation enacted in 1931 neither referred to issues such as compulsory licensing nor clearly distinguished between product and process patents. The new law (2008) is more comprehensive but its effects remain to be seen. Data shows that the weak national system of patent protection is an obstacle to innovation in both sectors, and international patents are considered more useful than national patents, however applying for international patents is costly for Iranian scientists. Further to the above, entrepreneurs perceive the new IP law (2008) preventing from patenting LMOs and their parts as another obstacle to innovation activities in the sector.

Further to the above weaknesses the Government domination of industry and slow privatisation, lack of modern methods of financing that offer low-risk capital to start-up firms, difficult access to machinery and equipment from abroad due to global sanctions on Iran and lack of a system to monitor the implementation of national strategies are also weaknesses of Iran's NSI.

MAJ and EPO have adopted a conservative attitude towards genetic engineering in post 2005 government. Lack of a national biosafety law was used as a reason to put all GM crop productions on halt until a national biosafety law was drafted, ratified an implemented. Power struggles over the location of NBC's Secretariat and CPB's Focal Point resulted in their relocation from MSRT to MAJ and eventually to EPO, putting the conservative EPO in charge of drafting the national biosafety law. Conflicting views on GM technology within the government and disagreements between scientific societies and the regulatory bodies (MAJ and EPO) delayed the national biosafety document by over five years. These developments were found to be the main reason for the slow-down in the sector's performance. The national biosafety law was finally ratified by the parliament in 2009. This law permits local GM production subject to acquirement of a production licence from NBC. The effects of this law on Iran's GM crop production remain to be seen.

7.5 Conclusions for Theory

In line with Gerschenkron's argument, we see that Iran is following a range of strategies and paths that both substitute for missing prerequisites as well as imitate and build upon developing and developed countries' model of growth, such as investment in science parks. With the changing economic circumstances government needs to provide new substitutions for missing prerequisites. With the private sector's growing contribution to the local production of high-value biopharmaceuticals the government needs to substitute for the unfair competition with the state owned large organisations. In addition, with the increasing number of new start-ups in the biotechnology sector the government needs to diversify sources of funding.

Although as Gerschenkron insisted, direct application of substitution strategies to other countries is inappropriate, the process of identifying the substitutes for missing prerequisites could potentially play a useful role in assisting developing countries to develop their own distinctive strategies for development. Each developing country embodies its own particular advantages and disadvantages, shaped by its stage of development. By observing the mechanisms of substitution in Iran, other developing countries might find new ways of overcoming disadvantages, including the lack of resources and capabilities needed for development. Each nation has its own set of missing prerequisites and (hopefully) distinctive methods for substituting for them, based not only on its particular conditions but also the changing external circumstances.

In line with the objectives of the thesis, the application of Gerschenkron's views has usefully helped to identify the extent to which the development of the biopharmaceutical and bioagricultural sectors in Iran is determined by the country's NSI characteristics. Empirical findings revealed that laws & regulations set by national authorities are the main determinants of biotechnology SI in Iran and the performance differences between the two sectors are due to differing ministerial regulations. While systemic failures in the bioagricultural sector are argued to be due to the institutional system lagging behind the sector's advanced R&D and innovation performance, systemic weaknesses in the biopharmaceutical sector are more in line with the developing status of the country.

Continuous government support has resulted in a slow but steady development leading to local production of modern biopharmaceuticals over the past five years. The biopharmaceutical institutional regime is more in line with the development of the sector and this has caused the sector to outshine the bioagricultural SI's performance. Although only 3% of drugs are imported, in terms of value these imports (including specialized biopharmaceutical drugs and APIs) account for one third of the drug budget (Annual Statistics Report, 2005). This situation has opened up an opportunity for new companies to emerge to develop and/or manufacture these high-value drugs (e.g. Cinnagen, Pouyesh Darou, and Zahravi). MHME's high value drug import substitution policy has resulted in continuous support for local production of modern biopharmaceuticals both in the pre and post 2005 government, facilitating the sectors progress. In addition MHME's regulatory measures to restrict selected imported drugs that are locally produced (e.g. case of Cinnovex versus Avonex) further demonstrates the Ministry's positive attitude towards building up local capabilities in biopharmaceutical production. MHME also has a positive attitude towards the use of genetic engineering in bioagriculture to significantly reduce the use of chemical pesticides in Iran.

The SSI concept is based on the idea that distinctive elements of economic sectors and technological fields determine the innovative capabilities and performance of different sectors. Sectoral elements of SI are believed to be typical to specific industrial sectors and somewhat invariant across countries (Kern, et al., 2006). Sectors can be characterised by specific knowledge bases, technologies, processes of production, cooperation patterns, demand and demography of firms and differ largely in several of these characteristics (Malerba, 2002). This was demonstrated in European biotechnology SI by Senker, et al., (2001) which identified that differences in demand and public acceptance and attitudes to applications of biotechnology in Europe are the main determinants of the differing performances. In Iran however the comparison of public acceptance for biopharmaceuticals and bioagricultural products does not highlight any distinctions between these sectors. Public awareness campaigns against the health threats of chemical pesticides and MHME's approval of the GM rice as a healthy alternative to the use of chemical pesticides and insecticides during the 3rd EDP have supported national demand for bioagricultural products. Iran is one of the largest importers of food crops, and with prices currently soaring, the public has not objected to bioagricultural products entering the local market. Media has also played a supportive role, in particular student news networks (e.g. ISNA) and pro GM campaigns by scientific societies (based on scientific evidence). In biopharmaceuticals too, innovation is supported by national demand characteristics. The large size of the market (country), and the import substitution strategy of the government affects national demand. MHME has realised that if it does not support local production of modern biopharmaceuticals (which are imported at high prices), cheap Indian and Chinese alternatives will soon replace these high-value products in the market instead.

The findings also demonstrate that in addition to public acceptance and attitudes to applications of biotechnology, industrial organisation and the character of biotechnology innovation processes which are considered to be typical sectoral elements also have important national determinants. The existence of natural resources in a country (such as oil, gas as well as flora and fauna in Iran), the geographic position, and the size of the home market are important national determinants of industrial organisation which can enable or hinder the development and exploitation of biotechnology and thus lead to important differences between nation-states. The character of biotechnology innovation processes too is influenced by national laws, regulations, traditions and standards, as in the thesis this was demonstrated. Failure to address the National Biosafety Law at the same pace as R&D developments in the bioagricultural sector (i.e. failure to provide a timely and adequate National Biosafety Law through systemic efforts) was a failure in the institutional development of the sector resulting in R&D capabilities caching up with the developed world while the institutions moved out of sync by remaining in line with the country's developing status. This finding supports the co-evolutionary model of dynamic change where timely and appropriate co-evolution of institutes and institutions is key to sustain and reap full benefit from technological change (von Tunzelmann, 2003).[172]

In addition, ministerial power struggles over the location of NBC in Iran and the resulting delay in the national biosafety document outline the importance of the role of political power struggles which are greatly understudied in NSI literature. The empirical findings of this study confirm Johnson's idea that destroying existing competences for political reasons related to the distribution of power may be more common in the developing context than in the developed context (Johnson, et al., 2003). This further confirms the need to adapt the SI approach to the situation in developing countries.

Internationalisation has challenged the significance of national dimension of SI as borders and geographical demarcations dissolve into a global technological system (Freeman, 1995). International SIs are believed to facilitate "transmission of best-practice techniques" and are also a "vehicle for the international flow of goods and services" (Archibugi, et al., 1999). Increasing power of TNCs and the growth of international R&D networks suggest that technological advances may be more properly viewed as products of a global technological system (Bartholomew, 1997). These give rise to debates as to whether increasing technological globalisation signal the convergence of technological capabilities across countries, and the declining role of the nation-state in technological development or whether NSIs maintain their importance in the face of the interlinked economy in particular in the context of a developing country.

Therefore with regards to the objective of adding to theoretical understanding and empirical knowledge of NSI in face of internationalisation, this study's findings reinforce the importance and relevance of NSI approach in particular in a 'developing country' like Iran. Technology transfers, both within a country and between countries are greatly influenced by the NSI characteristics, the institutional and organisational structures which support technological development and

[172] The Bioagricultural sector's mere focus on the creation of a bioagricultural 'knowledge base' at public research institutes resulted in failure to address institutional developments simultaneously, emphasising the significance of the 'moment of implementation' of national policies. The biopharmaceutical sector adopted a more systematic approach to the innovation process by simultaneously addressing the knowledge base and commercialisation of modern research, and witnessed better performances in both science and commercialisation (Reiss, et al., 2003).

innovation. The case of Iran confirms that 'national governments' can build or strengthen scientific and technical educational institutions and modify the form or operation of technology networks (Metz, et al., 2000).[173] While the broad and fuzzy nature of NSI approach is criticised by policy makers for being hard to implement, its flexibility should be used to capture the open and dynamic nature of different national economies. The NSI concept however, should consider the importance of international aspects of technology flows in order to provide a more complete picture in explaining national innovation performance. SSI and TSI can be regarded as complementary frameworks to NSI in order to address important aspects of innovation associated with national specialisations within global production and innovation networks (Kern, et al., 2006), (Nightingale, et al., 2008).

7.6 Unexpected Findings

While Gerschekron's theory suggests that the government can speed up economic development by overcoming the barriers to development, in the case of Iran the government eventually became an obstacle to innovation in the already advanced bioagricultural sector. While the government successfully built R&D capacity in the sector it failed to provide the regulatory environment within which the sector could thrive. The government as a barrier to development turns Gerschenkron's conclusion about the state as a substitute for 'economic backwardness' on its head.

The findings were unexpected at the outset of the project as the uneven development in the biotechnology sector of Iran turns out to have been caused less by technological failure than by regulatory failures on the part of government. This demonstrates that while the government can speed up economic development by overcoming barriers (through for example promoting successful access to technological knowledge, and R&D), it can also hamper innovation by failing to provide appropriate legislation and to adjust laws and regulations to the stage of technological development that the biotechnology sector of a developing country has achieved.

The government of a nation as a potential agent of economic development can influence the national economy which may be favourable to economic development or hamper it. The government can contribute to economic development by promoting – or failing to promote – political and institutional stability. This can also be hampering in case of already advanced technologies, such as GM crop technology in Iran where the government caused a major slow down by failing to provide an appropriate National Biosafety Legal Framework.

[173] Technology networks are the interrelated organisations generating, diffusing, and utilising technologies (Metz, et al., 2000).

7.7 Limitations of the Analysis

The study identified a limited number of 'quantitative' figures as indicators of innovation in the biotechnology sector of Iran. The indicators of innovation in the biotechnology sector of Iran need to be developed further. Also nothing specific is known about the processes for implementing the policies set out in various policy documents and that indeed is one of the major drawbacks of the country's NSI. Iran requires an explicit statement of technology policy. This policy document must consist of policy instruments, an indication of the responsible governmental agency that is to be charged with its implementation, the necessary budget and the precise time-frame for achieving the desired results. Simultaneous efforts must also be placed on developing statistical and other indicators for measuring and evaluating the effectiveness of specific policy instruments.

There was difficulty in getting data on the public biotechnology science base, either for research funding or for the training and production of PhDs. Small companies often did not have the time or were unready to provide information which they regarded as confidential. Also although NSI focuses on the systemic character of the whole system, the study has not captured sufficiently the links within or between the four networks used as the basis for data collection. This was partly related to the design of the project as well as the limitations of data. Also it was difficult to work out how to operationalise the identification of the detailed working of network links.

The generalisation of the specific case of Iran imposes further analytical challenges. While characteristics such as economic sanctions are specific, they are not limited to the case of Iran. In addition the utility of the NSI framework for developing countries with directed governance structures are not uncommon. Therefore the case of Iran provides valuable insight into issues of biotechnology development in the role of national government in building S&T capacity, the role of public research institutes in R&D, the role of foreign sources of technological knowledge and the effect of national institutions on the sector.

Another limitation of this study is in analysing processes of dynamics of change within the NSI Framework. The U/RI–Industry–Government relations are subject to institutional transformations. For example, academia can play a role as a source of technological development, in addition to its traditional role as a provider of trained persons and basic knowledge. Dynamics of technological change require a dynamic policy process in which goals, key issues and instruments are reformulated and reassessed over time.

7.8 Policy Implications

While sectoral determinants of SI are perceived as somewhat invariant across countries, discouraging nation-specific policies, the national determinants of SI in particular in developing countries should make policy makers reluctant to adopt foreign 'best practices' in innovation policies without a critical examination of the local environment. The transferability of policies and instruments is not self-evident. At the same time, there is a need for robust, predictable and stable policy frameworks that are not (heavily) changed or adapted to all the specific needs of sectors and industries. Without such stable and robust policy frameworks the actors in the system might use and distort the policy system for their own benefits. Ministries often have their own policy domains and are in charge of specific sectors or parts of SIs; these ministries tend to react defensively when others enter their policy domain. Extending the authority in the area of innovation policies over a number of government departments, without the existence of proper coordination mechanisms, results in an ineffective and unproductive environment. A central system of co-ordination, monitoring and implementation can be highly desirable. Moreover, there are many policies outside the innovation area that affect the processes of technical change and national/sectoral innovativeness, e.g., in the areas of education, market introduction, taxation, and legislation, which also need to be co-ordinated.

With regards to bioagricultural policies, GM crops designed to reduce levels of chemical pesticide and insecticide use could benefit rather than harm the environment as well as human health (both farmers and consumers). In addition to reduced cost of chemical pesticides, there will be reduced cost of medication for farmers and their children who spend their days in pesticide contaminated rice paddies.

To ensure public confidence, in parallel to building up research capabilities, it is also necessary to invest in systematic biosafety research and testing capabilities (e.g. field trials, animal feeding trials, environmental studies of effects on non-target organisms, etc.). This will provide a framework for communicating to the public information on safe and beneficial application of biotechnology to agriculture which helped Iranian scientists to argue their case based on scientific evidence.

In parallel to supporting R&D and innovation at public research institutes and private firms, the Iranian government needs to update its protocols for clinical trials and quality control to facilitate development of biotechnology in the country. For example in biopharmaceuticals the government should establish protocols for different phases of clinical trials and strengthen its regulatory bodies to centralise and coordinate the clinical trial of drugs. Similarly in bioagriculture and bio-food, methods and standards of quality control should be updated to test for microbial qualities of bio products. While Iran has an advanced system of monitoring the quality of chemical products (e.g. chemical fertilizers), the mechanisms and standards to conduct such control for bio products are still missing (e.g. bio-fertilisers need to be tested for quantity of the bacteria, their contamination, and the effect on the soil).

Private enterprises that base their innovation strategies on conditions of demand and competition are a necessity to derive larger economic benefits from innovation (UNCTAD, 2005). Only recently has Iran started realizing such larger benefits including opportunities for commercializing new products, emergence of spinoff enterprises and new entrepreneurs (e.g. through Biotechnology Incubators).

The new IP law of 2008 is yet to show its effect on incentives for entrepreneurship. The IP system should be strong both in legislation and in implementation in order for biotechnology firms to protect their R&D investments. The new law is said to be more comprehensive than the previous law, however biotechnology firms still distrust the national system of IP protection. The government should introduce specialised IP courts and expert judges in the field.

Biotechnology research is mainly carried out by research institutes, so an incentive system for the researchers in these institutes is needed to improve the productivity, quality and variety of research and move away from the dominance of academic criteria as the standard for evaluating research quality. As part of the incentive system, the scientists involved could be given a share of the royalties, if their research results in commercially viable products or processes. This will increase researchers' incentive to engage in commercialisable research and address the industry's needs.

The experiment of unique integrated research, education and production institutes (e.g. IPI and RVSRI) may have served a purpose in the past but their production activities don't have a profit motive. In order to build up a commercially viable biopharmaceutical industry, their production activities may have to be spun-off to separate, preferably private companies with a profit motive. At the moment, production activities, i.e. manufacturing drugs, are financed through the government budget (perhaps on a cost-plus-margin basis), so there is no incentive to improve productivity or lower production costs). Production levels are decided by the government, and the budget is provided accordingly. In addition these large state organizations that produce a major portion of the drugs required by Iran are not really companies, and if there is competition in the industry, they have an undue advantage over private companies. The production activities of these organizations could be transferred to new companies to be run with earnings from the sale of products rather than through the government budget. This should help the producing company retain its knowledge base and integrate it with the commercial realities. Such a spinoff will also drive the promotion of entrepreneurship in biopharmaceuticals.

7.9 Future Studies

A complementary study currently underway is the study by E. Souzanchi (SPRU DPhil Candidate) investigating the causes of the differing approaches of the different Ministries to biosafety issues in Iran using the concept of framing assumptions. It is also interesting to follow the development of

Iran’s biotechnology sector in face of institutional developments in the country and the move from a resource based economy towards a knowledge based economy.

The new position of the U/RIs within the dynamic NSI as sources of technological development calls for studying processes to link academic research to industries needs and policies to support new models of U/RI-firm collaboration.

Natural resource based economies are looking to diversify their industry by strengthening their NSIs because natural resources are exhaustible as well as export success in world markets increasingly demands knowledge-intensive production and innovation-based competition. The shift towards a more knowledge-based economy will require creating a NSI that would not only import and adapt technologies, but also build up upon them, develop new technologies and diffuse them economy-wide. Ready or simple access to technology does not automatically mean that the technologies obtained through transfer arrangements are effectively diffused and adapted to local conditions, resulting in dependence on endogenous technological capacity. Therefore there is need for exploring how NSI characteristics of natural resource based economies such as Iran influence/challenge the shift towards a more knowledge-based economy and what policy intervention is required to link the S&T infrastructure to the needs of the manufacturing sector generally, and to build up capabilities in high-tech areas such as biotechnology as well as low-tech industries.

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APPENDIX 1

Questionnaire A – Guide questions to Universities/Research Institutes

Introduction
When was the biotechnology department in your university/research institute established?
(Number of biotechnology researchers: 5 years ago___ Now____)
Briefly describe R&D activities at your department.
Do you undertake your own contract research (e.g. as a private individual within your department) or is all your work channelled through the university/institute?
Innovation in your department/institution:
Have you or your department developed any new or significantly improved biotech products?
Have you or your department developed any new or significantly improved biotech processes?
Technology transfer activities between U/RI and industry
Is your University/research department engaged in knowledge & technology transfer activities with the biotech industry? If yes in what form?
Has the industry made any financial commitment to support your University department/research institute?
Have there been any contract research projects to you to perform long-term research?
Has your research department been engaged in any studentship, postdoctoral fellowships with the industry?
Have you or your department been involved in collaborations with industry to carry out joint research?
If there are any collaboration between your U/RI and the biotech industry which of the following cases are they: □ Personal connection, □ Network related to a forum or an academic society, □ An organizational linkage or institution of the university, □ An organizational linkage or institution of the firm, □ Others, please specify
How successful and important would you regard such interaction, and what forms should it take in your view?
Have you given any other form of advice to the industry?
What would in your opinion facilitate technology transfer between research institutes and industry? What inhibits it?
Intellectual property
In the past 5 years: did your department or any member of your department undertake to protect your intellectual property rights (with patents, trademarks, copyrights, trade secrets agreements, or other?) If yes did you or your department also apply for any international patents?
Do you find the present IPR system for biotech generally helpful or unhelpful?
Role of government
Have you received support from the government for your research? If yes, in what forms?
Have you received support from the government for your innovations? If yes, in what forms?
How successful and important would you regard the government's role in advancing biotechnology in Iran, and what forms should it take in your view?
Role of other national U/RI
Have you had any interactions with other U/RI for your innovations? If yes, in what forms?
Have these interactions been helpful towards your innovation? In what ways?
Role of Foreign Universities/research institutes
Have you had any interactions with foreign U/RI for your innovations?
How successful and important would you regard such interactions, and what forms should it take in your view?
Role of foreign companies and consultants
Have you had any interactions with foreign companies and consultants for your innovations? If yes, in what forms?
How successful and important would you regard such interaction, and what forms should it take in your view?
Role of industry

Have you had any interactions with the biotech industry within Iran for your innovations? If yes, in what forms?
Have you had any interactions with the biotech industry outside Iran for your innovations? If yes, in what forms?
Have you had any interactions with other industries within Iran for your innovations? If yes, in what forms?
Have you had any interactions with other industries outside Iran for your innovations? If yes, in what forms?
How successful and important would you regard such interactions, and what forms should it take in your view?

Questionnaire B – Guide questions to GSOs

How does your organisation support Biotechnology related research in U/RIs?
How does your organisation support Biotechnology related innovation at the firm level?
How successful and important would you regard your role, and what forms should it take in your view?
Have you had any interactions with foreign organisations/ companies/ consultants to promote biotechnology in Iran? If yes, in what forms?
How successful and important would you regard such interaction, and what forms should it take in your view?
Which of the government human resource development activities have been less successful?
□ Developing HR in education
□ Developing HR in R&D
□ Developing HR in Industry
□ Developing HR in managing R&D
□ Developing HR in Science and Innovation Policy
What are the main sources of success in biotechnology innovation in Iran in your view?
What are the main obstacles to biotechnology innovation in Iran in your view?

Questionnaire C – Guide questions to Private Biotechnology Firms

<u>R&D</u>
How does R&D contribute to your company?
Is it the responsibility of a particular company division, all/most of top management, relatively junior appointees, or other?
Is your R&D conducted in house or outsourced?
Conducted R&D □ Yes □ No
□ particular company division □ all/most of top management □ relatively junior appointees □ or other
□ in house □ outsourced
<u>Innovation</u>
Did you develop any new or significantly improved products (goods or services) or implement any new or significantly improved processes in the past 5 years? If yes, can you briefly describe these?
In the past 5 years did you implement any new or significantly improved ways of adapting or marketing your products to your clients? If yes, can you briefly describe these?
Innovation level □ None □ new to firm □ new to (regional) market □ world first
Innovation type □ Product □ process □ organization □ market □ NA
<u>Intellectual property:</u>
In the past 5 years: did you undertake to protect your intellectual property rights (with patents, trademarks, copyrights, trade secrets agreements, or other)?
If yes did you also apply for any international patents?
Intellectual Property protection □ Patent □ copyright □ trademark □ other □ none
<u>Ownership, management and human resources</u>
Have there been any changes in ownership in the past 5 years?
What kinds of people and skills were involved in the growth stage?

Did the management structure or team change?
Leadership □ Founder □ family □ partners □ board □ external national (Iranian) □ international structure

<u>Business strategy</u>

Could you briefly describe your business strategy in the past 5 years?

Growth stage in the past 5 years	□ Start-up □ expansion □ mature □ diversification
Formal planning structure	□ Business plan □ strategic plan □ informal □ other □ none
Growth strategy	□ Control □ grow □ survive □ cost-cutting
Sources of business advice	□ Internal board □ coach □ consultant □ other (which?)

<u>External factors</u>

Most of the factors above have been largely internal to your firm. What were the most important external factors for the expansion or contraction of the firm in the past 5 years of the business (for example, the economic environment, the market, sources of funding, sources of information?)

Access to highly qualified personnel	□ No problem □ moderate problem □ major problem (specify?)
Market niche	□ Competitive □ non-competitive □ monopolistic
Relationship to client/market	□ None □ advisory □ collaborative
Relationship to supplier	□ None □ advisory □ collaborative
Source of funds	□ Own □ Private Bank □ Public/IPO □ Government □ other

<u>Role of other actors in innovation</u>

<u>Role of government</u>

Have you received support from the government for your innovations? If yes, in what forms?
How successful and important in your view is the government's role, and what forms should it take?
Relationship to government □ Close □ limited/sporadic □ none

<u>Role of national U/RI</u>

Have you had any interactions with universities for your innovations? If yes, in what forms?
□ Financial commitment of support □ Awarding universities contract research projects □ Awarding company studentships etc. □ Graduates training □ Joint research collaboration with universities □ Business co-partnership etc. □ Business advice □ Science/technical advice □ Others, please specify
Are you involved in any knowledge/Technology transfer with universities?
Is the collaboration with the university/research institute through: □ Personal connection □ Network related to a forum or an academic society □ An organizational linkage or institution of the university □ An organizational linkage or institution of the firm □ Others, please specify
How successful and important would you regard such interaction, and what forms should it take in your view?

<u>Role of foreign U/RI</u>

Have you had any interactions with foreign U/RI for your innovations?
How successful and important would you regard such interaction, and what forms should it take in your view?

<u>Role of other national companies and consultants</u>

Are you Engaged in alliances or any form of collaboration with other local firms? If yes, in what forms? □ For technology □ for production □ for marketing □ other □ no
How successful and important would you regard such interaction, and what forms should it take in your view?

<u>Role of foreign companies and consultants</u>

Have you had any interactions with foreign companies and consultants for your innovations? If yes, in what forms?
How successful and important would you regard such interaction, and what forms should it take in your view?

Barriers and Crises

What aspects of growth did you find most difficult in the past 5 years to overcome, for example:
□ financing □ marketing □ partnerships □ skills □ business advice □ government regulations □ competition □ Taxes □ market acceptance of new products or technologies □ Intellectual property issues □ others, please specify
Were there any crises (internal or external) that led to a major change in your management strategy?
□ Survived crises □ minor crises □ no crises □ took advantage of opportunities

APPENDIX 2

Table A - The field rankings for Iran released by the ISI (1996–2005)

No.	Field	Papers	Citations	Citations per paper	% contribution
1	Chemistry	6,100	24,176	3.96	30.6
2	Physics	1,933	7,565	3.91	9.7
3	Clinical medicine	1,986	5,480	2.76	10.0
4	Engineering	2,906	5,042	1.74	14.6
5	Pharmacology &toxicology	597	1,940	3.25	3.0
6	Plant and animal science	1,167	1,705	1.46	5.9
7	Materials science	990	1,589	1.61	5.0
8	Biology and biochemistry	565	1,345	2.38	2.8
9	Neuroscience and behaviour	272	1,074	3.95	1.4
10	Agricultural science	422	801	1.90	2.1
11	Geosciences	434	744	1.71	2.2
12	Environment/ecology	291	718	2.47	1.5
13	Mathematics	783	714	0.91	3.9
14	Molecular biology and genetics	129	546	4.23	0.6
15	Immunology	143	472	3.30	0.7
16	Psychiatry/psychology	125	435	3.48	0.6
17	Computer science	463	342	0.74	2.3
18	Space science	119	253	2.13	0.6
19	Social sciences, general	148	189	1.28	0.7
20	Economics and business	34	38	1.12	0.2
	All fields	19,900	55,507	2.79	

Table B - Number of university graduates in sciences and engineering (annually)

	Sciences				Engineering			
Year	BSc	MSc	PhD	Total	BE	ME	PhD	Total
1991-1992	4204	452	11	4667	5106	541	2	5649
1996-1997	7332	861	37	8230	8075	1469	39	9583
1999-2000	10763	1058	128	11949	10497	1914	65	12476
2000-2001	12516	1300	143	13959	11467	2241	130	13838
2001-2002	15885	1844	151	17880	12985	2650	145	15780
2002-2003	19264	2387	158	21809	14519	3067	163	17749
2003-2004	20865	2411	186	23462	15098	3228	199	18525
2004-2005	24131	3115	225	27471	17915	3950	242	22107

Source: Institute for Research and Planning in Higher Education (2009)[174]

[174] http://www.irphe.ir/Fa/index.htm

APPENDIX 3

Composition of agricultural research institutes and FTE research staff (2004)

Type of Agency			Number of research institutes	Number of research staff (FTE)
Government	Affiliated with AREEO	National research institutes	24	1584
		Provincial research centres	32	2199
		Subtotal	56	3783
	Affiliated with universities		6	64
	Affiliated with ministries		11	307
	Governmental agricultural production units (non-AREEO)		2	2
	Total government		75	4156
Non-profit	Total Non-profit		5	10
Higher education	Governmental		54	471
	Private		23	59
	Total Higher Education		77	530
Total Public			157	4696
Private Business enterprises			34	277
Total public and private			191	4973

Source: ASTI

APPENDIX 4

List of GM crop projects at Iranian U/RI

Crop	Projects	GM technology	Detail	Status
Alfalfa	1		Insect resistant	lab scale
Barley	4	Anther Culture		lab scale
		AFLP		lab scale
		RAPD		lab scale
		Microsatellite markers		lab scale
Wheat	4	Anther Culture		lab scale
		AFLP		lab scale
		RAPD		lab scale
		Microsatellite markers		lab scale
Canola	2	Morphogenesis, AGL1, AGL5, AGL8		lab scale
			Glyphosate tolerance	field trial
Chickpea	1		Drought and cold tolerant	lab scale
Cotton	6		Multiple resistance to Bt genes	lab scale
		Bt CrylA(b) transgenic	Lepidoptera	lab scale
		AFLP		lab scale
		RAPD		lab scale
		Microsatellite markers		lab scale
		Agrobacterium mediated transformation via heterol. bean chitinase gene	Heliotis armigera resistant	lab scale
Cumin	1	Glyphosate	GOX	lab scale
Date palm	1	Micro propagation		commer.
Fungus	1	Chitinase	Resistance to fungi	field trial
Lentil	1		Drought and cold tolerant	lab scale
Maize	2	Bt CrylA(b)	Lepidoptera resistant	lab scale
		Glucanase and chitinase	Resistance to fungi	lab scale
Olive	4	Micro propagation		field trial
		AFLP		lab scale
		RAPD		lab scale
		RAPD		lab scale
Pistachio	1	Micro propagation		field trial
Potato	2	Micro propagation		commer.
		Bt CryIII	Coleoptera	lab scale
Rice	7	Bt CrylA(b)	Lepidoptera	part commer.
		Microsatellite markers		lab scale
		AFLP		lab scale
		RAPD		lab scale
			Drought and salt tolerance	lab scale
		Chitinase and glucanase	Resistance to fungi	lab scale
		Glucanse	Resistance to fungi	lab scale
Sugar beet	2	Bt crylA(b)	Lepidoptera resistant	lab scale
			Rhizomonia resistant	field trial
Wheat	3	Genome sequencing	Fusarium head blight resistant	lab scale
		Chitinase and glucanase	Resistance to fungi	lab scale
			Drought and salt tolerance	lab scale

APPENDIX 5

List of Major AREEO affiliated research institutes in Iran:

Agricultural Biotechnology Research Institute of Iran (ABRII)
Agricultural Engineering Research Institute (AERI)
Animal Science Research Institute (ASRI)
Date Palm and Tropical Fruit Research Institute (DPTFRI)
Dry Land Agricultural Research Institute (DARI)
Engineering Research Institute (ERI)
Fisheries Research Institute of Iran (FRI)
Iran Citrus Research Institute (ICRI)
Institute for Cotton Research (ICR)
Institute of Technical & Vocational Higher Education
Iran Pistachio Research Institute (IPRI)
National Salinity Research Centre (NSRC)
Plant Pests and Diseases Research Institute (PPDRI)
Razi Vaccine and Serum Research Institute (RVSRI)
Research Institute of Forest and Rangeland (RIFR)
Rice Research Institute of Iran (RRII)
Rural Research Centre (RRC)
Seed and Plant Certification Research Institute (SPCRI)
Seed and Plant Improvement Research Institute (SPII)
Soil and Water Research Institute (SWRI)
Soil Conservation and Watershed Management Research Institute (SCWMRI)
Sugar Beet Seed Research Institute (SBSI)

Source: AREEO's website

APPENDIX 6

Biopharmaceutical research areas/activities of key U/RI departments

Institute	Research areas and activities
ARI	Currently ARI's biotech related research centres are the Reproductive Biotechnology Research Centre (RBRC), the Monoclonal Antibody Research Centre (MARC), and the Nano-Biotechnology Research Centre (NBRC). RBRC's research priorities are in recurrent abortion; endometriosis; idiopathic infertility; stem cells, embryo, transgenic animals; male & female infertility, and reproductive infections. RBRC's Department of Reproductive Genetic & Biotechnology identifies genetic fertility and infertility disorders in Iranian families. RBRC's Department of Reproductive Endocrinology & Embryology and the Department of Reproductive Infections research activities are in the recognition of operative factors in recurrent abortion, enhancement of quantitative and qualitative sperm parameters, and recognition of idiopathic infertility factors; RBRC's Department of Reproductive Immunology research is on immunologic factors in recurrent spontaneous abortion (RSA) and recurrent implantation failure (RIF) as immunologic factors are believed to cause more than 50% of abortions. The department also carries out research on immunologic aspects of endometriosis, immune-biology of normal pregnancy, immunologic factors of infertility, and immune-contraceptives. The Monoclonal Antibody Research Centre (MARC) of ARI conducts research on human and animal monoclonal antibodies (mAbs). In addition the centre produces, purifies, and characterizes mAbs required by researchers and firms. MARC mainly produces and characterizes a large number of different mAbs against sperm surface antigens, prostate specific antigen, ferritin, inhibin, tumour cell lines, and other cancer associated antigens. Based on the nature of the antigens, different techniques have been developed to characterize the antibodies. MARC is also involved in antibody engineering and has produced single chain antibodies (SCAbs) and is working on humanization of antibodies for therapeutic purposes. Besides the mAbs, more than 60 different polyclonal antibodies (pAbs) have been produced at large scale to cover the research needs of Iranian institutions. Nano-Biotechnology Research Centre (NBRC) of ARI is mainly active in the application of nano-particle antibody conjugates in diagnosis and treatment of cancer and chronic diseases. Due to the gap in the knowledge on toxicity, health related effects of nano-particles and their conjugates in humans, research activities of NBRC include assessing the immune response and toxicity of these particles in vitro but also in experimental biological systems. Notable Achievements include: Innovative activities of NBRC include combination of modern technologies such as proteomics, bioinformatics, DNA chips, recombinant antibodies, and nano-biotechnology to establish new approaches for treatment of chronic diseases.
IPI	The Medical Biotechnology Unit of BRC is involved in the development of recombinant vaccines and pharmaceutics (protein expressions, interferon and vaccine for H. pylori). The centre also offers services, such as protein characterization and gene expression. Further to recombinant pharmaceutics, a new drug discovery group has been established in the Medical Biotechnology unit to design and develop target based anti-infection compounds including new antifungal and anticancer agents. The unit is also involved in expression of two leishmania vaccine candidate (LmaCIN and gp63) and in vaccine development against HP infection producing new vaccines and diagnostic kits. Diagnostic kits for HIV and HP are also the result of the R&D carried out in the Medical Biotechnology unit including HIV proteins and H. pylori antigen cloning and expression. The ELISA based HIV diagnostic kit in the market is again the result of the R&D work of this unit and the facilities for the production of recombinant DNA at IPI. The Molecular Medicine Unit of BRC deals with molecular detection of prevalent genetic disorders and various infectious diseases in Iran, including carrier detection and prenatal diagnosis of alpha and beta Thalassemia, haemophilia A and B, Duchene Muscular Dystrophy and Becker Muscular Dystrophy. The The genetic disorder group of this unit (under Dr. Sirous Zeinali, Dr. Morteza Karimipoor and Dr. Tayebeh Hamzeloie) has also created a transgenic

	mouse expressing ovine beta lactoglobulin-calcitonin in its milk and gene therapy for beta-thalassemia.[175] The Malaria and vector Research Group, (supervised by Dr. Navid Dinparast and Dr. Sedigheh Zakeri), has initiated the molecular diagnosis of different plasmodiums and malaria vectors to further develop the knowledge of molecular genetics of these organisms in Iran. Notable Achievements include: The Hep C vaccine, Erythromycin and Erythropoietin are produced at IPI's production unit. The ELISA based HIV diagnostic kit in the market is the result of the R&D work of Medical Biotechnology Unit and the facilities for the production of recombinant DNA at IPI. One of the latest achievements at IPI is the production of IFN-β and IFN-γ. Vaccines against Leishmania and HP. Transgenic mouse producing Calcitonin in its milk (Calcitonin is used in the treatment of osteoporosis and other forms of bone degradation). The Transgene is a combination of the Calcitonin producing gene in fish and human. (Project didn't go beyond mouse because of financial reasons).
IROST	Isolation of micro-organisms producing anti-virus and anti-cancer substances, production of the calcytonin hormone by cloning, and laboratory production of cyclosporine. The centre also produces antibiotics, such as penicillin G, streptomycin and erythromycin in its pilot plant.
NIGEB	NIGEB's biopharmaceutical related departments and their research areas: Biochemistry – to study structure and reactions between bio-molecules and engineer them for use in industries); Physiology-pharmacology – effects of pharmaceutical and food products on cells and tissues of living organisms, particularly humans; Bio-informatics; Medical genetics – molecular diagnosis of genetic diseases, especially pre-natal diagnosis and identification of carriers of defective genes, determination of genomic diversity of communities and patients, gene therapy and genetic consultation; Immunology – understanding the defence mechanisms of the body, new vaccines, designing serologic molecular diagnostic methods, increasing the level of body immunity, and tissue and organ transplantation; Molecular medical pathology – understanding molecular mechanisms of human pathological diseases such as cancer and infectious and parasitic diseases in order to find ways of diagnosing, preventing and curing); and Plant biotechnology – molecular mechanisms of resistance to biotic and non-biotic stresses in plants; and molecular modification of plant species. Notable Achievements include: Research studies of genetic mutations among different ethnic groups in Iran, studies of multiple sclerosis (MS) and the cloning of auto-antigens involved in MS and other neurological diseases, and construction of DNA vaccine vectors for hepatitis B and C. The human growth Hormone (hGH), the first recombinant product in Iran was developed at NIGEB and transferred to Samen Pharmaceutical Company for commercial production. GM-CF (cytokine that functions as a white blood cell growth factor)
Royan Institute	The Department of Andrology-s research activities are in the area of male infertility and sperm morphology, motility, and function disorders. Current research projects include sperm disorders associated infertility, etiology and treatment of azoospermia and impotency, etiology of dry ejaculation and retrograde ejaculation, germ cell transplantation, and genetic studies of male infertility. The Department of Embryology conducts research on chromatin deficiency, embryo co-culture with different cell types, increasing gamete and embryo quality, in-vitro maturation of animal and human gametes (IVM), molecular aspects of embryo development, molecular aspects of gamete and embryo freezing, and nuclear transfer and animal cloning. The Department of Gynaecology and Endocrinology is active in female infertility treatment, prenatal diagnosis, and treatment of recurrent abortion to increase the implantation rate and reduce recurrent pregnancy loss. The Department of Epidemiology and Reproductive Health carries out research on epidemiology and causes of infertility. The Department of Reproductive Genetics provides genetic counselling, pre-implantation

[175] Sources: Interview with Dr Zeinali, founder of Medical Genetic Lab of Dr Zeinali, a private R&D lab involved in prenatal diagnosis of genetically inherited diseases.

	genetic diagnosis, and lymphocyte karyotyping as routine laboratory tests. The major research activities of the department are assessment of genetic causes of infertility and recurrent spontaneous abortion; cytogenetic evaluation of oocyte, sperm, and embryo; cytogenetic effects of embryo freezing, azoospermic factors, and mutations leading to congenital agenesis of vasodefran; and embryonic stem cell based studies. The DNA bank of RI was established in 2005 as a division of this department, giving essential service to the researchers by providing DNAs from infertile patients and patients with recurrent abortion. Finally the Department of Stem Cell Research is the pioneer in Iran's stem cell research activities. The department was established in 2002 to set up embryonic stem cell lines and differentiate them into cardiomyocytes, beta cells, and neural cells. Since then the department has expanded into 9 main research groups of embryonic/adult stem cell biology, neural cells, beta cells, germ cells, mesenchymal stem cells (bone/cartilage), eye transplantation, heart transplantation, liver transplantation, and proteomics. Following the department's latest achievements in the application of stem cells in treatment of cardiac arrest, chronic lower extremities ulcers, limbal stem cell deficiency, liver cirrhosis, and vitiligo, a centre for cell therapy has recently been launched at this department. In 2004, the Isfahan campus was established to expand RI's research activities in andrology, cloning and animal reproduction, embryonic stem cell research, and molecular genetics research. The research activities of this campus have resulted in outstanding achievements producing the first cloned mammal in the MENA region. The research activities on male infertility at this campus have so far resulted in the publication of over 20 papers in peer reviewed journals. In addition over 30 postgraduate students have completed their theses at this campus. The campus provides routine workshops, seminars and postgraduate short courses. The animal cloning activities at RI have put Iran's biotechnology research at the forefront in the MENA region. The production of transgenic animals at RI was initially based on bovine species but due to the long period of pregnancy in cows, the project was later changed and followed in ovine species. Iran's first cloned lamb (called Royana) was born on 30th September 2006 at the Isfahan campus of RI and is still alive. Iran's first cloned goat was born on 15th April of 2009 by caesarean, and is also still alive. RI also produced Iran's first cloned calf which died. The ultimate goal of this area of research is to attain recombinant drug technology in Iran through the following three steps: Producing mammalian embryos using IVF techniques. Producing cloned embryos by nuclear transfer from a somatic cell to an oocyte and transferring the embryo into the recipient uterus. Producing transgenic cell lines containing tPA.[176] The tPA gene is cut from the human genome and inserted into the recipient genome. After the cloning process, a transgenic animal is born which is able to secrete tPA in its milk. In addition to the above, research activities at RI have resulted in Iran becoming the first country in the MENA region (and the fifth in the world) to produce human induced pluripotent Stem Cells (iPSC). Human and mouse somatic cells were reprogrammed into an undifferentiated state exhibiting essential characteristics of embryonic stem cells and accelerating the cell production pace. RI researchers claim these reprogrammed pluripotent stem cells, also known as induced pluripotent stem cells (iPSC), maintain the developmental potential to differentiate into advanced derivatives of all three primary germ layers, which could be effective in the identification of new disease models and foetal abnormalities, drug development, gene therapy, and treatment of refractory and congenital genetic disorders. Notable Achievements include: The first IVF birth in Tehran (1993) The second ICSI birth in Iran (1995) Iran's second success in open testicular biopsy to treat severe male infertility (1996) The first frozen embryo birth in Iran (1996) The first ICSI birth by frozen sperm of a gonadectomized man (1999) Celebration of the 1000th birth by the assisted conception treatment in Iran (1999) The first human embryonic Stem Cell line establishment (2003) Establishment of Stem Cells research department (2003) The first PGD child born in Iran (2004) The first time use of Adult Stem Cell in treatment of MI during CABG (2004) Production of insulin producing cells from human embryonic stem cells (2004)

[176] Tissue plasminogen activator (tPA) is a protein involved in the breakdown of blood clots.

	Culture of human Limbal stem cells on Chorionic membrane for corneal injuries (2004) Establishment of the first organized Cord Blood Bank (2005) The first IVM-IVF lamb born in Iran (2006) The first cloned lamb born in Iran (2006) The first cloned goat born in Iran (2009) RI is currently involved in three Nano-biotechnology research projects under MHME.
RVSRI	Biopharmaceutical related R&D activities range from clinical cytogenetic and chromosome studies in cancerous cells, production of new generation recombinant vaccines through genetic engineering for livestock, birds, and humans, antigen development and diagnostic kits for medical and veterinary labs, genetic diagnosis of livestock and bird diseases, to PCR for clinical diagnostic applications and production of transgenic animals. Current biotechnology R&D projects include production of a monoclonal antibody for measles, creation of cell lines from mice foetuses through cloning, design and production of engineered skin tissue, molecular analysis of the CDS gene in cattle to diagnose genetic defects, production of hybrid cells, and production of recombinant vaccines. The institute mainly imports the strains for research purposes, cultures them locally and then scales them up, after which dosage and formulation are developed and the product is manufactured. Notable Achievements include: live attenuated trivalent (Sabin) oral poliomyelitis, diagnosis and isolation of strains of foot and mouth disease virus using molecular methods; and the design and manufacture of large fermenters for the production of vaccines for foot and mouth disease, aerobic and non-aerobic bacteria used for poultry and livestock, and diphtheria and human tetanus vaccines with domestic technology. Vaccines developed and produced at the institutes include measles, mumps, rubella (patented by RVSRI), Measles-Mumps-Rubella combined, tetanus (TT), diphtheria & tetanus combined for Children and Adults (DT), Diphtheria, Tetanus and Pertussis combined (DTP) vaccines. The institute has also produced a new variety of Leishmania Vaccine in 2008. At present RVSRI produces over 60 different biopharmaceuticals for veterinary and human use and exports them to 19 countries. For vaccine production, the institute uses locally produced fermenters. A spin-off company, "Jahad e Razi", handles commercial sales of RVSRI's products.
SBU	The institute's biopharmaceutical related research activities fall into two broad areas of basic and applied research. Basic research involves investigating new plants from medicinal families and isolating active ingredients; investigating traditional medicinal plants (e.g. hyprocumperfatum, an anti-depressant, investigated for its anti-inflammatory properties and compared with other similar plants); semi-synthesizing compounds by changing the molecular structure and comparing with the decimal for bio-activity; current work does not include research on using micro-organisms to change compounds or transgenic plants. Applied research at the institute involves isolating active ingredients for anti-inflammatory anti-nociceptive effects from medicinal plants; separating anti-fungal and anti-bacterial and oxidant compounds through bioassay methods and introducing them in pharmaceuticals; no cell culture is being carried out at the moment.
SBUMS	The Biopharmaceutical research group is active in research on microbiological cell cultures, bio-fermentation, anti-cancer biopolymers, and biotransformation related research.
TMU	Biomedical/biopharmaceutical research activities include extraction and purification of single-domain antibody fragments alongside Vascular endothelial growth factor; Interleukin-2 production in E. Coli, cloning, and extraction and study of structure and function of single and multi-domain proteins. The faculty of Pharmacology is active in production of diagnostic and biochemical kits. The main research activities have been focused on the production and purification of enzymes and determination of their characteristics. Presently, the expanded research activities include biologically changing steroids; isolating and identifying micro-organisms that produce antibiotics with a wide range of anti-fungi and anti-bacterial effects; isolating and identifying micro-organisms that produce enzymes with industrial and medical applications; producing recombinant proteins and recombinant pharmaceutical products. The Faculty of Medicine's research activities are in the areas of genetics and immunology. The Faculty of Medicine has been a pioneer in genetic engineering in Iran. Some of its most important research activities are the study on the nature and identity of the molecules, pathology and determination of mutations of ß-thalassemia in Iran for the production of related probes to use in prenatal diagnosis, as well as the application of genetic engineering and tissue culture techniques. Notable Achievements include: Three products have been produced and transferred to the industry after successful completion of the R&D and clinical trials at the department: Interferon alpha, GCSF, and Erythropoietin.

APPENDIX 7

Bioagricultural research areas/activities of key U/RI departments

Institute	Research areas and activities
ABRII	Enhanced salinity resistance, improved agronomic characteristics of wild species for cultivation in salt-affected soils, isolation and characterization of high affinity potassium transporter genes from a salt tolerant variety of rice, in collaboration with IRRI in a German/BMZ funded project. Analysis of the promoter is being carried out at ABRII to determine the factors affecting the expression of these proteins. Mapping QTLs for salinity tolerance genes. Enhanced resistance to biotic and abiotic stresses resistance to four different pests of rice up to the 6th generation. Isolation and characterization of candidate genes involved in pathogen resistance. Application of Molecular Markers to study genetic diversity and germplasm management. Characterizations of thousand Iranian rice germ plasma in collaboration with RRII and IRRI. Classification of wheat germplasm and fingerprinting walnut and olive trees. Molecular markers have been used to tag quality related genes such as aroma and gelatinization temperature (gt) at RRII. Haploid breeding for crop improvement and yield improvement of wheat X maize with enhanced resistance to yellow rust and leaf rust. Notable Achievements include: Creation of varieties of wheat resistant to salinity. Molecular location and breaking up of QTL for resistance to fusarium blight. Production of a new variety of transgenic rice resistant to stem borer. Production of transgenic cotton resistant to diseases and pests. Production of bio-fertilizers to provide nitrogen needed by rice fields. Production of bio pesticides.
NIGEB	Viral disease resistance, herbicide resistance, salt and drought tolerance, molecular biology of phosphate starvation response in plants, development of molecular markers for fusarium resistance in wheat, recombinant protein production in plants, and improvement of olive cultivation. Identification of plant viruses and diseases by molecular methods, optimization and establishment of plant transformation techniques for production of transgenic and molecular farming by using plant as a factory for production of important pharmaceutical proteins and industrial enzymes (expression of human growth hormone and other candidate genes in transgenic plants). Notable achievements include virus resistant sugar beet and canola.
IROST	Notable achievements include lysine production as livestock and poultry food supplement; bio-fertilizers and single cell protein production from agricultural by-products (sugar-beet waste and pistachio peelings), large scale production of lysine and giberrelic acid; lab scale production of enzymes such as alpha-amylase, gluco-amylase, gluco-isomerase, and pectinase; application of bacterial and fungal agents in agricultural pest control (microbial pesticides); isolation of azospirillum from the soil of different regions of Iran and assessment of its role in nitrogen stabilization; isolation and production of biopolymers to revive saline and desert lands; industrial scale production and marketing of bt-MH-14 based insecticide for combating malaria in southern and eastern provinces of Iran. Its slow release mechanism is effective in obtaining 100% control against malaria mosquito vectors with no adverse environmental impact.
RRII	Biotech is applied in two Departments of Agronomy and Plant Breeding (DAPB) and Plant Protection (DPP). DAPB produces inbred and hybrid rice varieties using mutation, tissue culture and recombinant DNA technologies in addition to conventional breeding. The main objectives of DAPB research activities are to improve grain quality and yield potential; to improve resistance to pests, diseases, drought, and salt; to develop early maturing varieties; conservation and utilization of rice germ plasma. DPP is involved in the biological control of major pests and diseases using beneficial organisms (predators, parasitoids, pathogens and antagonists), mass production and preservation methods of Trichogramma as biocontrol agent of striped stem borer (Chilo supperssalis), introducing new sources of resistance to blast disease and tolerant varieties to sheath blight disease. Basic studies on biology and genetic diversity of rice diseases, introducing alternative control methods to chemical control against rice pests, diseases and weeds.

APPENDIX 8

The list of biotechnology postgraduate degrees initiated during 1995-2000 period

PhD in biotechnology, University of Tehran;
PhD in biotechnological products, Pasteur Institute of Iran;
PhD in chemical engineering-biotechnology, Tarbiat Modarres University;
PhD in chemical engineering-biotechnology, Sharif University of Technology;
PhD in molecular genetics, Tarbiat Modarres University and NIGEB;
PhD in cellular and molecular biology, Kermanshah University and NIGEB;
PhD in plant modification-genetic engineering, University of Tehran;
MSc in agricultural biotechnology, University of Tehran;
MSc in medical biotechnology, Tarbiat Modarres University;
MSc in chemical engineering-biotechnology, Tarbiat Modarres University;
MSc in chemical engineering-biotechnology, Sharif University of Technology;
MSc in chemical engineering-biotechnology, Azad University;
MSc in chemical engineering-biotechnology, Science and Industry University;
MSc in chemical engineering-biotechnology, Amir Kabir University.

APPENDIX 9

AREEO's international collaborations

AREEO has collaborated with numerous international and regional research institutes, laboratories, and organisations. AREEO is a member of the Consultative Group of International Agricultural Research (CGIAR) and has strong linkages with the International Centre for Agricultural Research in the Dry Areas (ICARDA), the International Centre for Maize and Wheat Improvement (CIMMYT), and the International Water Management Institute (IWMI). Joint activities with IWMI involve research on water issues and the implementation of the 'Challenge Program on Water for Food' in Karkheh river basin in western Iran. CGIAR centres operate regional offices in Tehran and Karaj. Collaboration between AREEO and ICARDA concerns the improvement of agricultural production in the dry land of Iran, covering commodity research on a large number of crops, natural resource management, exchange of improved germplasm of ICARDA-mandated crops, as well as research capacity strengthening. AREEO works closely with CIMMYT in the field of wheat, maize, and triticale germplasm research. AREEO also collaborates with IRRI on improved, high-yielding varieties of rice, rice germplasm for resistance to salinity, blast, and other insects, and with the International Crops Research Institute for the Semi-Arid Tropics on research related to sorghum and chickpea germplasm, and on a program of breeding and plant protection under irrigated conditions. Other collaborations are with Bioversity International, the World Fish Centre, the International Potato Centre, and International Service for National Agricultural Research.
In addition AREEO has also linkages with the Association of Agricultural Research Institutions in the Near East and North Africa (AARINENA) and the Asia-Pacific Association of Agricultural Research Institutions (APAARI) and their affiliated agricultural R&D networks. AREEO hosts and supports the secretariats of the Regional Agricultural Information System of AARINENA and the Interregional Network on Cotton in Asia and North Africa, which is cosponsored by AARINENA, APAARI, and the Central Asia and Caucasus Association of Agricultural Research Institutions. AREEO has signed 'Memoranda of Use' to strengthen collaboration with the national agricultural research institutes of India, Pakistan, Syria, Sudan, Cuba, Turkey, Oman, Tajikistan, Azerbaijan, Russia, and China. It has also developed a partnership with several overseas universities, such as Wageningen Agricultural University in the Netherlands.

APPENDIX 10

In 1997, a Bt gene, developed at IRRI, was transferred into Tarom Molai, an Iranian aromatic rice cultivar, to get rice lines resistant to green rice caterpillars (Naranga aenescens) and striped stem borers (Chilo suppressalis). After 12 years, the world's first-ever released GM rice was developed at the ABRII at Karaj (30 km north of Tehran) in a joint effort with the IRRI. The Cryl Ab gene has been transferred into Tarom Molai through biolistic gun method. The selectable marker is hpt, and the promoter regulating the expression of CrylAb gene in green tissues is a derivative of maize C4 phosphoenolpyruvate carboxylase (Ghareyazie, et al., 1997). Three-year field trials proved that the insect resistance gave 10% higher yield compared to the unmodified control. The cry protein constitutes about 0.1% of total leaf soluble proteins. The stem-borer-resistant crop gives farmers a 10% yield advantage to reach 2.2 tons/acre (Ghareyazie, et al., 1997). The most important characteristic of this transgenic rice is that it expresses Cry1Ab protein only in its green tissues (not in the seed) and kills only striped stem borers and green rice caterpillars, with no harmful effects to humans or live farm organisms, as shown in data collected when the transgenic rice was fed to mice and chickens (Alinia, et al., 2000). It has been estimated that Bt-transgenic rice cultivation will prevent the loss of 200,000 tons of rice yield due to pests and result in a benefit to Iranian rice producers of about $US 125 million.
Over the last decade, Iran's Bt rice has undergone rigorous testing, including animal feed trials, composition analysis of nutritional values, field trials to study yield and environmental impact, and other risk assessments to fulfil safety requirements of the transgenic variety. From agricultural aspects, the study of 40 agronomic characters has shown that Bt rice is completely identical to its parental line. Since there are no wild relatives of Oryza in Iran, the possibility of gene flow is extremely low. This rice has shown complete and stable resistance to stem borer through the several generations studied (Alinia, et al., 2000). Field studies show that the introduction of the Bt rice has the potential for decreasing the amount of sprayed pesticides over 50% together with considerable increases in harvest yield (Mousavi, et al., 2007). The characteristics and safety of releasing Iran's first biotech crop Iran's GM rice was comprehensively assessed by a working group made up of 3 major Iranian societies of genetics, biotechnology, and (Malboobi, et al., 2005).

Over the past decade, Iran's Bt rice has undergone rigorous testing, including animal feed trials, composition analysis of nutritional values, field trials to study yield and environmental impact, and other risk assessments to fulfil safety requirements of the GM transgenic rice field release (Ghareyazie, et al., 1997), (Alinia, et al., 2000), (Malboobi, et al., 2007). From agricultural aspects, the study of 40 agronomic characters has shown that the GM rice is completely identical to its parental line. Since there are no wild relatives of Oryza in Iran, the possibility of gene flow is extremely low. The GM rice has showed complete resistance to stem borer, stable through the several generations studied. Field studies show that the introduction of the Bt rice has the potential to decrease the amount of sprayed pesticides by over 50% together with considerable increases in harvest yield. The GM rice has also been a role model for the development of other Iranian high-yielding crops now at field trial stage.
Summary of Iranian GM Bt rice's unique characteristics:
First GM rice in the world produced by Biolistic gene transfer method (Ghareyazie, et al., 1997)
High Dose resistance to the Stemborer and other Lepidopteran pests at any larva stage (Alinia, et al., 2000)
Existence of only one copy of the transgene in the Iranian Bt rice resulting in optimal gene expression, as multiple copies of the transgene may cause gene silencing. Numerous Molecular, bioassay and Greenhouse tests carried out on 15 Generations of the Tarom Molai rice showed that the gene expression was continuous and the Rice was ready for field trials.
Tissue specific expression of the protein Cry1Ab, due to the use of a special promoter, to control the expression of the Cry1Ab protein. First transgenic rice in the world that expressed the Cry1Ab protein only in the green tissues of the plant while the corn is Cry1Ab free at all times. Chen et al, 2005 reported that the Iranian GM Tarom Molai was the only rice that used the PEP Carboxylase promoter and causes the protein only to be expressed in the green tissues (Chen, et al., 2005).
Substantially equivalence to its non-transgenic counterpart
Decreased expression of the protein in ageing plant

Successful completion of animal feeding trial
Successful completion of a five year field trial
Gene escape issues – One concern is the possibility of gene escape to non-transgenic rice varieties. Although this is a valid concern, it is not relevant in the case of Iranian GM rice. In addition to the fact that tests so far have shown no signs of such gene escape, as rice is a non-native crop to Iran there are no plants in Iran that are recipient to such gene transfer.
Bt rice's possible effects on non-target organisms – Another concern may be the GM BT Rice's effect on non-target organisms. Tests so far have not shown any unintended effects on the population of such friendly organisms. In addition to lack of any scientific prove of such unintended effects, there is also the issue that such friendly organisms are severely affected by chemical fertilizers (Romeis, et al., 2006). In contrary, due to the reduced use of chemical toxins and fertilizers in the cultivation of GM BT rice, the population of such organisms in the field grows. Tests carried out on 'Sene Shekargare Andralus' and 'Trichoger Bees' have shown no adverse effects on these animals what so ever.
Human health issues – GM products shave been cultivated in the world for a decade and no adverse effects on human health have been shown. In addition the peasants and their children will be less exposed to chemical toxins and pesticides and will have to spend less on medication. Diminished use of chemical toxins and pesticides reduces the exposure of peasants and their children to such dangerous chemicals and reduces the risk of chronic toxicity symptoms.
Economic aspects – In addition to increased productivity of the crop, decreased costs of chemical pesticides and reduced medical costs associated with the use of chemicals have been shown to improve the farmer's financial situation and as well as the cost of producing the crop.
In conclusion, extensive assessments of scientific data available worldwide over the past 10 years on environmental effects of commercialized GM crops, provide no scientific evidence that the commercial cultivation of GM crops has caused environmental impacts beyond the impacts that have been caused by conventional agricultural management practices (Romeis, et al., 2006).