The Israel Academy of Sciences and Humanities

Report of the Committee for the Assessment of the State of Biomedical Research in Israel

Jerusalem,

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EXECUTIVE SUMMARY

A. Introduction

A healthy society is a prerequisite for the success of any modern society. Therefore, in many countries, a premium is put on investment in biomedical research, which helps us understand the etiology of many prevalent diseases and, ultimately, can lead to their cure. Such investments can also improve the level of patient care and public healthcare and promote the economic development of the pharmaceutical and biotech sectors. In many Western countries, the government supports biomedical research through agencies that are created solely for that purpose, such as INSERM in France, MRC in England and NIH in the United States. Israel, in contrast, has no organization or agency that exclusively supports biomedical research and the government does not allocate significant resources to support such research.

Several grant funds in Israel competitively fund biomedical research projects, along with those in other fields of research. However, the only government fund that exclusively funds biomedical research is that of the chief scientist of the Ministry of Health; and its budget is miniscule. There are also several sectorial funds, mostly from private donations, whose budget is earmarked for a specific medical issue or disease, for instance, that of the Israeli Cancer Society.

The current state of affairs does not allow Israeli biomedical investigators to reach their full potential. The reasons for this include the following:

- Limited amount of funds available for high-quality research
- Outdated research infrastructure
- Inability of young researchers to secure positions
- Large amount of time wasted in chasing after many small research grants.

Also, the level of research done in Israeli hospitals (where most clinical research is conducted) is much lower than research conducted in Israeli universities. One such indicator of this disparity is based on the citation index, where research papers

originating from Israeli hospitals receive, on the average, much lower scores than research papers originating in Israeli universities.

The Israel Academy of Sciences and Humanities, therefore, decided to conduct an in-depth study on the state of biomedical research in Israel. The current Committee for the Assessment of the State of Biomedical Research in Israel was convened on October 29, 2006, by the Academy's President Prof. Menachem Yaari, with Prof. Ruth Arnon, Vice President of the Academy, as its designated head. The mandate of the Committee is to:

- Study the current state of biomedical research (including clinical research) in Israel and the interface between biomedical research and the biotech industry
- Report its findings
- Where warranted, suggest ways to improve and better utilize the vast potential that Israel has in biomedical research.

The Committee has adopted the following definition for biomedical research, based on that of the NIH:

> **Biomedical research seeks out new knowledge in order to understand, prevent, diagnose, identify and cure sicknesses and disabilities and to enhance human health**.

The Committee worked separately on three separate areas:

- Basic biomedical research
- Clinical research
- Interface between biomedical research and the biotech industry.

It was understood from the onset that these three subjects are intertwined. The Committee met monthly for a year and a half, each session lasting approximately four hours. Researchers, doctors and administrators were invited to these meetings to share their knowledge. Memos, background papers and other necessary material were prepared in advance. A visiting committee of 3-4 experts from abroad was convened for each of the three subjects. These experts came to Israel for three days to visit, meet and hold discussions with appropriate people. They then submitted their reports,

which were taken into account in this final report of the Committee. The Committee's findings, divided by research area (1.3-1.5), and its recommendations (1.6) follow.

B. Findings of the Committee

1. Basic Biomedical Research

Basic research is the foundation on which all biomedical research, including more applied clinical and biotechnological research, is built. Most basic research is done in university laboratories. The Committee found that Israel currently invests an acceptable percentage of its Gross Domestic Product (GDP) in research *and* development. However, Israeli R&D funding tends to under-emphasize basic research, the source of most innovative ideas and discoveries. The Committee's impression is that the situation in biomedical basic research is of particular concern, and that it could have serious implications for Israeli clinical and applied biomedical research. A more detailed analysis of the relevant data is provided in Annex N.

At the moment, despite the problematic state of its clinical research, Israel is still above average in certain research areas. However, this is only because Israel is now using up its "scientific reserves," reserves that were accumulated due to national policies in previous years, rather than current policies.

Today, many Israeli researchers have a hard time keeping up with their colleagues abroad. They are limited by small budgets, antiquated laboratory infrastructure, lack of research grants and the inability to employ postdoctoral fellows (who do the brunt of basic research in leading research institutions abroad). Furthermore, Israeli basic biomedical researchers spend a sizable amount of time in securing funds and/or collaborations with their colleagues abroad. Since this is time not spent on research, the current situation does not allow Israel to live up to its full potential.

After careful investigation and deliberation, the Committee has concluded that to solve these problems, Israel should create a new national fund devoted exclusively to the support of biomedical research (see Section 6.1). This fund should be adequately capitalized and run by appropriate experts. Such a fund, in the Committee's view, would help Israel achieve its full potential in biomedical research.

2. Clinical Biomedical Research

Clinical research is mostly done in a hospital setting; and it can most readily be translated into better patient care. Clinical research also plays an important role in the development of pharmaceuticals, and in the conduct of clinical trials. Israeli hospitals run many clinical trials for pharmaceutical and medical device companies; but since the protocols followed are those of the companies paying for these trials, they do little to advance innovation in Israeli clinical research. They are, however, a welcome source of income for hospitals; and they do give hospital staff experience in running such trials. Such experienced personnel would be an asset if and when local researchers could field clinical trials of their own innovations.

Under the current contracts, physicians are not reimbursed for physician-initiated clinical studies. There is no national guidance or policy identifying which areas of clinical research are particularly important for Israel; and there is no national support (e.g. through a health-care tax) for clinical research. All decisions regarding the support of clinical research are made locally by the hospital's administrators and/or sponsors.

Physicians who want to do clinical research have many hurdles to overcome, particularly the lack of research time and lack of research money. There is also a lack of experienced mentors to guide young physician-researchers at the beginning of their careers. Even with all these obstacles, a small number of Israeli physicians have been able to conduct excellent clinical research. In all cases examined, this excellence was due to the hospital's positive attitude towards research and the researcher's success in raising private donations.

Israel's hospitals are owned and run by many different bodies, and there is no centralized mechanism for establishing a uniform clinical research policy. Thus, the Committee recommends creating a special unit within the new National Fund for Biomedical Research (Recommendation 1) to promote clinical research and physician-researcher careers in Israel through research grants, stipends and other measures.

3. Interface between Biomedical Research and Industry

Converting an idea or knowledge in biomedical research into an economically viable product is a long, expensive, multistep process. For these reasons, it is normally undertaken outside university research facilities. The last six years have seen a rapid expansion in the international biotech sector and substantial growth in the number of Israeli biotech start-up companies. However, given its sizable research base, Israel is surprisingly lagging in creating innovative technologies to transform into successful companies. The Committee believes this is due, in large part, to the inability of universities to (1) support biomedical research of potential economic value and (2) support *proof-of-concept* studies to adequately assess the economical potential of their discoveries (see below).

In contrast, technology-transfer mechanisms within Israel's universities seem adequate. These include (1) university-owned technology transfer companies which operate within the framework of the university and (2) programs developed by the Office of the Chief Scientist of the Ministry of Industry and Trade. All Israeli universities and privately owned (including "sick fund") hospitals have adequate patenting mechanisms in place. Discoveries made by government employees in government-owned hospitals are now patented indirectly, for example through health unions, and negotiations are underway to finalize rules and procedures for directly patenting discoveries made in government institutions. The Committee is in full agreement with these efforts. In order to prevent high-quality human resources from leaving government medical centers, there must be full parity between universities, private hospitals and government-owned hospitals as much as possible.

Regarding funding, the Israeli government declared that it regards the development and funding of Israeli biotech *industry* a priority. At the same time, it has been drastically cutting its funding of universities. Our international visiting review committees have noted that they know of no country that has been successful in developing its biotech industry while slashing its funding of the *research* institutions that fuel those same biotech companies.

Successfully developing new drugs requires both an adequate basic science research infrastructure and competent clinical research facilities for drug testing. The latter requires a network of good physicians and well-trained medical staff that can conduct complex medical trials. Therefore, Israel must develop all aspects of biomedical and clinical research for maximum success in this area.

All this being said, the Committee reiterates that, in Israel, the most critical stage ("bottleneck") in moving a new technology from the laboratory to a viable product seems to be the proof-of-concept study, in which the product is shown to work – with a success predictive of significant financial return - outside the laboratory on a small but realistic scale. This stage is no longer basic science, but it is not yet at a stage that private investors would regard as attractive. The chief scientist of the Ministry of Industry, Trade and Labor (MITL) has made only scant amounts of money available for such studies and there is a need for considerable additional government funding to specifically finance them. Our visiting committees have suggested several possibilities for structuring such a fund. Since this is beyond the expertise of the Committee, it has passed these recommendations on to appropriate authorities (such as the MITL).

C. Recommendations

The Committee's recommendations, based on the above findings are summarized under the following five headings:

1. ***Establishment of a National Fund for Biomedical Research (NFBR)***

a. This new fund should be separate and independent of all existing research funds. It will support both basic and clinical research with an emphasis on supporting physician-researchers. Translational research, i.e. research that can later be used to benefit the biomedical industries, should also be supported by this fund.
b. The Israel Academy of Sciences and Humanities, together with the Israel Science Foundation (ISF) and the Ministry of Health (MOH), should be responsible for establishing this fund.
c. The ISF has had some success in raising funds, with matching amounts from the Ministry of Finance, for specific areas of research (degenerative and

d. Once the fund reaches its goal of raising a substantial sum of money (hopefully within five years), it should be designated as an independent national fund.
e. The recommended amount to be allocated annually by the NFBR is 100 million dollars.

2. ***Additional funding for basic biomedical research***

Additional funding above and beyond what is given today should be given to basic biomedical research. Basic research is the basis for both clinical research and biotechnological industries. This additional funding also should come from the NFBR.

3. ***Strengthening clinical research at Israeli medical centers and developing appropriate career structures for clinical researchers***

a. In order to advance biomedical/clinical research at the medical centers, the NFBR will set up an independent unit to deal specifically with this issue.
b. This unit will seek to expand both the quantity and quality of clinical research and to help clinical researchers from the level of the medical student to senior researcher by means of grants and scholarships.
c. During the first three years, this unit will concentrate its efforts on Israel's six largest medical centers (Hadassah, Sheba, Rabin, Sourasky, Soroka and Rambam). Later, other medical centers will be able to join, based on criteria to be established by the unit.
d. Other medical centers will be able to establish centers of research excellence at the onset of this unit's establishment, and compete for individual and research group (as distinct from institutional) grants.
e. A detailed proposal for grants and scholarships is included as an addendum to this paper. The funds allocated for these grants and scholarships will be about 50 million NIS from the fifth year onward.

4. ***Supporting university-based research that can lead to biomedical and biotechnological applications***

a. Incentives should be provided to universities interested in developing biomedical and biotechnological research.
b. The NFBR should develop means to encourage universities to conduct research with practical implications.
c. The NFBR will not be able to support the later stages of product development (including proof-of-concept studies), due to its high cost. Funds will have to be raised from other sources (e.g. venture capital).
d. In light of this, the committee advises that the recommendation of the visiting committee on the subject of "translational research" be further explored. That recommendation refers to the consolidation of government and philanthropic resources and/or the creation of specifically targeted bonds for the funding of such projects.

5. ***Establishing a mechanism to evaluate Israeli biomedical research in comparison with that of other countries***

a. The Israeli Academy of Sciences should establish a mechanism to identify new areas of research and new techniques pursued abroad that are not developed or that are underdeveloped in Israel; and if needed, it should help establish such new fields of research and techniques in Israel, in accordance with its judgment.

6. ***Legislation regarding researcher intellectual property and patent rights in government-owned medical centers***

a. All aspects of the ownership of such intellectual property and patent rights should be clearly stated in Israeli patent law. Favorable legislation would motivate researchers to commercialize their discoveries.
b. The Committee recommended that the American model for intellectual property rights (as stated in the so-called Bayh-Dole Act of 1980) be adopted as a basis for protecting discoveries made by government employees.

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THE COMMITTEE'S REPORT

INTRODUCTION AND METHODS

A. Background

Internationally, biomedical research is a high priority research area. The U.S. allocates almost 50% of its basic science research budget to biomedical research and the UK plans to double its biomedical research expenditures over the next five years. This trend is evident in many other Western European countries as well; and it reflects the widespread realization that biomedical research helps us understand the etiology of many prevalent diseases and, ultimately, can lead to their cure.

Biomedical research also improves the quality of patient care. There is a direct correlation between the level of research and the level of patient care in a given hospital. Thus, the best hospitals are those which carry out extensive medical research supervised and/or performed by the hospital's medical staff. Prime examples include the teaching hospitals of Harvard, Columbia and John Hopkins University. There are also top-quality unaffiliated medical centers, such as the Sloan-Kettering Medical Center, known both for its excellent cancer patient care and cutting-edge research.

Biomedical research improves public health, a primary responsibility of any democratic government and a prerequisite for a productive population. Biomedical research also provides the foundation for a robust, economically productive biotech and pharmaceutical sector.

In many Western countries, the government supports biomedical research through agencies created solely for that purpose, such as INSERM in France, MRC in England and NIH in the United States. These organizations both support external research via competitive grants and conduct internal research in their own research centers. Such research reflects their current needs or their need to promote important but neglected fields. They also help young scientists by providing them with initial grants to establish themselves. More recently, they have become interested in "translational research," which facilitates the application of laboratory findings to patient care.

Israel, in contrast, has no organization or agency that exclusively supports biomedical research. In addition, although 44% of the Israel Science Foundation's (ISF) annual investment in basic research goes to the biological sciences, and over half of those studies are biomedical research, there is no formal interface between basic research and the clinical infrastructure, thus hampering the advancement of Israeli medical research.

B. Important Definitions

The Committee for the Assessment of the State of Biomedical Research in Israel: Its Current Status and Future Needs ("the Committee") has adopted the following definition for biomedical research, based on that of the NIH:

> **Biomedical research seeks out new knowledge in order to understand, prevent, diagnose, identify and cure sicknesses and disabilities and to enhance human health**.

The Committee has defined three sub-categories in biomedical research:

1. *Basic biomedical research.* The main objective of basic biomedical research is to advance the understanding of biological processes. This understanding is crucial to understanding the etiology of the diseases and developing pharmaceuticals. Strong basic biomedical research is essential in developing a robust pharmaceutical and biotechnological sector.

2. *Clinical biomedical research.* The classical definition of clinical research is "medical research conducted on human beings." The committee, however, adopted the following, broader definition given by the visiting expert committee:

> **The term "clinical research" no longer refers solely to the classical investigation of diseases in the whole patient. There is a continuous spectrum between the laboratory analysis of normal and abnormal genes, to molecular mechanisms of disease manifestations in the whole patient, to deriving novel treatment and population studies.**

3. *Translational biomedical research.* The practical application of basic research in either medicine or industry.

C. Appointment of the Committee for Assessing the State of Biomedical Research in Israel ("The Committee")

1. Mandate and members

The Committee was established on October 29th 2006 by the president of the Israel Academy. The mandate of the Committee is to:

(a) Survey the breadth and quality of basic biomedical research in Israel and its funding sources, determine the effects of current funding on the level of research and suggest ways for improving the current situation.

(b) Survey the clinical research conducted in Israel, gauge its integration with the medical system and academia, examine its funding and infrastructure, map the country's needs in this field and suggest ways for improving the current situation.

(c) Examine the interface between biomedical research and the biotechnological and pharmaceutical sector in Israel and elicit the factors that are essential for maximum utilization of new discoveries made by biomedical researchers.

Dr. Ruth Arnon, vice president of the Academy, was asked to head the committee; and its members were carefully selected to represent all relevant sectors. Dr. David Friedman served as committee coordinator. A full list of members is found on page 2; a short biography of the members is found in Annex E.

2. Ways and means

(a) General

In accordance to its mandate, the Committee worked independently on three separate areas:

- Basic biomedical research

- Clinical research
- Interface between biomedical research and the biotech industry

It was understood from the onset that these three subjects are intertwined. The Committee met monthly for a year and a half, each session lasting approximately four hours. All sessions were taped. Researchers, doctors and administrators were invited to these meetings to share their knowledge. Memos, background papers and other necessary material were prepared in advance. A visiting committee of 3-4 experts from abroad was convened for each of these three subjects. These experts came to Israel for three days during which they visited, met and held discussions with appropriate people. They then submitted their reports. Some issues were discussed in subcommittees. The Physician-Researcher Subcommittee was headed by Prof. Zeligson; the Development of New Areas of Research Subcommittee was headed by Prof. Simchen. The reports of the subcommittees can be found in Annex P. The reports of the expert committees were taken into account in this final report of the Committee.

(b) Background

Background material was prepared by Dr. David Friedman, the Committee's coordinator, and by outside experts. The Committee's source material can be found in Annex F.

(c) Meetings with senior researchers and department heads

For each of the three subjects, researchers, physicians, academic department heads and government representatives were asked to present a survey of the existing situation in their field. Each report included current working conditions, problems arising from those conditions, and an overall assessment of the state of research in its field.

In addition, senior and young researchers were invited to participate in discussions regarding basic biomedical research and clinical research to provide a more complete picture of the problems they face. Faculty deans, vice-presidents of research, Ministry of Health and other government officials and heads of granting organizations were

also invited, to discuss current problems on the institutional and national level. A list of invitees can be found in Annex G.

(d) Expert visiting committees from abroad

The scientific world generally regards an external visiting committee as an excellent way to objectively evaluate the level of achievement and efficiency of scientific institutions. These visiting committees are usually made up of respected experts experienced in both the research and administrative aspects of their field, and who have no connection to the institutions investigated. The Committee used this method to assess each of the three main topics above. It further insisted that members of the visiting committees also be capable of looking at biomedical research as a whole, from the level of the single researcher to the institutional and national level. Its choices relied on input from its members and from researchers abroad. Recruiting was not easy, since people of this caliber are usually quite busy; but fortunately, the committee succeeded in finding top-quality appointees.

Each visiting committee came to Israel for three full days of meetings with people from all different levels and fields. All members received extensive background material prior to their arrival, including data about their committee's tasks, and prior comparative analyses of Israel's research inputs/outputs as compared to other developed countries. A list of the members of the visiting committees along with short biographies is found in Annex G. It is apparent from the three-day schedules of the committees (Annex H, I) that much ground was covered in the relatively short time at their disposal. The mission statement of each visiting committee is found in Annex L,M,N.

FINDINGS OF THE COMMITTEE

A. Scope and quality of research done in Israel; an international comparison

1. Funding of basic research in Israel

The OECD does not have specific data regarding the scope of biomedical research in different countries. However, the OECD does have data regarding the levels of

investment in academic R&D (HERD, total all fields). Since biomedical research is typically between 30-40% of all such research, an estimate can be made regarding the funding levels in biomedical research in OECD countries. This estimate shows that, although Israel rates above average in both total R&D investment and in HERD investment, normalized to GDP, it rates below average in its funding *emphasis* on basic science research. For a detailed analysis see Annex N.

According to the Planning and Budgeting Committee of the Council for Higher Education, the number of professors and lecturers in Israeli universities – about 5,000 professors and 5,000 lecturers – has not changed in the last ten years. In contrast, the number of students during the same ten year period has grown by 300%! The teacher/student ratio has thus deteriorated greatly, negatively affecting both the quality of mentoring each student receives and the quality of research done by both young and experienced researchers.

2. **Quantity** of biomedical research done in Israel

One measurement used to quantify the quantity of national research output (but not necessarily quality) is the amount of scientific publications published annually per one million population. According to this measure, Israel is one of the world's leading nations. Israel's share of the world's scientific publications (all fields) between the years 1999-2003 was a disproportionate1.28%. This constitutes 1,549 publications per one million population, compared to 1,932 for Switzerland and 900 for the U.S. Israel ranked third behind Sweden and Switzerland for 1999-2003 (the last year for which data is available).

Israel was also among the five leading nations in the *quantity* of publications published relevant to *biomedical* research (this includes biology, molecular biology, biochemistry, immunology, neurology and clinical research). In fact, Israel ranked third worldwide in the number of publications in molecular biology and fourth in clinical research (details are given in Annex N).

The quantity of patents is often used to suggest a country's potential for translational research. Israel ranks second in the amount of patents per million population that were filed at the European Patent Office (the EPO) and ranks third in patents filed at the

U.S. Patent Office (USPTO). (This data was provided by the Ne'eman Foundation for the Advanced Research in Science and Technology, May 2007.) Also, OECD data show that, in 2003, Israel filed 80 patents in the biotechnology sector, compared to 76 for Sweden and 102 for Switzerland. Unfortunately, these positive patent performances have more to do with dividends from past government policies rather than the result of current government policies.

3. **Quality** of biomedical research done in Israel

Two measurements used to quantify the quality and impact of national research output – that is, whether it is influential or mediocre – are based on the number of times a paper is cited by others who regard it as important to their own research ("citations"). The two measures are: the average number of citations per published paper (CAV) and a country's CAV for a given field divided by the world average for that field (citation index, CI). Israel's CI ratings and rankings in basic biomedical research vary greatly by field of research. Israel ranks fourth worldwide in molecular biology; within the top ten percentile in many other fields; and, even in many lower-ranked fields, it still ranks above the world average (albeit not in immunology and microbiology, CI ≈0.92). Israel's high ranking in molecular biology is particularly gratifying, since it is a particularly important, competitive, prestigious and influential part of advanced modern biomedical research.

In stark contrast to all this, Israeli clinical biomedical research ranks 31st worldwide! Although the fraction of all Israeli publications in clinical research is about the same as in other countries (about 25% of total), Israel's citation index is (CI = 0.89 for 1999-2003) **well below** the world average.

B. State of basic biomedical research in Israel

1. General

Biomedical research is conducted globally. Israeli researchers are in direct competition with their counterparts worldwide, who are all part of an informal but exclusive "research club." Membership in this "club" allows researchers to access information well before it gets published, which greatly benefits Israeli research.

2. Way and means

The Committee's sessions included meetings with researchers from all research institutes in Israel, both young researchers and senior scientists. The Committee interviewed deans of faculties, vice-presidents for R&D and heads of grant funds. To further evaluate the basic biomedical research done in Israel, the Committee also relied upon the findings of its expert visiting committee:

Visiting Committee on Basic Research:

1. Prof. William E. Paul – NIH, U.S. (Chairman)
2. Prof. Eva Klein- Karolinska Institute, Sweden
3. Prof. George Klein – Karolinska Institute, Sweden
4. Prof. Andrew Marks- Columbia University, U.S.

A short biography of the visiting committee members and their mandate can be found in Appendix ….

3. Committee's findings

The majority of the basic biomedical research in Israel is done in universities, including the Weizmann Institute, all of which are research-oriented. However, the government's constant budget cuts make it increasingly difficult to further develop basic research initiatives. All faculty members in the universities are also lecturers and the increased teaching workload – due to the rising student population – makes it even more difficult to do research. Despite these handicaps, the visiting committee:

> was enormously impressed with the dedication to science and the talents of all with whom it spoke, but most particularly with the faculty who led individual laboratories and with the students who worked in those laboratories. The pool of talent represented by these individuals represents an enormous strength and a national resource for Israel. The accomplishment of many of the scientists with whom we spoke were at the highest level representing a credit to the State of Israel and providing important advances in biomedical science. Such advances can lead to the improvement of health for all and can provide the knowledge base for the development of new drugs, other therapeutics and vaccines that could markedly strengthen the biotech/pharma industry in Israel and make a major contribution to the Israeli economy.

The following major problems facing Israeli basic biomedical researchers were brought up before the Committee and the visiting committee. These are detailed below.

(a) Funding issues

The major Israeli competitive funding source for basic research grants is the Israel Science Foundation (ISF). Grants are for up to $50,000 a year for up to 5 (usually 4) years; and they are awarded based on scientific merit as determined by peer review. Most Israeli researchers are pleased with how the fund is run. The $50,000 annual maximum was a compromise, chosen to give a substantial sum of money for each project, while still funding as many applicants as possible. There are also many excellent research projects that cannot be funded due to budgetary constraints.

Visiting committee members remarked that a modern biomedical research laboratory needs at least $150,000 a year to be considered adequately funded. Israeli researchers agreed and commented that they must expend considerable energy to secure additional funding from other sources. Most complained about the valuable research time wasted in writing numerous proposals for small sums of money from other funds in Israel and abroad, from private donors, and (infrequently) from biotech industry. This puts them at a disadvantage compared to their colleagues in Europe and the United States, where grants are usually $150,000 or more a year for five years. The visiting committee concurred and reiterated this analysis and problem – in full – in their report (Annex A).

(b) Research infrastructure

Many researchers complained about Israel's aging academic research infrastructure, particularly large and expensive equipment used for research (e.g., electron microscopes and NMRI). These research tools are constantly being improved and, in order to compete scientifically, must be constantly upgraded. Central service laboratory facilities for DNA, RNA and protein sequencing also face major cutbacks in new equipment and in the trained personnel required to operate it (such equipment is often quite complex). This problem is becoming more acute as the government continues to cut university budgets.

(c) Size of research teams and quality of the researchers

The size of an average research laboratory in Israel is considerably smaller than that in the U.S. or Europe. This is a direct consequence of budget disparities. Since larger laboratories have greater research outputs and can capitalize on discoveries more rapidly and easily, initial discoveries in Israel are often more fully followed up and exploited outside of Israel after initial publication.

Much U.S. and European research is performed by experienced postdoctoral fellows; and their research group leader does not have to spend as much time in teaching and guiding them as he would with graduate students. In Israel, most talented postdocs accept positions abroad to gain experience in more advanced research and techniques vital to their development as scientists. Consequently, most Israeli academic laboratories have fewer postdocs and more PhD students, whose supervision imposes another time burden on their mentors. Although some postdocs do come to Israel from India and China, their scientific level is usually lower than that of their Israeli, European or American counterparts. The Committee suggested that a select group from the Budgeting and Planning Committee of the Council for Higher Education (VATAT), together with the Batsheva de Rothschild Foundation, find ways to identify good postdocs and ways to finance them.

(d) Unsatisfactory cooperation between university and hospital researchers

Some of the researchers interviewed do research on human tissue obtained from hospital laboratories. Others do research on human subjects, something that also require collaboration with hospital physicians. However, these academic researchers report that many of these doctors were "too busy to be bothered" with active research collaboration. Although some physicians were eager to be scientifically engaged, they were reportedly in the minority.

(e) New research fields abroad not represented in Israel

Being a small country, Israel cannot excel – or even be active – in all areas of biomedical research. At times, Israel is part of major new discoveries, e.g. stem cell research, but more often new discoveries are not readily exploited by Israeli researchers. Cloning techniques, for example, were first used in Israeli laboratories only years after their routine adoption abroad. Israel was also late in joining the Human Genome Program and in incorporating genomics into its biomedical research.

Such delays negatively impact Israeli research. The Committee, therefore, suggests establishing a mechanism to facilitate the adoption and exploitation of promising new fields and techniques pursued abroad, but that are not developed or are underdeveloped in Israel.

C. State of clinical biomedical research in Israel

1. Ways and means

The Committee met with many clinicians and research-physicians, at various stages of their professional careers, and with hospital directors and representatives of the Ministry of Health (MOH). It also invited an expert visiting committee to further assess this area.

Visiting Committee on Clinical Research:

1. Prof. John Mendelsohn – MD Anderson Cancer Center, U.S. (Chairman)
2. Prof. A. Michael Denman – University College, London, UK
3. Prof. Robert Schwartz – Tufts University, Boston, U.S.

A short biography of the visiting committee members and their mandate can be found in Appendix G. Their report can be found in Annex B.

2. Committee's findings

(a) Absence of a national policy for clinical research

From the many discussions held with the directors of the Israeli health system, it became apparent that there is no national policy to support or encourage clinical research. The only official national fund that supports clinical research is that of the chief scientist of the Ministry of Health. This fund is too small in size to have a serious impact on national clinical research. Funding for clinical research is usually at the discretion of the hospital's administrators as will be discussed below.

(b) Different hospital approaches to clinical research

Israeli hospitals are owned and operated by a diverse collection of dissimilar entities. The Israeli government owns and manages about 11 general hospitals. The Clalit Sick

Fund (*Kupat Cholim Clalit*) owns and manages 8 general hospitals. The remainder of the hospitals are privately owned. Other than the Hadassah and Sheba Medical Centers (and a few other hospitals) that actively support clinical research, most have no active policy, pursued in practice, to support clinical research. One director of the Clalit Sick Fund explicitly stated that their official policy is **not** to support clinical research, because their government-based funds are earmarked only for patient care.

The bottom line is that any clinical research done in Israeli hospitals is either "top-down," through the encouragement of hospital management, or "bottom-up" when staff physicians petition hospital management; but both require receptive management attitudes. As a rule, Israeli hospitals in Israel do not provide a friendly supportive environment for clinical research. Over time, however, many hospitals, particularly those affiliated with medical schools, have opened research laboratories. Most are supported by private donations, Israeli or foreign, and/or from internal hospital funds. The hospitals also fund research from money paid by private companies to conduct clinical trials of their products in Israeli hospitals.

Hospitals that encourage clinical research have an administrative arm, sort of a private research authority, to help assist researchers. Some hospitals also have ancillary research facilities to facilitate clinical research.

In summary, clinical research in Israeli hospitals is totally decentralized. There is no uniformity in hospitals' policy or support for clinical research and there is no governmental body that, in practice, sees itself as responsible for the state of clinical research in Israel.

(c) Quality of clinical research in Israel

The quality of clinical research in Israel is uneven due to the heterogeneity of research capabilities among hospitals and even among different departments in the same hospital. The Committee made the following observations:

(1) Undoubtedly, there are a number of excellent physician-researchers in Israeli who have founded world-class research laboratories in their hospitals. Two Committee members are themselves physician-researchers.

(2) Although many journal articles are published by Israeli clinicians (well over the world average, see A.2 above), the quality of these articles is markedly *below* the world average, according to citation index scores (see A.3 above).

(3) There is no one obvious reason to explain this unfortunate discrepancy, but the Committee notes that much of the clinical research done in Israel is product-related clinical trials sponsored by pharmaceutical companies. Since Israel is just one site for such multinational trials, the impact of any one paper regarding them could be minimal. Secondly, the *quantity* of papers published is one criteria for the career advancement of physicians in many Israeli hospitals, whereas their *quality* is not.

Even though the Committee's overall assessment of the state of Israeli clinical research is pessimistic, it is tempered by the number of medical centers and clinicians that do world-class clinical research on par with leading medical research centers abroad. Although the visiting committee only met with selected researchers, they were:

> impressed with the quality of the research presented, which was primarily laboratory-based. The achievements they described included many of the major subjects in clinical research…. Their enthusiasm and commitment were extremely encouraging….. It was evident to the committee that there is a core of talented medical investigators in Israel who are doing work that is competitive on an international scale….
>
> After meeting a number of Israel's bright, dedicated clinical researchers and learning about the innovative, exciting research programs they have succeeded in establishing in their hospitals, we are convinced that Israel has a largely untapped opportunity to make major contributions to clinical research in the future, to the betterment of medical knowledge, patient care and the growing biomedical component of Israel's knowledge- based economy.

(d) Other problems raised before the Committee

(1) Designating time for doing research

All the physicians interviewed said that the number one impediment for doing clinical research is the lack of research time. Physicians work long hours in their hospital's wards. The number of doctors in each department is based on the number of patients seen. Therefore, if a department head gives a physician free time to do research, he soon will find himself understaffed in the wards. It is, therefore, essential that the hospital receive financial compensation for time designated for research, so it can hire an additional doctor to take the researcher's place. This arrangement has been successfully tested and implemented on a small scale by the Batsheva de Rothschild Foundation, who give research grants to reimburse the physician-researchers' salary, plus an additional amount for research equipment. Funding was later assumed by the Morasha Foundation; and their young physician grantees have been able to establish themselves as researchers.

Other Israeli grant funds, such as the ISF, have problems allocating salary funds for the lead investigator. If and when a clinical research foundation is founded in Israel, this model of paying for designated research time can and should be implemented. Funding to free promising researchers from other duties, such as teaching, is already common in many other countries.

(2) Funding clinical research

No Israeli entity sees itself as primarily responsible for funding clinical research. The small amount of funds available from the MOH chief scientist is far from sufficient. The ISF does not have the tools to evaluate clinical research and therefore, until this year, had not even considered, much less funded, such research (by its somewhat narrow definition). Funding for hospital-based clinical research comes from private donations, Israeli and foreign funds, or from internal funds. Hospitals also fund research from money paid by private (largely pharmaceutical) companies to conduct clinical trials of their products in Israeli hospitals.

When established, the NFBR (see Recommendations 1, 3) should establish a funding mechanism to specifically fund hospital-based clinical research, which needs a different approach to assessment and financing. This way, Israeli citizens will be able to benefit from novel drugs and procedures developed by clinician-researchers here in

Israel. The NFBR should also help fund the new research infrastructure hospitals need to improve their research capabilities.

(3) Mentoring researchers

Most Israeli physicians who want to start doing research are young and inexperienced. Even those who previously went abroad to do research, still need considerable guidance in designing, implementing and analyzing experiments, methods and procedures. One such physician reported that the lack of mentors is one of their major obstacles in doing research. Hospitals should recognize this need and allow senior physician-researchers to spend more time mentoring younger ones. Some physicians told the Committee that they had taken an unpaid leave of absence to familiarize themselves with the latest scientific techniques and methods in university research laboratories.

D. Interface between biomedical research and industry

1. General

Basic research in science – and particularly biomedical science – often has practical implications. Most biotechnological and pharmaceutical industries are rooted in basic research; and worldwide experience confirms a direct correlation between a well-developed basic science infrastructure and a robust biotech sector. No wonder large U.S. science parks have been built near such outstanding universities as MIT, Harvard, Stanford, Caltech, the University of California, Duke and the University of North Carolina at Chapel Hill.

Converting an idea or knowledge in biomedical research into an economically viable product is a long, expensive, multistep process. Much of the needed expertise is not normally found in universities, and is usually undertaken outside university research facilities. The first step is to patent the invention. This gives the inventor and the assignee (usually his institution) ownership and intellectual property rights (i.p.) in his discovery.

The next step is called *proof-of-concept*, in which the invention is shown to work not only in a laboratory setting but also in the "real world," in a way that can convince

potential investors that the invention constitutes a potentially viable product. If it passes this stage, potential investors can justify investing money, time and effort to help it actually reach the marketplace. The intrinsic difficulty of funding this crucial proof-of-concept stage creates a "bottleneck" where many new inventions and discoveries languish. The invention is no longer basic science, but it is not yet sufficiently developed to attract investors either.

The next steps include clinical trials for pharmaceutical products and large-scale testing for other products. The major sums needed for these steps can only be provided by commercial sources, such as venture capital funds.

This commercialized process is both multi-step and multi-disciplinary, requiring cooperation among people from many different fields. Success depends on the capabilities of the scientists, institutional technology-transfer personnel, investors and others involved. An emerging new field, *translational research*, attempts to analyze, both theoretically and practically, the best ways to get a product from the laboratory to the market and (for biomedical research), the patient's bedside. This field is being rapidly developed in the United States; but it is not currently taught anywhere in Israel. Translational research may increase the odds of a product becoming a commercial success, and could benefit research institutes, industry and the state.

2. Situation in Israel

By the 1980s, Israel had already succeeded in converting basic biomedical science into successful applied products. Human growth hormone, interferon and beta-carotene were commercially developed based on basic science done at the Weizmann Institute. Exelon, one of the world's four leading drugs for Alzheimer's, was developed at Hebrew University. Today, the four most important drugs based on basic Israeli biomedical research generate annual sales of about 4 *billion* dollars. Many medical devices and diagnostic tools have also been developed from Israeli basic science.

All Israeli research institutions have technology transfer companies that patent their (worthy) discoveries and commercialize them via licensing agreements. They also

help create start-up companies and encourage collaboration between researchers in Israel and abroad.

The Office of the Chief Scientist (CS) of the Ministry of Industry, Trade and Labor (MITL) has established mechanisms to facilitate the interface between the university and industrial sectors (initially, the CS/MITL only supported R&D in the latter). These interfaces include its Magnet and Magneton programs, which provide collaborative funding (and Nofar, which helps transfer knowledge from universities to the industrial sector). Such joint research projects between one or more companies and universities improve the exploitation of discoveries made in academia.

By law, the CS/MITL cannot fund research exclusively done in the universities, even if it has obvious industrial applications; there must be some collaboration with industry.

The CS/MITL also has provided financial assistance to new start-up companies, often through "industrial incubators." Initially, government funded, they recently have been privatized and their funding now comes from industrial sources. The incubators assist the developer by providing him with space, research facilities, equipment and technical, organizational and financial assistance. In return, the start-up company gives the incubator a certain percentage stake in the company. The incubators also assume the risk if the start-up fails. Israel's industrial incubators have proven themselves very useful in helping start-up companies become viable.

3. State of biotech industry in Israel and abroad

The journal *Bio*, a U.S. biotechnology publication, reported that U.S. biotech company revenues jumped from $8 billion in 1992 to $50.7 billion in 2005. There was **no** comparable increase in the Israeli biotech industry. Some see this as a wasted opportunity, since (1) the biotech sector is research-intensive, (2) Israel is considered an advanced country in biomedical research, and (3) the Israeli biotech industry enjoys substantial government support. Thus, the Committee believes that Israel's biotech sector should have been larger and more successful than it was. This may well imply a failure to properly commercialize Israel's strong basic research potential.

4. Ways and means

The Committee concentrated its efforts on the various steps that universities take in commercializing their research and how they can be optimized. To do this, the Committee met with researchers who have successfully commercialized their research, researchers who are trying to do so, directors of university technology-transfer companies, key employees of the CS/MITL (see above), and representatives of Israel's pharmaceutical industry. The Committee also convened an expert committee:

Visiting Committee for Translational Research

1. Prof. Harvey Finberg – Institute of Medicine, U.S. National Academy of Science (Chairman)
2. Prof. Michael Rosenblatt - Tufts University, U.S.
3. Prof. Robert Califf - Duke University, U.S.

All three members have extensive experience in drug development and in the interface between academia and industry. Their biographies can be found in Appendix …

The visiting committee also met with some of the people who appeared before the Committee. They also met with others, including Dr. Eli Offer, the chief scientist of the MITL. They also visited the Weizmann Institute. The schedule of the meetings and a brief write-up of their discussions can be found in Annex J.

5. Problems raised before the Committee

(a) Importance of patents to promote knowledge transfer

A patent gives its owner certain rights to his intellectual property (i.p.), which can be a new idea, product, process, material and/or use. These are very difficult to commercialize without patent protection. The patent also provides an official stamp of approval that the invention is indeed novel and has not been previously invented. University-based knowledge-transfer companies are well aware that patenting promotes product commercialization and they readily invest in such patents.

The U.S. which has long understood the connection between i.p. rights and commercialization, enacted the Bayh-Dole Act (1980) to give universities and researchers i.p. rights to their findings (with some limitations), even if the research was done with government funding. This act greatly encouraged universities to commercialize discoveries made in their laboratories.

The universities in Israel have also adopted this model and, in most cases, an invention is patented under the name of the inventor with his institution as the assignee. Agreements between researchers and their institutions specify the percentages that each side gets if and when the invention becomes profitable. This arrangement also benefits the Israeli economy. Privately owned hospitals and those owned by the Clalit Sick Fund have similar arrangements; however, no such arrangement exists in government owned hospitals. Government officials told the Committee that, according to existing laws, any discovery made by any government employee in a government facility belongs to the government and cannot be patented. The Committee holds that this law should be changed, since this is a serious disincentive for researchers in government institutions who, unlike their counterparts in the private sector, cannot profit from their discoveries.

(b) Scope and quality of basic biomedical research influences the biotech industrial development

Biotech centers tend to develop near academic research centers that excel in basic biomedical research. The CS/MITL stated that Israel's policy is to encourage the development of its biotechnological industry; but, in reality, the Israeli government constantly and consistently reduces its funding of universities. This reduces the amount and level of Israel's academic research. The visiting committee noted that Israel:

> has a deserved reputation for innovation and successful discovery based on science focused in its universities. We found that this mission is now jeopardized by funding cutbacks. ***The visiting committee knows of no country that has succeeded in the biomedical industrial sphere while cutting back on the scientific enterprise that forms its foundation*** **[emphasis added].**

(c) Proof-of-concept studies as the rate-limiting factor in commercializing research

A discovery that seems promising in the laboratory often does not work in the "real world." For example, results in cell cultures and small animals may not be replicable in humans, or scaling-up may not be economically viable. Thus, proof-of-concept studies are conducted to better judge if a product can be commercialized. The expertise and equipment required for conducting such a study are generally not found in academia. The funding needed to do a proof-of-concept study is not trivial; but few venture capital firms are willing to assume the financial risk involved at that stage. Universities do not have the funding to undertake such studies, nor will the proposed NFBR (see Recommendation 4). The visiting committee made two interesting recommendations; but the Committee, lacking the expertise to evaluate them, decided to pass them along to those who can. They were:

(1) Consolidating government, philanthropic and institutional resources (a similar concept was successfully implemented in the Israeli nanotechnology sector).

(2) Going public, by floating a bond for an Israel Biomedicine Development Fund, to raise sufficient capital to fund proof-of-concept studies.

(d) Good clinical research infrastructure is important to successfully implement clinical biomedical research results

Utilizing the products of biomedical research entails human clinical trials, thus good clinical research capabilities should be important for realizing the full potential of biomedical research. After investigation, the visiting committee headed by Prof. Harvey Finberg found that Israel does not have a sufficiently good clinical research infrastructure to fully exploit its biomedical research discoveries. To quote from the visiting committee's report:

> A talented pool of physician-researchers is needed to provide insight into the applications of discoveries based on clinical evaluation and predictive assessments in early-phase human studies. This type of research cannot be done in spare time; instead, it requires high level clinical skills coupled with scientific expertise in a supportive environment with appropriate resources.
>
> A trained pool of clinical investigators is also needed. These experts must have skills in research design, biostatistics, epidemiology, the ethics of human studies, health services research, health economics and health policy. Their mission would include the design, analysis and presentation of clinical

research studies intended to develop new technologies and the evaluation of technologies to determine their value in practice. Without insight from such a group from the beginning, drug and device development is at significant risk of failure, if clinical benefits cannot be documented through unassailable clinical trials and outcomes studies.

The state of Israeli clinical infrastructure and recommendations for its improvement were discussed in the previous chapter. Those recommendations, if implemented, could help solve these problems as well.

RECOMMENDATIONS AND REASONING

Recommendation 1: The establishment of a National Fund for Biomedical Research (NFBR)

a. This fund should be separate and independent of all existing research funds. It will support both basic and clinical research with an emphasis on supporting physician-researchers. Translational research, i.e. research that can later be used to benefit the biomedical industries, should also be supported by this fund.

b. The Israel Academy of Sciences and Humanities ("the Academy"), together with the Israel Science Foundation (ISF) and the Ministry of Health (MOH), should be responsible for establishing this fund.

c. The ISF has had some success in raising funds for specific areas of research (e.g., degenerative and genetic diseases) with MOH matching funds. The Committee recommends that these funds be put into a separate fund within the ISF, to be the genesis of the National Fund for Biomedical Research (NFBR).

d. Once the NFBR reaches its goal of raising a substantial sum of money (hopefully within five years), it should be designated as an independent national fund.

e. The recommended amount to be allocated annually by the fund for research is 100 million dollars.

Reasoning:

Definition of biomedical research to be used by the NFBR

The Committee has adopted the following definition for biomedical research, based on that of the NIH:

> Biomedical research seeks out new knowledge in order to understand, prevent, diagnose, identify and cure sicknesses and disabilities and to enhance human health.

Lack of funding for biomedical research

Academic biomedical research is mostly funded by the ISF, and also by: the Research Fund of the chief scientist of the MOH, international funds (e.g., the NIH), disease-specific funds, private funds and private donations. Hospital-based clinical research (excluding commercial drug trials), an important part of biomedical research, has limited ISF and no real governmental funding. It is mostly funded by the hospitals themselves, largely from private donations. The consensus is that such clinical research in Israel is underfunded as compared to its needs and potential. The Shochat Committee also has recently recommended establishing a separate government fund for biomedical research. The Committee agrees with this recommendation, but believes that the budget envisioned by the Shochat Committee is too low.

Previous recommendations for the establishment of a biomedical fund

The need for a separate biomedical research fund has been understood by every committee dealing with Israeli biomedical research. Some of these are mentioned below:

(1) The National Council for Research and Development adopted the recommendation of the late Prof. Rami Rachamimoff, then MOH chief scientist, to establish a national health research fund. The council brought this suggestion to the Israeli government in December 2006. They also pointed out that Israel spends less of its total R&D budget on academic R&D (HERD/GERD = 13.6% in today's terms) than the OECD average (HERD/GERD = 17.8%).

(2) The establishment of a biomedical research fund was suggested to the Shochat Committee by the Israel Academy of Sciences and Humanities. The Shochat Committee gave its recommendations to the Israeli Government in July 2007; and these included the establishment of a competitive biomedical research fund with an annual budget of 100 million **NIS** ($1 = 3.7 NIS).

(3) The three expert visiting committees convened by the current Committee unanimously recommended the establishment of a national biomedical research fund in Israel.

Importance of the biomedical research fund being separate

Most developed countries have a separate fund or agency whose sole function is to fund biomedical research. Examples include the NIH in the U.S., MRC in the UK and INSERM in France. The reasons given for establishing such a separate, dedicated fund include:

(1) A biomedical research fund is a way of maximally utilizing the national research infrastructure to advance the health of nations in all aspects of prevention, detection, diagnosing and finding a cure. In addition, such a fund supports and encourages cooperation and collaboration between universities and hospitals.

(2) Existing Israeli grant-funding organizations almost always fund basic research only on an open, competitive basis. The proposed NFBR can and should also *initiate* and *proactively* support quality research in areas that serve Israel's health needs.

(3) The social and political elements that support medical research differ from those that support basic research as a whole. For this reason, NIH's budget doubled during 2002-2005, and the British government is planning to double the MRC budget over the next three years.

(4) All three visiting committees have pointed out that such a national fund will not only improve the quality of Israeli basic biomedical research, but will also advance Israel's biotechnological and pharmaceutical industries, thus improving the nation's economy.

Recommendation 2: Additional funding for basic biomedical research

Additional funding above and beyond what is given today should be given to basic research. Basic research is the basis for both clinical research and biotechnological industries. The additional funding should come from the above mentioned National Fund for Biomedical Research (NFBR).

Reasoning:

The Israel Science Foundation (ISF) does fund basic biomedical research in Israel. However, the amount that it can give does not fully fill the national need. From ISF's annual budget of about 60 million dollars, about 40% go to the life sciences, about half of which goes to biomedical research. This translates to about 12 million dollars a year for biomedical research. The Committee believes that much more money is needed to improve the quality of basic biomedical research in Israel. More research funding will help Israel utilize its full potential in this area by encouraging quality research which could later be translated into better health care and a more robust biotech industry.

Recommendation 3. Strengthening clinical research at Israeli medical centers and developing appropriate career structures for clinical researchers

a. In order to advance biomedical/clinical research at the medical centers, the Committee recommends that NFBR set up an independent unit to deal specifically with this issue.
b. This unit will seek to expand both the quantity and quality of clinical research and to help clinical researchers (from medical student to senior researcher) by means of grants and scholarships.
c. During its first three years, this unit will concentrate its efforts on Israel's six largest medical centers (Hadassah, Sheba, Rabin, Sourasky, Soroka and Rambam). Later, other medical centers will be able to join, based on criteria to be established by the unit.

d. Other medical centers also will be able to establish centers of research excellence even at the onset of this unit's establishment, and compete for individual and research group grants (as distinct from institutional grants).
e. A detailed proposal for grants and scholarships is included as an addendum to this paper. The funds allocated for these grants and scholarships will be about 50 million NIS from the fifth year onward.

Reasoning:

State and quality of clinical research in Israel

There is no national policy to actively support and encourage clinical research. Clinical research is mostly supported by the directors of individual medical centers. Indeed, the policy of the eight medical centers owned by the Clalit Sick Fund is **not** to support clinical research. Only the two Hadassah hospitals have regular budget lines for clinical research and internally funded full-time research staff positions. Although some other hospitals (e.g., Sheba, Ichilov) do good research, their funding has not been institutionalized. Furthermore, no agency or official body has taken charge of coordinating Israeli biomedical research policy.

As for the quality of Israeli clinical research, although some world-class researchers and areas of excellence exist, the overall level is below average for industrialized countries (Israel's CI is below both the OECD, EU and world averages). Many problems and obstacles prevent Israel from achieving its full potential in this field. They include:

(1) **Lack of dedicated time to do research.** This is the most acute problem in the hospital setting in Israel. Doctors have to work long hours tending patients, leaving them very little time for research. The only way time can be readily freed for research is by "buying time." If hospitals were paid for the time physicians spent on research, they could hire other physicians to maintain quality patient care.

(2) **Funding.** There is no agency or official body that sees itself as responsible for funding clinical research. The fund of the MOH Chief Scientist is small and relatively insignificant. It certainly cannot meet Israel's needs for clinical research funding.

(3) **Mentoring.** Another limiting factor is the lack of research mentors. A change in hospital policies is needed to encourage senior clinician-researchers to become mentors for younger physician-researchers.

(4) **Human Infrastructure.** Israel needs to develop an expert infrastructure in hospitals for doing high-level clinical research. This includes both scientists experienced in clinical research design, epidemiology and biostatistical analysis, and also other ancillary services that facilitate clinical research and researcher-initiated clinical trials.

Recommendation 4: Supporting university-based basic research that can lead to biomedical and biotechnological applications

a. Incentives should be provided to universities that are interested in developing basic research that can lead to biomedical and biotechnological applications.
b. The proposed NFBR (Recommendation 1) should develop means to encourage universities to conduct such research with practical implications.
c. NFBR will not be able to support the later stages of product development (including proof-of-concept studies), due to its high cost. Funds will have to be raised from other sources (e.g. venture capital).
d. In light of this, the committee advises that the recommendations of its visiting committee on translational research be further explored. These recommendations refer to the consolidation of government and philanthropic resources and/or the creation of specifically targeted bonds for the funding of such projects.

Reasoning:

Institutional Vision

Universities have *two* main purposes: teaching and research. In the U.S., a third purpose is added: to be an economic generator. The visiting committee felt that Israeli academia and the medical centers have not sufficiently adopted this last purpose. Both

universities and hospitals can become catalysts for economic development, especially in the biotech and pharmaceutical sectors.

Infrastructure

Practically, Israel will initially have to invest heavily in improving research infrastructure. Both basic research and applied research, both within universities and within hospitals, should be supported. This public support is greatly needed in the advanced stages of applied research, especially proof-of-concept studies. This would bridge the current gap in funding, to the stage where venture capital and other private sources can step in.

Scope of NFBR

The NFBR is not intended to support the development of a product all the way to its production stage. Rather, it is intended to give limited resources to research projects that have commercial potential.

Recommendation 5: Establishing a mechanism to evaluate Israeli biomedical research in comparison with other countries

> a. The Israeli Academy of Sciences should establish a mechanism to identify new areas of research and new technologies pursued abroad that are not developed or are underdeveloped in Israel; and, if needed, it should help establish such new fields of research and techniques in Israel, in accordance with its judgment.

Reasoning:

Staying Current

Research is not static. New areas and methods constantly arise, the most important of which influence the research done in many other related fields. Although Israel is strong in many areas of biomedical research, it is sometimes late in incorporating new research areas in its repertoire. For example, in the 1970s, hardly anybody was doing research in the biochemistry and enzymology of DNA. As a result, Israel was at least five years behind in adopting genetic engineering methods in its ongoing biomedical

research. Israel's contribution to the Human Genome Project also suffered because of this. Another recent example is Israel's lack of developed microbiology research, compared to the U.S. and Europe. Here, lagging could have far-reaching consequences in clinical biomedical research and biotechnology as well.

Role of the Academy

The Israel Academy of Sciences and Humanities would be asked to create a permanent body whose function is to follow the research being done in Israel and compare it to that being done in other developed nations. This body, along with the Academy, would be able to recommend pursuing new priority areas of research, according to Israel's needs.

A Proactive Strategy

The Academy would promote these newly identified areas of research by, for example, funding postdoctoral students to gain expertise abroad in these areas of research. The Academy, together with the Planning and Budgeting Committee of the Council for Higher Education (VATAT) and the Israel Science Foundation (ISF) – in conjunction with Israeli universities – could promise postdoctoral fellows a funded research position in Israel when they finish their training. In addition, the VATAT and ISF could offer researchers remaining here in Israel funding for projects in these high-priority fields, and part-time salaries. They could also give these areas priority in their funding decisions.

Recommendation 6. Legislation regarding researcher intellectual property rights in government-owned medical centers

a. All aspects of the ownership of intellectual property rights in government-owned medical centers should be clearly stated in Israeli patent law. Favorable legislation would motivate researchers to commercialize their discoveries.
b. The Committee recommended that the American model for intellectual property rights (as stated in the Bayh-Dole Act of 1980) be adopted as the basis for protecting discoveries made by government employees.

Reasoning:

A patent gives its owner certain rights to his intellectual property (i.p.), which can be an idea, product, process, new material and/or use. These are very difficult to commercialize without patent protection. The patent is also an official stamp of approval that the invention is indeed novel and has not been previously invented. University-based knowledge-transfer companies know patents provide an incentive to commercialize a product, and they invest heavily in patenting innovations. U.S. insight into the connection between i.p. rights and commercialization was the basis of the Bayh-Dole Act (1980) which gave universities and researchers i.p. rights to their findings, even if their funding came from government sources. The Bayh-Dole Act encouraged universities to commercialize discoveries made in their laboratories.

Israeli universities have also adopted this model and, in most cases, an invention is patented under the name of the inventor, with his institution as assignee. There are prior collective agreements between researchers and institutions specifying the percentages that each side gets if and when the invention becomes profitable. This arrangement benefits the Israeli economy as well. The privately owned hospitals and those owned by the Clalit Sick Fund have made similar arrangements. However, no such arrangement exists in government-owned hospitals. Government officials told the committee that, according to the existing laws, any discovery made by a government employee in a government facility belongs to the government and cannot be patented. The Committee holds that this law should be changed, since it is a disincentive for researchers in government institutions, who cannot profit directly from their discoveries.

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