האקדמיה הלאומית הישראלית למדעים
ACADEMIA SCIENTIARUM ISRAELITICA

Executive Summary

An International Comparative Workshop: Strategies for the National Support of Biomedical Research

Jerusalem, December 2-3, 2009
at The Israel Academy of Sciences and Humanities

The workshop took place upon completion and publication of the Report of The Committee for the Assessment of the State of Biomedical Research in Israel

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The Israel Academy of Sciences and Humanities

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Table of Contents

The Workshop Program

An International Comparative Workshop:
Strategies for the National Support of Biomedical Research

Wednesday and Thursday, December 2–3, 2009
at the Israel Academy of Sciences and Humanities

Wednesday, December 2nd 2009

09.00 - 09.30 **Opening Remarks and Greetings**
Prof. Menahem Yaari, President of the Israel Academy of Sciences and Humanities (IASH)
MK Yakov Litzman (Israel), Deputy Minister of Health
MK Meir Sheetrit (Israel), Chairperson, Science and Technology Committee, Knesset
Prof. Manuel Trajtenberg, Chairman of Planning & Budgeting Committee, Council of Higher Education
Prof. Ruth Arnon, Vice-President IASH and Chairperson, The Committee for the Assessment of the State of Biomedical Research in Israel

09.30 - 11.00 **The National Policy for the Support and Funding of Biomedical Research; Basic, Clinical and Translational**
Chair: Prof. Michael Sela, Weizmann Institute of Science, AISH Member
Prof. H. Fineberg, (USA) President of the Institute of Medicine of the National Academies

Prof. Willam Paul, (USA) National Institute of Health (NIH), NIAID
Prof. Christopher Kennard, (UK) Oxford University and Medical Research Council

11.30 - 13.00 **The National Policy for the Support and Funding of Biomedical Research** (continued)
Chair: Prof. Raphael Mechoulam, Hebrew University of Jerusalem, AISH Member
Prof. Jean-Francois Bach, (France) Permanent Secretary, Academie des Sciences, former Director of the Institute for Immunology, INSERM
Prof. Reinard Kurth, (Germany) Chairman of Ernst Schering Foundation, Former President of the Robert Koch Institute and Paul Ehrlich Institute
Prof. Olle Stendahl, (Sweden) Linkoping University, Former Secretary General of the Swedish Medical Research Council

14.00 - 15.30 **Biomedical R & D in Israel**
Chair: Prof. Uri Seligsohn, Sheba Medical Center and TA University, AISH Member

Policy, Support and Funding of R&D in Israel - Overview
Mr. Yigal Erlich, Deputy Chair of The National Council for R&D

Findings and Recommendations of the Committee for the Assessment of the State of Biomedical Research in Israel
Prof. Ruth Arnon, Vice-President of the Israel Academy of Sciences and Humanities and Chairperson of the Committee

The State of Clinical Research in Israel
Prof. Gabi Barabash, Tel Aviv Medical Center and TA University

Biomedical Funding by the Israel Science Foundation (ISF)
Prof. Benny Geiger, Weizmann Institute; Head of the Division of Life Sciences and Biomedical Research, ISF

16.00 - 17.00 **Summary and Discussion**

Thursday, December 3rd, 2009

09.00 - 10.30 **National Support of Biomedical Research** - Expert panel of all presenters - Israelis and guests
Chair: Prof. Alex Keynan, Israel Academy of Sciences and Humanities

11.00 - 12.30 **Expert Panel** (continued)

12.30 - 13.00 **Summary and Conclusion**
Prof. Ruth Arnon

The Workshop was made possible by the generous support of the Charles H. Revson Foundation, the Yad Hanadiv Foundation, and the Eli and Marilyn Goldfarb Grant.

Workshop Executive Summary

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Background

Concerned that Israel's current biomedical research system does not allow Israeli researchers to reach their full potential, the Israel Academy of Sciences and Humanities convened a special Committee for the Assessment of Biomedical Research in Israel to examine this topic in depth. The Committee, chaired by Prof. Ruth Arnon and supplemented by three Visiting Committees of international experts, submitted their final report in November 2008. This workshop, funded by the C. H. Revson Foundation (USA), extends their work by comparing the Israeli system, its funding mechanisms, and funding levels with that of its counterparts abroad.

The workshop was opened by Prof. Menahem Yaari, President of the Israel Academy, MK Yaakov Litzman, Deputy Minister of Health, MK Meir Sheetrit, Chairperson of the Knesset Committee on Science and Technology, and Prof. Manuel Trajtenberg, Chairperson of the Planning and Budgeting Committee (VATAT) of the Israel Council for Higher Education, all of whom expressed their strong commitment to improving Israeli biomedical research. Echoing the primary recommendation of the Arnon Committee – strongly endorsed by all three of its expert Visiting Committees – MK Sheetrit presented his own "dream that Israel have an Israeli National Institute of Health" to pursue these goals.

Prof. Daniel Hershkovitz, Israel's Minister of Science, is "very aware of the importance of funding biomedical research" and fully intends "to bring the conclusions of the Arnon report to the Interministerial Committee for S&T," which acts with "the full (decisionmaking) authority of the Government," to try to increase funding.

Presentations of Speakers from Abroad

Prof. Harvey Fineberg (USA), President of the U.S. Institute of

Medicine (NAS/IOM), began an informative series of national comparisons with an overview of the U.S. model for biomedical research funding. The U.S. spends over $130 billion on health-related R&D, divided by source as follows:

Industry	**$ 74.8 Billion**
Pharmaceutical	$ 37.7
Biotechnological	$ 27.5
Other	$ 9.6
Federal Government	**$ 38.6 Billion**
NIH	$ 29.3
Other	$ 9.3
Other Sources	**$ 17.1 Billion**
University Institutional Funds	$ 10.4
States, Philanthropy, Other	$ 6.7

In the U.S. model, all sectors invest heavily in health R&D. The most funds come from industry, although industry is increasingly leaving basic research. The national government's contribution is also incredibly high, even when normalized per capita or per GDP. That is, biomedical research matters to the U.S. both as a driver of better health and of economic growth. In fact, between 1982 and 2008 such R&D, as a percentage of total U.S. health costs (over $2 trillion a year!), has grown from 3.0% to 5.5%. Recent surveys indicate that 36% of all Americans want this percentage to increase even further to 7-10%; and another 34% want it even higher than that!

As in most advanced countries (except Israel), the government's money is allocated directly by the legislature (Congress) to separate, dedicated R&D agencies (NIH, NSF, etc.). In particular, it is not a vulnerable, fungible part of a ministry or department that primarily provides health care. This approach leads to much greater responsiveness and overall funding – since decisionmakers more readily vote for what they (or their constituents) want and control – but it also can lead to more variable funding levels (e.g., doubling followed by lower growth), political and interest group influence, earmarks, and lack of an overall national strategy. These weaknesses are outweighed by the model's strengths: the greater scale and diversity of funding, public support, transparent merit review and the encouragement of scientific entrepreneurship.

Fineberg concluded that, however funded, "We know of no country that has succeeded in building a successful biomedical industry without a strong basic research enterprise. You cannot piggyback forever on others. This is where policymakers have a (special) responsibility."

Prof. William Paul (USA) of the NIH/NIAID Laboratory of Immunology discussed the structure and funding of the U.S. National Institutes of Health (NIH), by far the main driver of U.S. biomedical research. The NIH consists of twenty institutes, each of which approaches and is funded individually by the U.S. Congress. These budgets thus reflect a national commitment to direct some of its funds specifically to biomedical research (unlike the NSF or ISF which accept all meritorious comers), and to give greater funding to some priorities over others. Within this decentralized environment, the NIH Director gives overall guidance and manages – a recent development – a relatively small "Common Fund" (only 1.7% of the total NIH budget).

Ninety percent of the NIH research budget provides extramural research grants (and <20% contracts), to U.S. universities, medical schools, research hospitals and medical research institutes. Individual research RO1 grants (3-5 years, up to $250,000 per year, total direct costs, and up to 70% more in indirect costs) predominate. However, some areas, particularly clinical research, require large diverse teams and facilities. The NIH currently funds about sixty large Clinical Translational-Science Awards, averaging about $9 million each. There are also Comprehensive Cancer Centers, an AIDS Clinical Trial Group, an Immune Tolerance Network, etc. Although only about 10% of the NIH budget supports NIH intramural research, that is still almost $3 billion; and the 1,200 principal investigators on the NIH's Bethesda Campus probably make it the world's largest single biomedical research center.

There are also special mechanisms to encourage innovative but high-risk research (e.g., Pioneer Awards) and to give greater preference to young investigators. NIH grants cover the full costs of the research, including the salaries of principal investigators who would otherwise receive university faculty funding. Finally, the NIH is now trying to reduce its review burden and turnaround time by limiting applications to only twelve pages. In 2009 the submission-to-decision time was as short as three months, which really helps researchers. Only one resubmission is allowed.

Paul also argued that "really innovative clinical research cannot be managed with research project grants alone. Advanced infrastructure is absolutely needed. Even in the U.S., a single $250,000 grant is probably inadequate to run a competitive laboratory. Recent technologies are quite remarkable, but next-generation sequencers cost a half-million dollars a pop. All of this has to be dealt with or you run the risk of being marginalized." He believes that Israel could be "an international force" and that it seems the "most efficient" of its peer countries; however, he notes that the inability of Israeli physicians to get "excused time" to do research is a major drag on Israeli clinical research.

Prof. Christopher Kennard (U.K.) from Oxford University and MRC, reported that the U.K. Medical Research Council (MRC) had an annual budget of £704 million (about $1.1 billion) in 2008/09. About half of this went to fund intramural research in three MRC institutes and 29 units, employing over 4,000 staff. The other half funds 3,300 extramural research grants. About $93 million funds training and career development programs. The MRC adheres to the "Haldane Principle," that the government provides the funds, but is not involved in decisionmaking.

The U.K. Department of Health (DOH) has historically funded another £800 million (about $1.3 billion) of National Health Service R&D in hospitals, although much was used, in practice for patient care. In 2006 the DOH program was converted into a new National Institute of Health Research (NIHR) and budgetarily combined with the MRC. Their current joint budget of £1.48 billion (about $2.37 billion) comes directly from the national Treasury. The influential Cooksie Report (2006) also led to the establishment of an Office for Strategic Coordination of Health Research (OSCHR), which coordinates government offices interested in health research to produce and promote a national health research strategy, in communication with appropriate industry and charities (whose leaders often sit on its board). The MRC's own strategic plan for 2009-14, Research Changes Lives, was recently published.

In general, the MRC takes the lead in discovery/exploratory research; and the NIHR takes the lead in applicative/translational research, including Phase II and Phase III clinical trials. The MRC also has a small central strategic fund of about £40 million ($64 million) for rapid review/response, and a series of initiatives targeted on research bottlenecks in translation (e.g., model and biomarker validation).

Finally, the U.K. is unique in having a private charity, The Wellcome Trust, that funds biomedical research at about the same level £702 million ($1.12 billion) as the national MRC. They also fund training and major facilitating-infrastructure centers (e.g., the Sanger Center). They have used some of their funding to leverage government co-funding of ten major clinical research centers throughout the U.K., a good way to encourage government involvement.

Prof. Jean-Francois Bach (France), Permanent Secretary of the French Academy of Sciences, pointed out that France is unique in that nearly all basic biological and biomedical research scientists – whether at CNRS (National Center for Scientific Research), ISERM (National Institute of Health and Medical Research), or elsewhere (INRA, CEA, etc.) – are officially government employees, with tenured positions at an early age (starting at age 35). Such lifetime security can encourage risk-taking and creativity (there's nothing to lose), but dead wood can never be pruned. The CNRS and ISERM are of similar size (about 3,000 scientists), but the CNRS has its own research buildings, while ISERM's units are all within hospitals, which does encourage clinical research. Excellence is the main criteria, whatever people work on, which can be problematic, as frontier fields come, evolve and go. As with all civil servants, most of the money (about 80%) goes to salaries, another serious constraint.

France also has several private research foundations. The Institut Pasteur and Institut Curie actually receive 2/3 of their funds from the government; but there are also charity-funded foundations such as the FRM (Foundation for Medical Research) and those devoted to specific diseases (cancer, multiple sclerosis, etc.). Recently, France has created two new agencies, ANR (National Research Agency) and AERES (Agency for Research Evaluation), to try to start doing things differently.

As for clinical research, Bach notes, "The situation of French hospitals has become terrible. People work from 8:00 in the morning to 8:00

in the evening. How can they find time to do clinical research? We feel that the only way to protect them is to create special Centers for Clinical Research Excellence," so we have started a Center for a Translational Science Research (CTRS) program. Starting next year (2010) we hope to get €100 million ($143 million) of government funding for five years for each center. All will be equipped and staffed at top international standards. We also expect a €500 million government-supported endowment fund, the income of which would be used to create cohorts of subjects and patients for clinical and epidemiological studies (possibly even involving industry). So change seems underway. Finally, €20 billion of France's proposed €30 billion stimulus loans are earmarked for research and academia. Over €15 billion ($21.4 billion) of that will probably go to stimulate biomedical research.

Prof. Reinhard Kurth (Germany) former director of the Robert Koch Institute reported on Germany's varied biomedical research landscape. Germany's universities are largely funded by the state governments, but budgets are tight; so much frontline research is done in Germany's large research societies. The largest, the Max Planck Society has 76 institutes with 13,000 staff and 6,400 junior and guest scientists. About 82% of its €1.72 billion ($2.46 billion) budget comes from federal and state funding (50:50). The Fraunhofer Society does applied research, two-thirds under contract (for government, industry, etc.). They have a €1.5 billion budget and 17,000 employees. The Helmholtz Association's fifteen research centers have a €2.35 billion budget (90% from the federal government) and 26,500 employees, although only two centers (Cancer, Infectious Biology) are specifically biomedical.

The Federal government also has 53 research facilities of its own, with 19,000 employees and an annual budget of €1.7 billion. Several (RK1, PE1, BZgA, etc.) are under the Federal Ministry of Health.

The Federal Ministry of Education and Research also provides €856 million for Life Sciences research, about 20% of its total project funding. The self-governing, German Research Foundation (DFG) has its own senate, president, etc. It's €1.92 billion annual budget comes from Germany's federal (60%) and state (40%) governments, and it is increased 3-5% a year. About €740 million go to the Life Sciences. As for other sources, about 100 of Germany's 7,000 private foundations focus on biosciences and medicine. Most are small, although the German Cancer Foundation raises about €90 million a year. About two-thirds (€40 billion) of all German R&D funds come from – and are spent in – industry; most support engineering or pharmaceutical company research.

Prof. Olle Stendahl (Sweden), former Secretary General of the Swedish Medical Research Council, notes that Sweden spends 3.5% of its total GDP on R&D (Israel = over 4%), of which 20-25%, about €2.4 billion ($3.4 billion) is biomedical research. The government provides about a quarter of that, about €100 a person a year. Foundations provide 10%; and industry, the rest. [For comparison, at Sweden's level, the Israeli government would spend about €700 million ($1 billion) on biomedical research annually.] Most government funds go to the four-year plan of the Ministry of Education and Research (MOER), a formal research bill passed by the national legislature. About 90% of the funds go to university-conducted research, not to government-run institutes or agencies.

The MOER gives grants both directly and through the Swedish Research Council (SRC, €300 million/year), which funds the Swedish Medical Research Council (€90 million/year), the board of which is dominated by rather independent-minded researchers. In practice, about 90% of the biomedical research funding ends up at Sweden's six medical schools. Clinical research receives about half of its funds from the same players, and half from the County Councils, which run Swedish healthcare. SRC funding has increased over the last five years, although clinical trials have decreased 20%. As in Israel, scientists are increasingly dependent on fragmented, short-term and/or external support. Sweden's university-driven, bottom-up system has its pluses; but without some dramatic top-down initiatives and more translational research to speed-up utilization, Stendahl worries that politicians may lost interest. However, biomedical research is really an exceptionally good investment for Sweden; just consider such products as Losec, Nexium, Seloken, Pulmicort ($3 billion, $4 billion, $1.5 billion, $1.0 billion, respectively).

Presentations of Israeli Speakers

Prof. Ruth Arnon, Vice President of the Israel Academy, and the Head of the Committee, then described the work, procedures, findings and six major recommendations of the Committee, as described in its Final Report (November 2008). The first and foremost recommendation was to establish an independent national foundation for biomedical research, at an internationally competitive funding level of $100 million a year (about $13 per capita, about the same as Sweden).

Prof. Benny Geiger, Head of the Division of Life Sciences and Biomedical Research of The Israel Science Foundation (ISF), reported that The ISF competitively funds investigator-submitted proposals, based on excellence as determined by external (mail) and internal (study section) peer review, in all fields. It has a total annual budget of about $79 million, predominantly from the government through VATAT, plus some private foundation funding. About a third of the new applicants receive grants of about $50,000 year for up to five years, which is small by U.S. and European standards ($100,000-$300,000). There are no preferred topics in this regular (predominant) part of the ISF program, which is, for convenience only, divided into: Exact Sciences and Technology, Life Sciences

and Medicine (LS), and the Humanities and Social Sciences. In practice, biomedical proposals tend to do less well than "all-LS" ones (24.4% compared to 29.6%); and hospital-affiliated researchers – who rarely have sufficient research time – tend to do less well than "all researchers" (19.2% compared to 30.7%).
Recent BIO-MED grants sponsored by the Legacy Heritage (Morasha) Foundation are larger ($100,000) and are specifically targeted to neurodegeneration and genetic disorders. They also reveal the small, exhaustible number of high-quality researchers in most specific subfields in our small country (e.g., decreasing preproposals: 130 (2008), 89 (2009), 59 (2010)). The Morasha Clinical Investigator Awards, of which 25 have been awarded (2007-09), are divided 50:50 between the hospital (to buy research time) and the investigator (for the project). As with other nimble private foundations, the Morasha Foundation has had a significant localized impact, increasing the ISF's total number of M.D.-researchers (2005-09) from 59 to 109, and proving the feasibility and desirability of such mechanisms on a larger scale. Both the ISF's regular and Morasha programs also fund equipment, centers-of-excellence and conferences. The bottom line? If Israel wants a competitive research community at world-class levels, it will have to fund it at world-class levels.

Mr. Yigal Erlich, Deputy Chairperson of the Israel National Council for R&D (NCRD) pointed out that high-tech capital investment in Israel is 90% concentrated in Information and Communications Technology (ICT), with little (10%) in Biotechnology. Although over 200 large foreign companies have bought up small Israeli companies and their technology, except for ten in medical devices, none are in biotechnology. Of Israel's 700 mostly small biotech companies, 365 are in medical devices, so even those financiers thinking Israel, think devices, not drugs. Israel's Ministry of Industry and Trade, which provides R&D matching funds, is "neutral."

Prof. Gabi Barbash, Director of the Tel-Aviv Sourasky Medical Center, reported on another concern of the Committee, the physician-researcher as an "endangered species." They are rare because they must master two difficult professions and then compete for the very scarce time and other resources needed to be even barely competitive – all this without the resources, status and intellectual property protection given their colleagues in academia, and despite the temptations of a lucrative private practice. Yet good physicians who are good researchers can make truly unique contributions; and they should be actively encouraged.

Open Discussion

In the second day's open-discussion session, Prof. Fineberg noted that "responsiveness to constituents" is a major factor in a Congressman's decisionmaking and reelection, so when volunteer advocacy groups mobilize public and media opinion around better health or specific diseases, big amounts of government money can flow from their confluence of interests. Israeli researchers, despite their reluctance, must learn to promote biomedical research the way companies promote a new soft-drink: identify what "will resonate with the public, how you can make your case. Speak to your legislators, invite them to your laboratories." Although concerned about possible media distortion, he also noted that "We are generally slow, in science, to think strategically about the media … (you should be) thinking very hard about media personalities who could take up this cause." Prof. Arnon agreed that "We have somewhat missed out on harnessing public opinion. The (Israeli) population, in general, does not feel that it is affected by research. This could be a new avenue (to pursue)." Prof. Bach reported being "surprised that it's difficult to convince (Israel's) government to help medical research. Politically that should be very popular!"

Prof. Kurth noted that success is not automatic, "One has to establish (and earn) confidence" with politicians and journalists. Prof. Kennard emphasized the importance of "pointing out the economic benefits of biomedical research." Several Israeli speakers cautioned that when the Treasury sees that Israeli scientists can do good science with such small amounts, it says "Why should we give more?" They think: Let big countries like the U.S. and France do the research, and we will spend the money elsewhere. They need to understand that biomedical research is not a waste, but a very important national investment.

Another major issue was achieving the right balance between targeted (prioritized) and undirected (open) research. Prof. Paul pointed out that, although scientists often don't like it, there are times when a rapid research response to an urgent health problem (e.g. SARS) is essential. Prof. Paul noted the difficulty of evaluating the success of such interventions (compared to no intervention), because the control experiment cannot be done; but in the case of HIV/AIDS, lots of good researchers were attracted, and in the end "brilliant work was done." Directed research can also help boost emerging fields and neglected (but important) fields. Finally, directed research represents a spectrum, running from contract research (when you largely know what you will get) to a broad priority like "translational research," which is largely undirected within its own limits. As Prof. Arnon pointed out, balance is the key.

The third topic was clinical research, including drug trials (not always stimulating), case reports (not always compelling), and epidemiological studies (often country-specific). Prof. Bach gave an overview of the field; and Prof. Seligsohn reported on the six main problems facing clinical researchers in Israel (protected time, salaries, grant funding, infrastructure, erosion of the research atmosphere in hospitals, lack of mentoring) and some steps Israel could take to meet them. Profs. Stendahl and Kennard noted that Sweden and the U.K. face similar problems, and discussed how they try to improve incentives, centers of excellence and mentoring. Profs. Paul and Kurth also reported on efforts along those lines in their countries.

Israeli speakers noted the need for a peer-review system for hospital research (much of which is privately funded), for more attention to publication quality (quantity is usually high) in promotion decisions, and other ways to boost clinical research quality. This will also require money and infrastructure, because we "will never get there by piggybacking on research done elsewhere." Two speakers from the Hadassah Medical Center, described their activities and the difference that infrastructure, committed management, and a supportive hospital research culture can make.

In conclusion, Prof. Keynan noted that "it is possible to do biomedical research in Israel at a high-level, as compared to other countries;" but that will also require comparable budgets and infrastructure. Prof. Arnon summarized the discussions and noted that the Israeli participants had learned a lot from the comparisons presented by their distinguished foreign guests. We now have to follow-up their remarks and recommendations. "It is benafsheinu (vital) for Israeli clinical and biomedical research."

The Committee Report - Executive Summary

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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.

In addition, 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 an 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 genetic diseases). The Committee recommends that these funds be put into a separate fund within the ISF that will be the genesis of the National Fund for Biomedical Research (NFBR).

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.